Technical Aspects of Non-HEU Mo-99 & Tc-99m Production: An IAEA Update

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International Atomic Energy Agency

Mo-99 Topical Meeting
11-15 September 2016  St Louis, MO
International Atomic Energy Agency (IAEA)

1953 : UN General Assembly
1957 : IAEA born-Vienna; 56 MS
2005 : Nobel Peace Prize
2016 : 168 MS; ~ 2500 staff

Statutory Mandate
The Agency shall seek to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world.

Mission
To assist its Member States, in the context of social and economic goals, in planning for and using nuclear science and technology for various peaceful purposes, including the generation of electricity, and facilitate the transfer of such technology and knowledge in a sustainable manner to developing Member States.
IAEA Organization for Mo-99 Activities

- Nuclear Energy
- Nuclear Fuel Cycle and Waste Technology
- Research Reactors
- Radioisotope products
- Physical and Chemical Sciences
- Physics- RR Applications
- Human Health
- Nuclear Medicine
IAEA’s Mo-99/Tc-99m related activities

- Stability of supply of Mo-99 in Member States
- HEU minimization
- Indigenous production using non-HEU targets
- Small-scale production of Mo-99 or Tc-99m for local use and associated regulatory aspects
- New alternatives to Tc-99m radiopharmaceuticals
- Coordination and participation in the OECD-NEA’s HLG-MR
Mechanisms for assistance

• **Coordinated Research Projects (CRPs)**—professionals/experts from 15-20 member countries (MS) participate in a research project of common interest, share the knowledge and experience and often achieve tangible results/success.

• **Training events**—need based; budget dependent thematic training events in specific topics- 15-20 MS professionals trained with focus on important aspects.

• **Thematic technical meetings**: professionals (typically 30-40) with expertise in the ‘theme’ from the MSs present their work; discussions often lead to further actions

• **Publications**

• **Conferences**
Coordinated Research Projects
Developing Techniques for Small Scale Indigenous Molybdenum-99 Production Using LEU Fission or Neutron Activation ($n, \gamma$)

- 2005-2011
- 14 Member States
Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99m

- 2011-2015
- 18 participants from 16 Member States
- Production of Tc-99m in cyclotron - very successful
- Technology to produce several (>30) Ci Tc-99m per run in medical cyclotrons of energies below 24 MeV proven; clinical trials under way; regulatory approvals sought
- Self-sufficiency in hospitals/towns/country
- Good option for hospital or radiopharmacy; local productions
- Target specifications; reuse of targets etc. need consideration

Comparison of cyclotron- and reactor-based Tc-99m pertechnetate for the Univ. of Alberta Clinical Trial (cancer thyroid patients imaged post-thyroidectomy)
Sharing and Developing Protocols to Further Minimize Radioactive Gaseous Releases to the Environment in the Manufacture of Medical Radioisotopes, as GMP

- 2014 - ongoing
- Initiated as result of a request from a five Member States - May 2014
- First Research & Coordination Meeting - August 2015
- Second Research & Coordination Meeting – planned 1Q 2017
- Participants and observers from Australia, Belgium, Canada, France, Germany, Indonesia, The Netherlands, Pakistan, Poland, Rep. of Korea, USA.
New Ways of Producing Tc-99m and Tc-99m Generators

- Planned new CRP for 2017
- Recommendation from Technical Meeting on same topic (March 2016)
- Aimed as use of low specific activity Mo-99 for generator preparation and accelerator production of Tc-99m
Training Events
Objectives:
• Assist in organization of Round Robin for Mo-99 production by $^0n_1$ capture
• Promote non-HEU production pathways
• Facilitate estimates for local supply of Mo-99

Means:
• Provision of samples and procedures
• Advice and evaluation by international experts
• Irradiation results analysis, both individual & group
• Follow up workshops
• Expert missions to identified labs

Results:
• 16 RR facilities
• Analysis - December 2015 workshop
• Demonstrated that ~1-3Ci/g specific saturation activities with flux of $1 \times 10^{14}$ cm$^{-2}$s$^{-1}$
• Summary paper accepted for publication in the Journal of Radioanalytical and Nuclear Chemistry

Specific saturation activities for Mo at a thermal neutron flux of $1 \times 10^{13}$ cm$^{-2}$s$^{-1}$
Supporting the Global Deployment of Mo-99 Production Capacity for Nuclear Medicine Applications without the Use of HEU

- Started 2013
- Aimed at assisting small-scale, national-level producers in setting up their production capability
  - NOT aimed at creating commercial producers
- Supports LEU fission or n,\( \gamma \) -based production
- Expert missions to Mexico, Morocco, Peru, Poland and Romania (Egypt and Malaysia conducted earlier)
Interregional Training Courses & Workshops

- **India** (Board of Radiation and Isotope Technology)
  - 22-27 June 2015
  - 15 participants from 12 MS
  - Lectures, demonstrations and visits:
    - Production and supply of Mo-99
    - Aspects related to (n,gamma) production
    - Generators with low specific Mo-99 (gel generator)
    - Solvent extraction of Tc-99m
    - Hot cells
    - Regulatory issues

- **Kazakhstan** (Institute of Nuclear Physics)
  - Planned for 2017, in tandem with the closing of the round robin activity

- **Round Robin Workshop**
  - To explore the use of Tc-99m radioactivity concentration units and high capacity absorbers for Mo
  - Planned for 2017
Thematic Technical Meetings
Global Capabilities for the Production and Manufacture of Molybdenum-99 Targets

• 20-21 October 2015
• 31 participants from 15 Member States + EU Commission
• Objectives:
  • Discuss current and upcoming techniques and capabilities for the manufacture of targets used in the production of Mo-99

LEU foil target (USA)  Irradiation baskets (Belgium)  Target holder and plates (Korea)
Regulatory Aspects of Radiopharmaceutical Production

• 7-11 December 2015
• 9 participants from 8 Member States
• Objectives and recommendations:
  - To share experience of current radiopharmaceutical regulation status in participating MSs;
  - To define a work plan for IAEA to support MSs that require assistance in this issue, in the form of education, training and harmonization tools;
  - To evaluate the need for an IAEA publication with recommendations of how new facilities or those that need renovation can comply with national regulations.
New Ways of Producing Tc-99m and Tc-99m Generators

- 14-18 March 2016
- 17 participants from 8 Member States
- Objectives:
  - Evaluate alternative routes for the production of Tc-99m and Mo-99
  - Evaluate optimization of available generators
  - Evaluate current status and potential development of Mo-99/Tc-99m generators using low specific activity Mo-99
- Recommendations:
  - Round-robin
  - Training course
  - New CRP
  - Publication
- Concerns
  - Supply of enriched Mo target materials
  - Regulatory issues

TCM-AUTOSOLEX Separation module with Control Unit (India)
IAEA Publications
Publications on Mo-99/Tc-99m

- Reference Plan for Self Sufficiency in the Supply of Selected Radioisotopes Produced in Research Reactors: Latin America Case Study

- Publication in progress
Conferences & Upcoming Activities
Upcoming IAEA Conferences

IMIC 2016 (Oct 10-14, 2016)

- Special Plenary Session on 12 Oct.
- Session VI : Radiopharmacy
  - Kevin Charlton – OECD role (HLG-MR)
  - Sally Schwarz – GMP in US (FDA; IND)
  - Adriano Duatti – Cardiac agents (Tc-99m, TI-201 & PET)

2019 – International Symposium on Trends in Radiopharmaceuticals
(approved) proposed date 06-10 May 2019
Upcoming Activities

CRPs
• 27 Feb. – 3 March 2017 (*proposed*): RCM #2 of Emissions CRP
• TBD – New Ways of Producing Tc-99m and Tc-99m Generators

Training Events
• 2017 – Interregional Training Course in Kazakhstan
• 2017 – Round robin on absorbers

Thematic Technical Meetings
• 2017 – 2nd Mo-99 target meeting
• 2017 – Workshop on Regulatory Aspects of Radiopharmaceutical Production
Thank You!