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NUCLEAR MEDICINE AS RADIONUCLIDE IN RADIOPHARMACEUTICALS IN SCINTIGRAPHY

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ABSTRACT

Radiopharmaceuticals are a special class of drugs. They include diagnostic agents, such as molecular imaging probes, contrast agents or tracers, as well as agents that treat diseases, called radio therapeutics. A radiopharmaceutical contains a radioactive isotope that emits energy, which can be detected or used to provide an image (diagnostic agent) or is directly therapeutic within a diseased tissue. Millions of patients receive radiopharmaceuticals annually for a wide variety of medical procedures ranging from the assessment of cardiac function to staging and treatment of cancer. Diagnostic radiopharmaceuticals are administered to a patient and enable physicians and researchers to non-invasively see the biochemical activity of cells, to diagnose or stage disease, identify which patients are best suited for a particular treatment, and help monitor a patient's response to treatment. The imaging probes selectively locate at the site of disease, and release positrons or gamma rays that can be detected and digitally imaged with specialized cameras, producing images through positron emission tomography (PET) or single photon emission computed tomography (SPECT). The probes accumulate at the site of disease and the images appear as colored or dark regions in partial or whole body structural images provided by computed tomography (CT) or magnetic resonance imaging (MRI). Community Preservation and Development Corporation (CPDC) currently markets and distributes diagnostic radiopharmaceuticals and is providing next generation imaging probes for our partners' clinical trials. Therapeutic radiopharmaceuticals are administered to a patient to selectively seek out and deliver cell-killing radiation to the site of disease. These drugs are designed to bind selectively to specific biochemical protein receptors on or within cells at the site of the

disease. Therapeutic radiopharmaceuticals can take many forms including highly selective proteins and antibodies, peptides or small molecules.

KEYWORDS: Atomic number, Atomic weight, Isotope, Radioactive decay, Half life, Shelf life, α particle emission, β particle emission, γ particle emission, Becquerel, Curie, Radionuclide, Nuclear fission, Positron Emission Tomography (PET), Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), X-rays.

INTRODUCTION

A radionuclide (radioactive nuclide, radioisotope or radioactive isotope) is an atom that has excess nuclear energy, making it unstable. This excess energy can be used in one of three ways: emitted from the nucleus as gamma [γ] radiation; transferred to one of its electrons to release it as a conversion electron; or used to create and emit a new particle (alpha [α] particle or beta [β] particle) from the nucleus. During those processes, the radionuclide is said to undergo radioactive decay. These emissions are considered ionizing radiation because they are powerful enough to liberate an electron from another atom. The radioactive decay can produce a stable nuclide or will sometimes produce a new unstable radionuclide which may undergo further decay.

Figure 1: Radiopharmaceuticals.

Radioactive decay is a random process at the level of single atoms: it is impossible to predict when one particular atom will decay. However, for a collection of atoms of a single element the decay rate and thus the half-life ($t_{1/2}$) for that collection can be calculated from their measured decay constants. The range of the half-lives of radioactive atoms has no known limits and spans a time range of over 55 orders of magnitude. Radionuclides occur naturally or are artificially produced in nuclear reactors, cyclotrons, particle accelerators or

radionuclide generators. There are about 730 radionuclides with half-lives longer than 60 minutes. Thirty-two of those are primordial radionuclides that were created before the earth was formed. At least another 60 radionuclides are detectable in nature, either as daughters of primordial radionuclides or as radionuclides produced through natural production on Earth by cosmic radiation. More than 2400 radionuclides have half-lives less than 60 minutes.

Most of those are only produced artificially and have very short half-lives. For comparison, there are about 254 stable nuclides. All chemical elements can exist as radionuclides. Even the lightest element, hydrogen [$_1H^1$], has a well-known radionuclide, deuterium [$_1H^2$] and tritium [$_1H^3$]. Elements heavier than lead and the elements technetium [$_{43}Tc^{98}$] and promethium [$_{61}Pm^{145}$], exist only as radionuclides. Unplanned exposure to radionuclides generally has a harmful effect on living organisms including humans, although low levels of exposure occur naturally without harm. The degree of harm will depend on the nature and extent of the radiation produced the amount and nature of exposure (close contact, inhalation or ingestion) and the biochemical properties of the element; with increased risk of cancer the most usual consequence. However, radionuclides with suitable properties are used in nuclear medicine for both diagnosis and treatment. An imaging tracer made with radionuclides is called a radioactive tracer. A pharmaceutical drug made with radionuclides is called a radiopharmaceutical.[1]

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).

Figure 2: Nuclear medicine therapy.

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 radionuclide 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 than 12 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 radionuclide impurity content may be such that an unacceptable radiation dose would be delivered to the patient. The shelf-life of a multi-dose 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 multi-dose container of an 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 radio-labeling process with a resultant radiopharmaceutical preparation.

Kit for radiopharmaceutical preparation: In general a vial containing the non-radionuclide 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 multi-dose 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.

Figure 3: Diagnostic radiopharmaceuticals.

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 isotopic composition of the target material 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.[2]

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 [$_{92}U^{238}$] by neutrons in a nuclear reactor. For example, iodine-131 [$_{53}I^{127}$], molybdenum-99 [$_{42}Mo^{96}$] and xenon-133 [$_{54}Xe^{131}$] can be produced in this way. Radionuclides from such a process must be carefully controlled in order to minimize the radionuclide impurities.

Charged particle bombardment: Radionuclides may be produced by bombarding target materials with charged particles in particle accelerators 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 (radionuclide impurities) and thus ultimately the radionuclide 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 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 $\lambda=0.693/t_{1/2}$.

$$\mathbf{A=N\lambda=N[0.693/t_{1/2}]}$$

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. 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. 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 single dose containers. If, however, such a preparation is supplied in a multi-dose 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 multi-dose 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.

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.

Radionuclidic purity: Requirements for radionuclide purity are specified in two ways:

1. By expression of a minimum level of radionuclide purity. Unless otherwise stated in the individual monograph, the gamma-ray spectrum should not be significantly different from that of a standardized solution of the radionuclide before the expiry date is reached.
2. By expression of maximum levels of specific radionuclide impurities in the individual monographs. In general, such impurities are those that are known to be likely to arise during the production of the material – for example, thallium-202 ($t_{1/2}$=12.23d) in the preparation of thallium-201 ($t_{1/2}$=73.5h).

Radiochemical purity: Radiochemical purity is assessed by a variety of analytical techniques such as liquid chromatography, paper chromatography, thin-layer chromatography and electrophoresis. After or during separation, the distribution of radioactivity on the chromatogram is determined. Different measuring techniques are used depending on the nature of the radiation and the chromatographic technique. The quantity of substance applied to the chromatographic support (paper, plate or column) is often extremely small (because of the high sensitivity of detection of the radioactivity) and particular care has to be taken in interpretation with regard to the formation of artifacts. The addition of carriers for both the radiopharmaceutical itself and the suspected impurities is sometimes helpful. There is, however, a risk that when a carrier of the radiopharmaceutical is added it may interact with the radiochemical impurity, leading to underestimation of these impurities. In cases where simple chromatographic methods fail to characterize the labeled compound satisfactorily, high performance liquid chromatography could be useful. In some cases, it is necessary to determine the biological distribution of the radiopharmaceutical in a suitable test animal.[3]

Chemical Purity: Chemical purity refers to the proportion of the preparation that is in the specified chemical form regardless of the presence of radioactivity; it may be determined by accepted methods of analysis. The chemical purity of a preparation is often no guide to its radiochemical purity. Preparations, especially those resulting from exchange reactions (for example, a preparation of o-iodohippuric acid in which some of the iodine atoms are replaced by atoms of iodine-131), may be of high chemical purity but may contain impurities of high specific activity (that is, a tiny weight of an radiochemical impurity may be associated with a relatively large amount of the radionuclide). In general, chemical impurities in preparations of radiopharmaceuticals are objectionable only if they are toxic or if they modify the physiological processes that are under study or if they result in undesirable interactions (e.g. aluminium can induce flocculation of Tc99m sulphur colloid). Special attention is necessary for impurities with a pharmacologically active or pharmacodynamic effect even for very low amounts (for example, receptor ligands). Where appropriate, the stereo-isomeric purity has to be verified. In general, the type of limits for inorganic impurities such as arsenic and heavy metals that is specified in monographs for pharmaceutical substances are also valid for radiopharmaceuticals.

pH: For radioactive solutions the pH may be measured using paper pH indicator strips, provided that the pH strips have been validated using an appropriate range of non-radioactive buffers.

Sterility: A number of monographs for radiopharmaceuticals contain the requirement that the preparation is sterile. Such preparations comply with test for sterility. Special difficulties arise, however, in carrying out the test for sterility for radiopharmaceutical preparations because of the short half life of most radionuclides, small size of batches and the radiation hazards. The half-life of many radiopharmaceuticals is so short that, while the sterility test may be initiated prior to release, it will be completed retrospectively. 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), sampling the batch may not be possible.

Bacterial endotoxins/pyrogens: Where appropriate, an individual monograph for a radiopharmaceutical preparation requires compliance with bacterial endotoxins. Validation of the test is necessary to exclude any interference or artifact due to the nature of the radiopharmaceutical. The levels of radioactivity should be standardized as some types of radioactivity and radionuclides, especially high levels of activities, can interfere with the test.

The pH of some radiopharmaceutical preparations will require to be adjusted to pH 6.5-7.5 to achieve optimal results. Where it is not possible to eliminate interference with the test for bacterial endotoxins due to the nature of the radiopharmaceutical, compliance with test for pyrogens may be specified.

Labeling: Every radiopharmaceutical preparation must comply with the labeling requirements established under Good Manufacturing Practice. The label on the primary container should include:
(1) A statement that the product is radioactive or the international symbol for radioactivity (2) The name of the radiopharmaceutical preparation (3) Where appropriate, that the preparation is for diagnostic or for therapeutic use (4) The route of administration (5) The total radioactivity present at a stated date and, where necessary, time; for solutions, a statement of the radioactivity in a suitable volume (for example, in MBq per ml of the solution) may be given instead (6) The expiry date and, where necessary, time (7) The batch (lot) number assigned by the manufacturer (8) For solutions, the total volume (9) Any special storage requirements with respect to temperature and light (10) Where applicable, the name and concentration of any added microbial preservatives or, where necessary, that no antimicrobial preservative has been added.

Storage: Radiopharmaceuticals should be kept in well-closed containers and stored in an area assigned for the purpose. The storage conditions should be such that the maximum radiation dose rate to which persons may be exposed is reduced to an acceptable level. Care should be taken to comply with national regulations for protection against ionizing radiation. Radiopharmaceutical preparations that are intended for parenteral use should be kept in a glass vial, ampoule or syringe that is sufficiently transparent to permit the visual inspection of the contents. Glass containers may darken under the effect of radiation.

Terminology

Nuclide: A unique atom characterized by its atomic number (Z=number of protons in the nucleus) and its atomic mass number (A=total number of neutrons and protons in the nucleus) ${}_{Z}M^{A}$ and having stability such that its lifetime is measurable. All atoms sharing the same atomic number are the same element.

Isotopes: Atoms of the same element with different atomic mass numbers are called isotopes.

Radioactivity: The property of certain nuclides of emitting radiation by the spontaneous transformation of their nuclei into those of other nuclides. The term "disintegration" is widely used as an alternative to the term "transformation". Transformation is preferred as it includes, without semantic difficulties, those processes in which no particles are emitted from the nucleus.

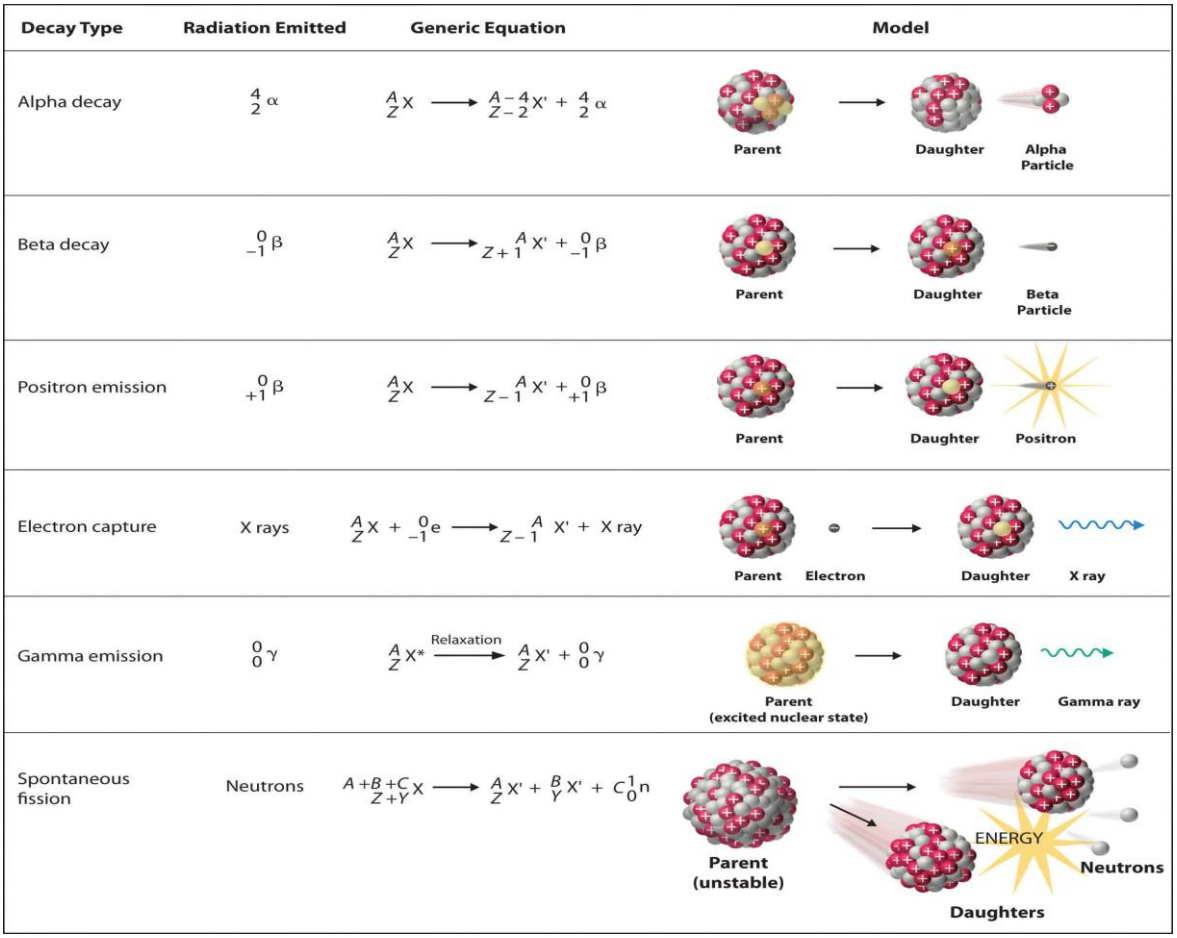

Figure 4: Radioactive decay.

Radioactive decay: The property of unstable nuclides during which they undergo a spontaneous transformation within the nucleus. This change results in the emission of energetic particles or electromagnetic energy from the atoms and the production of an altered nucleus. The term "disintegration" is widely used as an alternative to the term "transformation". Transformation is preferred as it includes, without semantic difficulties, those processes in which no particles are emitted from the nucleus.

Atomic Number (Z) $M^{\text{Atomic Weight (A)}}$

Alpha decay: ${}_{Z}M^{A} \longrightarrow {}_{Z-2}M^{A-4} + {}_{2}\alpha^{4}$ [An alpha particle (A=4, Z=2) emitted from nucleus]

Proton emission: ${}_{Z}M^{A} \longrightarrow {}_{Z-1}M^{A-1} + {}_{1}p^{1}$ [A proton ejected from nucleus; (A−1, Z−1)]

Neutron emission: ${}_{Z}M^{A} \longrightarrow {}_{Z-1}M^{A} + {}_{1}n^{0}$ [A neutron ejected from nucleus; (A−1, Z)]

Double proton emission: ${}_{Z}M^{A} \longrightarrow {}_{Z-2}M^{A-2} + 2\ {}_{1}p^{1}$ [Two protons ejected from nucleus simultaneously; (A−2, Z−2)]

Beta decay: ${}_{Z}M^{A} \longrightarrow {}_{Z+1}M^{A} + {}_{-1}\beta^{0}$ [A nucleus emits an electron and an electron antineutrino; (A, Z+1)]

Positron emission (β+ decay): ${}_{Z}M^{A} \longrightarrow {}_{Z-1}M^{A} + {}_{+1}\beta^{0}$ [A nucleus emits a positron and an electron neutrino; (A, Z−1)]

Gamma decay: ${}_{Z}M^{A} \longrightarrow {}_{Z}M^{A} + {}_{0}\gamma^{0}$ [Excited nucleus releases a high-energy photon (gamma ray); (A, Z)]

Units of radioactivity: The activity of a quantity of radioactive material is expressed in terms of the number of spontaneous nuclear transformations taking place in unit time. The SI unit of activity is the Becquerel (Bq), a special name for the reciprocal second (s^{-1}). The expression of activity in terms of the Becquerel therefore indicates the number of transformations per second. The historical unit of activity is the curie. The curie (Ci) is equivalent to 3.7×10^{10} Bq. The conversion factors between Becquerel and curie and its submultiples are given in Table-1.[4]

Half-life period: The time in which the radioactivity decreases to one-half its original value. The rate of radioactive decay is constant and characteristic for each individual radionuclide. The exponential decay curve is described mathematically by the equation: $\mathbf{N=N_0\mathfrak{E}^{-\lambda t}}$

Where N is the number of atoms at elapsed time t, N_o is the number of atoms when t=0 and λ is the disintegration constant characteristic of each individual radionuclide. The half-life period is related to the disintegration constant by the equation: Radioactive decay corrections are calculated from the exponential equation, or from decay tables, or are obtained from a decay curve plotted for the particular radionuclide involved.

Table 1: Units of radioactivity.

Number of atoms transforming per second	SI unit: Becquerel (Bq)	historical unit: curie (Ci)
1	1 Bq	27 picocurie (pCi)
1000	1 kilobecquerel (kBq)	27 nanocurie (nCi)
1×10^{6}	1 megabecquerel (MBq)	27 microcurie (μCi)
1×10^{9}	1 gigabecquerel (GBq)	27 millicurie (mCi)
37	37 Bq	1 (nCi)
37,000	37 kBq	1 (μCi)
3.7×10^{7}	37 MBq	1 (mCi)
3.7×10^{10}	37 GBq	1 Ci

Physical half-life: The physical half-life of a radionuclide ($t_{½}p$) is the time in which the amount of radioactivity decreases to one half of its original value. Although the time of decay of an individual atom cannot be determined, large numbers of atoms will obey statistical considerations and calculations of activity versus time can be carried out. The rate of decay for a collection of atoms (N) of the same radionuclide is constant and characteristic for each individual radionuclide. The exponential decay is described by the equation: $N=N_oe^{-\lambda t}$; Where N is the number of atoms after an elapsed time t. N_o is the number of atoms at time t=0 and λ is the decay constant characteristic for a given nuclide. This relationship is commonly referred to as the decay law equation. Where the activity of a quantity of radioactive substance is known at a certain time its activity at any other time can be determined by using the decay law relationship. The physical half-life is related to the decay constant by the equation: $t_{1/2}=0.693/\lambda$

In addition to the use of the decay law formula radioactivity can be determined at different times using decay tables or decay curves plotted for the specific radionuclide.[5]

Biological half-life: The biological half-life ($t_{½}b$) of a radiopharmaceutical is the time taken for the concentration of the pharmaceutical to be reduced 50% of its maximum concentration in a given tissue, organ or whole body, not considering radioactive decay.

Effective half-life: The effective half-life ($t_{½}e$) is the actual half-life of a radiopharmaceutical in a given tissue, organ or whole body and is determined by a relationship including both the physical half life and biological half-lives. The effective half-life is important in calculation of the optimal dose of radiopharmaceutical to be administered and in monitoring the amount of radiation exposure. It can be calculated from the formula:
$t_{1/2}e=[t_{1/2p}\times t_{1/2b}]/[t_{1/2p}+t_{1/2b}]$; Where $t_{1/2p}$ and $t_{1/2b}$ are the physical and biological half-lives respectively.

Radionuclidic purity: The radionuclide purity of a preparation is that percentage of the total radioactivity that is present in the form of the stated radionuclide. Some radionuclides decay into nuclides that are themselves radioactive: these are referred to as mother (or parent) and daughter radionuclides respectively. Such daughter radionuclides are often excluded when calculating the radionuclide purity; for example, iodine-131 [$_{53}I^{127}$] will always contain its daughter xenon-131 m [$_{54}Xe^{131}$], but this would not be considered an impurity because its presence is unavoidable. In employing the definition, the radioactivity must be measured in

appropriate units: that is, in the number of nuclear transformations that occur in unit time (in terms Becquerel). If, for example, a preparation stated to be iodine-125 is known to contain 99MBq of iodine-125 and 1MBq of iodine-126 and no other radionuclide, then the preparation is said to be of 99% radionuclide purity. It will be noted that the relative amounts of iodine125 and iodine-126, and hence the radionuclide purity, will change with time. An expression of radionuclide purity must therefore contain a statement of the time, such as: "Not more than 1% of the total radioactivity is due to iodine-126 at the reference date stated on the label". It is clear that, in order to give a statement of the radionuclide purity of a preparation, the activities (and hence the identities) of every radionuclide present must be known. There are no simple and certain means of identifying and measuring all the radionuclide impurities that might be present in a preparation. An expression of radionuclide purity must either depend upon the judgment of the person concerned, or it must be qualified by reference to the method employed, for example: "No radionuclide impurities were detected by gamma scintillation spectrometry using a sodium iodide detector."

Radioactive concentration: The radioactive concentration of a solution refers to the amount radioactivity per unit volume of the solution. As with all statements involving radioactivity, it is necessary to include a reference date and time of standardization. For radionuclides with a half-life period of less than one day, a more precise statement of the reference time is required. In addition, the term radioactive concentration is generally applied to solutions of a radioactive solute. The radioactive concentration of a solution refers to the amount of radioactivity per unit volume of the solution. An example of units for radioactive concentration would be megaBecquerels per millilitre (MBq/ml). Since the radioactive concentration will change with time due to decrease in the nuclide radioactivity it is always necessary to provide a reference time. For short lived radionuclides the reference time will be more precise including time of day in addition to date.[6]

Specific radioactivity: (or specific activity)**:** The specific activity of a preparation of a radioactive material is the radioactivity per unit mass of the element or of the compound concerned. The specific activity of a given radioisotope refers to the disintegration rate per unit mass of the element. For example, a fresh solution of 99mTc will have a specific activity of: As=N×A Where As=specific activity and N=the number of 99mTc atoms in one gram of pure technetium. N is calculated as: N=6.023×1023 (atoms/mole)/(99 grams/mole) However, the following note must be taken into consideration to calculate the specific activity of a

formulated compound. It is usual to specify the radionuclide concerned and also it is necessary to express the time thus: "100MBq of iodine-131 per mg of MIBG at 12.00 hours GMT on 1 January 2006". Specific radioactivity is often not determined directly but is calculated from knowledge of the radioactive concentration of the solution and of the chemical concentration of the radioactive compound. Thus, if a solution contains x MBq of I^{131} per ml, and if the I^{131} is entirely in the chemical form of MIBG of which the concentration is y mg per ml, then at that time the specific activity is: x/y mCi of iodine-131 per mg of MIBG. Where necessary, the radiochemical purity of the preparation must be taken into account.

The term employed in radiochemical work is "specific activity". As the word, "activity" has other connotations in a pharmacopoeia, the term should, where necessary, be modified to "specific radioactivity" to avoid ambiguity.

Radiochemical purity: The radiochemical purity of a preparation is that percentage of the stated radionuclide that is present in the stated chemical form. As radiochemical purity may change with time, mainly because of radiation decomposition, the result of the radiochemical purity test should be started at given date and if necessary hour indicating when the test was carried out. The radiochemical purity limit should be valid during the whole shelf-life. If, for example, a preparation of 99mTc-DTPA is stated to be 99% radiochemically pure, then 99% of the technetium-99m is present in the form of DTPA (diethylenetriamine-pentaacetic acid) complex. Radiochemical impurities might include such substances as reduced-hydrolyzed 99mTc or free 99mTc-pertechnetate anion The possible presence of radionuclide impurities is not taken into account in the definition. If the radionuclide impurity is not isotopic with the stated radionuclide, then it cannot possibly be in the identical chemical form. If the radionuclide impurity is isotopic with the stated radionuclide, it could be, and indeed is likely to be, in the same chemical form. Radiochemical impurities may arise during the preparation of the material or during storage, because of ordinary chemical decomposition or, what is often more important, because of radiation decomposition (that is, because of the physical and chemical effects of the radiation-radiolysis).

Critical Organ: The Critical Organ is the organ or tissue which receives the highest radiation dose. This may not be the target tissue and therefore the dose to the critical organ will determine the maximum safe dose which can be administered. This is primarily of importance with respect to therapeutic radiopharmaceuticals.

Natural: On Earth, naturally occurring radionuclides fall into three categories: primordial radionuclides, secondary radionuclides, and cosmogenic radionuclides. Radionuclides are produced in stellar nucleo-synthesis and supernova explosions along with stable nuclides. Most decay quickly but can still be observed astronomically and can play a part in understanding astronomic processes. *Primordial radionuclides*, such as uranium and thorium, exist in the present time because their half-lives are so long (>100 million years) that they have not yet completely decayed. Some radionuclides have half-lives so long (many times the age of the universe) that decay has only recently been detected, and for most practical purposes they can be considered stable, most notably bismuth-209: detection of this decay meant that bismuth was no longer considered stable. It is possible decay may be observed in other nuclides adding to this list of primordial radionuclides. *Secondary radionuclides* are radiogenic isotopes derived from the decay of primordial radionuclides. They have shorter half-lives than primordial radionuclides. They arise in the decay chain of the primordial isotopes thorium-232, uranium-238 and uranium-235. Examples include the natural isotopes of polonium and radium. Cosmogenic isotopes, such as carbon-14, are present because they are continually being formed in the atmosphere due to cosmic rays. Many of these radionuclides exist only in trace amounts in nature, including all cosmogenic nuclides. Secondary radionuclides will occur in proportion to their half-lives, so short-lived ones will be very rare. Thus polonium can be found in uranium ores at about 0.1 mg per metric ton (1 part in 1010). Further radionunclides may occur in nature in virtually undetectable amounts as a result of rare events such as spontaneous fission or uncommon cosmic ray interactions.

Nuclear fission: Radionuclides are produced as an unavoidable result of nuclear fission and thermonuclear explosions. The process of nuclear fission creates a wide range of fission products, most of which are radionuclides. Further radionuclides can be created from irradiation of the nuclear fuel (creating a range of actinides) and of the surrounding structures, yielding activation products. This complex mixture of radionuclides with different chemistries and radioactivity makes handling nuclear waste and dealing with nuclear fallout particularly problematic.[7]

Table 2: Medical radioisotopes.

Radioisotope	Half-life	Use
Chromium-51 ($_{24}Cr^{52}$)	27.7 days	Used to label red blood cells and quantify gastro-intestinal protein loss.
Iodine-131 ($_{53}I^{127}$)	8.02 days	Used to diagnose and treat various diseases associated with the human thyroid.
Iridium-192 ($_{77}Ir^{192}$)	73.83 days	Supplied in wire form for use as an internal radiotherapy source for certain cancers, including those of the head and breast.
Molybdenum-99 ($_{42}Mo^{96}$)	66 hours	Used as the 'parent' in a generator to produce technetium-99m, the most widely used radioisotope in nuclear medicine.
Phosphorus-32 ($_{15}P^{31}$)	14.28 days	Used in the treatment of excess red blood cells.
Samarium-153 ($_{62}Sm^{150}$)	46.7 hours	Used to reduce the pain associated with bony metastases of primary tumours.
Technetium-99m ($_{43}Tc^{98}$)	6.01 hours	Used to image the brain, thyroid, lungs, liver, spleen, kidney, gall bladder, skeleton, blood pool, bone marrow, heart blood pool, salivary and lacrimal glands, and to detect infection.
Yttrium-90 ($_{39}Y^{89}$)	64 hours	Used for liver cancer therapy.

Table 3: Cyclotron-produced medical radioisotopes.

Radioisotope	Half-life	Use
Copper-64 ($_{29}Cu^{63.5}$)	12.7 hours	Used to study genetic disease affecting copper metabolism; in Positron Emission Tomography; and also has potential therapeutic uses.
Gallium-67 ($_{31}Ga^{70}$)	78.25 hours	Used in imaging to detect tumours and infections.
Iodine-123 ($_{53}I^{127}$)	13.2 hours	Used in imaging to monitor thyroid function and detect adrenal dysfunction.
Thallium-201 ($_{81}Tl^{204}$)	72.9 hours	Used in imaging to detect the location of damaged heart muscle.
Carbon-11 ($_{6}C^{12}$)	20.3 minutes	These are used in Positron Emission Tomography to study brain physiology and pathology; for detecting the location of epileptic foci; and in dementia, and psychiatry and neuropharmacology studies. They are also used to detect heart problems and diagnose certain types of cancer.
Nitrogen-13 ($_{7}N^{14}$)	10 minutes	
Oxygen-15 ($_{8}O^{16}$)	122 minutes	
Fluorine-18 ($_{9}F^{19}$)	1.83 hours	

Table 4: Naturally occurring radioisotopes used in industry and science.

Radioisotope	Half-life	Use
Carbon-14 ($_{6}C^{12}$)	5715 years	Used to measure the age of organic material that is up to 50 000 years old.
Chlorine-36 ($_{17}Cl^{35.5)}$	301000 years	Used to measure sources of chloride and the age of water that is up to 2 million years old.
Lead-210 ($_{82}Pb^{207}$)	22.6 years	Used to date layers of sand and soil laid down up to 80 years ago.
Hydrogen-3 (tritium) ($_{1}H^{3}$)	12.32 years	Used to measure the age of 'young' groundwater (up to 30 years old).

Table 5: Artificially produced radioisotopes used in industry and science.

Radioisotope	Half-life	Use
Americium-241 ($_{95}Am^{241}$)	232.7 years	Used in neutron gauging and smoke detectors.
Cobalt-60 ($_{27}Co^{59}$)	5.27 years	Used in gamma radiography, gauging, and commercial medical equipment sterilization.
Caesium-137 ($_{55}Cs^{133}$)	30.07 years	Used in radiotracing to identify sources of soil erosion and depositing; also for thickness gauging.
Gold-198 ($_{79}Au^{197}$)	2.7 days	Used to trace factory waste causing ocean pollution, and to trace sand movement in river beds and on ocean floors.
Gold-198 ($_{79}Au^{197}$)	2.7 days	Used to study sewage and liquid waste movements. Nb technetium-99m is generated from its reactor-produced 'parent', molybdenum-99.
Technetium-99m ($_{43}Tc^{98}$)	6.01 days	
Iridium-192 ($_{77}Ir^{192}$)	73.8 days	Used in gamma radiography
Iridium-192 ($_{77}Ir^{192}$)	73.8 days	Used to trace sand to study coastal erosion
Gold-198 ($_{79}Au^{197}$)	2.7 days	
Chromium-51 ($_{24}Cr^{52}$)	27.7 days	
Tritiated water T_2O or ^3H_2O	12.32 years	Used as a tracer to study sewage and liquid wastes.
Ytterbium-169 ($_{70}Yb^{173}$)	32 days	Used in gamma radiography
Zinc-65 ($_{30}Zn^{65}$)	243.87 days	Used to predict the behavior of heavy metal components in effluents from mining waste water.
Manganese-54 ($_{25}Mn^{55}$)	312.1 days	

Synthetic: Artificial nuclide americium-241 emitting alpha particles inserted into a cloud chamber for visualization Synthetic radionuclides are deliberately synthesized using nuclear reactors, particle accelerators or radionuclide generators:

As well as being extracted from nuclear waste, radioisotopes can be produced deliberately with nuclear reactors, exploiting the high flux of neutrons present. These neutrons activate elements placed within the reactor. A typical product from a nuclear reactor is iridium-192. The elements that have a large propensity to take up the neutrons in the reactor are said to have a high neutron cross-section. Particle accelerators such as cyclotrons accelerate particles to bombard a target to produce radionuclides. Cyclotrons accelerate protons at a target to produce positron-emitting radionuclides, e.g. fluorine-18. Radionuclide generators contain a parent radionuclide that decays to produce a radioactive daughter. The parent is usually produced in a nuclear reactor. A typical example is the technetium-99m generator used in nuclear medicine. The parent produced in the reactor is molybdenum-99.

Uses: Radionuclides are used in two major ways: either for their radiation alone (irradiation, nuclear batteries) or for the combination of chemical properties and their radiation (tracers, biopharmaceuticals). In biology, radionuclides of carbon can serve as radioactive tracers because they are chemically very similar to the nonradioactive nuclides, so most chemical, biological, and ecological processes treat them in a nearly identical way. One can then

examine the result with a radiation detector, such as a Geiger counter, to determine where the provided atoms were incorporated. For example, one might culture plants in an environment in which the carbon dioxide contained radioactive carbon; then the parts of the plant that incorporate atmospheric carbon would be radioactive. Radionuclides can be used to monitor processes such as DNA replication or amino acid transport.

In nuclear medicine, radioisotopes are used for diagnosis, treatment, and research. Radioactive chemical tracers emitting gamma rays or positrons can provide diagnostic information about internal anatomy and the functioning of specific organs, including the human brain. This is used in some forms of tomography: single-photon emission computed tomography and positron emission tomography (PET) scanning and Cherenkov luminescence imaging. Radioisotopes are also a method of treatment in hemopoietic forms of tumors; the success for treatment of solid tumors has been limited. More powerful gamma sources sterilize syringes and other medical equipment.

In food preservation, radiation is used to stop the sprouting of root crops after harvesting, to kill parasites and pests, and to control the ripening of stored fruit and vegetables. In industry, and in mining, radionuclides are used to examine welds, to detect leaks, to study the rate of wear, erosion and corrosion of metals, and for on-stream analysis of a wide range of minerals and fuels. In spacecraft and elsewhere, radionuclides are used to provide power and heat, notably through radioisotope thermoelectric generators (RTGs). In astronomy and cosmology radionuclides play a role in understanding stellar and planetary process. In particle physics, radionuclides help discover new physics (physics beyond the Standard Model) by measuring the energy and momentum of their beta decay products. In ecology, radionuclides are used to trace and analyze pollutants, to study the movement of surface water, and to measure water runoffs from rain and snow, as well as the flow rates of streams and rivers. In geology, archaeology, and paleontology, natural radionuclides are used to measure ages of rocks, minerals, and fossil materials.[8]

Physical characteristics of clinically relevant radionuclides: Information on the physical characteristics of key radionuclide used in nuclear medicine is provided in the following table. For more detailed information on physical characteristics including parent half-life, daughter half-life, decay mode, energy, end-point energy intensity, dose and daughter nucleus refer to IAEA nuclear data base.

List of Radiopharmaceuticals Used In Nuclear Medicine

1. Carbon-11: Chemical Symbol: 11C [$_6C^{12}$], Chemical Form: Carbon-11+Choline, Half-life: 20.334 minutes. Manufacturer: Mayo Clinic, *Diagnostic use: Indicated for PET imaging of patients with suspected prostate cancer recurrence based upon elevated blood prostate specific antigen (PSA) levels following initial therapy and non-informative bone scintigraphy, computerized tomography (CT) or magnetic resonance imaging (MRI) to help identify potential sites of prostate cancer recurrence for subsequent histologic confirmation.*

2. Carbon-14: Chemical Symbol: 14C [$_6C^{12}$], Chemical Form: Carbon-14+urea, Half-life: 5,730 years, Manufacturer: Kimberly-Clark, Trade name(s): PYtest, *Diagnostic use: Detection of gastric urease as an aid in the diagnosis of H.pylori infection in the stomach.*

3. Fluorine-18: Chemical Symbol: 18F [$_9F^{19}$], Chemical Form: Fluorine-18+florbetapir, Half-life: 109.771 minutes, Manufacturer: Eli Lilly, Trade name(s): Amyvid™, *Diagnostic use: Indicated for PET imaging of patients with suspected prostate cancer recurrence based upon elevated blood prostate specific antigen (PSA) levels following initial therapy and non-informative bone scintigraphy, computerized tomography (CT) or magnetic resonance imaging (MRI) to help identify potential sites of prostate cancer recurrence for subsequent histologic confirmation.*

4. Fluorine-18: Chemical Symbol: 18F [$_9F^{19}$], Chemical Form: Fluorine-18+sodium fluoride, Half-life: 109.771 minutes, *Diagnostic use: PET bone imaging agent to delineate areas of altered osteogenesis.*

5. Fluorine-18: Chemical Symbol: 18F [$_9F^{19}$], Chemical Form: Fluorine-18+fludeoxyglucose, Half-life: 109.771 minutes, *Diagnostic use: As a PET imaging agent to: > Assess abnormal glucose metabolism in oncology > Assess myocardial hibernation > Identify regions of abnormal glucose metabolism associated with foci of epileptic seizures.*

6. Gallium-67: Chemical Symbol: 67Ga [$_{31}Ga^{70}$], Chemical Form: Gallium-67+Gallium Citrate, Half-life: 3.26 days, Manufacturer(s): Covidlen, Lantheus Medical Imaging, Trade name(s): Neoscan (GE), DuPont Ga-67, Mallinckrodt Ga-67, *Diagnostic use: Useful to demonstrate the presence/extent of: >Hodgkin's disease >Lymphoma >Bronchogenic carcinoma >Aid in detecting some acute inflammatory lesions.*

7. Indium-111: Chemical Symbol: 111In [$_{49}In^{115}$], Chemical Form: Indium-111+Capromab Pendetide, Half-life: 2.80 days, Manufacturer: Jazz Pharmaceuticals, Trade name(s): ProstaScint®, *Diagnostic use: A diagnostic imaging agent in newly-diagnosed patients with biopsy-proven prostate cancer, thought to be clinically-localized after standard diagnostic evaluation (e.g. chest x-ray, bone scan, CT scan, or MRI), who are at high-risk for pelvic*

lymph node metastases. A diagnostic imaging agent in post-prostatectomy patients with a rising PSA and a negative or equivocal standard metastatic evaluation in whom there is a high clinical suspicion of occult metastatic disease.

8. Indium-111: Chemical Symbol: 111In [$_{49}In^{115}$], Chemical Form: Indium-111+Chloride, Half-life: 2.80 days, Manufacturer: GE Healthcare, Covidien, Trade name(s): Indiclor (Nycomed), Mallinckrodt In-111Cl, *Diagnostic use: For labeling monoclonal antibodies and peptides.*

9. Indium-111: Chemical Symbol: 111In [$_{49}In^{115}$], Chemical Form: Indium-111+Diethylenetriamine pentaacetic Acid (DTPA), Half-life: 2.80 days, Manufacturer: GE Healthcare, Trade name(s): Indium DTPA In 111, *Diagnostic use: For use in radionuclide cisternography, Cerebro spinal fluid imaging.*

10. Indium-111: Chemical Symbol: 111In [$_{49}In^{115}$], Chemical Form: Indium-111+Oxyquinoline, Half-life: 2.80 days, Manufacturer: GE Healthcare, Trade name(s): Indium-111+oxine, *Diagnostic use: Indicated for radio-labeling autologous leukocytes which may be used as an adjunct in the detection of inflammatory processes to which leukocytes migrate, such as those associated with abscesses or other infection.*

11. Indium-111: Chemical Symbol: 111In [$_{49}In^{115}$], Chemical Form: Indium-111+Pentetreotide, Half-life: 2.80 days, Manufacturer: Covidien, Trade name(s): Octreoscan™, *Diagnostic use: An agent for the scintigraphic localization of primaryand metastatic neuroendocrine tumors bearing somatostatin receptors. Imaging of neuroendocrine tumors.*

12. Indium-111: Chemical Symbol: 111In [$_{49}In^{115}$], Chemical Form: Indium-111+Satumomab Pendetide, Half-life: 2.80 days, Trade name(s): OncoScint, *Diagnostic use: Imaging of metastatic disease associated with colorectal and ovarian cancer.*

13. Iodine-123: Chemical Symbol: 123I [$_{53}I^{127}$], Chemical Form: Iodine-123+Iobenguane, Half-life: 13.22 hours, Manufacturer: GE Healthcare, Trade name(s): AdreView™, *Diagnostic use: Indicated for use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests. Neuroendocrine tumor imaging.*

14. Iodine-123: Chemical Symbol: 123I [$_{53}I^{127}$], Chemical Form: Iodine–123+Ioflupane, Half-life: 13.22 hours, Manufacturer(s): GE Healthcare, Trade name(s): DaTscan™, *Diagnostic use: Indicated for striatal dopamine transporter visualization using SPECT brain imaging to assist in the evaluation of adult patients with suspected Parkinsonian syndromes*

(PS) in whom it may help differentiate essential tremor due to PS (idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy)

15. Iodine-123: Chemical Symbol: 123I [$_{53}I^{127}$], Chemical Form: Iodine–123+Sodium iodide, Half-life: 13.22 hours, Manufacturer(s): Cardinal Health, Covidien, Trade name(s): Mallinckrodt, Amersham, *Diagnostic use: Indicated for use in the evaluation of thyroid: Function and Morphology.*

16. Iodine-125: Chemical Symbol: 125I [$_{53}I^{127}$], Chemical Form: Iodine–125+Human serum albumin, Half-life: 59.4 days, Manufacturer(s): IsoTex Diagnostics, Trade name(s): Isojex, Jeanatope, *Diagnostic use: Indicated for use in the determination of: Total blood and Plasma volume.*

17. Iodine-125: Chemical Symbol: 125I [$_{53}I^{127}$], Chemical Form: Iodine–125+Iothalamate, Half-life: 59.4 days, Manufacturer(s): IsoTex Diagnostics, Trade name(s): Glofil, *Diagnostic use: Indicated for evaluation of glomerular filtration.*

18. Iodine-131: Chemical Symbol: 131I [$_{53}I^{127}$], Chemical Form: Iodine–131+human serum albumin, Half-life: 8.0197 days, Manufacturer(s): IsoTex Diagnostics, Trade name(s): Megatope, *Diagnostic use: Indicated for use in determinations of: Total blood and plasma volumes, Cardiac output, Cardiac and pulmonary blood volumes and circulation times, Protein turnover studies, Heart and great vessel delineation, Localization of the placenta and Localization of cerebral neoplasm.*

19. Iodine-131: Chemical Symbol: 131I [$_{53}I^{127}$], Chemical Form: Iodine–131+sodium iodide, Half-life: 8.0197 days, Manufacturer(s): Covidien, DRAXIMAGE, Trade name(s): HICON™, *Diagnostic use: Performance of the radioactive iodide (RAI) uptake test to evaluate thyroid function, Localizing metastases associated with thyroid malignancies Therapeutic, Treatment of hyperthyroidism and Treatment of carcinoma of the thyroid.*

20. Iodine-131: Chemical Symbol: 131I [$_{53}I^{127}$], Chemical Form: Iodine–131+tositumomab, Half-life: 8.0197 days, Manufacturer(s): GlaxoSmithKline, Trade name(s): BEXXAR®, *Diagnostic use: Indicated for: Treatment of patients with CD20 antigen-expressing relapsed or refractory, low grade, follicular, or transformed non-Hodgkin's lymphoma, including patients with Rituximab-refractory nonHodgkin's lymphoma.*

21. Molybdenum 99: Chemical Symbol: 99Mo [$_{42}Mo^{96}$], Chemical Form: Mo-99 generator, Half-life: 2.7489 days, Manufacturer(s): Covidien, Lantheus Medical Imaging, Trade name(s): Ultra-TechneKow® DTE, Technelite®, *Diagnostic use: Generation of Tc-99m sodium pertechnetate for administration or radiopharmaceutical preparation.*

22. Nitrogen-13: Chemical Symbol: 13N [$_{7}N^{14}$], Chemical Form: Nitrogen-13+Ammonia, Half-life: 9.97 min, *Diagnostic use: Indicated for diagnostic Positron Emission Tomography (PET) imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.*

23. Radium-223: Chemical Symbol: 223Ra [$_{88}Ra^{226}$], Chemical Form: Radium-223 dichloride, Half-life: 11.4 day, Manufacturer(s): Bayer HealthCare Pharmaceuticals Inc., Trade name(s): Xofigo®, *Diagnostic use: Indicated for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease.*

24. Rubidium-82: Chemical Symbol: 85Rb [$_{37}Rb^{85}$], Chemical Form: Rubidium-82 chloride, Half-life: 1.27 minutes, Manufacturer(s): Bracco Diagnostics, Trade name(s): Cardiogen-82®, *Diagnostic use: PET myocardial perfusion agent that is useful in distinguishing normal from abnormal myocardium in patients with suspected myocardial infarction.*

25. Samarium-153: Chemical Symbol: 153Sa [$_{62}Sa^{150}$], Chemical Form: Samarium-153+EDTMP, Half-life: 46.3 hours, Manufacturer(s): Jazz Pharmaceuticals, Trade name(s): Quadramet®, *Diagnostic use: Indicated for relief of pain in patients with confirmed osteoblastic metastatic bone lesions that enhance on radionuclide bone scan.*

26. Strontium-89: Chemical Symbol: 89Sr [$_{36}Sr^{88}$], Chemical Form: Strontium-89 chloride, Half-life: 50 days, Manufacturer(s): Bio-Nucleonics, GE Healthcare, Trade name(s): Metastron, *Diagnostic use: Indicated for the relief of bone pain in patients with painful skeletal metastases that have been confirmed prior to therapy.*

27. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m bicisate, Half-life: 6.0058 hours, Manufacturer(s): Lantheus Medical Imaging, Trade name(s): Neurolite®, *Diagnostic use: SPECT imaging as an adjunct to conventional CT or MRI imaging in the localization of stroke in patients in whom stroke has already been diagnosed.*

28. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m disofenin, Half-life: 6.0058 hours, Manufacturer(s): Pharmalucence, Trade name(s): Hepatolite®, *Diagnostic use: Diagnosis of acute cholecystitis as well as to rule out the occurrence of acute cholecystitis in suspected patients with right upper quadrant pain, fever, jaundice, right upper quadrant tenderness and mass or rebound tenderness, but not limited to these signs and symptoms.*

29. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m exametazine, Half-life: 6.0058 hours, Manufacturer(s): GE Healthcare, Trade name(s):

Ceretec™, *Diagnostic use: As an adjunct in the detection of altered regional cerebral perfusion in stroke, Leukocyte labeled scintigraphy as an adjunct in the localization of intra abdominal infection and inflammatory bowel disease.*

30. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m macroaggregated albumin, Half-life: 6.0058 hours, Manufacturer(s): DRAXIMAGE, Trade name(s): Pulmolite – CIS, Macrotec (Bracco), Technescan MAA (Mallinckrodt), Amersham MAA, *Diagnostic use: An adjunct in the evaluation of pulmonary perfusion (adult and pediatric) and Evaluation of peritoneo-venous (LaVeen) shunt patency.*

31. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m+mebrofenin, Half-life: 6.0058 hours, Manufacturer(s): Bracco Diagnostics, Pharmalucence, Trade name(s): Choletec®, *Diagnostic use: As a hepatobiliary imaging agent.*

32. Technetium-99M: Chemical Symbol: 99mTc[$_{43}Tc^{98}$], Chemical Form: Technetium-99m medronate, Half-life: 6.0058 hours, Manufacturer(s): Bracco Diagnostics, DRAXIMAGE, GE Healthcare, Pharmalucence, Trade name(s): MDP-Bracco™, MDP-25, MDP Multidose, *Diagnostic use: As a bone imaging agent to delineate areas of altered osteogenesis.*

33. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m mertiatide, Half-life: 6.0058 hours, Manufacturer(s): Covidien, Trade name(s): Technescan MAG3™, *Diagnostic use: In patients > 30 days of age as a renal imaging agent for use in the diagnosis of: Congenital and acquired abnormalities, Renal failure, Urinary tract obstruction and calculi, Diagnostic aid in providing of Renal function, Split function, Renal angiograms, Renogram curves for whole kidney and renal cortex.*

34. Technetium-99M: Chemical Symbol: 99mTc[$_{43}Tc^{98}$], Chemical Form: Technetium-99m oxidronate, Half-life: 6.0058 hours, Manufacturer(s): Covidien, Trade name(s): Technescan™HDP, *Diagnostic use: As a bone imaging agent to delineate areas of altered osteogenesis (adult and pediatric use).*

35. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m pentetate, Half-life: 6.0058 hours, Manufacturer(s): DRAXIMAGE, Trade name(s): *Diagnostic use: Brain imaging, Kidney imaging: - To assess renal perfusion - To estimate glomerular filtration rate.*

36. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m pyrophosphate, Half-life: 6.0058 hours, Manufacturer(s): Pharmalucence, Covidien, Trade name(s): Technescan™ PYP™, *Diagnostic use: As a bone imaging agent to delineate areas of altered osteogenesis, As a cardiac imaging agent used as an adjunct in the diagnosis of*

acute myocardial infarction, As a blood pool imaging agent useful for: - Gated blood pool imaging - Detection of sites of gastrointestinal bleeding.

37. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m red blood cells, Half-life: 6.0058 hours, Manufacturer(s): Covidien, Trade name(s): UltraTag™, *Diagnostic use: Tc99m-labeled red blood cells are used for: Blood pool imaging including cardiac first pass and gated equilibrium imaging, Detection of sites of gastrointestinal bleeding.*

38. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m sestamibi, Half-life: 6.0058 hours, Manufacturer(s): Cardinal Health, Covidien, DRAXIMAGE, Lantheus Medical Imaging, Pharmalucence, Trade name(s): Cardiolite®, *Diagnostic use: Myocardial perfusion agent that is indicated for: Detecting coronary artery disease by localizing myocardial ischemia (reversible defects) and infarction (non-reversible defects), Evaluating myocardial function, Developing information for use in patient management decisions, Planar breast imaging as a second line diagnostic drug after mammography to assist in the evaluation of breast lesions in patients with an abnormal mammogram or a palpable breast mass.*

39. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m sodium pertechnetate, Half-life: 6.0058 hours, Manufacturer(s): Covidien, Lantheus Medical Imaging, *Diagnostic use: Brain Imaging (including cerebral radionuclide angiography), Thyroid Imaging, Salivary Gland Imaging, Placenta Localization, Blood Pool Imaging (including radionuclide angiography), Urinary Bladder Imaging (direct isotopic cystography) for the detection of vesico-ureteral reflux, Nasolacrimal Drainage System Imaging (adult and pediatric use).*

40. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m succimer, Half-life: 6.0058 hours, Manufacturer(s): GE Healthcare, *Diagnostic use: An aid in the scintigraphic evaluation of renal parenchymal disorders.*

41. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m sulfur colloid, Half-life: 6.0058 hours, Manufacturer(s): Pharmalucence, *Diagnostic use: Imaging areas of functioning retriculoendothelial cells in the liver, spleen and bone marrow, It is used orally for: Esophageal transit studies, Gastroesophageal reflux scintigraphy, Detection of pulmonary aspiration of gastric contents, Aid in the evaluation of peritoneo-venous (LeVeen) shunt patency, To assist in the localization of lymph nodes draining a primary tumor in patients with breast cancer or malignant melanoma when used with a hand-held gamma counter. (adult and pediatric use).*

42. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m tetrofosmin, Half-life: 6.0058 hours, Manufacturer(s): GE Healthcare, Trade name(s): Myoview™, *Diagnostic use: Myocardial perfusion agent that is indicated for: Detecting coronary artery disease by localizing myocardial ischemia (reversible defects) and infarction (non-reversible defects), The assessment of left ventricular function (left ventricular ejection fraction and wall motion).*

43. Technetium-99M: Chemical Symbol: 99mTc [$_{43}Tc^{98}$], Chemical Form: Technetium-99m tilmanocept, Half-life: 6.0058 hours, Manufacturer(s): Navidea Biopharmaceuticals, Inc. Trade name(s): Lymphoseek®, *Diagnostic use: Indicated for lymphatic mapping with a handheld gamma counter to assist in the localization of lymph nodes draining a primary tumor site in patients with breast cancer or melanoma.*

44. Thallium-201: Chemical Symbol: 201Tl [$_{81}Tl^{204}$], Chemical Form: Thallium-201 chloride, Half-life: 72.912 hrs, Manufacturer(s): Covidien, GE Healthcare, Lantheus Medical Imaging, Trade name(s): DuPont, Mallinckrodt, Amersham, *Diagnostic use: Useful in myocardial perfusion imaging for the diagnosis and localization of myocardial infarction, As an adjunct in the diagnosis of ischemic heart disease (atherosclerotic coronary artery disease), Localization of sites of parathyroid hyperactivity in patients with elevated serum calcium and parathyroid hormone levels.*

45. Xenon-133: Chemical Symbol: 133Xe [$_{54}Xe^{131}$], Chemical Form: Xenon-133 gas, Half-life: 5.2475 days, Manufacturer(s): Lantheus Medical Imaging, Trade name(s): Xeneisol, *Diagnostic use: The evaluation of pulmonary function and for imaging the lungs, Assessment of cerebral flow.*

46. Yttrium-90: Chemical Symbol: $_{39}Y^{90}$, Chemical Form: Yttrium-90 chloride, Half-life: 64 hrs, Manufacturer(s): Eckert & Ziegler Nuclitec, MDS Nordion, *Diagnostic use: Indicated for radiolabeling: Zevalin® used for radioimmunotherapy procedures.*

47. Yttrium-90: Chemical Symbol: $_{39}Y^{90}$, Chemical Form: Yttrium-90+ibritumomab tiuxetan, Half-life: 64 hrs, Manufacturer(s): Spectrum Pharmaceuticals, Trade name(s): Zevalin, *Diagnostic use: Indicated for the: Treatment of relapsed or refractory, low-grade or follicular ß-cell non-Hodgkin's lymphoma (NHL), Treatment of previously untreated follicular NHL in patients who achieve a partial or complete response to first-line chemotherapy*.[9]

Medical Applications: Radioactive drugs, or radiopharmaceuticals, are used clinically for the diagnosis, investigation and occasionally for the therapy, of many human illnesses. The

first radiopharmaceutical to be widely used was the fission product, iodine-131, in the form of the simple salt, sodium iodide, the use of which was established in the late forties as a diagnostic test for certain thyroid disorders. Because the drug could be administered orally, in solution, it was referred to in the press as the "Atomic Cocktail". Since those pioneering days, the practice of nuclear medicine has soared in most developed countries. Approximately 10,000,000 people in the United States are tested diagnostically each year with a radioactive drug, either *in-vivo* or *in-vitro*. The total value of the radiopharmaceuticals used throughout the world is approaching $(US) 10^8 per year, with over two-thirds of the total being produced by private companies. The world-wide use of these drugs is growing at a rate of 15 - 20% per year.

Board of Radiation and Isotope Technology (BRIT) produces and supplies a wide range of radiopharmaceuticals to hospitals and medical institutions to enable various diagnostic and therapeutic studies on patients. BRIT has recently added [Lu^{177}]-Lu-DOTATATE (LUM-3) and [I^{131}]-Lipiodol (IOM 40) as new therapeutic radiopharmaceuticals products. These radiopharmaceutical products undergo strict quality analysis and quality control tests including sterility, pyrogen tests and bio-distribution studies and are manufactured in strict compliance with regulations in India as per the Radiopharmaceutical Committee (RPC) guidelines.

Table 6: Application of Radiopharmaceuticals.

Radiopharmaceutical	**Application**
I^{131}+Sodium iodide	Thyroid uptake
I^{131}+Rose Bengal	Liver scan
I^{131}+Hippuran	Kidney scan
I^{131}+Human Serum Albumin	Blood volume, circulatory studies
I^{131}+Iodinated Oils	Fat absorption studies
Cr^{51}+Sodium chromate	Spleen scanning (by tagging red blood cells)
Co^{57}+Vitamin B^{12}	Pernicious anemia diagnosis
Au^{198}+Gold colloid (less than 1µ)	Liver scan
Hg^{197}+Chlormerodrin	Brain and kidney scans
Se^{75}+Selenomethionine	Pancreas scan
I^{131} or Tc^{99m} – Macro-aggregated serum albumin (30-50µ)	Lung scan
F^{18}-Sodium fluoride	Bone scan

Lu^{177}-DOTATATE Injection Code: LUM-3 available in 100 mCi and 200 mCi doses. Production is on fortnightly basis. The product is useful for PRRT of sstr positive Neuroendocrine tumors.

I^{131}-Lipiodol Injection Code: IOM 40 available in 75 mCi dose. Production is on a monthly basis. The product is useful in treatment of hepatocellular carcinoma.

[Tc^{99m}]-Technetium is formed from the decay of a parent radionuclide, molybdenum-99, which through this parent-daughter process, can be provided in a convenient, readily available form such as the recently introduced COLTECH Technetium Generator. There are other Column Generator products such as geltech generator and TCM 2 solvent extraction generator which can also be used for preparation of [Tc^{99m}]-Technetium labeled radiopharmaceuticals with Technetium Cold Kits supplied by BRIT.

Technetium Cold Kits (TCK) are prepared under aseptic, sterile and pyrogen free conditions. When reconstituted with sterile, pyrogen free sodium [Tc^{99m}]-pertechnetate solution as per the prescribed procedure they yield desired injectable 99mTc - radiopharmaceutical.

BRIT has recently introduced high dose sodium [I^{131}]-iodide capsules in the range of 25 mCi to 100 mCi (IOM 5B). Frequency of supply for I-131 labeled MIBG (IOM 50) has also been enhanced considerably.

PHM-3 sodium [P^{32}] orthophoshate injection for Bone Pain Palliation (Weekly), PHM-4 samarium [P^{32}] phosphate colloidal injection for Radiation Synovectomy (Weekly), SAM-2 [Sm^{153}] samarium-EDTMP injection for Bone Pain Palliation (Fortnightly), CRM-1 sodium [Cr^{51}]chromate injection Blood Volume Studies Bi-annually.

BRIT is engaged in production and supply of radioimmunoassay (RIA) and immunoradiometric assay (IRMA) kits for various hormones. BRIT has developed a novel method for the preparation of Magnetic cellulose* and a new type of magnetic cellulose* suitable for immunoassays and other biological applications. (* Patent pending) BRIT also gives technical assistance in setting-up of RIA laboratories, training of manpower, custom-made kit development including for veterinary applications.

***In-vitro* application:** There are a number of *in-vitro* clinical tests which employ radioactive reagents, but the most important one in present use is the radioimmunoassay for body hormones. Although a number of variations of this test have been developed, the essential features common to all are: 1. A protein which selectively interacts with the hormone (binding agent). This protein may be naturally-occurring, e.g. a globulin, or a non-naturally occurring antibody. The latter is produced by a crossed-species reaction, e.g. the injection of

human (or pork) insulin into a rabbit, which causes the formation of rabbit antibodies to the human insulin. 2. A hormone preparation which has been labeled with a radioactive atom. 3. An effective method to separate the free hormone from the hormone bound to the protein. The total amount of the labeled hormone preparation and the binding protein, followed by separation of the bound from unbound hormone. By measuring the radioactivity in each fraction, one obtains a bound: unbound ratio which is referred to a standard curve to obtain the concentration of the hormone in the plasma. Radioimmunoassay is an exceedingly sensitive method which is capable of measuring most hormones at the nanogram to picogram level. It is also very specific since the antibody binds its specific hormone very selectively. A surprisingly wide range of hormones and other antigens can be assayed by this method. A few examples are assays for insulin, thyroxin, prostaglandins, digitoxin, human growth hormone, and the "hepatitis associated" antigen, the test for which can minimize hepatitis injection through blood transfusions by pre-testing donors.

***In-vivo* application:** Radiopharmaceuticals are used *in-vivo* to obtain clinical information by measuring the spatial distribution of the drug in an organ (scintigraphy), or by measuring the uptake or throughput of the drug within the organ (uptake or organ-function test). A scintigraphic measurement produces a two dimensional "picture" or scan (or three dimensional if a tomographic device is used) which shows whether or not the radiopharmaceutical is distributed over the organ in a "normal" manner. If the radioactivity scan shows abnormal areas, these can indicate the presence of a tumor or the reduced viability of that portion of the organ. The uptake test is best typified by the thyroid radioiodine uptake measurement. The rate at which the thyroid removes radioactive iodide from the blood stream furnishes important information regarding the physiological state of this gland. Similarly, kidney function can be evaluated by measuring the rate of accumulation of a radiopharmaceutical, such as 197 Hg chlormerodrin, in both kidneys at the same time. There are less than 50 radiopharmaceuticals for *in-vivo* administration which are in common use. Many of them are used for identical diagnostic tests, the choice of a particular one frequently depending on the personal preferences of the practitioner. The development of more effective radiopharmaceuticals is being intensively investigated in several score laboratories all over the world and it is likely that the drugs used in nuclear medicine will be altered considerably during the next 10 to 20 years.

Isotope Generators: One of the major developments of the past ten years has been the commercial introduction of the isotope generator into nuclear medicine. This device is based on a mother daughter isotope decay scheme, the former being relatively long-lived and the latter short-lived. The long-lived mother isotope is shipped to the hospital. By simple manipulations, it is possible to obtain the desired daughter isotope from the generator in sterile apyrogenic solution. The impetus for the rapid acceptance of generators has been the awareness that the radiation dose to the patient should not be above acceptable levels, and should also be minimized. The simplest way to do this is to employ a radioisotope with a convenient short half-life, so that after the medical information is obtained, the isotope rapidly decays away. Other incidental desirable properties are the absence of beta ray emission, which causes unnecessary radiations exposure, and a high degree of localization of the radiopharmaceutical in the target organ or region of body (high target to non-target ratio of incorporation), followed by rapid biological clearance from the body. The technicium-99m generator is employed in over 2000 hospitals at the present time. The parent isotope, molybdenum 99 (half life 67 hours), absorbed on an alumina column, is shipped weekly. The technetium-99m (half-life 6 hours) can be eluted once or twice daily, and in this chemical form, the pertechnetate ion, it can be used directly for brain and thyroid scanning. Various commercial kits have been developed which permit the conversion under sterile conditions of the pertechnetate into other useful radiopharmaceuticals, e.g. technetium-sulfur colloid (liver scanning), technetium labeled serum albumin (blood pool studies) and macro-aggregated serum albumin (lung scanning). Some useful isotope generators of radiopharmaceutical interest are shown in Table-2.

Medical Cyclotrons: Another effort to produce short-lived isotopes and isotopes not otherwise accessible by reactor irradiation has been the installation of ' compact" or "medical" cyclotrons adjacent to nuclear medicine clinics. At the present time, there are about 30 such installations, which are producing such isotopes as U, C, N^{13}, O^{15}, F^{18}, Fe^{52}, Ga^{67} and I^{123}, each of which offers desirable characteristics for use in a radiopharmaceutical.[10]

Therapeutic Applications: Todate, there have been relatively few therapeutic applications of radiopharmaceuticals. The early successes in treating certain thyroid diseases with radioactive iodine have been followed by a few other major breakthroughs. Certain leukemic diseases have responded to therapeutic doses. Radiopharmaceutical therapy is still a frontier in nuclear medicine. During the past twenty-five years, nuclear medicine has developed into a

widely accepted medical discipline and has been one of the major positive contributions to human welfare to arise out of the atomic era. The Agency is playing an active role in transmitting these techniques to developing nations for the betterment of health throughout the world.

CONCLUSION

Radioisotopes are widely used in medicine, industry and scientific research, and new applications for their use are constantly being developed. Radioisotopes are radioactive isotopes of an element. Different isotopes of the same element have the same number of protons in their atomic nuclei but differing numbers of neutrons. They can also be defined as atoms that contain an unstable combination of neutrons and protons. The combination can occur naturally, as in radium-226, or by artificially altering the atoms. In some cases, a nuclear reactor is used, in others, a cyclotron. The best known example is uranium. All but 0.7 per cent of naturally-occurring uranium is uranium-238; the rest is the less stable, or more radioactive, uranium-235, which has three less neutrons.

Atoms containing this unstable combination regain stability by shedding radioactive energy, hence the term radioisotope. The process of shedding the excess radioactive energy is called radioactive decay. The radioactive decay process of each type of radioisotope is unique and is measured with a time period called a half-life. Radioisotopes are an essential part of radiopharmaceuticals. In fact, they have been used routinely in medicine for more than 30 years. On average, one in every two Australians can expect at some stage in his or her life to undergo a nuclear medicine procedure that uses a radioisotope for diagnostic or therapeutic purposes. Some radioisotopes used in nuclear medicine have very short half-lives, which mean they decay quickly; others with longer half-lives take more time to decay, which makes them suitable for therapeutic purposes. Industry uses radioisotopes in a variety of ways to improve productivity and gain information that cannot be obtained in any other way. Radioisotopes are commonly used in industrial radiography, which uses a gamma source to conduct stress testing or check the integrity of welds. A common example is to test aeroplane jet engine turbines for structural integrity. Radioisotopes are also used by industry for gauging (to measure levels of liquid inside containers, for example) or to measure the thickness of materials. Radioisotopes are also widely used in scientific research, and are employed in a range of applications, from tracing the flow of contaminants in biological systems, to determining metabolic processes in small Australian animals. They are also used

on behalf of international nuclear safeguards agencies to detect clandestine nuclear activities from distinctive radioisotopes produced in weapons programs. A sealed radioactive source is an encapsulated quantity of a radioisotope used to provide a beam of ionizing radiation. Industrial sources usually contain radioisotopes that emit gamma or X-rays.

Nuclear medicine uses small amounts of radiation to provide information about a person's body and the functioning of specific organs, ongoing biological processes, or the disease state of a specific illness. In most cases, the information is used by physicians to make an accurate diagnosis of the patient's illness. In certain cases radiation can be used to treat diseased organs or tumors. Medical radioisotopes are made from materials bombarded by neutrons in a reactor, or by protons in an accelerator called a cyclotron. ANSTO uses both methods. Radioisotopes are an essential part of radiopharmaceuticals. Some hospitals have their own cyclotrons, which are generally used to make radiopharmaceuticals with short half-lives of seconds or minutes.

A radiopharmaceutical is a molecule that consists of a radioisotope tracer attached to a pharmaceutical. After entering the body, the radio-labeled pharmaceutical will accumulate in a specific organ or tumor tissue. The radioisotope attached to the targeting pharmaceutical will undergo decay and produce specific amounts of radiation that can be used to diagnose or treat human diseases and injuries. The amount of radiopharmaceutical administered is carefully selected to ensure each patient's safety. About 25 types of radiopharmaceuticals are routinely used in Australia's nuclear medicine centers. The most common is technetium-99m, which has its origins as uranium silicide sealed in an aluminium strip placed in the OPAL reactor's neutron-rich reflector vessel surrounding the core. After processing, the resulting molybdenum-99 is removed and placed into devices called technetium generators where it changes to technetium-99m. These generators are distributed by Australian Nuclear Science and Technology Organization (ANSTO) to medical centers throughout Australia and the near Asia Pacific region. The short half-life of 6 hours and the weak energy gamma ray it emits makes technetium-99m ideal for imaging organs of the body for disease detection without delivering a significant radiation dose to the patient. The generator remains effective for several days of use and is then returned to ANSTO for replenishment. One of the shorter half-life (eight days) radiopharmaceuticals is iodine-131, used to fight thyroid cancer. Because the thyroid gland produces the body's supply of iodine, the gland naturally accumulates iodine-131 injected into patient. Its radioactivity attacks nearby cancer cells with minimal effect on

healthy tissue. Nuclear imaging is a technique that uses radioisotopes that emit gamma rays from within the body.

There is a significant difference between nuclear imaging and other medical imaging systems such as CT (computerized tomography), MRI (magnetic resonance imaging) or X-rays.

The main difference between nuclear imaging and other imaging systems is that, in nuclear imaging, the source of the emitted radiation is within the body. Nuclear imaging shows the position and concentration of the radioisotope. If very little of the radioisotope has been taken up a 'cold spot' will show on the screen indicating, perhaps, that blood is not getting through. A 'hot spot' on the other hand may indicate excess radioactivity uptake in the tissue or organ that may be due to a diseased state, such as an infection or cancer. Both bone and soft tissue can be imaged successfully with this system. A radiopharmaceutical is given orally, injected or inhaled and is detected by a gamma camera which is used to create a computer-enhanced image that can be viewed by the physician. Nuclear imaging measures the function (by measuring blood flow, distribution or accumulation of the radioisotope) of a part of the body and does not provide highly resolved anatomical images of body structures.

Positron Emission Tomography (PET) scans: A widely used imaging technique for detecting cancers and examining metabolic activity in humans and animals. A small amount of short-lived, positron-emitting radioactive isotope is injected into the body on a carrier molecule such as glucose. Glucose carries the positron emitter to areas of high metabolic activity, such as a growing cancer. The positrons which are emitted quickly, form positronium with an electron from the bio-molecules in the body and then annihilate producing gamma rays. Special detectors can track this process and enables the detection of cancers or abnormalities in brain function.

Computed Tomography (CT) scans: A CT scan, sometimes called CAT (Computerized Axial Tomography) scan, uses special X-ray equipment to obtain image data from hundreds of different angles around, or 'slices' through, the body. The information is then processed to show a 3-D cross-section of body tissues and organs. Since they provide views of the body slice by slice, CT scans provide much more comprehensive information than conventional X-rays. CT imaging is particularly useful because it can show several types of tissue-lung, bone, soft tissue and blood vessels - with greater clarity than X-ray images.

PET scans are frequently combined with CT scans, with the PET scan providing functional information (where the radioisotope has accumulated) and the CT scan refining the location. The primary advantage of PET imaging is that it can provide the examining physician with quantified data about the radiopharmaceutical distribution in the absorbing tissue or organ.

What can nuclear imaging tell us? The information obtained by nuclear imaging tells an experienced physician much about how a given part of a person's body is functioning. By using nuclear imaging to obtain a bone scan for example, physicians can detect the presence of secondary cancer 'spread' up to two years ahead of a standard X-ray. It highlights the almost microscopic remodeling attempts of the skeleton as it fights the invading cancer cells.

A Radiopharmaceutical is a drug that can be used either for diagnostic or therapeutic purposes. It is composed of a radioisotope bond to an organic molecule. The organic molecule conveys the radioisotope to specific organs, tissues or cells. The radioisotope is selected for its properties. Radioisotopes emitting penetrating gamma rays are used for diagnostic (imaging) where the radiation has to escape the body before being detected by a specific device (SPECT/PET cameras). Typically, the radiation emitted by isotope used for imaging vanishes completely after 1 day through radioactive decay and normal body excretion. The most common isotopes for imaging are: Tc^{99m}, I^{123}, I^{131}, Tl^{201}, In^{111} and F^{18}. Radioisotopes emitting short range particles (alpha or beta) are used for therapy due to their power to lose all their energy over a very short distance, therefore causing a lot of local damage (such as cell destruction). This property is used for therapeutic purposes: cancer cells destruction, pain treatment in palliative care for bone cancer or arthritis. Such isotopes stay longer in the body than imaging ones; this is intentional in order to increase treatment efficiency, but this remains limited to several days. The most common therapeutic isotopes are: I^{131}, Y^{90}, Rh^{188} and Lu^{177}. Radiopharmaceutical radioiodine radiotracer tracer. Manufacturing such radio labeled molecules requires pharmaceutical industry expertise within the safety constraints of a nuclear facility. Therefore, such a facility must comply with the Good Manufacturing Practice of the pharmaceutical industry while at the same time adhering to the As Low As Reasonably Achievable principle of the nuclear industry, aimed at protecting the workers, the environment and the patient. The largest facilities for producing radiopharmaceuticals are located in Europe and North America. Before being accessible for routine clinical use, the radiopharmaceutical has to demonstrate its harmlessness for the patient and its benefit for the treatment, like any classical drug. This demonstration process is

strictly regulated by the Food and Drug Administration (FDA) in the United States and the European Medicines Agency (EMA) in Europe. The typical duration for such a process is typically 5 to 8 years, from the initial discovery to the availability for the physicians.

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