Production of Radioisotopes in Pakistan Research Reactor: past, present and future

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ABSTRACT

Production of radioisotopes started since Pakistan Research Reactor-1 went critical in December 1965. Pakistan Institute of Nuclear Science and Technology (PINSTECH) Islamabad is operating two research reactors (PARR-1 and 2) to provide services to the users for the production of radioisotopes and for neutron irradiation. Beam work usually includes using neutron beams outside of the PARR-1 for a variety of analytical purposes. Facility for neutron radiography, prompt gamma neutron activation analysis, neutron scattering for material analysis have been functioning. Improvements in the instrumentation and control system of PARR-1 are continuously being made to enhance the safety and availability of the system. Production of radioisotopes ranges from micro- curie to curie level. Solid, liquid and gas targets have been irradiated for generation of alpha, beta and gamma emitting radionuclides. A large number of no-carrier-added radionuclides have been produced for applications in medicine, agriculture, hydrology and industry. Sealed radioactive sources were also manufactures to distribute in colleges and universities for basic physics experiments. The most widely used radiotherapeutic radionuclide Iodine-131 has been regularly produced for the last three decades using PARR-1. The n, gamma and fission molybdenum-99, parent of technetium-99m used in 80% of diagnostic nuclear medicine procedures is also produced. Production of sealed radioactive sources of Cobalt-60, Cesium-137 and Irridium-192 etc. has been planned.

Main Features of Pakistan Research Reactor 1 and 2

General Data	PARR-1	PARR-2
Construction date:	1-5-1963	1-1-1988
Criticality date:	21-12-1965	2-11-1989
Initial cost:	6.6 M US$	2 M US$
Per day cost:	15000 US$	2000 US$
Total staff:	30	10
Operator:	13	7

Main Features of Pakistan Research Reactor 1 and 2

Technical Data	PARR-1	PARR-2
Reactor type	Pool	Tank-in-poon
Thermal power, steady	**kW:** 10,000.000	**kW:** 30.000
Max flux SS, thermal, n/cm^2-s	1.5 x10^{14}	1.0 x10^{12}
Max flux SS, fast, n/cm^2-s	6.0 x10^{13}	3.2 x10^{11}
Moderator and coolant	Light water	Light water
Reflector	Graphite, water	Beryllium, water
Control rod material	Ag, In, Cd	Cd
Criticality with LEU	Oct 1991	**-**
Power increase	9 MW in May 1992	**-**
Power increase	10 MW in Feb 1998	**-**

Main Features of Pakistan Research Reactor 1 and 2

Fuel Data	PARR-1	PARR-2
Min critical mass	**kg U-235:** 4.42	**kg U-235:** 0.98
Normal core loading	**kg U-235:** 6.59	**kg U-235:** 1.00
Fuel material	U_3Si_2-Al	U-Al alloy (UAl_4-Al)
Enrichment min%	19.99	90.20
Enrichment max%	19.99	90.20
Origin of fissile material	USA, China	China

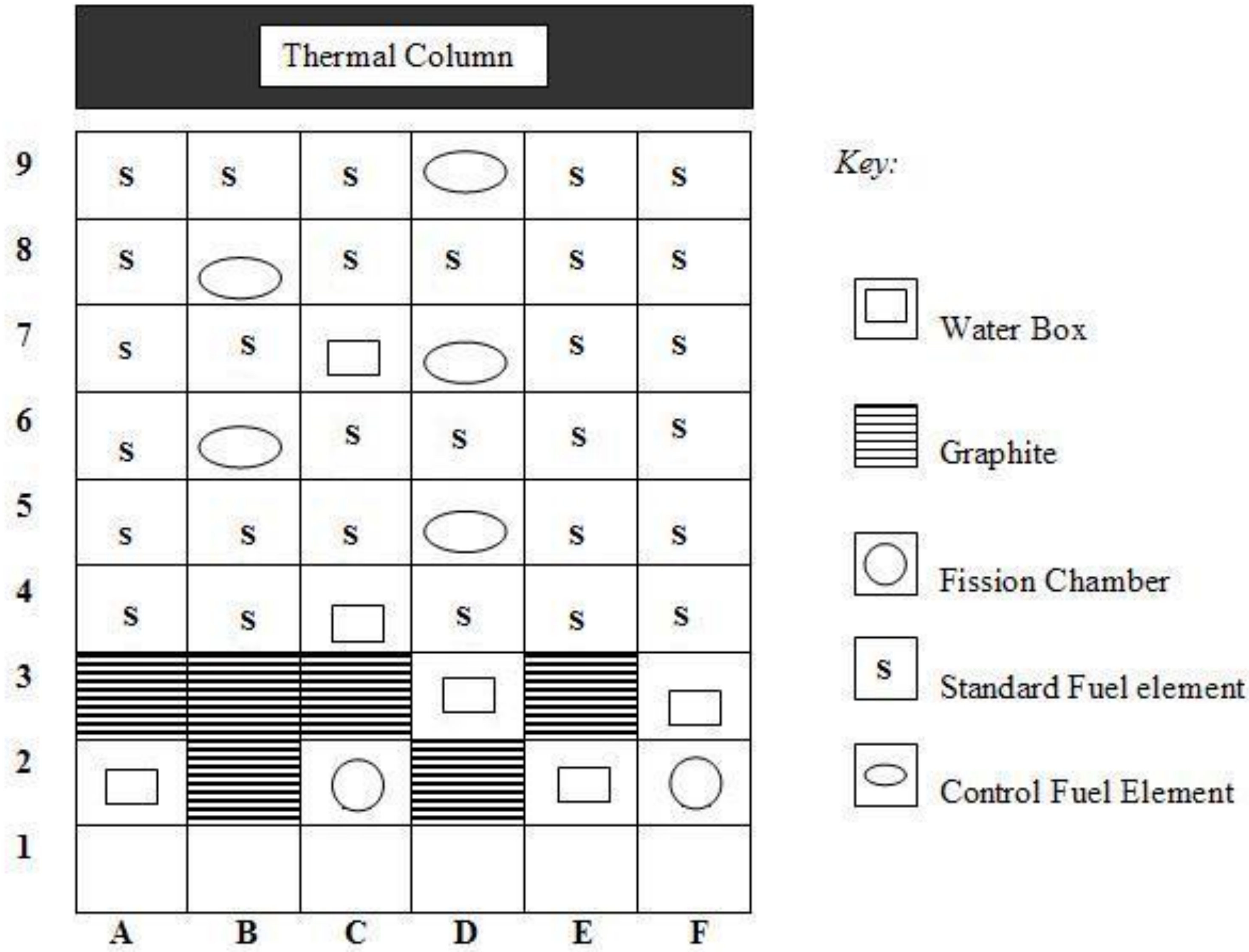
Main Features of Pakistan Research Reactor 1 and 2

Experimental Data	PARR-1	PARR-2
Channels	**Horizontal:** 7	**Vertical:** 10
max flux n/cm^2-s	**Horizontal:** 4.7 x10^{13}	**Vertical:** 1 x10^{12}
Horizontal use	Basic research	**Small irradiation sites:** 8x7 cm^3
Vertical use	Neutron activation analysis	
Core irradiation facilities	2	**Large irradiation sites:**2x25 cm^3
Core max flux n/cm^2-s	1.5 x10^{14}	
Reflector irradiation facilities	3	10

Main Features of Pakistan Research Reactor 1 and 2

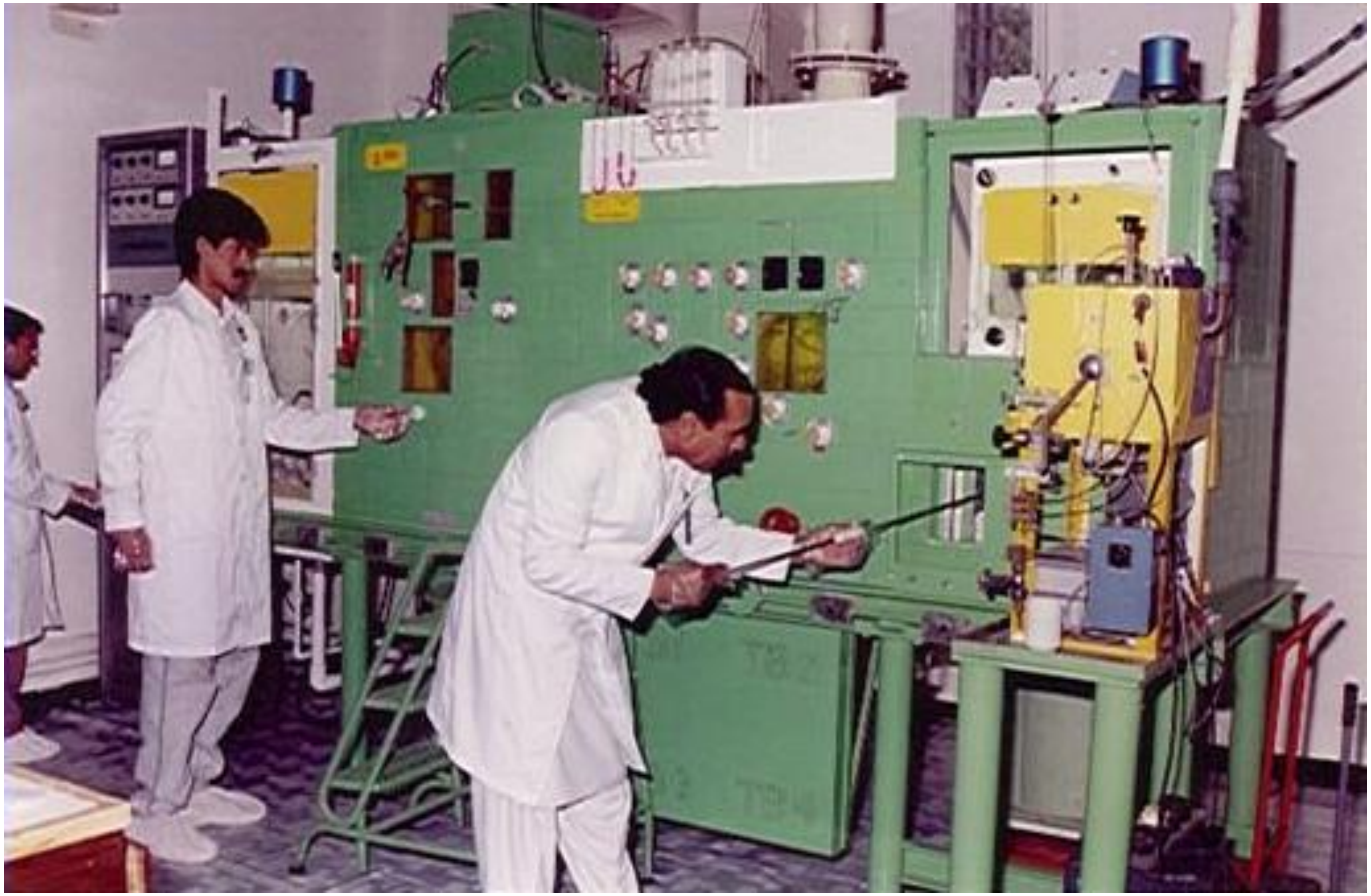
Utilization	PARR-1	PARR-2
Basic/applied research	Neutron diffraction, n,γ reaction	NAA, Radioisotopes
Isotope production	I-131, P-32, Br-82 etc.,	Short lived
Neutron scattering	Two Diffractometers	-
Neutron radiography	one	-
Nuclear chemistry	NAA, radiochemistry	NAA, radiochemistry
Training	Reactor supervisors, operators, students	Reactor supervisors, operators, students

Configuration of core PARR-1



Radioisotope Processing Facilities

- IODINE-131 Production Cell (Wet Distillation Technique). Maximum capacity per batch **10 Ci/370 GBq**.
- Iodine-131 Production Cell (Dry Distillation Technique). Maximum capacity per batch **10 Ci/370 GBq**.
- Phosphorus-32 Production Cell (Dry Distillation Technique). Maximum capacity per batch **10 Ci/370 GBq**.
- Sulpher-35 Production Glove Box
- Molybdenum-99 Loading Facility for preparation of ^{99m}Tc generators.(100Ci/batch)
- Mo-99 Production facility (under commissioning phase)
- Hot Cell with Master Slave Manipulators.
- Fume Hoods and Glove Boxes (for small scale production of different radionuclides and R&D work)
- Workshop for target preparation and sealed source fabrication
- Laboratories for determination of radionuclidic, radiochemical and biological purity



^{131}I Processing Plant (Wet Distillation)

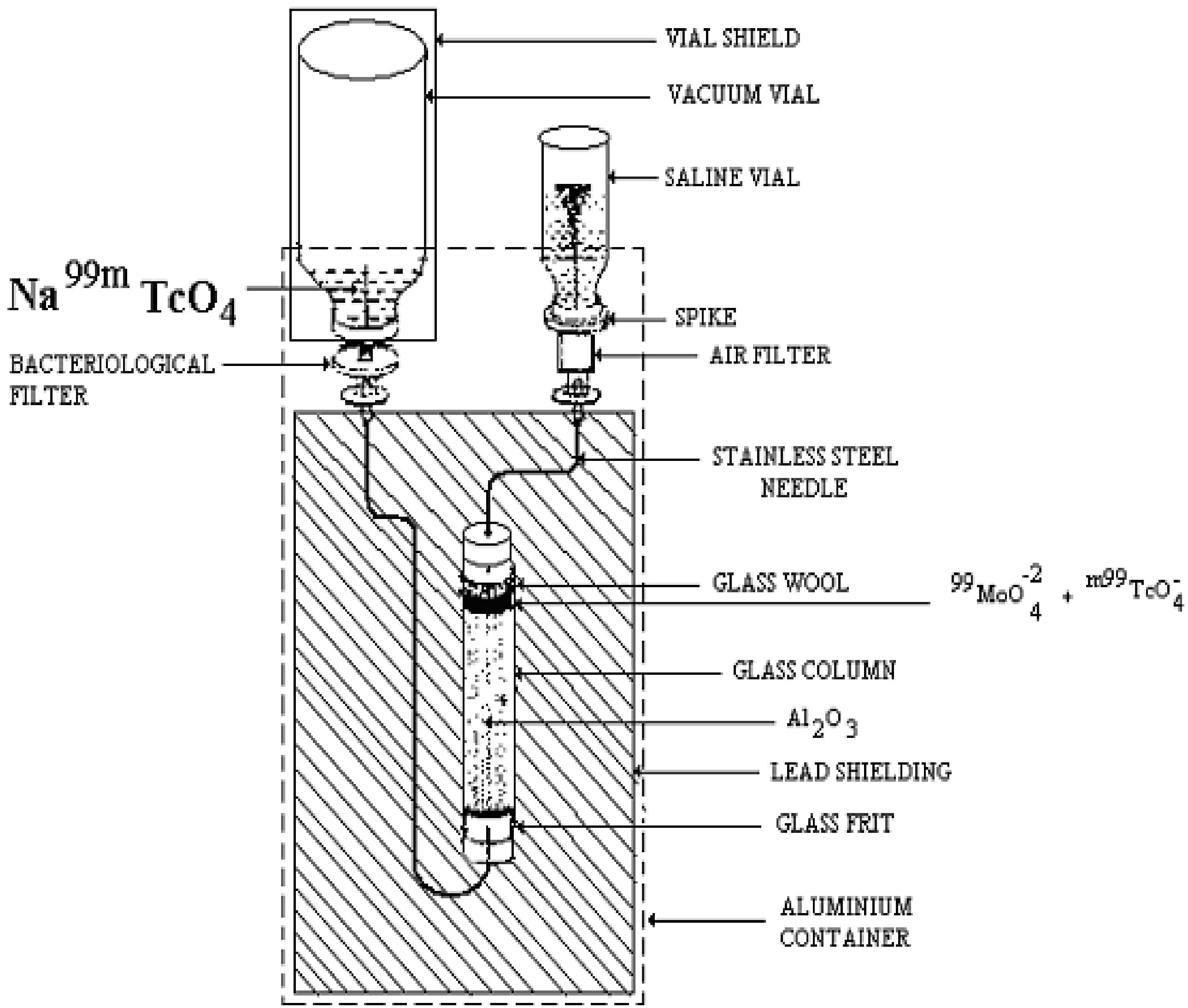
^{131}I Processing Plant (Dry Distillation)

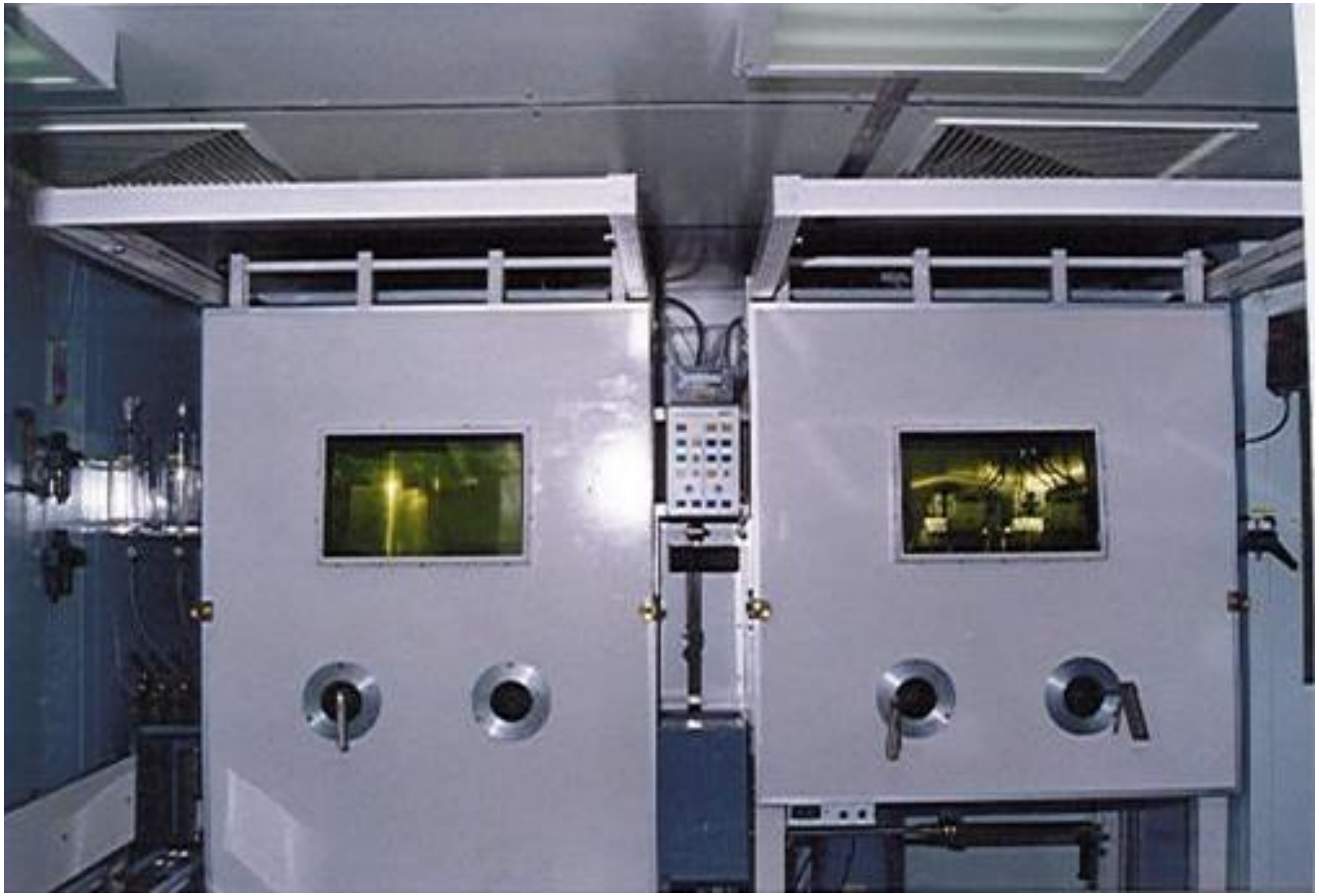
^{32}P Processing Plant

Clean Room for Radiopharmaceutical kits Production

^{99m}Tc Generators

Scheme of PAKGEN ^{99m}Tc Generator

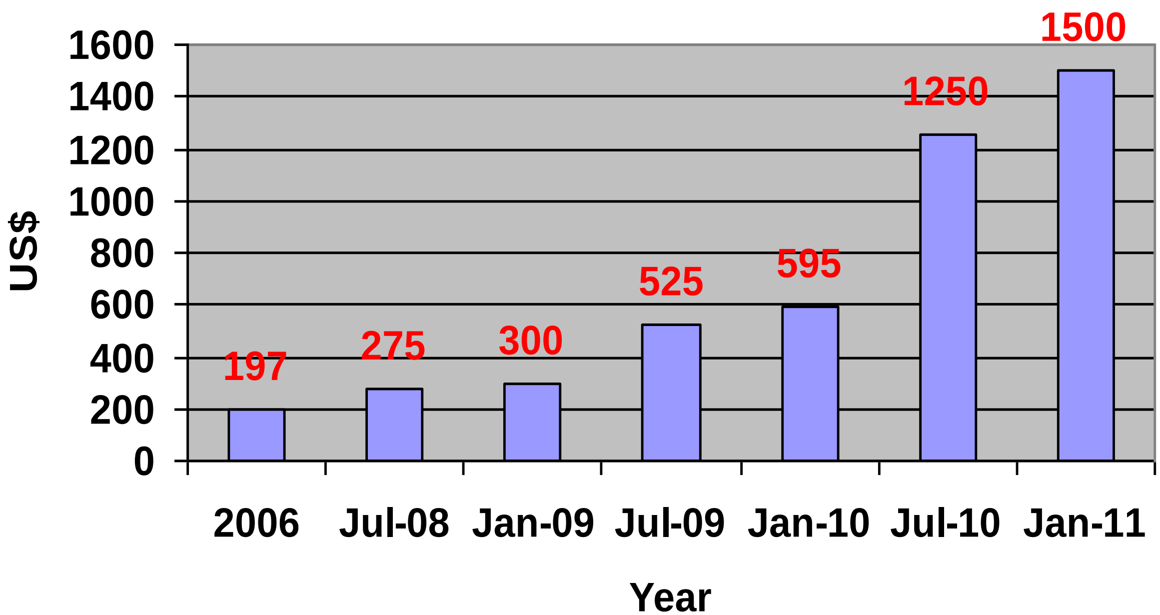




^{99m}Tc Generator Plant (hot cells)

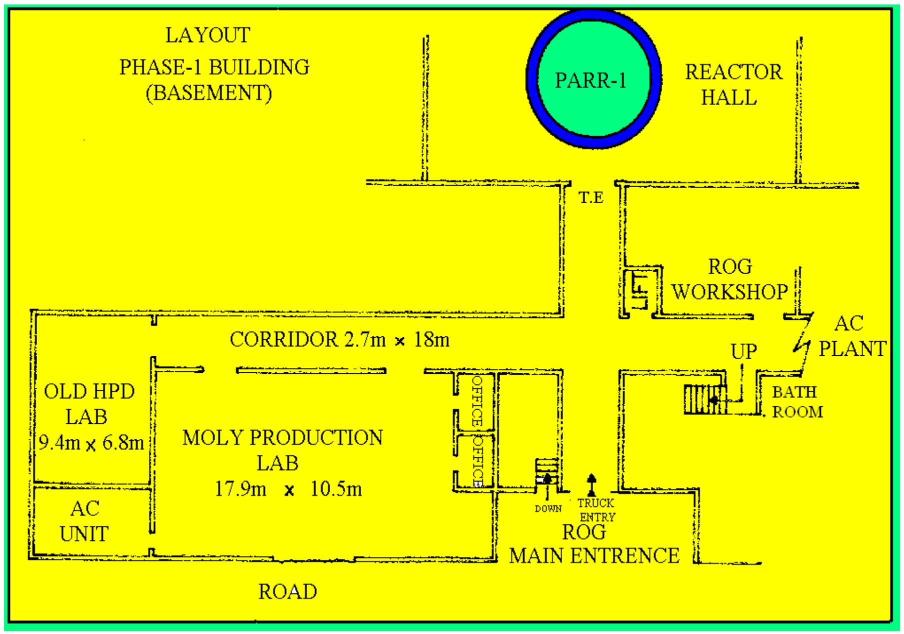
Inner layout of Hot cell of ^{99m}Tc Generator lab

Fission Mo-99



Price for 1Ci reference day activity

Molybdenum-99 Production Facility at PINSTECH



Location of Facility

Hot-Cells of facility

Establishment of Mo-99 Production Plant
Capacity: 500 Ci/Batch

• Project Profile

Sponsor: Planning Commission of Pakistan (S&T)

❑ **Approved on**	March 2004
❑ **Implementation period**	July 2004 –June 2007
❑ **Funds allocated**	Rs. 212 M (3.55 M $)
❑ **Agreement with** Waelischmiller Germany	January, 2005
❑ **Contract value**	€ **2.54 M + $ 0.10 M**
❑ **Installation Work Started**	June, 2006
❑ **Waelischmiller Germany faced insolvency**	December 2007
❑ **New Agreement with ITD, Germany**	27 August, 2008
❑ **Project to be completed**	**June**, 2010

OBJECTIVES

- **Local production of fission ^{99}Mo for the preparation of Pakgen ^{99m}Tc generators**
- **Export of ^{99}Mo and Pakgen ^{99m}Tc generators to neighboring countries to enhance commercialization**
- **Extraction of ^{131}I and ^{133}Xe as by product**
- **Separation of ^{90}Sr and ^{137}Cs**
- **Self reliance in terms of consistent supply and economic uplift**

Advantages of Mo-99 extraction process developed at PINSTECH

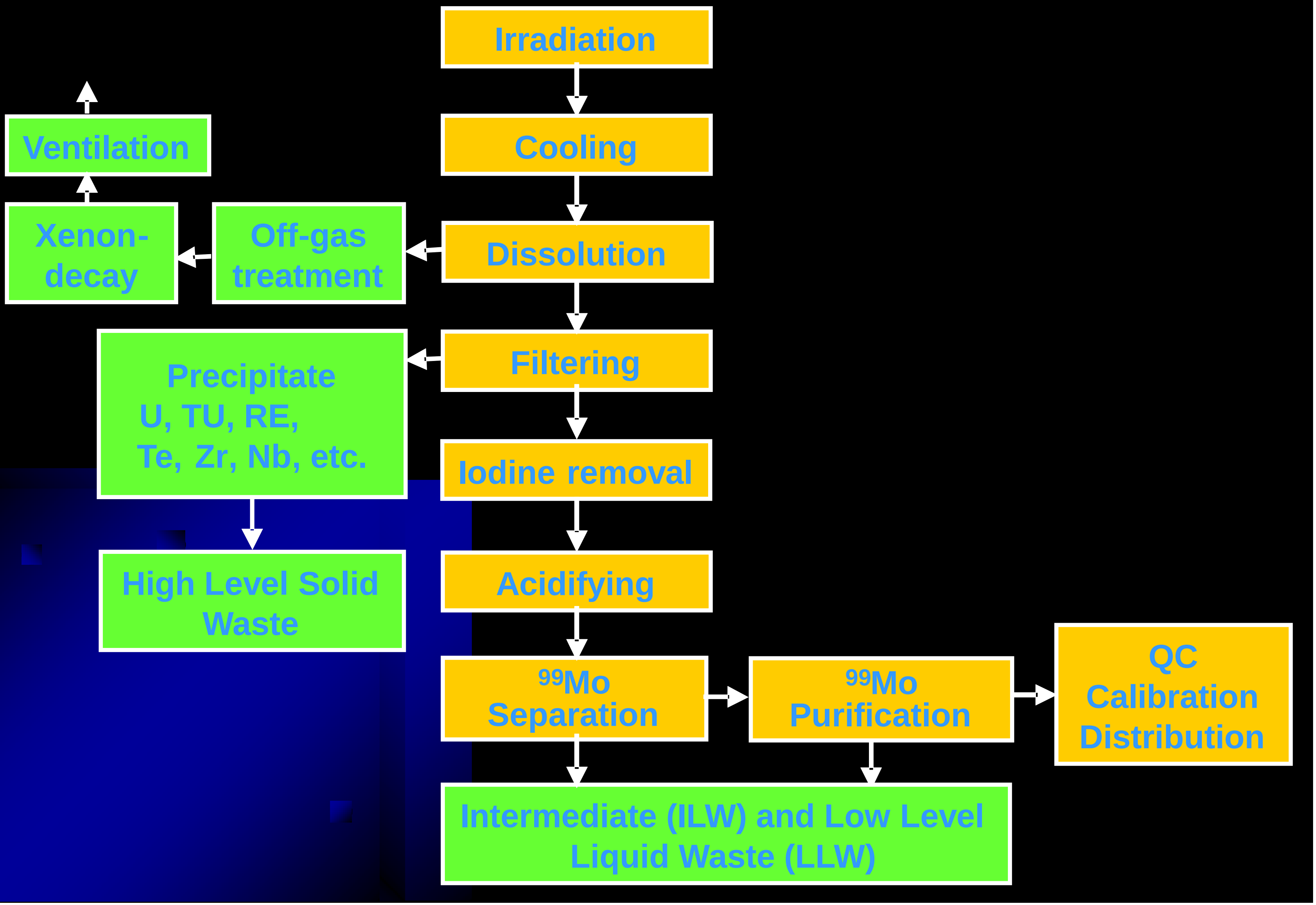
- A new chemical process was developed at PINSTECH with the help of German expert for separation of Mo-99 from fission products
- Optimization of parameters was achieved in IPD laboratory
- Fission Iodine-131 and Xenon-133 as by-product
- Spent HEU in small SS container for easy disposal

Parameters to meet country's need

Target irradiation

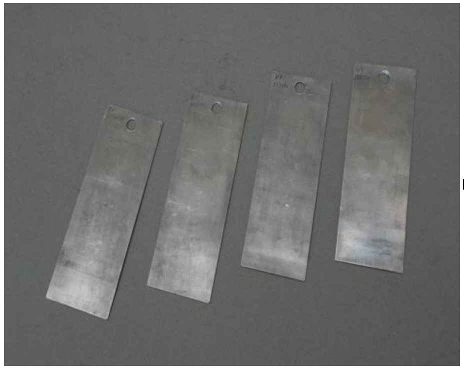
Number of target plates	3
Uranium per target plate	1.667 g
Enrichment	93 % U-235 (1.55 g)
Irradiation time	12 hours
Neutron flux	1.5 x 10^{14}/cm^2 sec
Cooling period	24 hours
Activity of Mo-99 at EOI	153 Ci
Mo-99 after 48 hour (separation)	92.4 Ci
Separation yield (70%)	64.68 Ci
Reference day activity (4-day)	23.63 Ci
PINSTECH imports Mo-99	16 Ci

Mo-99 Separation Technique

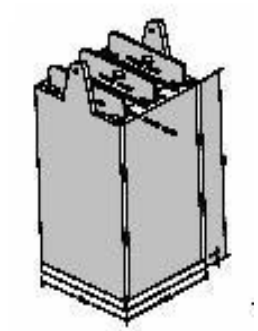


^{99}Mo Production Facility

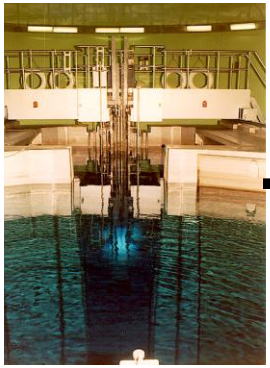
Step1: Target Irradiation



Target plates



Target Holder for PARR-1



PARR-1 Core

Target basket for transportation

Target Container

Step2: Target transportation from PARR-1 to Mo-99 Facility & container docking

Fork lifter for transportation of target container

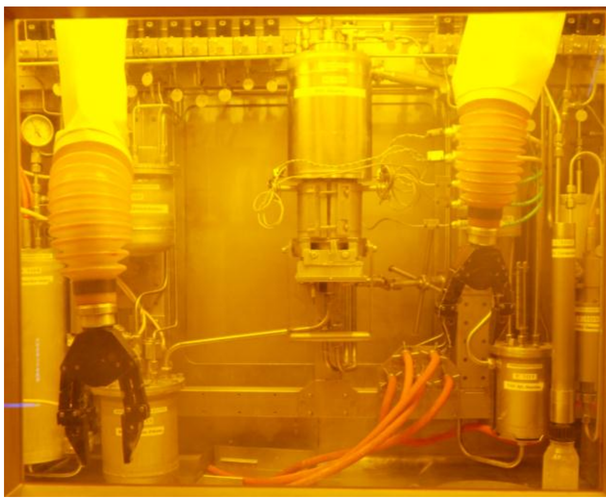
Mo-99 Hot-cell (1-3)

Docking of container below hot cell-1 of Mo-99 Facility

Target basket for dissolver

^{99}Mo Production Facility (Continued)

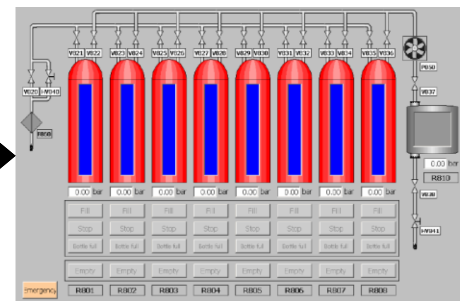
Step3: Hot Cell 1 Processes (Dissolution, Filtration, Iodine removal & acidification)



In-cell equipment of Hot cell-1

Filter cake

Solid waste container

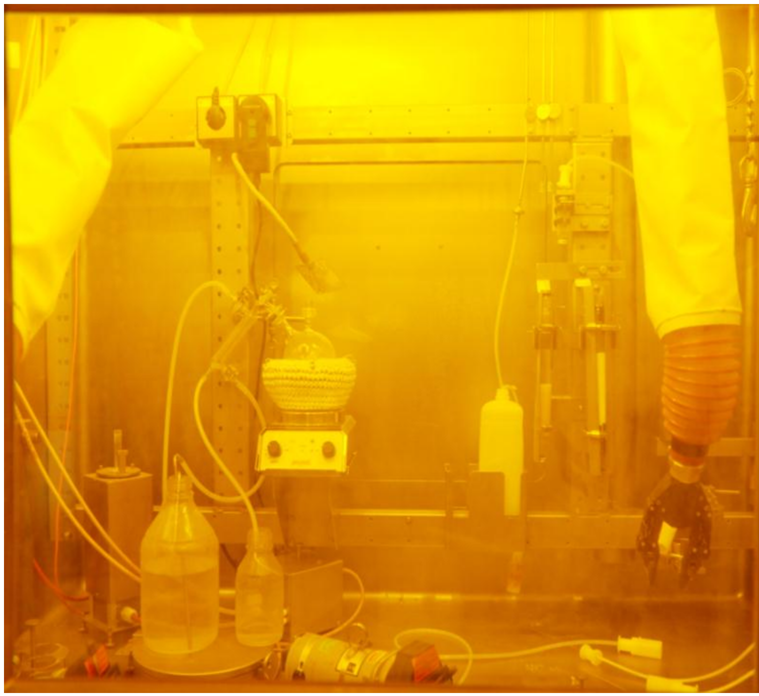


Xenon delay and decay cascade

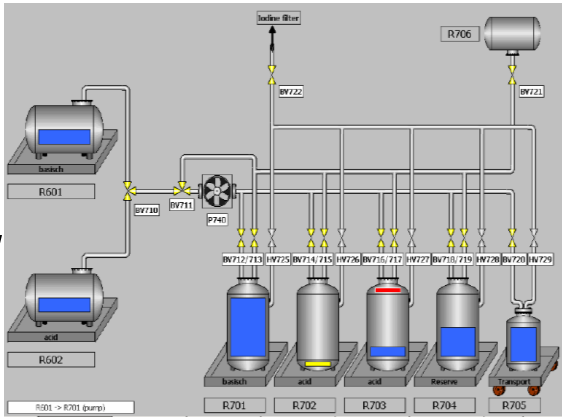
Filter tower for retaining radio-iodine

^{99}Mo Production Facility (Continued)

Step 4: Hot Cell 2 Processes (Mo-99 Separation and Purification)



In-cell equipment of Hot cell-2

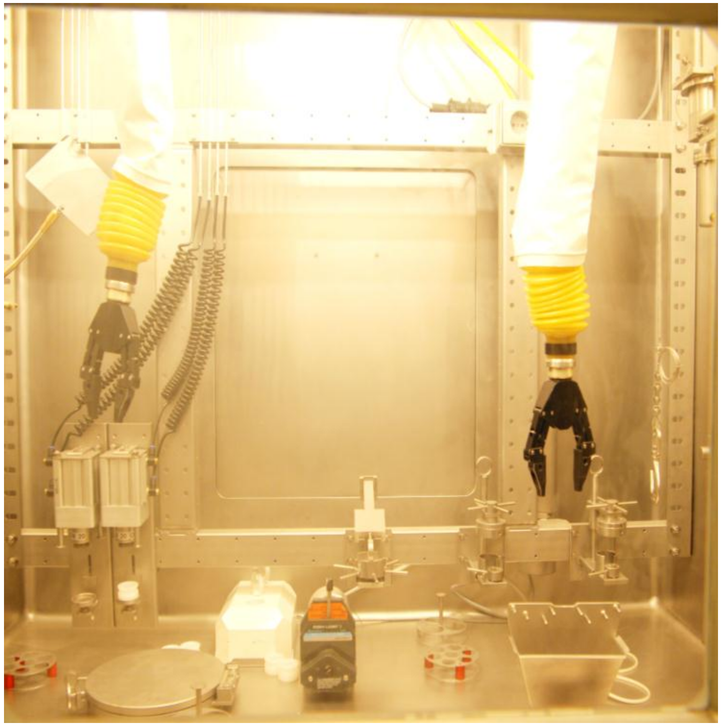


Intermediate decay and storage system for liquid radioactive waste

Medium level waste container

^{99}Mo Production Facility (Continued)

Step 5: Hot Cell 3 Processes (Mo-99 Dispensing and transportation to generator production facility)



In-cell equipment of Hot cell-3

Product container

Transport of Product container

^{99}Mo Production Facility (Continued)

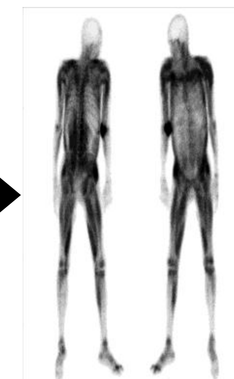
Step 6: Mo-99/Tc-99m Generator production facility and its use in medical center for scanning

Mo-99/Tc-99m Generator production facility

Mo-99/Tc-99m generator

Nuclear Medical Center

Gamma camera Imaging



Scan

Radioisotopes produced in PARR-1

S. No.	Radio nuclide	Chemical form	Maximum Activity / Batch	Year
1	Na-24	Sodium carbonate	50 mCi	1966
2	P-32	Sodium phosphate	50 mCi > 1 Ci	1978 1986
3	S-35	Sodium sulphate	10 mCi	1995
4	Sc-46	Scandium glass	50 Ci	1967
5	Sc-47	Scandium chloride	mCi	2005
6	Cr-51	Sodium chromate, EDTA Complex	100 mCi 100 mCi	1972
7	Fe-59	Ferric chloride	5 mCi	1995
8	Co-60	Metal	10 mCi	1980
9	Cu-64	Copper chloride	50 mCi	1988

Radioisotopes produced in PARR-1

S. No.	Radio nuclide	Chemical form	Maximum Activity / Batch	Year
10	Zn-65	Zinc chloride	mCi	1989
11	Se-75	L-Selenomethionine	10 mCi	1982
12	As-77	Arsenic chloride	mCi	2007
13	Br-82	Potassium bromide Ammonium bromide Dibromobenzene	~ 1 Ci ~ 1 Ci ~ 1 Ci	1972
14	Mo-99	^{99m}Tc-Generator (n,γ)	150 mCi	1973
15	Mo-99	^{99m}Tc-Generator fission Local production	1Ci 500 mCi	2002 2010
16	Ag-111	Silver chloride	5 mCi	1995
17	Sn-113	Tin chloride	mCi	1996
18	Cd-115	Cadmium chloride	15 mCi	1996

Radioisotopes produced in PARR-1

S. No.	Radio nuclide	Chemical form	Max Activity Batch	Year
19	Sb-125	Antimony chloride	mCi	1989
20	I-131	Sodium Iodide, oral sol Sodium ortho-idohippurate MIBG	7 Ci 20 mCi 30 mCi	1979 1980 2000
21	Ba-133	Barium chloride	micro Ci	1996
22	Cs-134	Cesium chloride	100 mCi	1993
23	La-140	Lanthanum chloride	1Ci	2003
24	Sm-153	EDTMP	1Ci	1999
25	Eu-152/154	Metal	10 mCi	1995
26	Ho-166m	Holmium oxide	Micro Ci	1995
27	Ho-166	particles	>100 mCi	1995

Radioisotopes produced in PARR-1

S. No.	Radio nuclide	Chemical form	Max Activity Batch	Year
28	Lu-177	EDTMP	500 mCi	2008
29	Re-186/188	EHDP	100 mCi	1995
30	W-188	Re-188 generator	5 mCi	1995
31	Au-198	Colloidal, gold chloride, Potassium auro cyanide	1Ci	1974
32	Au-199	Gold chloride	1Ci	2003
33	Hg-197	Neohydrin	100 mCi	1977
34	Hg-203	Neohydrin	10 mCi	1977
35	Po-210	metal	Ci	1982

In-vivo kits for ^{99m}Tc-radiopharmaceuticals

No	Freeze-dried kits	PINSTECH Supply	Studies/Imaging
1	PINSCAN DTPA	1987	Kidney
2	PINSCAN EHIDA	1987	Hepatobiliany
3	PINSCAN Tin colloid	1990	Liver
4	PINSCAN Ca Hepta Gluconate	1990	Kidney
5	PINSCAN DMSA III	1990	Renal
6	PINSCAN DISIDA	1990	Hepatobiliary
7	PINSCAN PIPIDA	1990	Hepatobiliary
8	PINSCAN BRIDA	1990	Hepatobiliary
9	PINSCAN Sucralfate / Ulsanic	1991	Stomach
10	PINSCAN MDP	1992	Bone
11	PINSCAN Pyrophosphate	1994	RBC/ MUGA

In-vivo kits for ^{99m}Tc-radiopharmaceuticals

No	Freeze-dried kits	PINSTECH Supply	Studies/Imaging
12	PINSCAN MIBI	1995	Heart
13	PINSCAN EHDP	1996	Bone
14	PINSCAN Phytate	1996	Liver / spleen
15	PINSCAN MAG-3	1996	Kidney
16	PINSCAN DMSA V	2000	Head Neck carcinoma
17	PINSCAN HMPAO	2001	Brain
18	PINSCAN Dextran	2002	Lymph nod
19	PINSCAN Ciprofloxacin	2003	Infection
20	PINSCAN Ubiquicidin	2003	Infection
21	PINSCAN Tetraphosmin	2008	Heart

IAEA TC and CRP projects

No	Contract No	Title	Work done
1	PAK/6/012 1989-1992	Preparation and quality control of radipharmaceuticals with special emphasis on the “Bulk production of Tc-99m radiopharmaceuticals kits	Clean Room Facility. 15 Cold kits are regularly produced
2	PAK/4/040 1998-2000	Establishment of loading facility for the production of Tc-99m generators for Nuclear Medicine.	Generator Production Laboratory. More than 30 generators are weekly produced
3	PAK/8668 1994-1998	Preparation and evaluation of radioisotopes for therapeutic applications.	^{186}Re-HEDP, ^{153}Sm-EDTMP and MDP complexes
4	PAK/8970 1995-1999	Tc-99m labeled peptides for imaging of peripheral receptors.	^{125}I-RC-160 ^{99m}Tc-RC-160

IAEA TC and CRP projects

No	Contract	Title	Work done
5	PAK/10107 1998-2002	Labeled Biomolecules with Sm-153, Re-188 and Y-90 for Targeted Radiotherapy.	^{188}Re,^{99m}Tc and ^{131}I-Lanreotide
6	PK/11263 2000 -2003	Development of Kits for Tc-99m radiopharmaceutical for infection imaging.	^{99m}Tc-UBI ^{99m}Tc-HYNIC-UBI
7	PK/12130 2002-2005	Laboratory evaluation of beta emitting radionuclides (^{131}I, ^{177}Lu, ^{166}Ho) and radiopharmaceuticals for radiotherapy	^{131}I, ^{153}Sm,^{166}Ho,^{177}Lu DOTATATE
8	PK/13929 2006-2010	Optimization of the preparation and quality control of ^{177}Lu based therapeutic radiopharmaceuticals	^{177}Lu-EDTMP ^{177}Lu-HA
9	PK/13362 2005-continue	Establish techniques for small scale indigenous molybdenum-99 production using LEU fission or neutron activation	Safety analysis; neutronic and thermal hydraulic analysis, radioactive waste management,

Beta particle emitting radionuclides produced at PINSTECH

No	Radionuclide	Half-life	Target	Separation technique
10	^{131}I	8.02 d	TeO^2	Dry distillation
11	^{153}Sm	46.75 h	Sm	Carrier added
12	^{166}Ho	26.8 h	Ho	Carrier added
13	^{186}Re	90.64 h	Re	Carrier added
14	^{188}Re	16.98 h	^{188}W	precipitation
15	^{177}Lu	6.71 d	Lu	Carrier added
16	^{199}Au	3.139 d	Pt	Adsorption

Beta particle emitting radionuclides produced at PINSTECH

No	Radionuclide	Half-life	Target	Separation technique
1	^{32}p	14.2 d	S	Dry distillation
2	^{47}Sc	3.41 d	Ti	Silica gel column
3	$^{64}Cu/^{67}Cu$	12.7/61.9 h	Zn	Ion exchange
4	^{77}As	1.6 d	Ge	HZO column
5	^{90}Y	64.1 h	^{90}Sr	Precipitation
6	^{90}Y	64.1 h	Y	Carrier added
7	^{111}Ag	7.45 d	Pd	Ion exchange /adsorption
8	^{113m}In	99.48 m	^{113}Sn	Ion exchange
9	^{115m}In	4.49 h	^{115}Cd	Ion exchange

Radionuclide Generators

No	Generator	Adsorbent	Eluant	Yield
1	$^{99}Mo/^{99m}Tc$	Hydrated titanium dioxide	0.9 % saline	85 %
2	$^{99}Mo/^{99m}Tc$	Alumina	0.9 % saline	85 %
3	$^{115}Cd/^{115m}In$	AG 50W-X8	DTPA/EDTA	95 %
4	$^{113}Sn/^{113m}In$ $^{115}Cd/^{115m}In$	Hydrated antimony pentaoxide	0.5 M HCl	66 % 87 %
5	$^{109}Pd/^{109m}Ag$	AG 50W-X8	0.9% saline	45 %
6	$^{109}Cd/^{109m}Ag$	AG 50W-X8	0.1 M Na Cl	40-70%

Concentrator systems for ^{99m}Tc, ^{188}Re and ^{68}Ga

No	Radionuclide	Eluant	Concentrator adsorbent	Fold
1	^{99m}Tc generator ^{188}Re generator	Acetone	Alumina	10
2	^{99m}Tc generator ^{188}Re generator	0.7 M acetic acid + 0.0225 M NaCl	QMA Sep-Pak	4.5 4
3	^{99m}Tc generator ^{188}Re generator	Saline	Ag and Alumina	50
4	$^{188}ReO4^{-}$	MEK	-	High
5	$^{99m}TcO4^{-}$	0.15 M HCl	Lead (Pb)	50
6	$^{99m}TcO4^{-}$	0.02 M Na_2SO_4	Alumina	2
7	$^{99m}TcO4^{-}$	0.02 M Na_2SO_4	Lead cation and alumina	38
8	^{68}Ga	MEK	-	High

THANKS