

Activities in Support of Production of Mo-99 and Mo-99/Tc-99m Generators

Valeriia Starovoitova, Amirreza Jalilian, Aruna Korde

Radioisotope Products and Radiation Technology Section Department of Nuclear Sciences and Applications International Atomic Energy Agency

October 2022



IAEA Organization – RPRT Section



RPRT Activities Relevant to Mo-99

- Research and Development
- Implementation of Technologies
- Education / Training / Qualification

Areas:

- Production of radioisotopes and radiopharmaceuticals
- Accelerator-based radiation technologies for industry, environment, and cultural heritage
- Sealed radiation sources for NDT and other applications





Mo-99 production routes: Nuclear reactors 32 60 Years



Mo-99 production routes: Accelerators

"The supply of medical radioisotopes-Review of potential Molybdenum-99/Technetium-99m production technologies". Nuclear Energy Agency-OECD November 2010



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
- Monograph approved in Europe
- 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)

Photonuclear Route for Producing Tc-99m and Tc-99m (Generators

- First Meeting: 11-15 December 2017
- 18 approved proposals
- 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 Mo-99 (Mo-100 (γ,n) reaction)







Production of Radiopharmaceuticals





Tc-99m Radiopharmaceuticals (generators)



most widely used generator system

mother nuclide ${}^{99}Mo$ (t_{1/2}=67 h) decays into the daughter nuclide ${}^{99m}Tc$ (t_{1/2}=6 h)







Ms Margaret Greene, Tc-99m generator, BNL

Over 5,000 lives will be directly impacted by Tc-99m in the next 90 minutes!!





From "Pangea Project", ePatient Nuclear Medicine & Molecular Imaging, Vol.1 N. 2.



Total worldwide recorded clinical trials on Tc-99m RPs



www.clinicaltrail.gov



Newly recruiting clinical trials planned Tc-99m RPs



www.clinicaltrail.gov

Trends of research articles on "Tc-99m" keyword according to PubMed



Trends of clinical trial articles on "Tc-99m" keyword according to PubMed



IAEA Coordinated Research Projects on Mo-99 and Tc-99m

- *"Immunoscintigraphy using technetium-99m labelled anti embryonic antigen monoclonal antibodies for the detection of colonic cancer"* E13007, **1989**
- *"Evaluation of use of bulk reagents for production of technetium-99m radiopharmaceuticals and kits, F22016 during 1991-1995*
- *"Production of technetium-99m generators based on low temperature sublimation and gel elution "F22018", 1991-1995*
- *"99mTc-Labelled Peptides for Imaging Peripheral Receptors" F22023, 1995*
- Clinical IAEA CRP project with the title of "Evaluation of Tc-99m based radiopharmaceuticals in the diagnosis and management of breast cancer patients, 1997-2000
- "Development of agents for imaging central neural systems (CNS) receptors based on Technetium-99m, during 1995–2001
- "Developing Techniques for Small Scale Indigenous Molybdenum 99 Production Using Low Enriched Uranium (LEU) Fission or Neutron Activation" T12018
- Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99m" F22062;
- "Development of ^{99m}Tc Radiopharmaceuticals for Sentinel Node Detection and Cancer Diagnosis" F22045, 2007-2010
- 2000 with the title of "Development of kits for Tc-99m radiopharmaceuticals for infection imaging, F22032
- "Development of 99mTc Based Small Bio Molecules Using Novel 99mTc Cores" F22038 performed during 2003-2006
- Development and Quality Control of Hospital Prepared Radiopharmaceuticals for Infection Imaging for Use in HIV/AIDS Positive Patients" 2004 2010
- IAEA CRP (2017-2021) was completed with the title of "New Ways of Producing Tc-99m and Tc-99m Generators (Beyond Fission and Cyclotron Methods)" F22068

TABLE 1. IAEA PUBLICATIONS RELATED TO Tc-99m RADIOPHARMACEUTICALS



*TRS = <u>Technical Reports Series</u>; <u>RRR = Radioisotopes and Radiopharmaceuticals Reports</u>; <u>NES = Nuclear Energy Series</u>; Tec-Doc = Technical Document.

Title	Date of publication	CRP code	Reference	Format*
DevelopmentofKitsfor99mTcRadiopharmaceuticals for Infection Imaging	2004	F22032	[18]	TECDOC
99mTc labelled peptides for imaging of peripheral receptors	2001	F22023	[19]	TECDOC
Labelling of Small Biomolecules Using Novel Technetium-99m Cores	2007	F22038	[20]	TRS
"Technetium-99mRadiopharmaceuticals:Manufacture of Kits"	2008	n.a.	[21]	RRS
Technetium-99m Radiopharmaceuticals: Status and Trends"	2010	n.a.	[22]	<u>RRS</u>
Non-HEUProductionTechnologiesforMolybdenum-99 and Technetium-99m	2013	n.a.	[23]	NES
Cyclotron Based Production of Technetium-99m	2017	F22062	[24]	<u>RRR</u>
Feasibility of producing molybdenum-99 on a small-scale using fission of low enriched uranium or neutron activation of natural molybdenum (iaea.org)	2015	T12018	[25]	TRS
Development of 99mTc Radiopharmaceuticals for Sentinel Node Detection and Cancer Diagnosis	2015	F22045	[26]	RRS

A new IAEA TECDOC, PROGRESS ON Tc-99m RADIOPHARMACEUTICALS (under preparation) ¹⁶

Recent activities



Technical Meeting on "Recent advances on Tc-99m Kits and Radiopharmaceuticals for molecular imaging" (May 2021)

 Consultants' Meeting; IAEA Future Activities on Tc-99m Kits and Radiopharmaceuticals (Virtual), 25-29 April 2022

A New CRP is under planning for 2024 onwards:

- New molecules
- New labeling methods
- New targets

IAEA TECDOC

PROGRESS ON Tc-99m RADIOPHARMACEUTICALS





[^{99m}Tc]Tc-HYNICTOC.

*HYNIC-E-[c(RGDfK)]*₂ *chemical structure*



^{99m}Tc-EC20 (^{99m}Tc-Etarfolatide)

Collaboration WHO - IAEA

- Update on the monograph for radiopharmaceuticals
- Review of general monograph for radiopharmaceuticals
- Guidelines for GMP for radiopharmaceutical production:
 - Good radiopharmaceutical practices: update guideline on Annex 3 (2003): meeting with experts in November 2018
 - The guidelines were open for discussion in 2019
 - A meeting took place in 2019 for pubic consultation
 - Another meeting in 2019 to evaluate comments
 - Guidelines were published in 2020





WHO Expert Committee on Specifications for Pharmaceutical Preparations



Update of TECDOC 1051



- TECDOC 1051, Management of Radioactive Waste from ⁹⁹Mo Production, was published in 1998 based on meetings held in 1995-96
- The IAEA Reactor Research Section Plans an Update to the TECDOC to include:
 - Additional Waste Processing Techniques and Technology
 - Approaches for Small Quantity Producers
 - Uranium Recycling
 - Managing / minimizing / recovery of gaseous wastes
 - Other topics to be identified

Plan for Update of TECDOC 1051



- Research Reactor Section to seek approval of publication in 4Q22
- Consultancy Meeting planned in January 2023 to define contents and identify contributors
- Technical Meeting planed for 3Q23 for broad input on content and format
- Publication expected in 2024

Contact John Dewes (J.Dewes@iaea.org) for more information or to participate!

RPRT Activities: Training Opportunities

- World Nuclear University (WNU) School on Radiation Technologies: a two-week programme for young professionals → Fall 2023
- WTTC School hands-on workshop at TRIUMF: half day lectures and half-day lab practice in TRIUMF labs
- IAEA/KOICA/KAERI annual trainings





RPRT Activities: Conferences

- ISTR-23, 2nd International Symposium on Trends in Radiopharmaceuticals April 17-21, 2023
- Special session or side event on Mo-99
- Abstract submission deadline: October 31, 2022



THANK YOU FOR YOUR ATTENTION!

REAL PROPERTY AND ADDRESS OF

TE CONTRACTOR A CONT TE CONTRACTOR A CONT TE CONTRACTOR A CON TE CONTRACTOR A CONT TE CONTRACTOR A CONT W LEADERS THE WAY AND

TABLET DE LE RESERVE DE LE RESERVE