THE IMPORTANT AND CLINICAL PHARMACEUTICAL ASPECTS OF RADIOPHARMACEUTICAL USAGE

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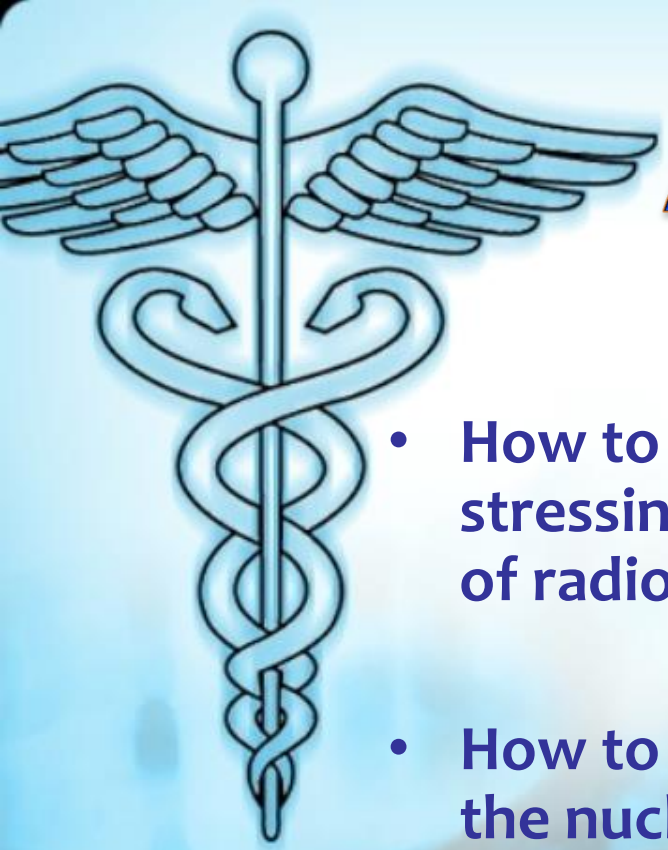


Aim:

- How to develop the new radiopharmaceutical stressing and keeping the pharmaceutical aspects of radiopharmaceuticals
- How to implement the new radiopharmaceutical in the nuclear medicine clinical practice and in the methods of quality assurance

Radiopharmacy is a specialty area of pharmacy practice dedicated to the compounding and dispensing of radioactive materials for use in nuclear medicine procedures."

Radiopharmaceuticals

- **Selection of pharmaceutical based on organ-specific question.**
- **Labeling of pharmaceutical with radioactive isotopes.**
- **Radiopharmaceuticals should not disturb the process under investigation**

Types of Radiopharmaceuticals

- Ready-to-use licensed radiopharmaceuticals: prepared and delivered to hospital by RP-manufacturer

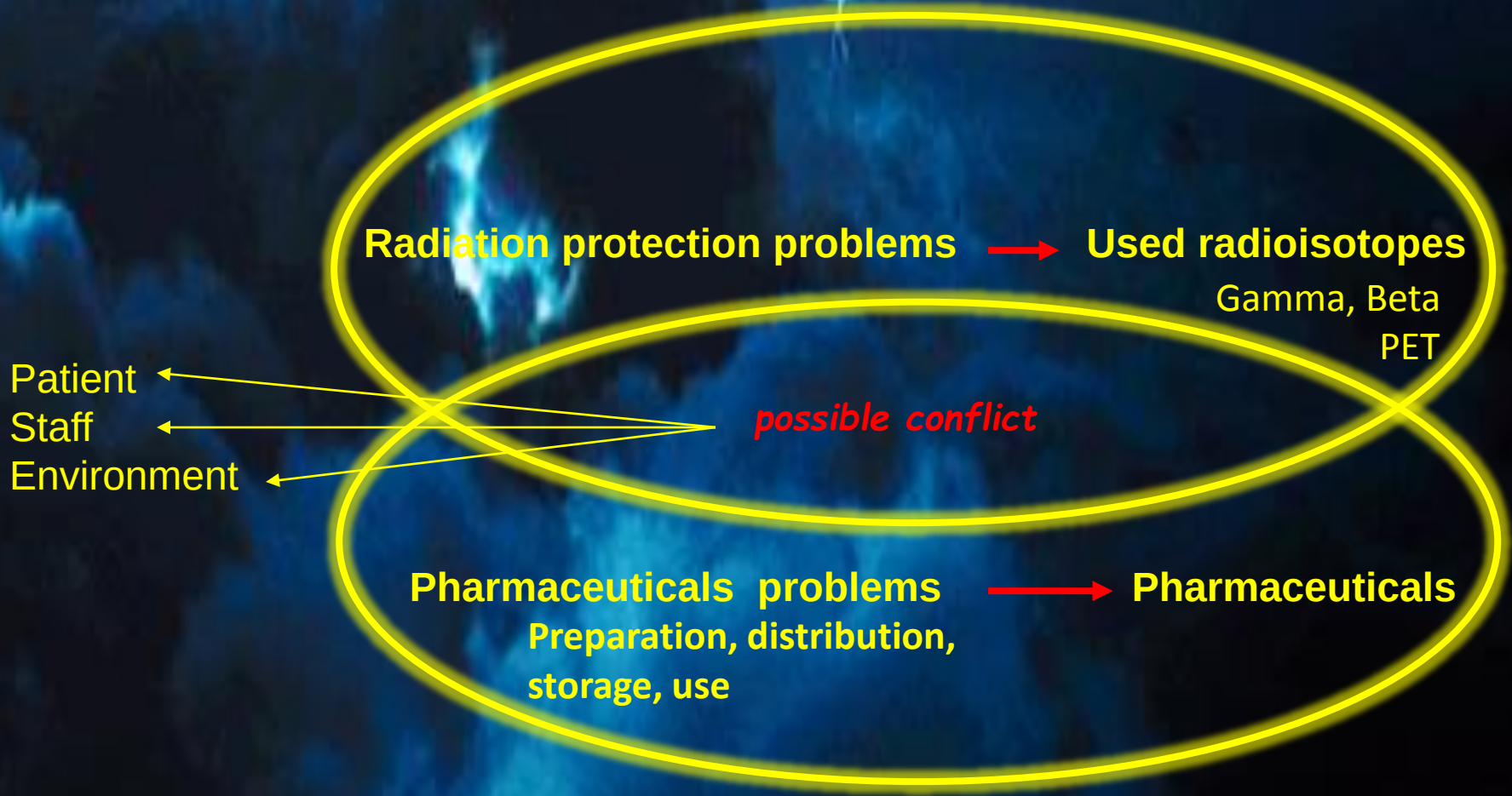
- Radiopharmaceuticals prepared just before use in the nuclear medicine department using licensed labelling kits and eluate of a licensed technetium-99m generator or licensed precursor radionuclide

- Radiopharmaceuticals synthesized on site in (mostly) several steps starting from raw materials and (in house) cyclotron produced radionuclide (most radiopharmaceuticals for positron emission tomography (PET)

- radiolabelled patient's autologous blood cells

- Most radiopharmaceuticals are used for medical diagnosis
- Contain only small amounts of the active substances with a radionuclide attached to them to allow scintigraphic imaging or measurement of biodistribution
- Not often show any measurable pharmacodynamic effect
- Radiation is a general property of all radiopharmaceuticals, and give to the patient an inevitable radiation dose
- In therapeutic radiopharmaceuticals, the radiation effect is the wanted property
- Evaluation of the safety and efficacy should include radiopharmaceutical and radiation hygiene aspects and radiation dosimetry in addition to general parameters.

RADIOPHARMACEUTICALS



PHYSICO-CHEMICAL, BIOLOGICAL OR MICROBIOLOGICAL TESTS OF RADIOPHARMACEUTICALS AS MEDICINAL PRODUCTS

1. **Qualitative and quantitative specifics of the constituents and development pharmaceutics**
2. **Description of method of preparation (**obtaining and maintaining sterility during manufacture (preparation and assembly) - **validation of processes**
3. **Control of starting materials**
4. **Control tests on the finished product**
5. **Stability tests**
6. **Toxicological and Pharmacological Tests -** toxicity may be associated with a radiation dose
7. **Single dose/repeated dose toxicity**
8. **Examination of reproductive function and foetal toxicity**
9. **Mutagenic potential / Carcinogenic potential**
10. **Pharmacodynamics / Pharmacokinetics**

Something more to discuss:

Controversial aspects of the regulatory framework for compounding of radiopharmaceuticals used in positron emission tomography (PET)

Positron emission tomography (PET) is a unique diagnostic modality in that it provides images of the human body's basic biochemical functioning. PET radiopharmaceuticals are unique among radiopharmaceuticals because of their short physical half-lives, ranging from a few seconds to several hours.

Pharmaceutical drug authorities around the world (FDA, EMEA, EDQM) considered the production of PET radiopharmaceuticals to be significantly different from the production of conventional drugs in a number of important aspects:

- short physical half-lives of PET radioisotopes
- prolonged preparation time significantly erodes the useful clinical life of PET radiopharmaceuticals
- must be administered to patients shortly after production
- the quantities of active ingredients contained in each lot of a PET radiopharmaceuticals generally vary from microgram to nanogram amounts
- PET radiopharmaceuticalsdo are not usually in a general drug distribution chain (the entire lot/one vial) is usually distributed directly from the PET facility to a single nuclear medicine department to a nuclear pharmacy for dispensing.

Established procedures and current good manufacturing practice (CGMP) requirements for PET radiopharmaceuticals conflict with differentiation between manufacturing and compounding.

COMPOUNDING BY PHARMACISTS IS IMPLIED, BUT SPECIFIC MENTION OF "PHARMACIST" NEEDS TO BE INCLUDED

And something else: Clinical trials using radiopharmaceutical:

Highly Regulated Profession – physician

✓ **Good starting point:**

- **They have already all documentation…**
- **They have already got wipe tests and calibrations and phantoms and surveys…**
- **They have already got MDs, specialy in Nuclear medicine and PhDs…**

Wrong consideration:

"They are using low risk diagnostic doses anyway…"
"Radiopharmaceuticals don't have side effects…"
"Patients get images which can help their diagnosis…"

CLINICAL DOCUMENTATION

Diagnostic radiopharmaceuticals will be different in many ways from therapeutic radiopharmaceuticals

1. **Clinical pharmacology**

Pharmacodynamics / Pharmacokinetics

2. Clinical trials - to prove their safety in use and their value as diagnostic or therapeutic agents

- **Diagnostic/therapeutic efficacy**
- **Adverse reactions**
- **Interactions**
- **Dosage**

Things to remember…

- All regulations and guidance for clinical trials exist to protect human subjects
- Fraud and unethical practices still occur today
- The *appearance* of fraud or unethical behavior can be detrimental to the investigator and sponsor
- Sponsors expect nuclear medicine investigators and study coordinators to be knowledgeable about the regulations and guidance documents


La belleza perece en la vida pero es inmortal en el arte.
Leonardo Da Vinci