IAEA support for accelerator-based radioisotopes and radiopharmaceuticals production

Amir Jalilian
Radioisotope and Radiopharmaceutical Chemist

Radioisotope Products and Radiation Technology Section, NAPC, IAEA

IAEA
International Atomic Energy Agency

Contents

1 Service to MS regarding cyclotrons
2 Radioisotopes from cyclotrons
3 Radiopharmaceuticals
4 New Radiopharmaceuticals
5 IAEA activities on radiopharmaceuticals

IAEA Projects: on radioisotopes and radiopharmaceuticals

Coordinated Research Projects (R&D) related to radiopharmaceuticals, active 3, closed 35, 2 new, 5 completed, 2 planned

Technical Cooperation Projects (implementation), related to radiopharmaceuticals 86

Regular program activities

Networks & coalitions

Publications

Participation in complimentary international activities

Collaborating Centers

Meetings / Conferences

General Conference side-events and Scientific Forum

Missions

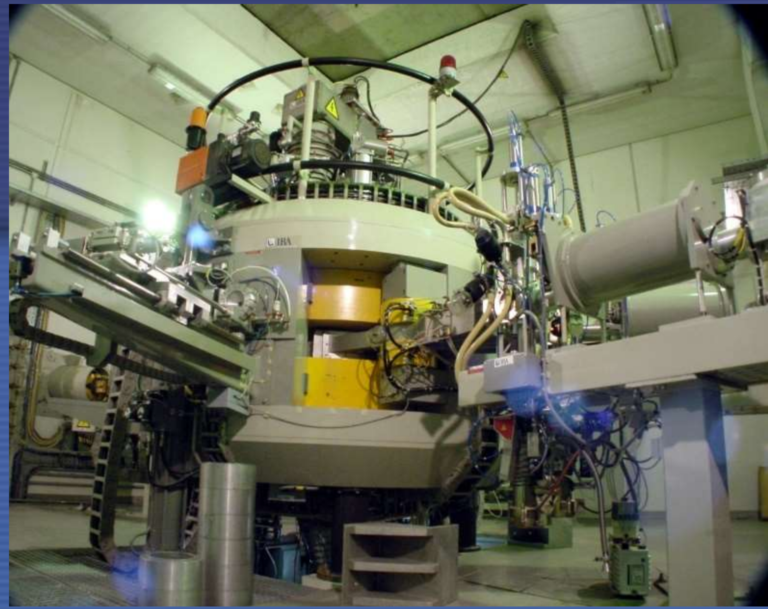
IAEA

Radioisotopes for radiopharmaceuticals - Diagnostic

Positron emission Tomography (PET) usually prepared by a Cyclotron

Isotope	^{11}C	^{13}N	^{15}O	^{18}F
Half-life	20 min	10 min	2 min	110 min
Production	$^{14}N(p,\alpha)^{11}C$	$^{16}O(p,\alpha)^{13}N$	$^{15}N(p,n)^{15}O$	$^{18}O(p,n)^{18}F$ enriched

Isotope	^{64}Cu	^{68}Ga	^{82}Rb	^{89}Zr
Half-life	12.7 h	68 min	1.25 min	78.4 h
Production	$^{64}Ni(p,n)^{64}Cu$ enriched	Generator (^{68}Ge-^{68}Ga) $^{nat}Ga(p,xn)^{68}Ge$ High energy Cyclotron	Generator (^{82}Sr-^{82}Rb) $^{85}Rb(p,4n)^{82}Sr$ High energy Cyclotron	$^{89}Y(p,n)^{89}Zr$

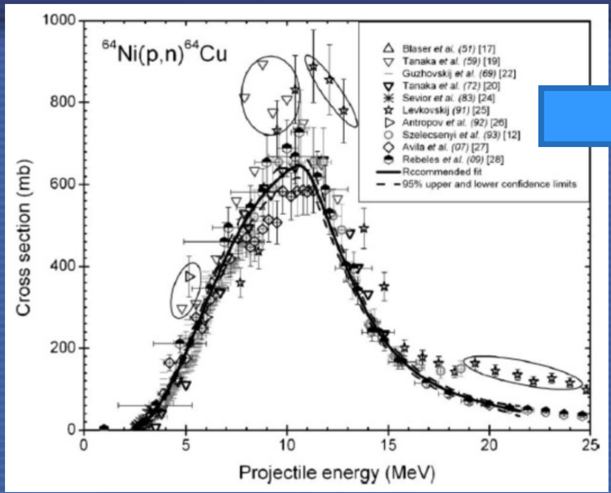


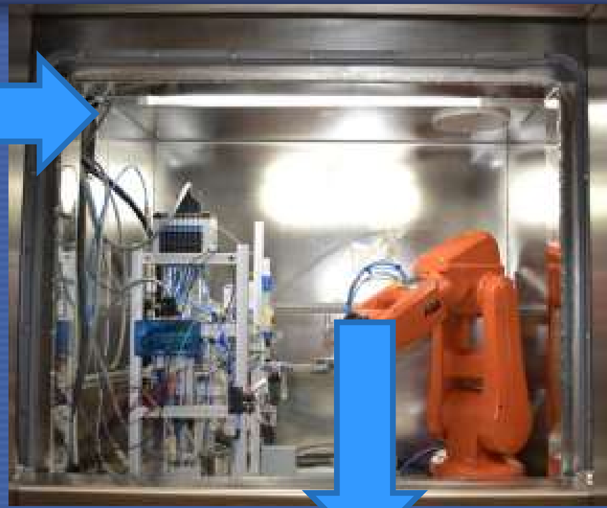
Synthesis module

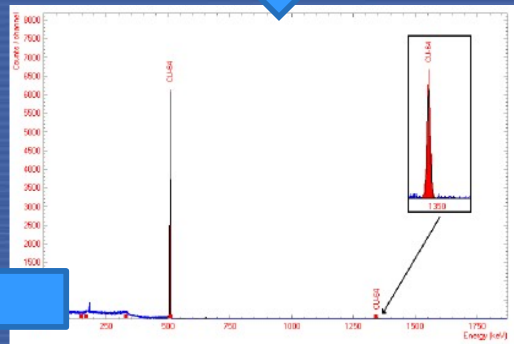
Layout

IAEA

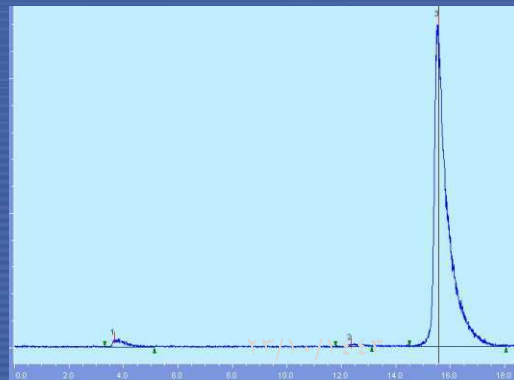
A summary of technical steps for radioisotope production in cyclotron using a solid target







Radioisotope Solution for radiopharmaceuticals development

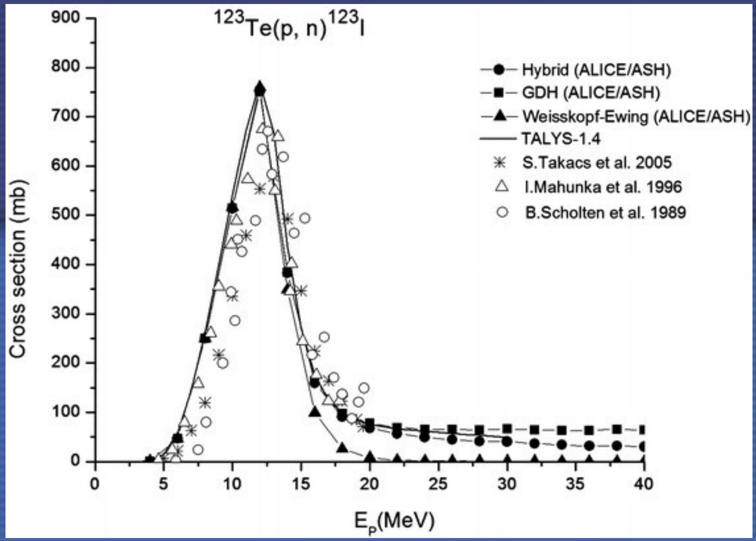


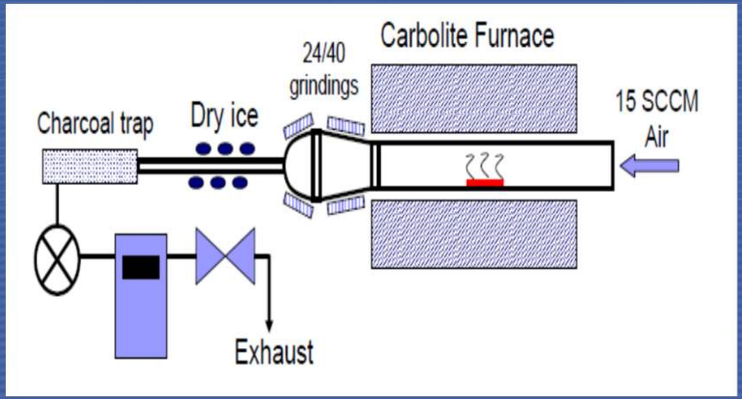
Recovery process

JALILIAN A, IAEA

gas/solid target; I-123

- 12.7 half life
- commonly production method
- One photon decay
- Low dose needed in human
- Used as
  - Radiopharmaceutical; NaI
  - precursor

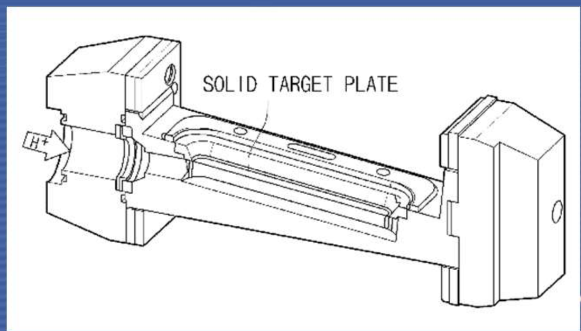




Metal radionuclides produced in cyclotron using solid targets

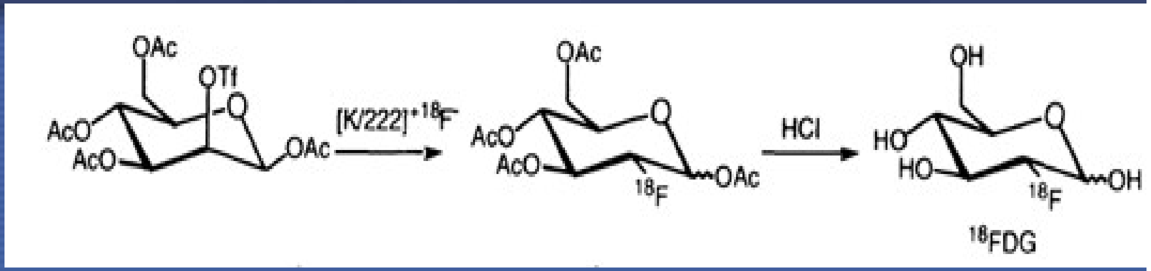
- Tl-201 Tl-203
- Ga-67 Zn-68
- Cu-64 Ni-64
- Zr-89 Y-nat
- Co-57 Ni-58
- Pd-103 Rh-nat
- Cu-61 Zn-nat

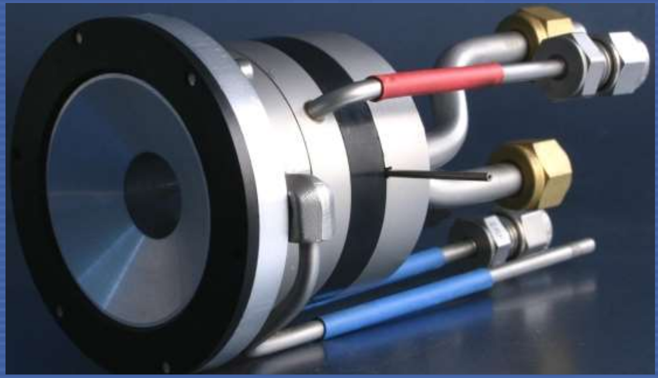
I-124 Te-124
Y-86 Sr-nat
Tc-99m Mo-100
Tc-94 Mo-94
Ga-68 Zn-68
…………

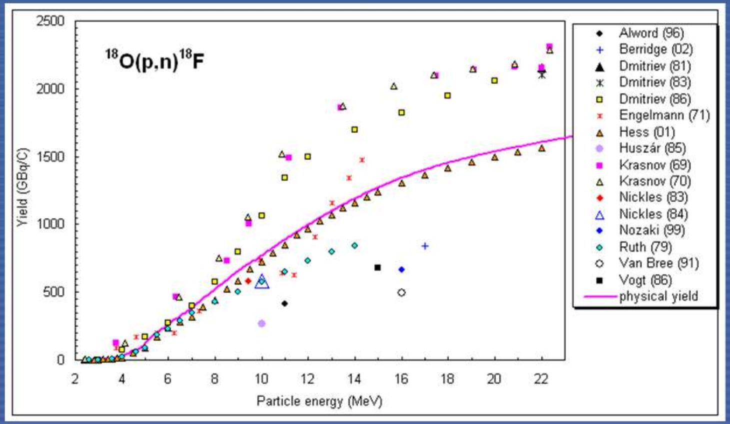


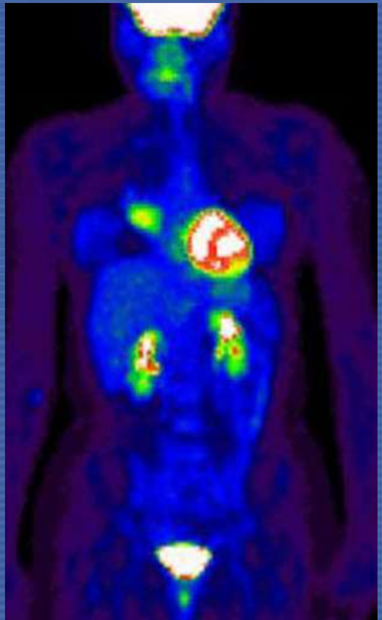
Non metal; F-18 radiopharmaceuticals

- F-18 110 min half life
- The mostly used PET radionuclide
- Suitable positron energy
- Stable C-F bond
- C-F/C-H size resemblance
- C-F bond is usually an enzyme inhibitor
- A hydrophilic bond

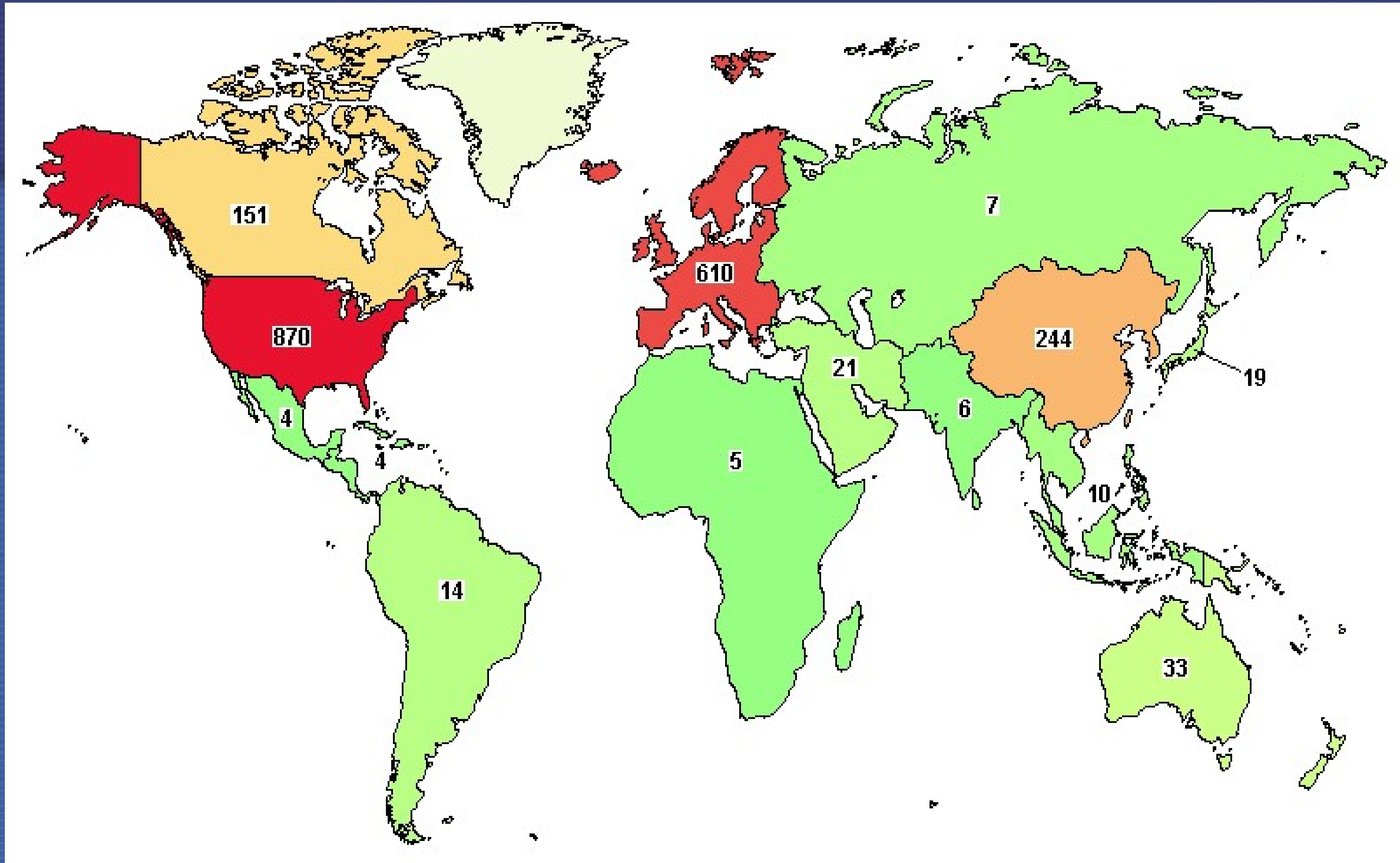








IAEA



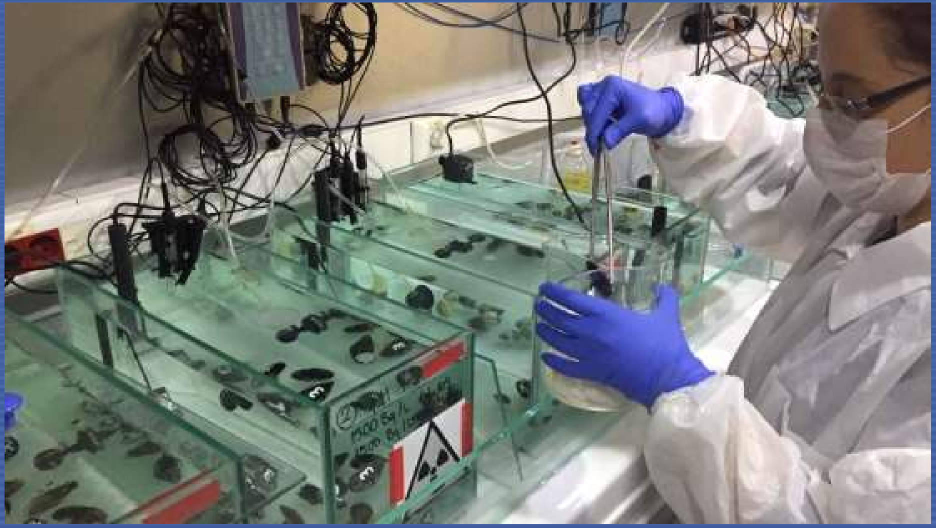
- worldwide distribution of clinical trials on ^{18}F-radiopharmaceuticals extracted from Clinicaltrial.gov,

IAEA

Cyclotron related Coordinated Research Projects (CRPs)

Finalised CRPs:

- Production and utilization of Emerging Positron Emitters for Medical Applications with an Emphasis on Cu-64 and I-124 (2010-2014)
- Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99m (2011-2015)
- Development and preclinical evaluations of therapeutic radiopharmaceuticals based on Lu-177 and Y-90 labelled monoclonal antibodies and peptides (2011-2015)

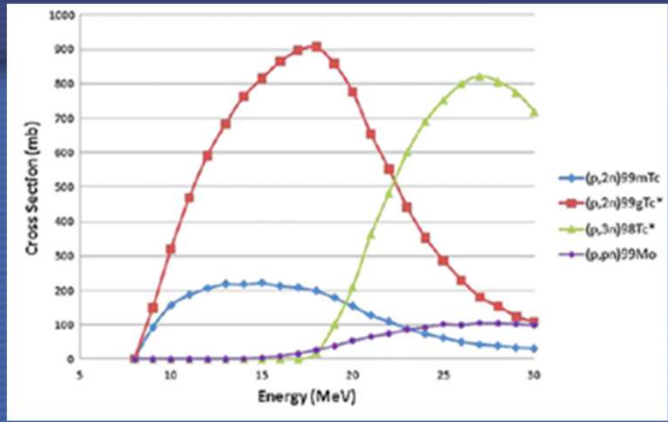


IAEA

Accelerator-based Alternatives to Non-HEU production of Mo-99/Tc-99m

Finalised CRPs:

- 2011-2015
- 18 participants from 16 Member States
- Production of Tc-99m in cyclotron
- Technology to produce several (>30) Ci Tc-99m per run in medical cyclotrons of energies below 24 MeV proven;



Irradiation Parameters

COUNCIL OF EUROPE / CONSEIL DE L'EUROPE

European Directorate for the Quality of Medicines & HealthCare / Direction européenne de la qualité du médicament & soins de santé

EUROPEAN PHARMACOPOEIA COMMISSION

EP/fp
Working document, with no legally binding status, intended exclusively for the addressees and their associates, under the responsibility of the addressees (listed opposite). Level 4

PA/PH/Exp. 14/T (14) 12 COM

BILINGUE

Strasbourg, October 2016

GROUP 14

(RADIOACTIVE COMPOUNDS / COMPOSES RADIOACTIFS)

Sodium pertechnetate (99mTc) injection (cyclotron-produced)

Sodium pertechnetate (99mTc) injection (cyclotron-produced)

Monograph N°: 2891

Cette monographie / Ce chapitre général sera présenté(e) à la Commission pour adoption du contenu technique et rédactionnel. Tout commentaire sur le texte doit être soumis par écrit en utilisant l'outil Document Review Tool (DRT) via l'extranet.
This monograph / general chapter will be submitted to the Commission for adoption of technical and editorial content. If comments are to be made on the text, they should be submitted in writing using the Document Review Tool (DRT) via the extranet.

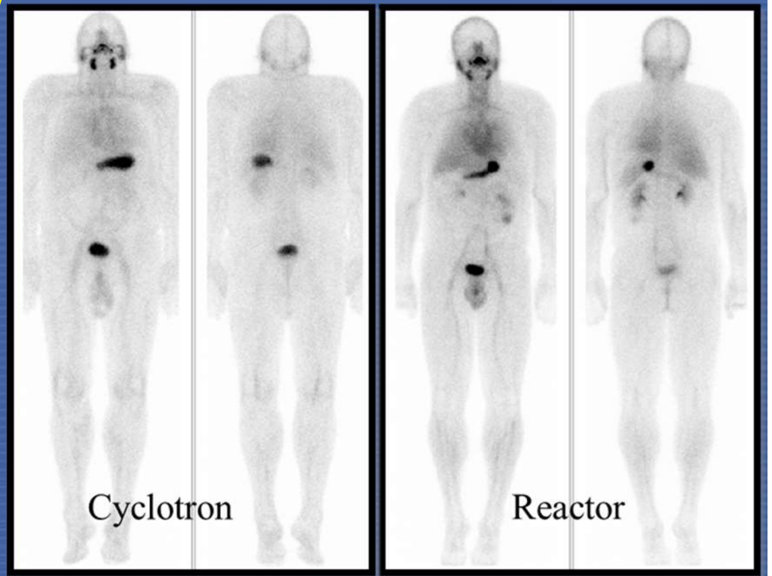
Distribution

For action:
COM European Pharmacopoeia Commission

For information:
14 Radioactive compounds
ANP National Pharmacopoeia Authorities
COM 156 COM 156th
CRP Production & compounding of radiopharmaceutical preparations
PRES Praesidium
PRP Precursors for radiopharmaceutical preparations

This document will not be redistributed in sessions. Ce document ne sera pas redistribué lors des sessions.

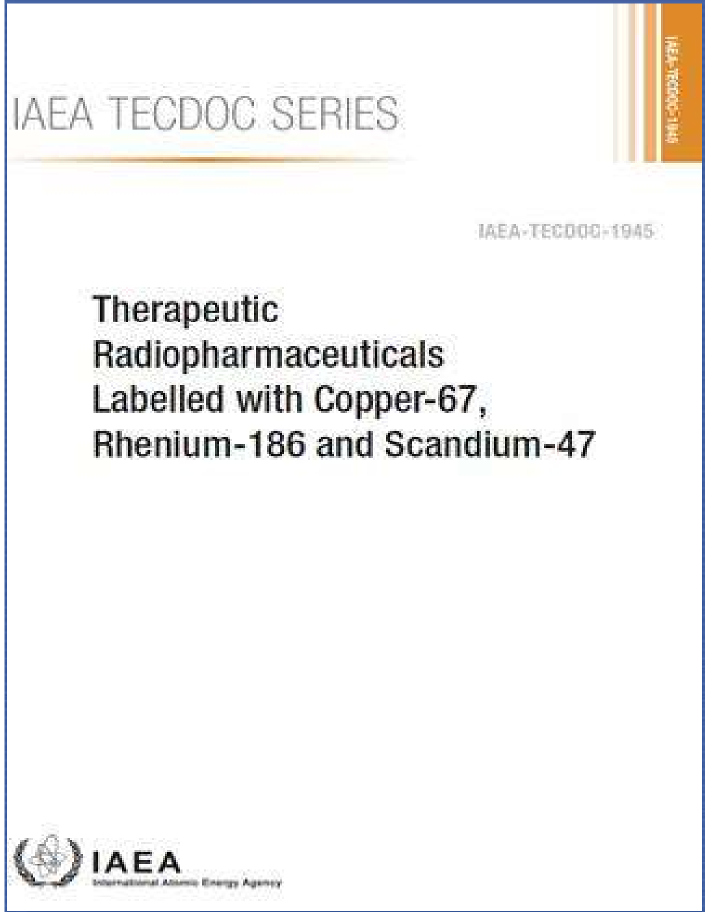
EDQM address: 7 allée Kastner, CS 30026, FR-67081 Strasbourg (France)



Comparison of cyclotron- and reactor-based Tc-99m pertechnetate for the Univ. of Alberta Clinical Trial (cancer thyroid patients imaged post-thyroidectomy)

Finalised CRP

F22053: Therapeutic Radiopharmaceuticals Labelled with New Emerging Radionuclides (^{67}Cu, ^{186}Re, ^{47}Sc) – (2016)

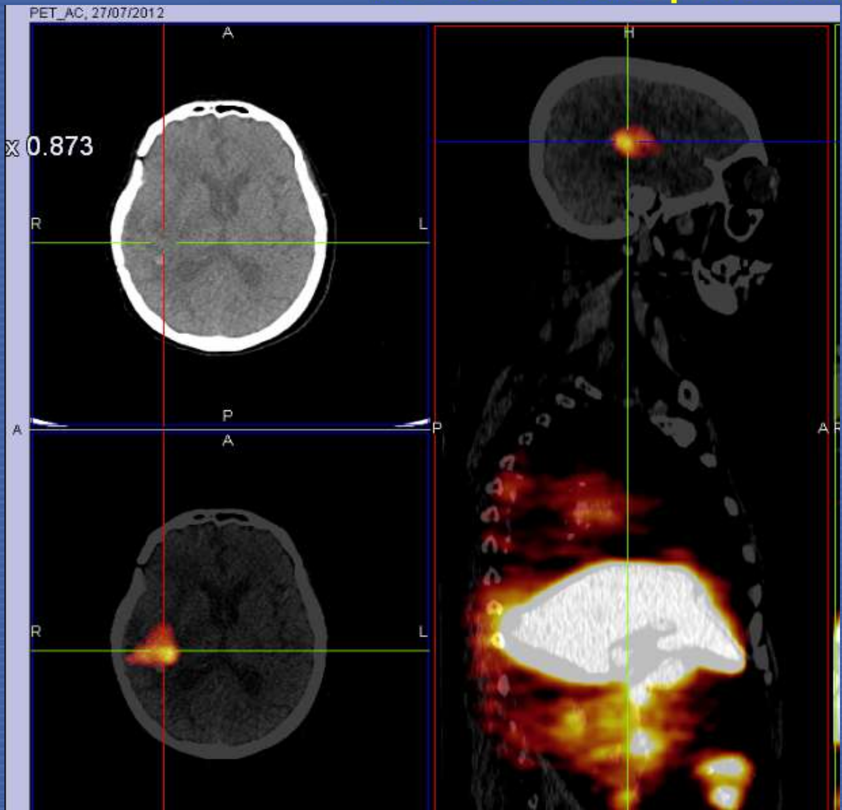


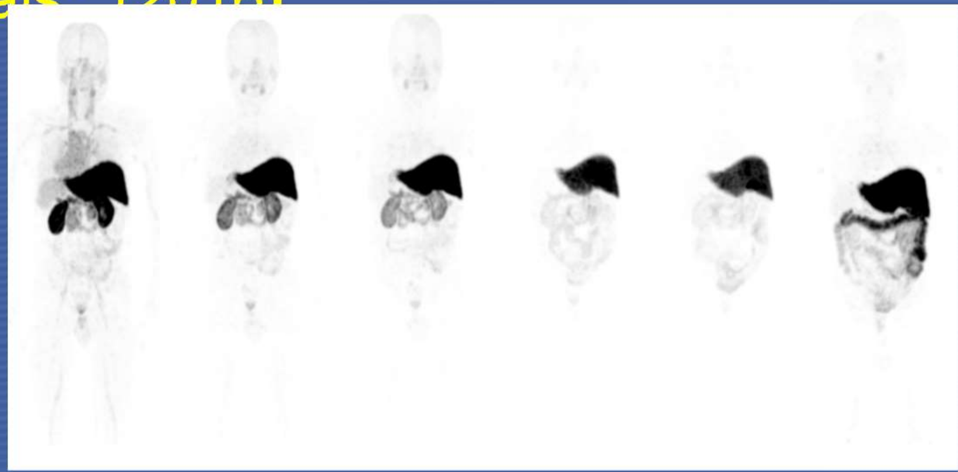
RN	Half-life	Imaging emissions	Therapy emissions	Production methods	Decay product
^{47}Sc	3.3492 d	γ 159.38 keV (68.3 % 4)	β⁻ (100 %) $E_{\beta max}$ = 440.9 keV (68.4 % 6) $E_{\beta max}$ = 600.3 keV (31.6 % 6) $E_{\beta mean}$ = 162.0 keV	^{48}Ti(p,2p) ^{49}Ti(p,^{3}He) ^{50}Ti(p,α) ^{47}Ti(n,p)	^{47}Ti (stable)
^{67}Cu	61.83 h	γ 93.31 keV (16.1 % 2) γ 184.58 keV (48.7 % 3)	β⁻ (100 %) $E_{\beta max}$ = 377.1 keV (57 % 6) $E_{\beta max}$ = 468.4 keV (22.0 % 22) $E_{\beta max}$ = 561.7 keV (20.0 % 20) $E_{\beta mean}$ = 141 keV	^{68}Zn(p,2p) ^{70}Zn(p,α) ^{67}Zn(n,p) ^{68}Zn(γ,p) ^{68}Zn(n,x)	^{67}Zn (stable)
^{186}Re	3.7183 d	γ 137.16 keV (9.47 % 3)	β⁻ (92.53 % 10) $E_{\beta max}$ = 932.3 keV (21.54 % 14) $E_{\beta max}$ = 1 069.5 keV (70.99 % 14) $E_{\beta mean}$ = 346.7 keV	^{186}W(p,n) ^{186}W(d,2n) ^{192}Os(p,α3n)	^{186}Os (stable) ^{186}W (stable)

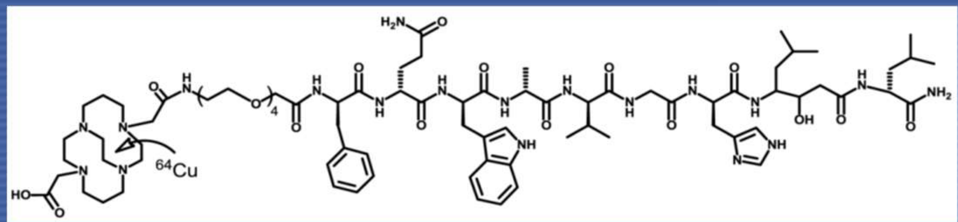
Radioisotope production technologies

Finalised CRP

"Cu-64 theranostic radiopharmaceuticals" (2016)







Copper-64 Radiopharmaceuticals; Production, Quality Control and Clinical Applications

IAEA Technical Report Series

December 2019

PAGE BREAK

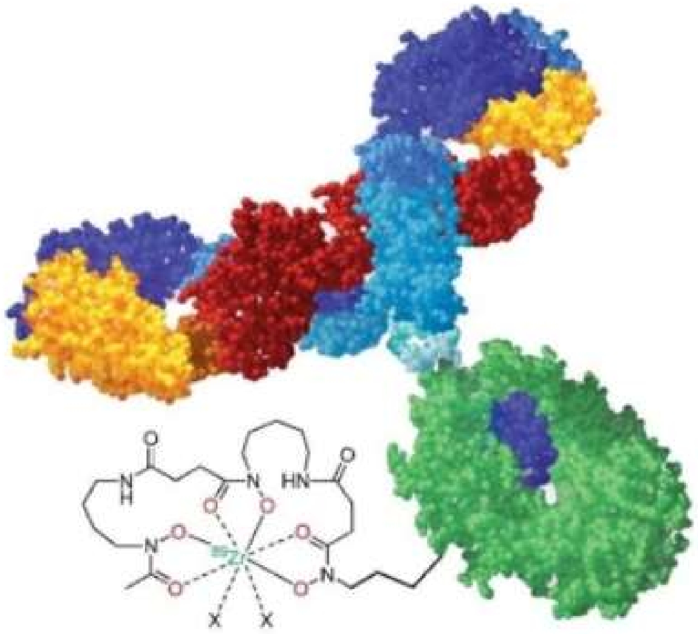
IAEA

New CRP: Zr-89 Production and Zr-89 Radiopharmaceuticals (F22071)

New Coordinated Research Project

Aruna Korde, IAEA Department of Nuclear Sciences and Applications

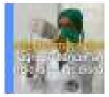
DEC
19
2018



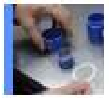
Schematic figure overview of a Zr-89 labelled monoclonal antibody. (Image: IAEA)

Related Stories

New Technique to Fight Prostate Cancer: IAEA organizes first-of-a-kind training for Radiopharmacists



How Radiopharmaceuticals Help Diagnose Cancer and Cardiovascular Disease



African Radiopharmacists Put New Skills to Use

Related Resources

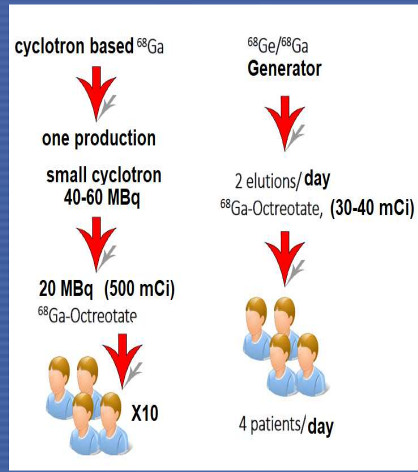
- Radiopharmaceuticals for Cost Effective Management of Cancer
- Coordinated Research Activities
- Radioisotope Products and Radiation Technology Section

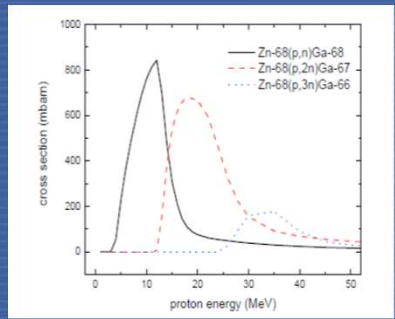
CRP at a Glance

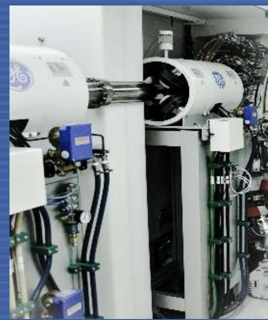
This Coordinated Research Project (CRP) will identify important technical issues related to the production of Zirconium-89 (Zr-89) and the development

Production routes of Ga-68

- ^{68}Ge-^{68}Ga Generator
- Convenient method for hospital radiopharmacy
  - Deliver limited activities of ^{68}Ga per elution
  - Limited lifetime, 6-9 months/~500 elutions
  - Constraining waiting time between two elutions
  - Long-lived ^{68}Ge impurity (Possible breakthrough)
  - Expensive
- Direct production using cyclotron
  - ^{68}Zn (p,n) ^{68}Ga
  - Solid target : plate, foil
  - Liquid target : $^{68}ZnCl_2$, $^{68}Zn(NO_3)_2$ – dil HNO_3
  - Challenges : Targetry, separation chemistry, Recycling
- FDA Approved:
  - Cyclotron-Produced Ga-68 DOTATOC on October 20, 2020
  - Ga-68 PSMA-11 on December 1, 2020







Liquid Zn target for direct production of ^{68}Ga

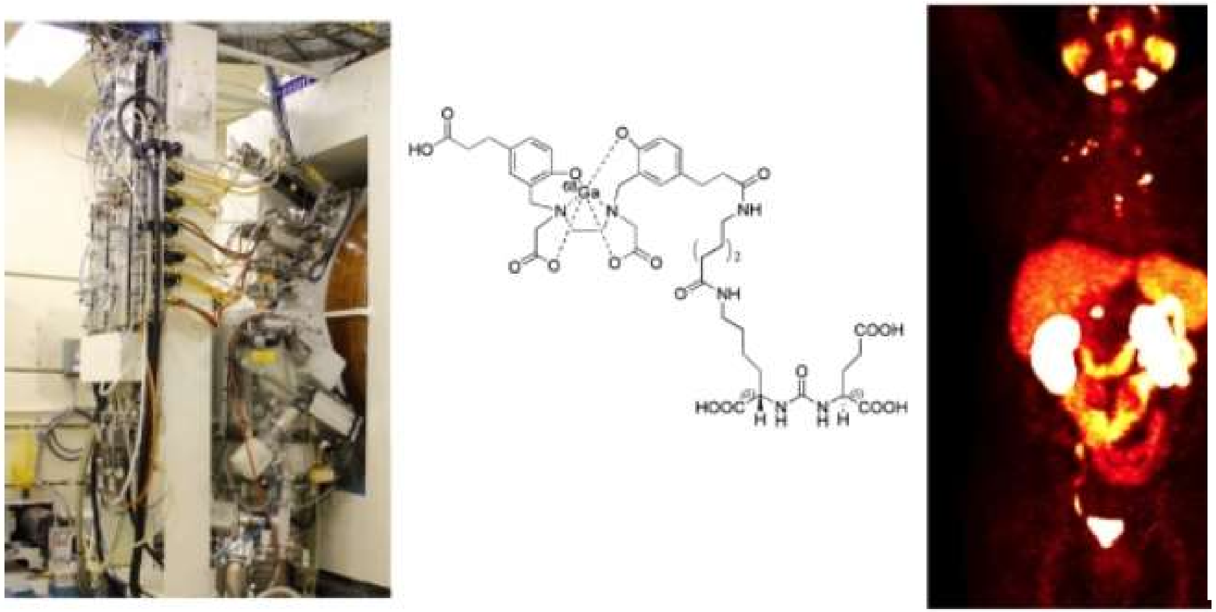
IAEA

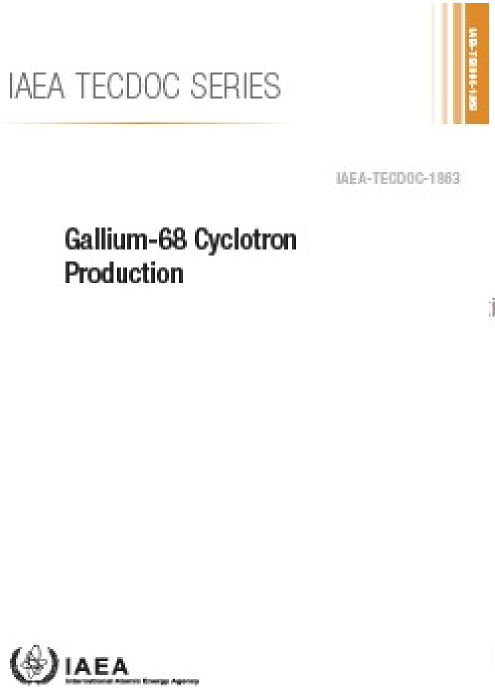
New CRP: Production of Cyclotron-Based Gallium-68 Radioisotope and Related Radiopharmaceuticals (F22073)

New Coordinated Research Project

Amir Jalilian, IAEA Department of Nuclear Sciences and Applications

APR
8
2020





The production of Gallium 68 and other radioisotopes in cyclotrons is a critical tool in nuclear medicine and diagnostic imaging, and is often used in PET images in cancer therapy. (Image: Lowe, Pandey and DeGrado/Department of Radiology Mayo Clinic Rochester)

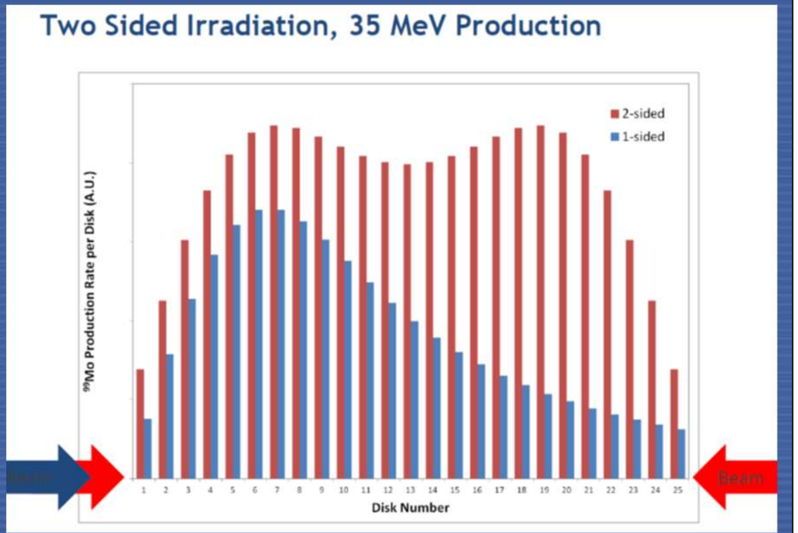
Production

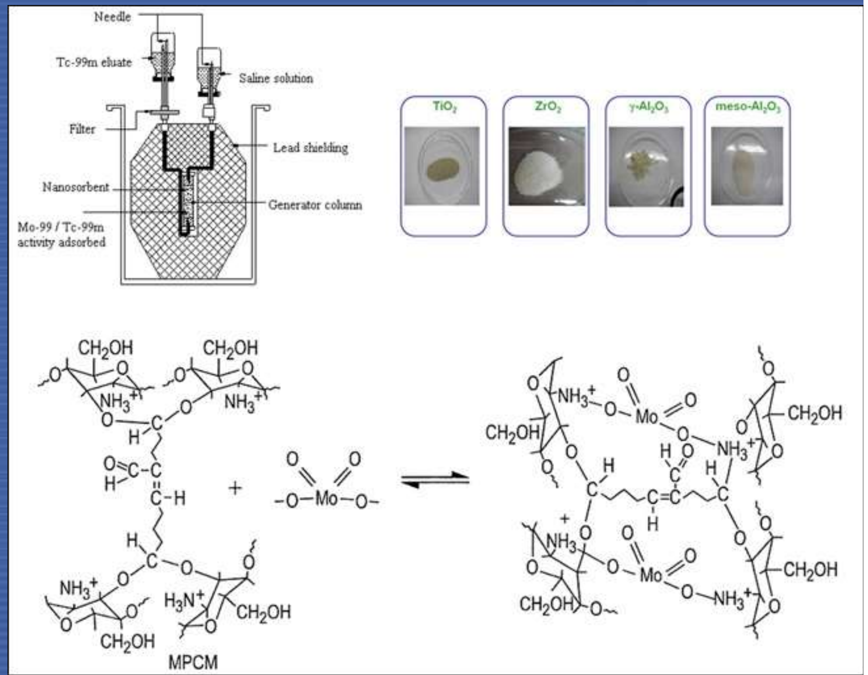
Development of Ga-68 based PET-Radiopharmaceuticals for Management of Cancer and other Chronic Diseases

Theranostic radiopharmaceuticals are molecules that can safely carry

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)





IAEA

- https://www.iaea.org/newscenter/news/new-crp-new-ways-of-producing-tc-99m-and-tc-99m-generators

publications

Links to the recent IAEA publications related to cyclotrons:

-
- 1- https://www.iaea.org/publications/13484/gallium-68-cyclotron-production
- 2- https://www.iaea.org/publications/10791/cyclotron-produced-radionuclides-emerging-positron-emitters-for-medical-applications-64cu-and-124i
- 3- https://www.iaea.org/publications/13422/quality-control-in-the-production-of-radiopharmaceuticals
- 4- https://www.iaea.org/publications/10829/good-practice-for-introducing-radiopharmaceuticals-for-clinical-use
- 5- https://www.iaea.org/publications/8783/cyclotron-produced-radionuclides-operation-and-maintenance-of-gas-and-liquid-targets
- 6- https://www.iaea.org/publications/8529/cyclotron-produced-radionuclides-guidance-on-facility-design-and-production-of-fluorodeoxyglucose-fdg
- 7- https://www.iaea.org/publications/7849/cyclotron-produced-radionuclides-principles-and-practice
- 8- https://www.iaea.org/publications/8046/cyclotron-produced-radionuclides-guidelines-for-setting-up-a-facility
- 9- https://www.iaea.org/publications/10990/cyclotron-based-production-of-technetium-99m

IAEA

IAEA | Accelerator Knowledge Portal

Cyclotron Database | AccApp'20 | Useful Resources ▾ | Case Studies | IBA Beamtime | Workspaces ▾

Cyclotrons used for Radionuclide Production

Cyclotron community

Cyclotron Events

Cyclotron Resources

This database was created as a follow-up action to the older hard-copy "Directory of Cyclotrons" developed i
1983 and updated in 1998 and 2006 by the "Radioisotope Products and Radiation Technology Section, Divis
of Physical and Chemical Sciences, IAEA" and international experts. The database was established and is
currently under revision in response to the request of Member States and world-wide interest in the installatic
and application of cyclotrons for medical radioisotope production. In order to add or edit information about yo
facility you can:

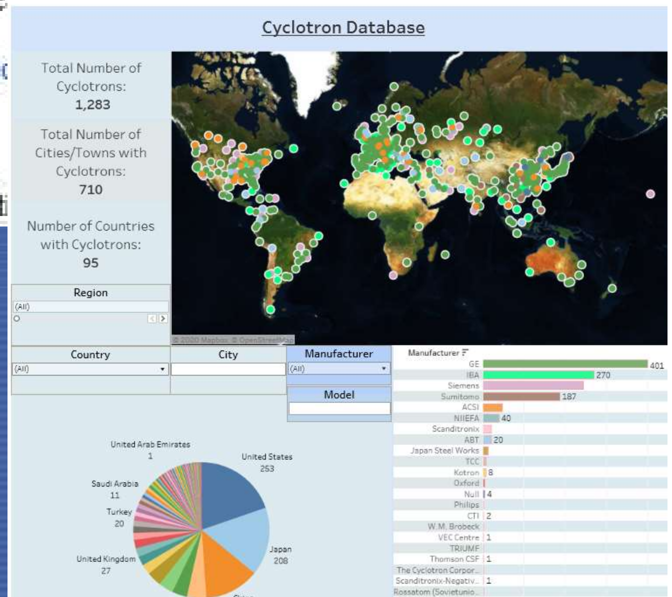
In order to add or edit information about your facility you c

- download and fill the dedicated form and send it via cycl

or

- fill a dedicated online form. You will receive a receipt noti

Cyclotron Database



https://nucleus.iaea.org/sites/accelerators/Pages/Cyclotron.aspx

IAEA

IAEA
International Atomic Energy Agency

Press centre Employment Contact

TOPICS SERVICES RESOURCES NEWS & EVENTS ABOUT US

Search

Network of Women in Radiopharmaceutical Sciences

The IAEA Network of Women in Radiopharmaceutical Sciences is a professional network aiming at supporting, promoting and empowering women in radiopharmaceutical sciences.

Established in 2019 as an interest group under the umbrella of the Women in Nuclear Global, the network aims at increasing the representation of female scientists and managers, especially in higher professional roles and decision-making positions, in the multidisciplinary field of radiopharmaceutical sciences.

To join the group, please fill out the membership form and send it at WRSNETWORK.Contact-Point@iaea.org.

Coordinator: Aruna Korde, Radiopharmaceutical Scientist, IAEA

Related resources

- Radioisotope Products and Radiation Technology Section
- Department of Nuclear Sciences and Applications
- Membership form
- Coordinator
- Advisory Committee

IAEA

Network of Women in Radiopharmaceutical Sciences | IAEA

World Health Organization

DRAFT WORKING DOCUMENT FOR COMMENTS:

International Atomic Energy Agency (IAEA)/ World Health Organization (WHO) guideline on good manufacturing practices for investigational radiopharmaceutical products

Please send your comments to **Dr Sabine Kopp**, Team Lead, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (kopps@who.int), with a copy to Ms Claire Vogel (vogelc@who.int) before **30 April 2021**. Please use the "Table of Comments" for this purpose.

Our working documents are sent out electronically and are also placed on the WHO Medicines website (https://www.who.int/teams/health-product-and-policy-standards/standards-and-specifications/pharmaceuticals/current-projects) for comments under the "*Working documents in public consultation*" link. If you wish to receive all our draft guidelines, please send your email address to jonessi@who.int and your name will be added to our electronic mailing list.

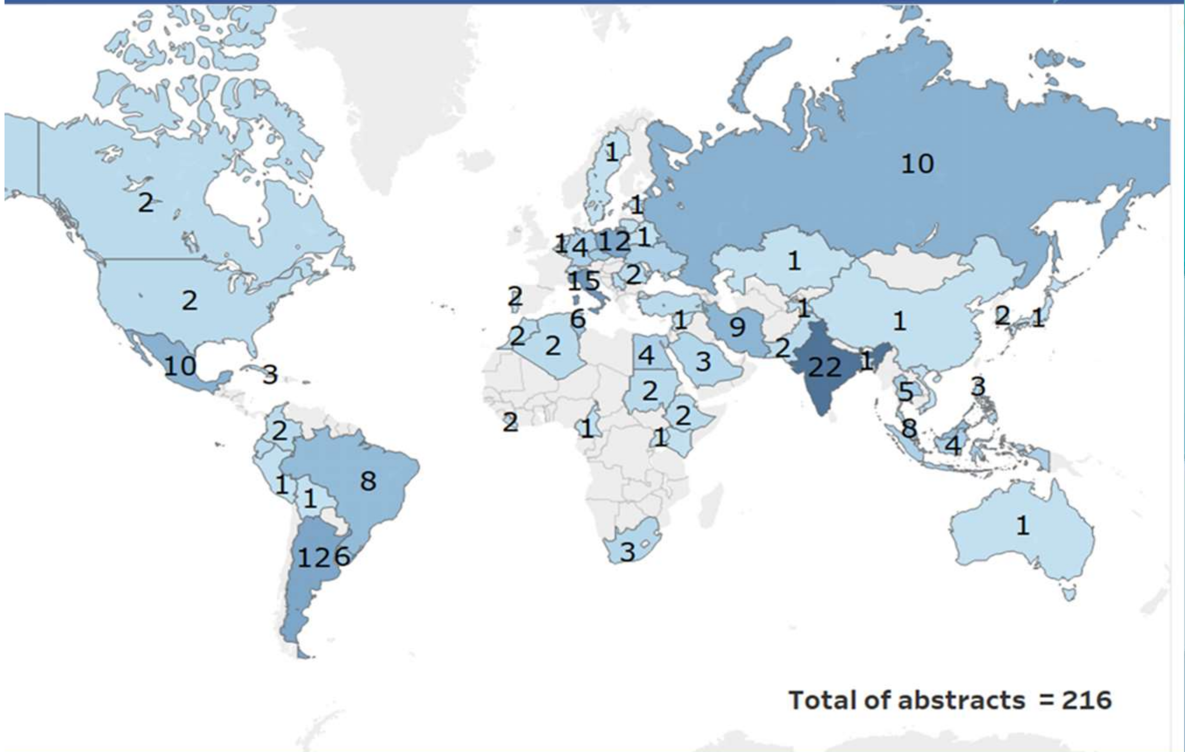
IAEA

qas21_878_iaea_who_gmp_for_radiopharmaceutical_products.pdf

❖The *Conference on "Trends in Radiopharmaceuticals"– (ISTR 2019*) was held in October 2019 at the IAEA HQ.

216 Abstracts

58 Member States



Get Ready! For ISTR 2023 **in April 2023 at the IAEA HQ!!!!!!!!!**

IAEA

Amir Jalilian;

a.jalilian@iaea.org

IAEA

International Atomic Energy Agency