8-Radio Pharmaceuticals – Handling and packaging- Dr.CKD

Introduction Radiopharmaceuticals are unique medicinal formulations containing radioisotopes which are used in major clinical areas for diagnosis and/or therapy. The facilities and procedures for the production, use, and storage of radiopharmaceuticals are subject to licensing by national and/or regional authorities. This licensing includes compliance both with regulations governing pharmaceutical preparations and with those governing radioactive materials. Additional regulations may apply for issues such as transportation or dispensing of radiopharmaceuticals. Each producer or user must be thoroughly cognizant of the national requirements pertaining to the articles concerned. Regulations concerning pharmaceutical preparations include the application of current Good Manufacturing Practices (GMP). Guidelines are available in Quality assurance of pharmaceuticals, Volume 2: Good manufacturing Document QAS/08.262/FINAL page 2 practices and inspection (WHO, Geneva, 2004); for the current WHO recommendations consult the WHO Medicines web site (http://www.who.int/medicines). Regulations governing radioactive materials include those on safe handling and production of radioisotopes. See International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources (IAEA, Vienna, 2003, CD-ROM Edition) Safety Series No. 115/CD and Radiological Protection for Medical Exposure to Ionizing Radiation Safety Guide (IAEA, Vienna, 2002) Safety Standard Series No. RSG-1.5. Consult the IAEA website for the current Safety Standards and publications (http://www-ns.iaea.org/standards/). **********new page********** Radiopharmaceuticals This general monograph is intended to be read in conjunction with the individual monographs on radiopharmaceutical preparations. A radiopharmaceutical preparation that is subject of an individual monograph in The International Pharmacopoeia complies with the general requirements stated below and with the general monograph for the relevant dosage form (most commonly that for Parenteral preparations) as modified by any of the requirements given below and by any specific instruction included in the individual monograph. Additional information • See Annex for terminology applied to radiopharmaceuticals Shelf-life The shelf-life (expiry period) of a radiopharmaceutical preparation depends primarily on the physical half-life of the radioisotope, the radiochemical stability and the content of longer-lived radionuclidic impurities in the preparation under consideration. Many radiopharmaceutical preparations contain radioisotopes with very short half-lives and such preparations therefore have very short shelf-lives. Such preparations require an expiry date and time to be indicated. For example, technetium based preparations and positron emission tomography (PET) preparations are normally intended to be used within less than12 hours (some within minutes) of preparation. At the end of the expiry period, the radioactivity will have decreased to the extent where insufficient radioactivity remains to serve the intended purpose or where the dose of active ingredient must be increased so much that undesirable physiological responses occur. In addition, chemical or radiation decomposition may have reduced the radiochemical purity to an unacceptable extent. In addition the radionuclidic impurity Document QAS/08.262/FINAL page 3 content may be such that an unacceptable radiation dose would be delivered to the patient. The shelf-life of a multidose radiopharmaceutical preparation, after aseptic withdrawal of the first dose, will also depend on microbiological considerations. For radiopharmaceutical preparations containing radioisotopes with long half-lives, microbiological considerations may take precedence over those based on the physical half-life of the radioisotope. For example, once the first dose has been aseptically withdrawn from a multidose container of a iodine-containing injection, the container should be stored at a temperature between 2° and

8°C and the contents used within 7 days. Definition Radiopharmaceuticals can be divided into four categories: Radiopharmaceutical preparation A radiopharmaceutical preparation is a medicinal product in a ready-to-use form suitable for human use that contains a radionuclide. The radionuclide is integral to the medicinal application of the preparation, making it appropriate for one or more diagnostic or therapeutic applications. Radionuclide generator A system in which a daughter radionuclide (short half-life) is separated by elution or by other means from a parent radionuclide (long half-life) and later used for production of a radiopharmaceutical preparation. Radiopharmaceutical precursor A radionuclide produced for the radiolabelling process with a resultant radiopharmaceutical preparation. Kit for radiopharmaceutical preparation In general a vial containing the nonradionuclide components of a radiopharmaceutical preparation , usually in the form of a sterilized, validated product to which the appropriate radionuclide is added or in which the appropriate radionuclide is diluted before medical use. In most cases the kit is a multidose vial and production of the radiopharmaceutical preparation may require additional steps such as boiling, heating, filtration and buffering. Radiopharmaceutical preparations derived from kits are normally intended for use within 12 hours of preparation. Manufacture The manufacturing process for radiopharmaceutical preparations should meet the requirements of Good Manufacturing Practice. The manufacturer is responsible for ensuring the quality of his products, and especially for examining preparations of short-lived radionuclides for long-lived impurities after a suitable period of decay. In this way, the manufacturer ensures that the manufacturing processes employed are producing materials of appropriate quality. In particular, the radionuclide composition of certain preparations is determined by the chemical and Document QAS/08.262/FINAL page 4 isotopic composition of the target material (see below) and trial preparations are advisable when new batches of target material are employed. When the size of a batch of a radiopharmaceutical preparation is limited to one or few units (for example, certain therapeutic preparations or very short-lived preparations) parametric release of the product manufactured by a fully validated process is the method of choice. When the half-life is very short (for example, less than 20 minutes), the administration to the patient is usually on-line within a validated production system. Radionuclide production In general ways of manufacturing radionuclides for use in radiopharmaceutical preparations are: Nuclear fission Nuclides with high atomic number are fissionable and a common reaction is the fission of uranium-235 by neutrons in a nuclear reactor. For example, iodine-131, molybdenum-99 and xenon-133 can be produced in this way. Radionuclides from such a process must be carefully controlled in order to minimize the radionuclidic impurities. Charged particle bombardment Radionuclides may be produced by bombarding target materials with charged particles in particle accelarators such as cyclotrons. Neutron bombardment Radionuclides may be produced by bombarding target materials with neutrons in nuclear reactors . The desired nuclear reaction will be influenced by the energy of the incident particle and by the isotopic composition and purity of the target material. Radionuclide generator systems Radionuclides of short half-life may be produced by means of a radionuclide generator system involving separation of the daughter radionuclide from a long-lived parent by chemical or physical separation. Starting materials (including excipients) In the manufacture of radiopharmaceutical preparations, measures are taken to ensure that all ingredients are of appropriate quality, including those starting materials, such as precursors for synthesis, that are produced on a small scale and supplied by specialized producers or laboratories for use in the radiopharmaceutical industry. The actual quantity of radioactive material compared with quantities of excipients is normally very small therefore excipients can greatly influence the quality of the radiopharmaceutical preparation. Target materials The composition and purity of the target material and the nature and energy of the incident particle will determine the relative percentages of the principal

radionuclide and other potential radionuclides (radionuclidic impurities) and thus ultimately the radionuclidic purity. For very short lived radionuclides including the ones present in most positron emission tomography tracers (PET) tracers the determination of the chemical state and purity of radionuclide before patient use is difficult. Therefore before clinical use of these radionuclides, extensive validations and strict operational conditions are essential. Strict control of Document QAS/08.262/FINAL page 5 range of specified quantity and quality is also essential. Any subsequent change in operational conditions should be re-validated. Each batch of target material must be tested and validated in special production runs before its use in routine radionuclide production and manufacture of the preparation, to ensure that under specified conditions, the target yields a radionuclide in the desired quantity and quality. Carriers A carrier, in the form of inactive material, either isotopic with the radionuclide, or non-isotopic, but chemically similar to the radionuclide, may be added during processing and dispensing of a radiopharmaceutical preparation to permit ready handling. In some situations it will be necessary to add carrier to enhance chemical, physical or biological properties of the radiopharmaceutical preparation. The amount of carrier added must be sufficiently small for it not to cause undesirable physiological effects. The mass of an element formed in a nuclear reaction may be exceeded by that of the inactive isotope present in the target material or in the reagents used in the separation procedures. Carrier-free Radioactive preparations in which no carrier is intentionally added during the manufacture or processing may be referred to as carrier-free. The designation no-carrier-added is sometimes used to indicate that no dilution of the specific activity has taken place by design, although carrier may be present due to the natural presence of a non-radioactive element or compound accumulated during the production of the radionuclide or preparation of the compound in question. Carrier-free specific activity can be determined by a consideration of the relationship between activity A, the number of radioactive atoms present N and the decay constant λ where λ = 0.693/T1/2. □ □ □ □ □ □ □ □ □ = = 2/1 .0 693 T A Nλ N The specific activity of radioactive materials that are not carrier-free can be determined by measuring both the radioactivity and the total amount of the element or compound of interest. Accurate determination, where a material has a high specific activity, may be difficult due to limitations in obtaining an accurate determination of the amount of the substance present by standard physical or chemical analysis. Production of Radiopharmaceutical preparation Radiopharmaceutical preparations may contain the types of excipients permitted by the general monograph for the relevant the dosage form. Sterilization Radiopharmaceutical preparations intended for parenteral administration are sterilized by a suitable method (see 5.8 Methods of sterilization). Whenever possible, terminal sterilization is recommended, although for many radiopharmaceutical preparations, the nature of the preparation is such that filtration is the method of choice. Document QAS/08.262/FINAL page 6 All sterilization processes are validated. When the size of the batch of a radiopharmaceutical is limited to one or few samples (e.g. therapeutic or very short-lived radiopharmaceutical preparations) parametric release of the product manufactured by a fully validated process is the method of choice. When the half-life is very short (e.g. less than 20 minutes), the administration of the radiopharmaceutical to the patient is generally on-line with a validated production system. Addition of antimicrobial preservatives Radiopharmaceutical injections are commonly supplied in multidose containers. The requirement of the general monograph for Parenteral preparations that such injections should contain a suitable antimicrobial preservative in a suitable concentration does not necessarily apply to radiopharmaceutical preparations. The nature of the antimicrobial preservative, if present, is stated on the label or, where applicable, that no antimicrobial preservative is present. Radiopharmaceutical injections for which the shelf-life is greater than one day and that do not contain an antimicrobial preservative should be supplied in singledose containers. If, however, such a preparation is

supplied in a multidose container, it should be used within 24 hours of aseptic withdrawal of the first dose. Radiopharmaceutical injections for which the shelf-life is greater than one day and that do contain an antimicrobial preservative may be supplied in multidose containers. After aseptic withdrawal of the first dose, the container should be stored at a temperature between 2° and 8°C and the contents used within 7 days. Warning/Caution: Adequate shielding1 must be used to protect laboratory personnel from ionizing radiation. Instruments must be suitably shielded from background radiation. 1 See Supplementary information chapter on Radiopharmaceuticals and International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources (IAEA, Vienna, 2003, CD-ROM Edition) Safety Series No. 115/CD and Radiological Protection for Medical Exposure to Ionizing Radiation Safety Guide (IAEA, Vienna, 2002) Safety Standard Series No. RS-G-1.5. Consult the IAEA website for the current Safety Standards and publications (http://www-ns.iaea.org/standards/). Identity tests Tests for identity of the radionuclide are included in the individual monographs for radiopharmaceutical preparations. The radionuclide is generally identified by its half-life or by the nature and energy of its radiation or by both as stated in the monograph. Half-life measurement The preparation to be tested should be tested after appropriate dilution to avoid dead time losses using an ionization chamber, a Geiger-Muller counter, a scintillation counter or a semiconductor detector. The activity must be sufficiently high to allow detection during several estimated half-lives. The measured half-life should not deviate by more than 5% from the half-life stated in the individual monograph..

A radiopharmaceutical is a preparation intended for in-vivo use that contains a radionuclide in the form of a simple salt or a complex. It may exist as a solid, liquid, gas or a pseudo gas. The chemical and physical identity and a form of a radiopharmaceutical are very important because in each case, once administered the radiopharmaceutical is intended to target certain tissues, binding sites, biochemical pathways. A radiopharmaceutical can be used for either diagnostic or therapeutic purposes depending on its specific physicochemical and radiation properties. The characteristic of radioactive decay is what makes radioisotopes useful in their medical applications; however, different applications will take advantage of radioactive emissions in different ways. Radioactive materials are regularly used to treat medical conditions, diagnosis pathology, visualize and measure physiological functions, and localize structures and pathways. This review describes both the therapeutic as well as diagnostic uses of radiopharmaceuticals.

By definition a radiopharmaceutical is a radioactive pharmaceutical agent that is used for diagnostic or therapeutic procedures. Over the past three decades the discipline of nuclear pharmacy or radio-pharmacy has become highly specialized and contributed positively to the practice of nuclear medicine. Nuclear pharmacy the first specialty in pharmacy recognized in 1978 by the Board of the Pharmaceutical specialties focuses on the safe and effective use of radioactive drugs or radiopharmaceuticals.

The application of radiopharmaceuticals is divided into two major areas, diagnostic and therapeutic the diagnostic side is well established. While the therapeutic side of nuclear medicine is evolving e.g. more than 100 radiopharmaceutical products are available with the largest proportion of these having application in cardiology (e.g. myocardial perfusion,) oncology (e.g. tumour imaging and localization) and neurology (e.g. cerebral perfusion) diagnostically they are also used for infection imaging and nephrology. Historically nuclear medicine has been well established as a therapeutic modality for thyroid cancer, Graves's disease, hyperthyroidism and bone pain palliation associated with skeletal metastasis. However, recent radiopharmaceuticals e.g. iodine- 131 or iodine 125 labelled MIBG (m-iodobenzyl guanidine) are being used to treat pheochromocytoma and neuroblastoma and radiolabeled somatostatin analogues are used for the treatment of neuro endocrine tumors e.g. neuroblastoma.

A radiopharmaceutical consists of drug component and a radioactive component. Most radio nuclides contain a component that emits gamma radiation. Substances that have the same number of protons but have varying numbers of neutrons are called radio nuclides. Radio nuclides may be stable or unstable those that are unstable are radioactive because their nuclei undergo rearrangement while changing to a stable state and energy is given off. An important distinction between radiopharmaceuticals and traditional drugs is lack of pharmacological activity on the part of radiopharmaceuticals. For intensive purposes radiopharmaceuticals have been used as tracers of physiologic processes. There huge advantage is that their radioactivity allows non invasive external monitoring or targeted therapeutic irradiation with very little effect on the biologic processes in the body indeed radiopharmaceuticals have an excellent safety record and their incidence of adverse effects is extremely low [1].

THERAPEUTICAPPLICATIONS

Therapeutic Radiopharmaceuticals are radio labelled molecules designed to deliver therapeutic doses of ionizing radiation to specific diseased sites. Therapeutic applications of radiopharmaceuticals have emerged from the concept that certain radio nuclides possessing particulate emission such as alpha and beta radiations or low-energy low-range electrons (Auger electrons) possess the ability to destroy diseased tissues. The dual facets of these agents constitute either curative or palliative measures in treatment modalities. Contrary to the usual requirement that intravenous injections be true solutions, some radiopharmaceuticals are deliberately particulate to achieve site-specific localization of radioactivity in the body. These specialized dosage forms permit imaging of, for example, the principal organs of the reticulo-endothelial system (liver, spleen, and bone marrow) with radio labeled colloidal particles, the cardiac blood pool with radiolabeled red blood cells, and lung perfusion with albumin aggregates.

Radioisotopes may be used internally or externally. If the radioisotopes are used externally or as implants in sealed capsules in a tissue, the dose could be terminated by removal of the sources. If they are given internally as unsealed source, the dose cannot be stopped by removal of the source. The total dose in therapeutic applications may be calculated on the basis of effective half- life of the isotope, concentration of the isotope and the type and energy of radiation emitted[2].

In therapeutic uses, the deleterious effect of high-energy radiation on human cells is used. Therapeutic radioisotopes are generally longer lived than those in diagnostic use and possess higher energies[3]. A few examples of how radioisotopes are used for therapeutic purposes are summarized below.

Non-Hodgkin'sLymphomaTherapy

Therapeutic treatments are given using a radioisotope attached to an antibody to deliver radioactivity to specific cells are called radioimmunotherapy (RIT). Radiopharmaceuticals I-131 tositumomab and Y-90 ibritumomab and Y90epratuzunab are used to treat Non-Hodgkin's lymphoma[3].

TreatmentofCancers and Tumours[4]

· Americium 241 used as antineoplastic.
· Californium 252 used as antineoplastic."
· Cobalt 60 used as antineoplastic.
· Gold1 94 used as antineoplasatic.
· Holmium 66 (26 h) being developed for diagnosis and treatment of liver tumours.
· Iodine-125 (60 d) used in cancer brachytherapy (prostate and brain).
· Iodine 123 used as antineoplastic.
· Iodine 131 used as antineoplastic.
· Rhenium 186 (3.8 d) used for pain relief in bone cancer. Beta emitter with weak gamma for imaging.
· Iridium 192 (74 d) supplied in wire form for use as an internal radiotherapy source for cancer treatment (used then removed).
· Palladium 103 (17 d) used to make brachytherapy permanent implant seeds for early stage prostate cancer.
· Samarium 153 (47 h) Sm-153 is very effective in relieving the pain of secondary cancers lodged in the

bone, sold as Quadramet. Also very effective for prostate and breast cancer.
· Strontium 89 (50 d) very effective in reducing the pain of prostate and bone cancer
· Yttrium 90 (64 h) used for cancer brachytherapy and as silicate colloid for the relieving.

Treatment of Thyroid Disease with Iodine 131
· I-131 is therapeutically used for to treat thyroid cancer, hyperthyroidism (including Graves' disease, toxic multinodular goiter, and toxic autonomously functioning thyroid nodules), and Nontoxic multinodular goiter. vita tissues. I-131 has a physical half-life of 8.1 days. It emits beta particles (average energy of 0.192 MeV, maximum energy of 0.61 MeV

· I-131 to ablate any remaining tissue, as well as to treat residual thyroid cancer or metastatic thyroid cancer.

Palliative Treatment of Bone Metastasis
· Various radioisotopes and pharmaceuticals are used to deliver palliative treatment of bone metastases, including samarium-153 (Sm-153), strontium-89 (Sr-89) chloride, and phosphorus-32 (P-32) sodium phosphate. The two most common side effects occurring from radiopharmaceutical therapy for metastatic bone disease are initial increased bone pain (flare) and a decrease in WBC and platelet counts.

· Samarium-153 EDTMP (lexidronan): The most commonly used radioisotope for this treatment in the United States is Sm-153. Sm-153 has a physical half-life of 1.9 days and emits beta particles with an average energy of 0.23 MeV (maximum energy of 0.81 MeV). Sm-153 has a soft-tissue range of approximately 0.6mm, keeping radioactive damage to tissue localized in bone matter. Sm-153 also has a gamma ray emission of 103 keV, which allows diagnostic imaging of the radioisotope distribution to be performed. Sm-153 will localize specifically in osteoblastic sites (sites of bone proliferation). Sm-153 is administered intravenously.

· Strontium-89 chloride: Sr-89 incorporates itself into the bone similarly to calcium. Its primary area of localization is in areas of osteoblastic activity. Sr-89 has a physical half-life of 50.5 days and emits beta particles with an average of 0.58 MeV (maximum energy of 1.46MeV). Sr-89 has a soft-tissue range of approximately 2.4mm, keeping radiation damage localized in the bone tissue.

· Phosphorous-32 sodium phosphate: P-32 is one of the first radioisotopes used for palliative treatment of bone metastases. It incorporates itself into the cortex of the bone as well as into the nucleic acids of growing bone matter. Its beta particle emission has an average energy of 0.70MeV (maximum energy 1.71MeV) and a soft tissue range of approximately 3.0mm, limiting damage to organs surrounding the skeleton. Its physical half-life is 14.3 days. P-32 can be administered orally or intravenously[3].

Treatment of Arthritis[4]
· Erbium-169 (9.4 d): Use for relieving arthritis pain in synovial joints.
· Yttrium-90 (64 h): as silicate colloid for the relieving the pain of arthritis in larger synovial joints. Pure beta emitter.

Diagnostic Radiopharmaceuticals
· Every organ in our bodies acts differently from a chemical point of view. Doctors and chemists have identified a number of chemicals which are absorbed by specific organs. The thyroid, for example, takes up iodine, the brain consumes quantities of glucose, and so on. With this knowledge, radiopharmacists are able to attach various radioisotopes to biologically active substances. Once a radioactive form of one of these substances enters the body, it is incorporated into the normal biological processes and excreted in the usual ways.
· Diagnostic radiopharmaceuticals can be used to examine blood flow to the brain, functioning of the liver, lungs, heart or kidneys, to assess bone growth, and to confirm other diagnostic procedures. Another important use is to predict the effects of surgery and assess changes since treatment.
· The amount of the radiopharmaceutical given to a patient is just sufficient to obtain the required information before its decay. The radiation dose received is medically insignificant. The patient

experiences no discomfort during the test and after a short time there is no trace that the test was ever done. The non-invasive nature of this technology, together with the ability to observe an organ functioning from outside the body, makes this technique a powerful diagnostic tool.
· A radioisotope used for diagnosis must emit gamma rays of sufficient energy to escape from the body and it must have a half-life short enough for it to decay away soon after imaging is completed[3].

Diagnostic Radiopharmaceuticals[5,6,7,8,9,10,11,12]

• Ammonia N 13 Injection is a radioactive diagnostic agent for Positron Emission Tomography (PET) indicated for diagnostic PET imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.
• Chromium 51 (28 d) as chromium chloride injection: Used to label red blood cells and quantify gastro intestinal protein loss cyanocobalamine preparation used for diagnosis of pernicious anaemia.
• Dysprosium 165 (2 h) used as an aggregated hydroxide for synovectomy treatment of arthritis.
• Floufine 18 Asfluoro2 Deoxy D-Gluocose (fdg) used for cxerebral, myocardial and tumor gluocose metabolism.
• Holmium 166 (26 h) being developed for diagnosis and treatment of liver tumours.
• Iodine 125 (60 d) as iothalamate sodium used diagnostically to evaluate the filtration rate of kidneys and to diagnose deep vein thrombosis in the leg. It is also widely used in radioimmuno assays to show the presence of hormones in minute quantities
• Iodine 131 (8 d):as sodium iodide 131 used as a diagnostic aid for studying the function of the thyroid gland and in scanning the thyroid for determining size, position and possible tumour location. Iodine 131 as sodium iodohippurate as a diagnostic for studying kidney function.
• Iron 59 (46 d) as ferric chloride solution used in studies of iron metabolism in the spleen.
• Lofetamine HCl 123 commonly known as IMP used for non invasive evaluation of local cerebral blood flow in cerebrovascular accidents.
• Oxygen15 as H215 O in equiliubrium studies of tissue water content and as a tracer for regional blood flow.
• Potassium 42 (12 h) as potassium chloride injection, used for the determination of exchangeable potassium in coronary blood flow.
• Rubidium 86 as Rubidium chloride injection used for determination of myocardial blood flow.
• Selenium 75 (120 d), used in the form of seleno-methionine to study the production of digestive enzymes.
• Sodium 24 (15 h) as sodium chloride injection to study sodium exchange.
• Xenon-133 (5 d) used for pulmonary (lung) ventilation studies.
• Gallium 67 (78 h) as gallium citrate used for tumour imaging and localisation of inflammatory lesions (infections).
• Indium 111 (2.8 d) used Strontium 92 (25 d) as indium111 pentetreotide used in imaging of neuroendocrine tumors.asindium 111 oxyquinoline for radiolabeling autologous leukocytes and platelets; as indium 111 cepromab penditide. It is monoclonal antibody for imaging prostate cancer.
• Strontium 89 chloride is in a class of drugs known as radioisotopes. It delivers radiation to cancer sites and ultimately decreases bone pain. The length of treatment depends on the types of drugs you are taking, how well your body responds to them, and the type of cancer you have.
• Thallium 201 (73 h) thallous chloride used for diagnosis of coronary artery disease other heart conditions such as heart muscle death and for location of low-grade lymphomas.

PACKAGING, TRANSPORTATION AND STORAGE OF RADIOACTIVE MATERIALS

Identify three types of packaging for radioactive materials · Describe package testing procedures for radioactive materials · Describe the type of information required on radioactive placards and labels · List five types of radioactive shipments · Explain how radioactive materials are transported · Identify six types of radioactive waste · Explain how radioactive materials are stored PACKAGING All shipments of radioactive materials whether form industry or government, must be packaged and transported according to strict Federal regulations. These regulations protect the public, transportation workers, and the environment from potential exposure to radiation. These regulations can be found in 49 CFR parts 100 to 177. Types of Packaging The most effective way to reduce the risk associated with transporting radioactive materials is to follow the appropriate packaging standards specified by DOT and, when required, NRC or DOE regulations. The type of packaging used is determined by the activity, type, and form of the material to be shipped. Depending on these factors, radioactive material is shipped in one of three types of containers. · Industrial packaging · Type A packaging · Type B packaging Industrial Packaging Materials that present little hazard from radiation exposure, due to their low level of radioactivity, are shipped in industrial packages. These are also known as strong, tight containers. This type of container will retain and protect the contents during normal transportation activities. Slightly contaminated clothing, laboratory samples, and smoke detectors are examples of materials that may be shipped in industrial packages. Type A Packages Radioactive materials with higher specific activity levels are shipped in Type A packages. These packages must demonstrate their ability to withstand a series of tests without releasing the contents. Regulations require that the package protect its contents and maintain sufficient shielding under conditions normally encountered during transportation. Typically, Type A packages are used to transport radiopharmaceuticals (radioactive materials for medical use) and certain regulatory qualified industrial products. Type B Packages Radioactive materials that exceed the limits of Type A package requirements must be shipped in Type B packages. Shippers use this type of package to transport materials that would present a radiation hazard to the public or the environment if there were a major 1 release. For this reason, a Type B package design must not only demonstrate its ability to withstand tests simulating normal shipping conditions, but it must also withstand severe accident conditions without releasing its contents. Type B packages are used to transport materials with high levels of radioactivity, such as spent fuel from nuclear power plants. These large, heavy packages provide shielding against the radiation. The size of the Type B packages can range from small containers to those weighing over 100 tons. Package Testing Radioactive materials are packaged according to their form, quantity, and concentration. DOE ensures that when radioactive materials are transported, they are packaged carefully to protect the public, transportation workers, and the environment. DOT and NRC regulate the testing of radioactive material package designs. DOT is responsible for specifying the required test conditions for packages. NRC certifies that packages designed for materials with higher levels of radioactivity, such as spent fuel, meet DOT's test requirements. Type A Packaging Testing Type A package designs must withstand four tests simulating normal transport conditions. These include: · Water spray for one hour to simulate rainfall of two inches per hour · Free fall dorp test onto a hard flat surface · Compression of at least five times the weight of the package · Penetration test by dropping a

13 pound, 1.25 inch diameter bar vertically onto the package from a height of 3.3 feet The NRC has established strict performance standards and testing requirements for Type B package designs. Computer analyses and scale model testing demonstrate the structural integrity of the design. Type B Packaging Testing Type B packaging must withstand Type A packaging testing criteria as well as four additional tests. · A 30 foot drop onto a flat, unyielding surface so that the package's weakest point is struck · A 40 inch free drop onto a 6 inch diameter steel rod at least 8 inches long, striking the package at its most vulnerable spot · Exposure of the entire package to 1475 degrees F for 30 minutes · Immersion of the package under 15 feet of water for at least 8 hours 2 Crash tests using actual spent fuel package prototypes have been used to verify the accuracy of the computer models. For example, a truck carrying a prototype-shipping package was crashed into a 900-ton concrete wall at 81 miles an hour. The truck was demolished, but the package was damaged only slightly. Special Form and Fissile Materials Special form materials are radioactive isotopes enclosed in sealed capsules. They are designed to withstand a fire and a high degree of damage, so they are rarely a problem unless the source is removed from the capsule. If you suspect that a source has been removed from the capsule, stay away from the area and notify the appropriate radiation authorities. Containers for fissile materials are also designed to withstand a great deal of stress, so it is not likely these materials will present a hazard. These materials are not flammable. In addition, the packaging is designed to withstand total engulfment by fire at temperatures of 1475 degrees F for a period of 30 minutes. Placards and Labels Placards are required on vehicles transporting one or more packages bearing Radioactive Yellow III labels, even if the cargo is in Type A packages. High level radioactive materials, such as spent nuclear fuel, require a diamond shaped placard with a larger white square with a black border. Non-bulk containers of radioactive materials must be marked with the shipping names, product identification, and shippers name and address. Labels identify the contents and radioactivity level according to three categories: · Radioactive – White I: almost no radiation. The maximum allowable radioactivity is 0.5 mrem/hr on the package surface. · Radioactive – Yellow II: low radiation levels. The maximum allowable radioactivity is 50 mrem/hr on the package surface, and one mrem/hr at three feet from the package. · Radioactive – Yellow III: higher levels of radiation. Maximum allowable radioactivity is 200 mrem/hr on the package surface, and 10 mrem/hr at three feet from the package. This is required for fissile Class III materials or large quantity shipments of any radiation level. (Fissile refers to elements in which fission reaction can be induced. This reaction will cause fissile atoms to become unstable and release energy and radiation.) Vehicles carrying packages with Yellow III labels must have a radioactive placard on both sides and both ends of the vehicle. Each of these labels also includes lines on which the contents are identified and level of radioactivity is stated in terms of curies. The Yellow II and Yellow III labels have additional items called the transport index box. (The top of the diamonds for 3 Radioactive II and III are actually yellow.) For the majority of shipments, the number in the transport index box indicates the maximum radiation level measured (in mrem/hr) at one meter from the surface of the package. In the examples above, a transport index of 0.1 on the Radioactive III label indicates that radiation measured 1 meter from the surface of the package should be less than 0.1 mrem/hr. With the exception of exclusive use shipments, the maximum transport index for any shipment is 10 mrem/hr. Packages that carry radioactive materials are designed to absorb radiation if it is released from the container. There are other regulations pertaining to the transport index as well, Though not as commonly used. Regulations limit exposure by restricting the total of all the transport indexes on any one vehicle, usually to less than 50. Exposure is

also limited by requiring tests for radioactive contamination on the outside of the packages before shipping. If a total shipment exceeds 200 mrem/hr, the vehicle must be designated exclusively for the purpose of transporting that shipment. Above the transport index is the contents line, which identifies the material inside the package. Reusable shipping containers that are empty, but possibly contaminated inside, are labeled with the word “empty”. 4 TRANSPORTATION Radioactive materials are shipped safely every day. DOE regulations covering these materials strictly control the types that can be carried, their quantities, and the packaging. In addition hazard communication standards help ensure that those who handle or come into contact with these materials – including emergency responders – will be able to identify the cargo and understand the hazards. Types of Shipments Radioactive materials that are shipped include: · Uranium ores · Nuclear fuel assemblies · Spent fuel · Radioisotopes · Radioactive waste Uranium ores and associated chemical products are shipped form mines and mills to purification processors. Irradiated material is shipped to manufacturers of metal and ceramic fuel assemblies. Nuclear fuel assemblies are the source of energy for commercial nuclear power plants and their production of electricity. Fuel elements are also produced for research reactors and national defense programs. Spent or “used” fuel is moved to a geologic repository for permanent disposal. Commercial spent fuel is now being temporarily stored at power plants, while Government owned spent fuel from test or research reactors is stored at DOE sites. Radioisotopes are transported from reactors to medical facilities, research laboratories and defense sites, as well as to a variety of industries and manufacturing facilities. Radioactive waste results from processes that use radioactive materials and must be transported to storage or disposal sites. Transportation accidents involving radioactive materials are very rare. Of 500 billion total shipments in this country every year, 100 million (.02%) contain hazardous materials, and only 3 million (.0006%) contain radioactive materials. Hospitals, factories, research facilities, nuclear power plants and other users of radioactive material are often at some distance from the locations that supply this material. In addition, they are often far from the waste storage and disposal sites. 5 Radiological Shipments by Industry Medical/ Research Uranium Compounds Empty Containers Nuclear Fuel Spent Fuel Rad Waste Misc. 54.5% 10.7% 6% 1.8% 0.2% 14.8% 12% Strict federal regulations established and enforced by the Department of Transportation (DOT) and the Nuclear Regulatory Commission (NRC) govern the packaging, labeling, documentation and routing of shipments of radioactive materials. All modes of transportation (highway, rail, air or waterway) and all carriers (private and government) are covered by these regulations. Transportation of Radioactive Materials by Highway Highway cargo tanks ship most radioactive waste. Trucks transport a wide variety of both low-level and high-level radioactive materials, including fission products used to manufacture nuclear fuel. Transportation of these materials is highly regulated. Among other restrictions, carriers are required to follow the most direct interstate rout, bypassing heavily populated areas when possible. When transportation incidents occur, they are most likely the result of a cargo tank accident. However, containers used for shipping high level radioactive materials are very strong, and releases are extremely rare. South Gate, CA February 1993 A vial of potentially deadly radioactive cesium 137 was either lost or stolen while in transit along Interstate 5. The vial (measuring 3.5” by .75”) was being shipped from northern California to South Gate. Cesium 137 is used to sterilize medical equipment. This material is usually encapsulated in two steel tubes and welded closed. Because of its high level of radioactivity, cesium 137 is stored underwater and must be remotely handled during use and loading for transport. Officials using a Geiger counter eventually found the small container beside an on-ramp to the Long

Beach freeway. Had it not been for an anonymous tip, the container might not have been found. -- “Hazardous Materials Emergencies,” John R. Cashman, 1995 6 Transportation of Radioactive Materials by Rail Rail is the second most frequent method of transporting radioactive materials. Generally, trains carry only large volumes of material, such as uranium hexafluoride. Rail accidents can be particularly dangerous for two reasons. For one, extremely large quantities are involved. Secondly, a serious accident can damage several rail cars, resulting in combinations of hazardous materials. The preferred method of shipping radioactive materials and waste is by unit train, which runs directly between its point of origin and its destination. It receives priority right-ofway and expedited switching, and does not receive or unload any additional cargo along the way. The radioactive loads are contained by a disposable liner and a hard cover and carried in gondola cars. Rail cars placarded RADIOACTIVE cannot be placed next to a locomotive or an occupied caboose. A buffer car loaded with any non-radioactive material must be placed between a car carrying radioactive materials and a locomotive or caboose. Federal regulations and DOE require shippers and carriers to have emergency plans in place in case an accident involving a rail car occurs. DOE also requires railroads to document their compliance with regulations and laws before and during shipment of radioactive materials. This documentation ensures that railroad tracks and rail structures such as culverts and crossings are in safe condition before any materials are shipped. Also, DOE is working with states along shipment routes to train and brief responders on their transportation plans. This training program, in fact, is part of DOE’s effort to increase awareness and response capabilities along its transportation routes. In the unlikely event of an accident involving DOE regulated radioactive materials, DOE will ensure that any release is cleaned up, and that any other remedial actions are taken. Transportation by Air DOT strictly limits air shipment of radioactive materials. One exception is radiopharmaceuticals. Radiopharmaceuticals are radioactive drugs use to diagnose or treat illnesses, and are frequently short-lived, small and light weight. Often they must be delivered quickly to hospitals and medical laboratories, so air shipment is generally the best method. Air shipment of radioactive materials is not regulated by the Code of Federal Regulations, as are most other methods. Regulations for air transport are issued by the International Atomic Energy Agency (IAEA). With the exception of nuclear weapons, large quantities of radioactive materials are rarely shipped by air. The military and its contract carriers are notable exceptions. 7 Transportation of Radioactive Materials by Water Only a small percentage of radioactive materials are shipped by water, primarily because this type of transportation is slow and geographically limited. Materials that are occasionally transported via waterways include spent nuclear fuel, uranium metal, uranium hexafluoride, and low-level waste. When shipped by water, these materials are identified as “marine pollutants” and noted as such on the manifest. The IAEA and the International Marine Organization (IMO) govern international water transport of radioactive materials. DOT and NRC regulate transportation in US waters. In addition, DOE has conducted extensive tests to ensure the safety of ships carrying radioactive cargo. Shipments that exceed a certain level of radioactivity must be shipped exclusively on vessels hired specifically for that purpose. STORAGE When radioactive materials are depleted or their usefulness, they are considered waste and must be stored at a government approved disposal facility. Storing Radioactive Waste Each type of waste is sent to a disposal site that is appropriate for its characteristics. High Level Waste High level waste results from the reprocessing of spent nuclear fuel in a commercial or defense facility. Reprocessing can recover the unstable radioactive materials for research and defense programs. High level waste is currently stored in underground tanks

and vaults at government sites. Some of this waste will be solidified in a glass form, packaged in stainless steel canisters, and placed in heavily shielded casks for transport to a permanent geologic repository. Spent Fuel Spent fuel results from producing electricity at nuclear power plants or from operating other reactors such as research reactors. After the usable fuel has been expended, highly radioactive fuel assemblies remain. The U.S. does not reprocess spent fuel from power plants, but has reprocessed spent fuel from many types of reactors in the past. Spent fuel is shipped as a solid, and is packaged 8 in casks for transport. Currently, spent fuel is stored in pools of water, above ground vaults, or concrete casks onsite at reactor or commercial power plants. Spent fuel from DOE owned reactors is stored where it is produced or at other DOE sites. Like high-level waste, spent fuel will eventually be shipped to permanent geologic repositories. Under the Nuclear Waste Policy Act, DOE is responsible for transporting spent fuel from power plants, as well as defense related high-level radioactive waste, to permanent repositories. Transuranic Waste Transuranic waste contains manmade elements heavier than uranium, thus the name trans (or beyond) uranic. Transuranic waste results from defense production activities and includes contaminated protective clothing, tools, glassware, and equipment. Most is now stored at government sites throughout the country. Although most transuranic waste is no more radioactive than low-level waste, it is radioactive for a longer period of time. In the past, transuranic waste was shipped in rail cars, but shipments to the Waste Isolation Pilot Plant (WIPP) in New Mexico will be made by truck in a specially designed packaging called the TRUPACT-II. WIPP is designed to demonstrate the disposal of transuranic waste in deep, geologically stable salt beds. If the demonstration project is successful, the site will become a permanent disposal facility for transuranic waste. Low-Level Waste Low-level waste results from research, medical, and industrial processes that use radioactive materials. Commercial power plant operations and defense related activities, including weapons disassembly and cleanup of production sites, also produce some lowlevel waste. Low-level waste consists of contaminated rags, papers, filters, tools, equipment, and discarded protective clothing. Typically, low-level waste contains small amounts of short-lived radioactive material dispersed in large quantities of non-radioactive material. It is far less hazardous than high-level waste and is usually packaged in sturdy wooden or steel crates and steel drums for shipment to storage or disposal sites. Low-level waste is sent to disposal sites licensed by the U.S. Nuclear Regulatory Commission. Several commercial sites accept waste from producers of low-level waste, and some states have formed regional compacts to dispose of low-level waste when these facilities close. Sites have been established throughout the DOE complex for disposal of DOE low-level waste. 9 Mixed Waste Mixed waste is waste that contains both hazardous chemical components and radioactive components and is subject to the requirements of the Atomic Energy Act and the Resource Conservation and Recovery Act. Mixed waste is treated, packaged, and shipped offsite to DOE or commercial disposal sites by most DOE facilities that produce it. Envirocare of Utah, Inc. recently began accepting DOE mixed waste shipments for disposal. The waste is encapsulated in melted recycled plastic and disposed of in an onsite landfill. Uranium Mill Tailings Uranium mill tailings are radioactive rack and soil byproducts from uranium mining and milling. Mill tailings contain small amounts of naturally occurring radium that decays and emits a radioactive gas called radon. When radon gas is released into the atmosphere, it disperses harmlessly. However, radon gas might be dangerous if it is inhaled in high concentrations over a long period of time. Uranium mill tailings are transported to several disposal facilities specifically designed to accept them. When the disposal site reaches capacity, it is sealed to prevent dispersion of radon gas.

CHAPTER:9
PROFESSIONAL RELATIONS AND PRACTICES OF HOSPITAL PHARMACIST

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PHARMACIST

- The profession of pharmacy exists to safeguard the health of the public.
- The ***pharmacist*** is one who is licensed to prepare and dispense medications, counsel patients, and monitor outcomes pursuant to a prescription from a licensed health professional.
- Pharmacists work primarily in community and hospital pharmacies
- Other fields - managed care, mail-order pharmacy, home healthcare, long-term care, nuclear pharmacy, academia, drug information, sales, marketing, or research.

HOSPITAL PHARMACY

A ***hospital pharmacy*** is an institutional pharmacy that dispenses and prepares drugs and provides clinical services in a hospital setting.

- One fourth of all pharmacists work in a hospital setting :
  - an institution that offers 24-hour healthcare service; that has six or more beds, a governing authority, and an organized medical staff; and that offers nursing and pharmacy services
  - carries out the functions of maintaining drug treatment records and ordering, stocking, compounding, repackaging, and dispensing medications and other supplies .

- The pharmacy technician in a hospital setting :
  - takes part in functions involving delivery, stocking, or inventorying of medications anywhere in the hospital
  - may operate manual or computerized robotic dispensing machinery
- Hospital pharmacies (and drugstore chains) are more likely than community pharmacies to require that pharmacy technicians be certified.

HOSPITAL PHARMACIST

- Dispenses oral medications.
- Prepares and dispenses parenteral medications.
- Sometimes specializes, with advanced training in an area of patient care.
- Educates and counsels patients.
- Provides drug information.
- Administers a department
  - develops policies and procedures
  - purchases drugs and supplies
  - monitors drug use in the hospital

PROFESSIONAL RELATIONS:

- According to code of ethics, to assist members in maintaining proper professional conduct while carrying out their duties as hospital pharmacists.

- It is divided into five parts, each specifying a hospital pharmacist's proper relationship:-

1. with the general public and patients.

2.with the pharmacy profession and fellow pharmacists.

3. with the members of other health care professions.

4. with the hospital or the employing institution.

5. with the pharmaceutical industry.

- ***With the general public and patients:***

- observe the laws, and in particular those related to the practice of pharmacy
- regard the health and safety of patients as his/her prime concern, and respect the confidentiality of patients' information;
- refuse to manufacture, supply or lend support to the promotion of sub-standard preparations or other unworthy products;
- to assist and educate patients and the general public on matters related to the usage of drugs and pharmaceutical products.

- ***With the pharmacy profession and fellow pharmacists:***

-uphold the honour and dignity of the pharmacy profession .

-endeavour to provide and maintain hospital pharmacy services up to the highest standard of the profession.

-assist fellow pharmacists with information and advice.

- ***With the members of other health care professions:***

- collaborate with members of other health care professions in order to optimize patient care.

-provide unbiased, scientifically-based information related to drugs and pharmaceutical products to other health care professionals.

-not publicly criticize the ability or performance of other health care professionals, although matters concerning drugs and pharmaceutical products may be expressed in private to the professional involved.

□ ***With the hospital or the employing institution:***

- observe the policies and standards of the hospital or the employing institution and act in its best interest.

- not agree to practice under any working condition which may interfere with his/her professional autonomy nor impose such conditions on their pharmacists.

- ***With the pharmaceutical industry.***

-act honorably in dealings with members of the pharmaceutical industry.

-not associate himself/herself with the advertisement of pharmaceutical products.

ROLE OF THE PHARMACIST

Today's pharmacist:

- ***Compounds*** and dispenses drugs.

- Gathers information about patients
- Counsels on possible side effects and adverse reactions
- Monitors for drug interactions
- Screens, monitors, and advises for self-treatment with ***over-the-counter (OTC)*** products sold without a prescription

- Provides drug information to other healthcare professionals
- Advises on home healthcare supplies and medical equipment