Perspectives of international organisations: International Atomic Energy Agency

Aruna Korde
a.korde@iaea.org
This project has received funding from the European Commission under Service Contract N° ENER/2022/NUCL/Si2.869532.0
IAEA Activities in radiopharmaceuticals

- To support Member States for Radioisotope and radiopharmaceutical production to ensure availability of safe and effective products of appropriate quality for patients use

Radioisotope production & Radiopharmaceutical Developments
- Preclinical
- Translation

Coordinated research projects (CRPs)
- Technical Meetings/Consultancy Meetings
- Technical Cooperation Projects ~110
- Collaborations
- WHO, SRS...

Capacity Building
- Human resource development
- WHO, SRS...

Conferences
- Publications
- CRP REPORTS

On going three, starting in 2023-1, In 2024-1
- Education (e-learning, Training Modules, Syllabus for Universities)

Supporting activities for GMP Guidelines, health regulation, Monographs

Collaborating Centres: CIRC, ICNAS, INSTTN

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How RPh were prepared historically? what changed today-regulations???

Use of I-131 for treatment since early 1940’s

Original Tc-99m generator 1958 shown without shielding

Initial synthesis module for $^{18}$F FDG

Some examples of recent facilities established through IAEA Technical cooperation Projects in radiopharmaceutical area
What is regulated for Radiopharmaceuticals

- Commercial Distribution
- RP Preparation/Production (Premises, Production process personnel, etc.)
- Quality control, specification, acceptance criteria
- First in human Translation

- Marketing Authorization
- Facility Licensing, GMP inspections, radiation safety regulations, transportation, waste managements
- Pharmacopoeia Specifications
- Clinical trials regulations
IAEA-RPRC Activities in radiopharmaceuticals regulations

• Regulatory basis for the use of radiopharmaceuticals
  • Marketing authorization
  • The small scale, non-commercial preparation of radiopharmaceuticals: Compounding, Magistral preparation and Extemporaneous Preparation
  • Clinical trials

• There are several factors that contribute to making the access to RPs challenging, and amongst them, the pharmaceutical regulatory framework and associated guidelines play a very important role in many ways.

• We receive several requests from MS to support capacity building and guidance for effective implementation of radiopharmaceutical oversight
  • Regional and national projects cover RP regulation activities, enabling conducting training programs, fellowships, expert missions
  • Specific Technical Meetings for Health regulations of RPH were conducted in 2017, 2023
  • Collaborations with WHO for International Pharmacopoeia and guidelines
• Preclinical evaluation is an integral part of the development of any drug, including radiopharmaceuticals.
• Different in vitro techniques are required to ascertain the biological properties of radiolabelled molecules in order to obtain approval for testing in laboratory animals.
• In many instances, it’s necessary to determine safety and efficacy of the new radiopharmaceutical products by suitable animal studies prior to translation for clinical trials.

The IAEA Conducted Technical Meeting on Non-clinical testing of radiopharmaceuticals: regulatory consideration Nov 2021

Annex 2

International Atomic Energy Agency and World Health Organization guideline on good manufacturing practices for radiopharmaceutical products

Acknowledgements

This guideline was prepared by the following experts (in alphabetical order): Mr P.O. Bremer (Norway), Mr C. Fallaiz (Belgium), Dr S. Kopp (World Health Organization [WHO], Switzerland), Mr P.B. Kulkarni (India), Mr D.V.S. Narasimhan (International Atomic Energy Agency [IAEA], Austria), Mr K.R. Park (Republic of Korea), Dr A. van Zyl (South Africa), Ms S. Vasanavuthana (Thailand) and Mrs H. Vera Ruiz (IAEA, Austria).

These guidelines were updated by the following experts (in alphabetical order): Ms Y.M. Chevalme (France), Dr S. Kopp (WHO, Switzerland), Ms A. Korde (IAEA, Austria), Mr S.K. Lynchnchen (United States of America), Mr J.A. Osso Junior (IAEA, Austria), Mr A. Ross (Canada) and Mr S. Todde (Italy).

Annex 3

IAEA/WHO guideline on good manufacturing practices for investigational radiopharmaceutical products

Background

In view of the rapidly expanding field of molecular imaging and targeted radiopharmaceutical therapy, combined with the absence of dedicated guidance specific to the manufacture of investigational radiopharmaceuticals used in both early and late clinical trials, the World Health Organization (WHO), in partnership with the International Atomic Energy Agency (IAEA), has raised the urgency for the generation of a new IAEA/WHO guideline on good manufacturing practices for investigational radiopharmaceutical products.

The objective of this guideline is to meet current expectations and trends in good manufacturing practices specific to investigational radiopharmaceuticals used in clinical trials (that is, phase I, phase II and phase III trials) and to harmonize the text with the principles from other related international guidelines.

This text was developed in alignment with the Good manufacturing practices: supplementary guidelines for the manufacture of investigational pharmaceutical products for clinical trials in humans (1). A draft working

Approved by WHO Expert Committee on Specifications for Pharmaceutical Preparations during their 57th Meeting 9-13 Oct 2023
The TM held in hybrid-mode had the participation of 37 experts, 11 joining in person and 26 joining on-line. Brought together researchers, regulators, producers, academicians in RPh. Representatives of US-FDA, EMA and other regulatory agencies from different MS, professional Societies: SRS, EANM and WHO.

Radiation safety regulations and pharmaceutical/drug oversight are well established in many MS (were not discussed during this TM). whereas establishing pharmaceutical framework for radiopharmaceuticals require special regulatory consideration due to their distinct characteristics than conventional pharmaceutical products.

The TM strongly advocated creating an international expert group to provide regulatory guidance on RPs for MS. This will facilitate common understanding of the requirements and their compliance.
Major findings, Observations and take-home message from TM

• Large diversity (heterogenicity) in radiopharmaceutical regulatory management - procedures and practices - as well as underlying legal framework - is noticeable.
• Regulation of radiopharmaceuticals should be risk based – the more risk, the more regulatory oversight and manufacturing process controls are required.
• Lack of- or mis-communication between radiation safety and pharmaceutical authorities often results in the lack of availability of certain radiopharmaceuticals or delays in approvals.
• Successful development of new radiopharmaceuticals requires dialog between Investigators and regulators.
• Regulatory Definition of Radiopharmaceuticals (incl. e.g. kits, precursors, generators) are often interpreted differently and result in variations in regulatory requirements.
• Definition of responsibilities and qualification of personnel were also observed to be a major challenge in many MS.
• Current status: Position paper in drafting stage, Expert working group establishment is under consideration.