Production of ^{99}Mo at IPEN-CNEN/SP-Brazil

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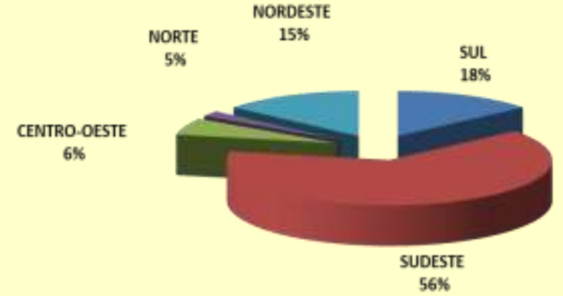
Mo-99 2013 TOPICAL MEETING ON MOLYBDENUM-99 TECHNOLOGICAL DEVELOPMENT
April 1-4, 2013
Embassy Suites Downtown - Lakeshore
Chicago, Illinois

BRAZIL – NUCLEAR MEDICINE

- ***Radiopharmacy market in Brazil: 365 Diagnostic Clinics, Hospitals, and Centers of Nuclear Medicine.***
- ***75% of them are located at Southeast and South of Brazil.***
- ***192 γ-cameras, 176 SPECT, 30 SPECT/CT***
- ***72 PET installations***
- ***33 hospitals with beds for therapy***
- ***Nearly 2,000,000 patients/year***
- ***Population: 190,732,694 (2010)***
- ***56.5% located at Southeast and South***



Ministério da Ciência, Tecnologia e Inovação

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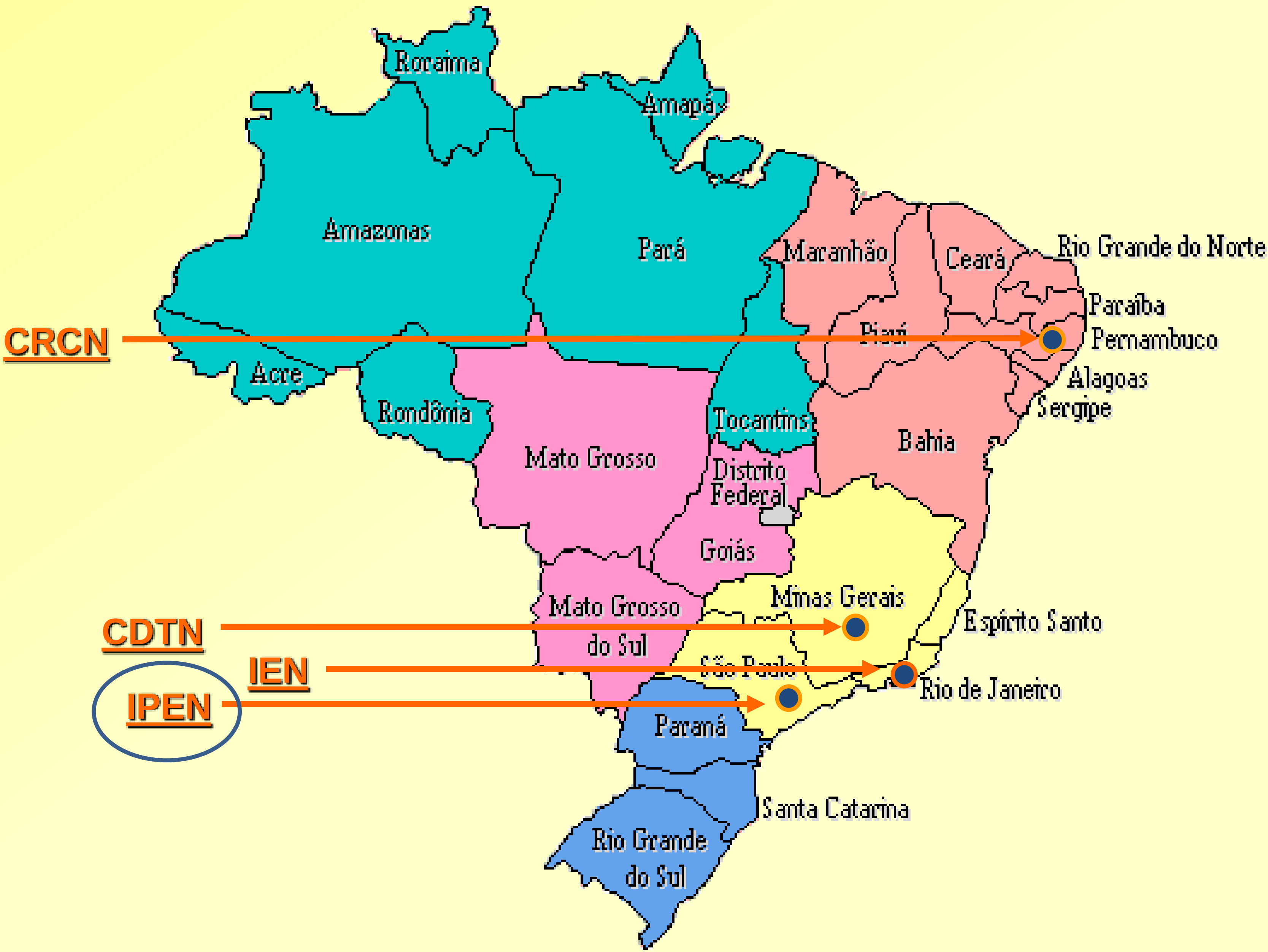
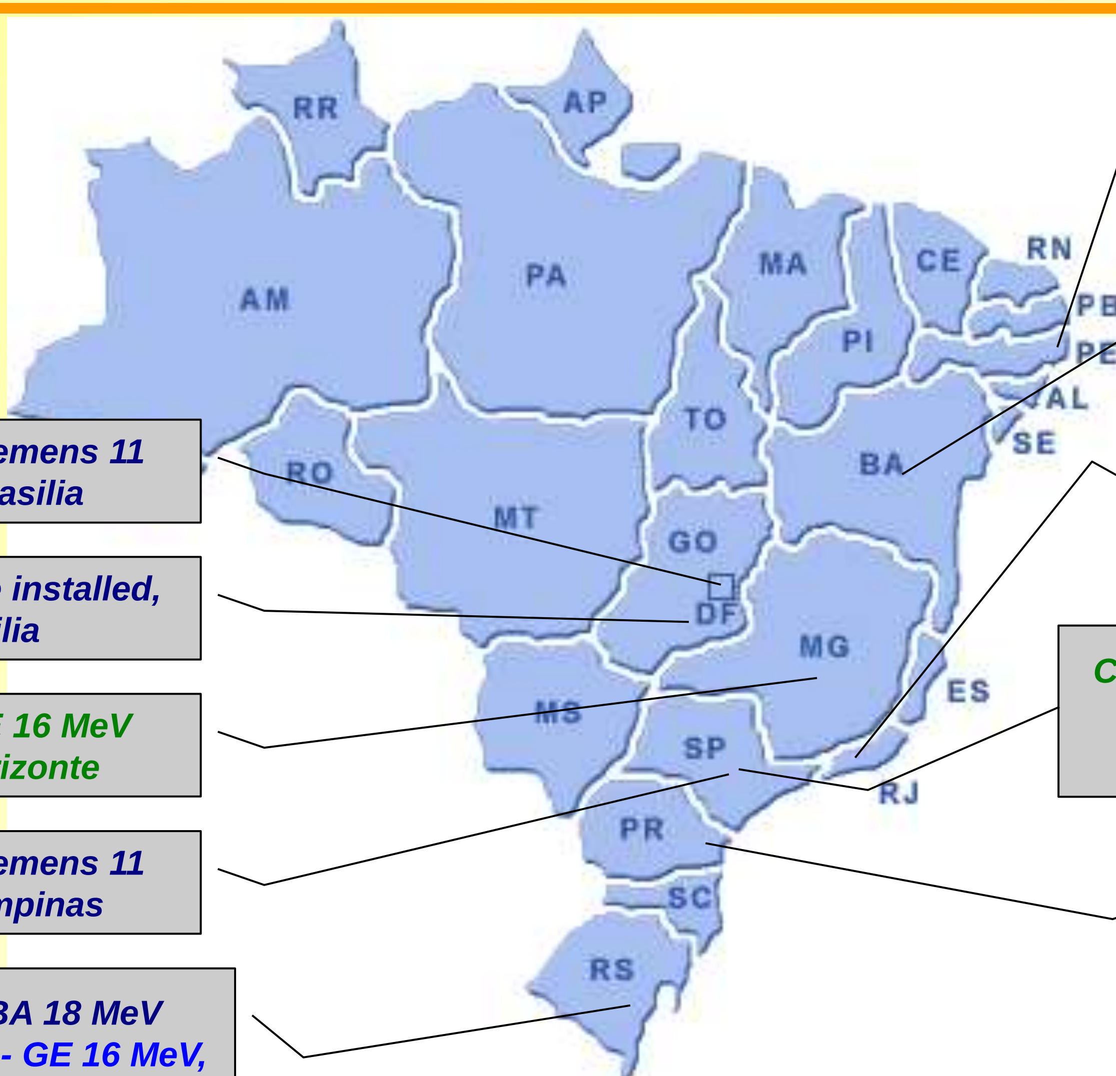


BRAZIL – Cyclotrons installations in 2012



CNEN - GE 16 MeV
Recife

Private, Bahia

CNEN- Siemens 11 MeV ;
CV 28
Rio de Janeiro

CNEN- IBA 18 MeV and 30 MeV,
São Paulo
CMN -GE 16 MeV

Private, to be installed

Private - Siemens 11 MeV, Brasilia

Private to be installed, Brasilia

CNEN - GE 16 MeV
Belo Horizonte

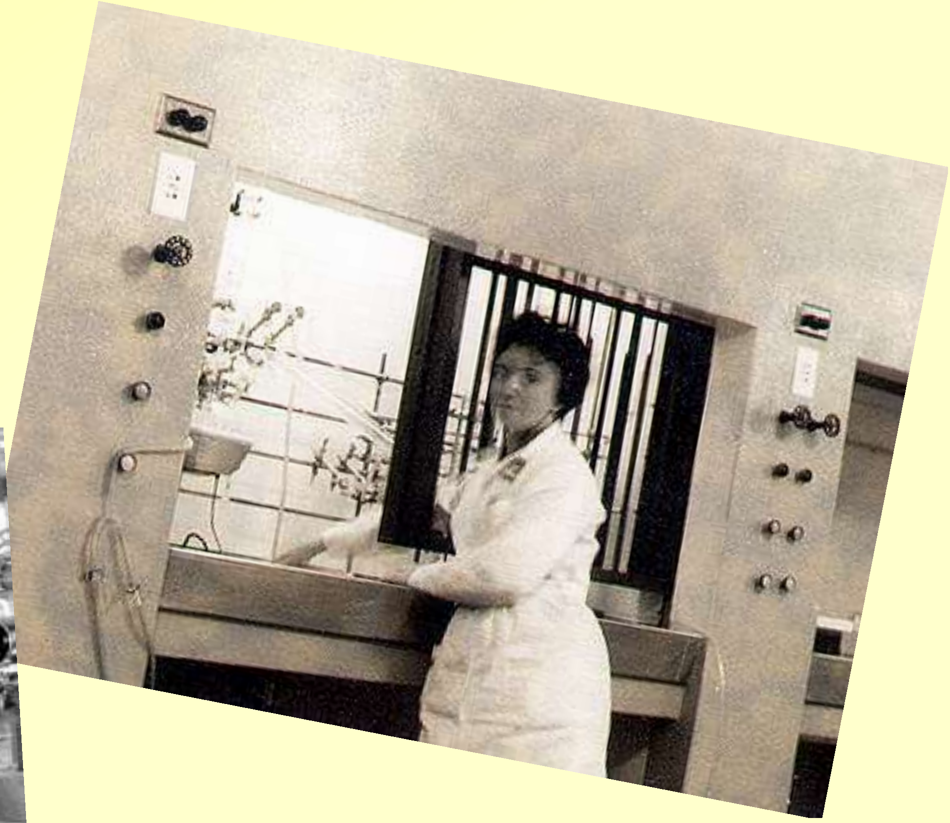
Private - Siemens 11 MeV, Campinas

Private - IBA 18 MeV
Private PUC. - GE 16 MeV,
Porto Alegre

IPEN

- *IPEN is the biggest Nuclear Research Institute in Brazil*
- *Nearly 1,000 employees and 1,000 students*
- *Radiopharmacy Center: 100 employes and 40 students*

… The beginning...



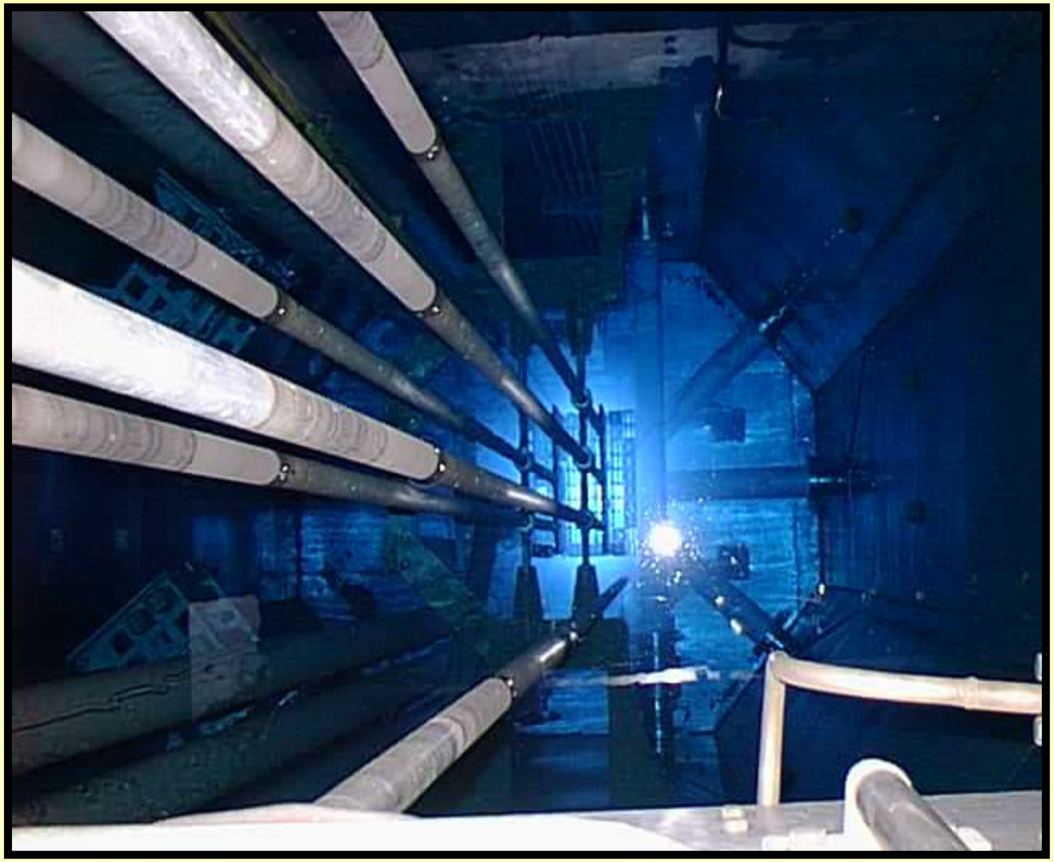
… Now…

IPEN – NUCLEAR REACTOR

Technical Characteristics

- **Swimming pool reactor**
- **Power: 4.5 MW**
- **Termal neutron flux =**

  1-3x10^{13} n/cm^{2}.s
- **^{235}U enriched 19.75%**
- **Maximum Termal neutron flux (5MW) = 1.17x10^{14} n/cm^{2}.s**
- **Reflector: graphite**
- **Moderator: water**
- **First criticality: 1957**
- **Manufacturer: Babcock & Wilcox Co**



Operating in continuous periods of 64 h/week at 4.5 MW and 5 MW (January/2013).

Presently, I-131 and Sm-153

Cyclotron

Cyclone-30 IBA

IPEN

(30 MeV)

Cyclone-18 IBA

- began operation: August 2008

Control room

Radiopharmacy Directory IPEN-CNEN/SP

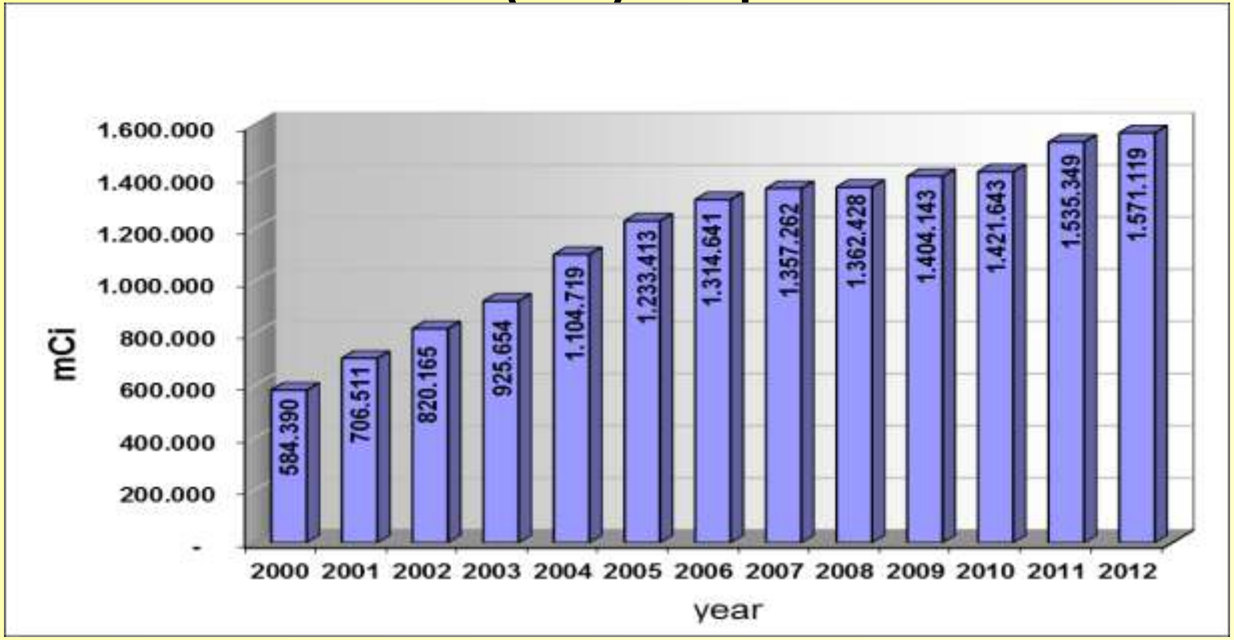
Radiopharmaceuticals produced at IPEN

Product - RI	Use
Sodium Iodide – ^{131}I	Oral
Sodium iodide – ^{131}I capsules	
Sodium Iodide – ^{123}I	
Gallium citrate – ^{67}Ga	Injectable
Thalium chloride – ^{201}Tl	
Sodium Chromate – ^{51}Cr	
Generator ^{99}Mo – ^{99m}Tc	

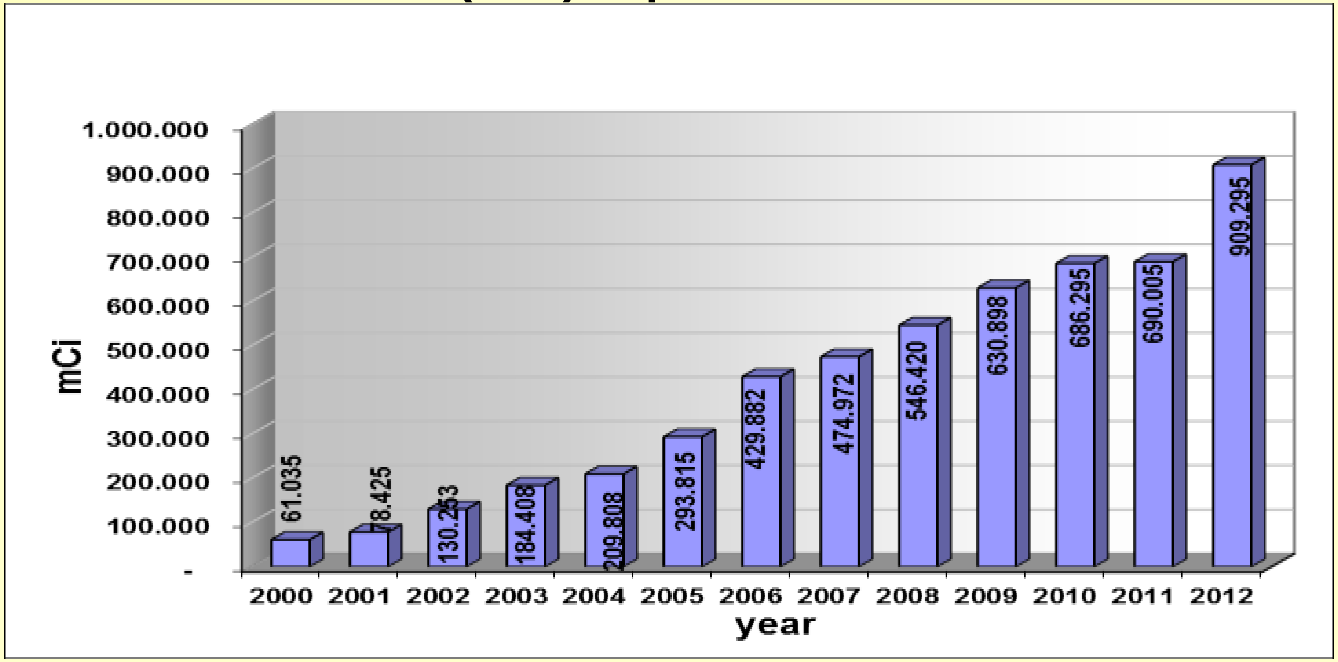
Radiopharmaceuticals

Labeled Molecules	
Therapy	**Diagnostic**
MIBG – ^{131}I	MIBG – ^{123}I
Octreotate – ^{177}Lu	Octreotide – ^{111}In
EDTMP – ^{153}Sm	FDG – ^{18}F
HA – $^{153}Sm/^{90}Y$ Citrate – ^{90}Y	SAH– ^{51}Cr SAH – ^{131}I
Lipiodol – ^{131}I	IOH – ^{131}I EDTA – ^{51}Cr
	Fluoride-^{18}F Octreotate-^{68}Ga

Demand for I-131 (mCi) in liquid form



Demand for I-131 (mCi) capsules



^{99}Mo/^{99m}Tc generator Ipen

- 385 generators/week

- (250,500,750,1000, 1250, 1500 and 2000 mCi)

- 2-3 productions/week

Kits for labelling with Tc-99m

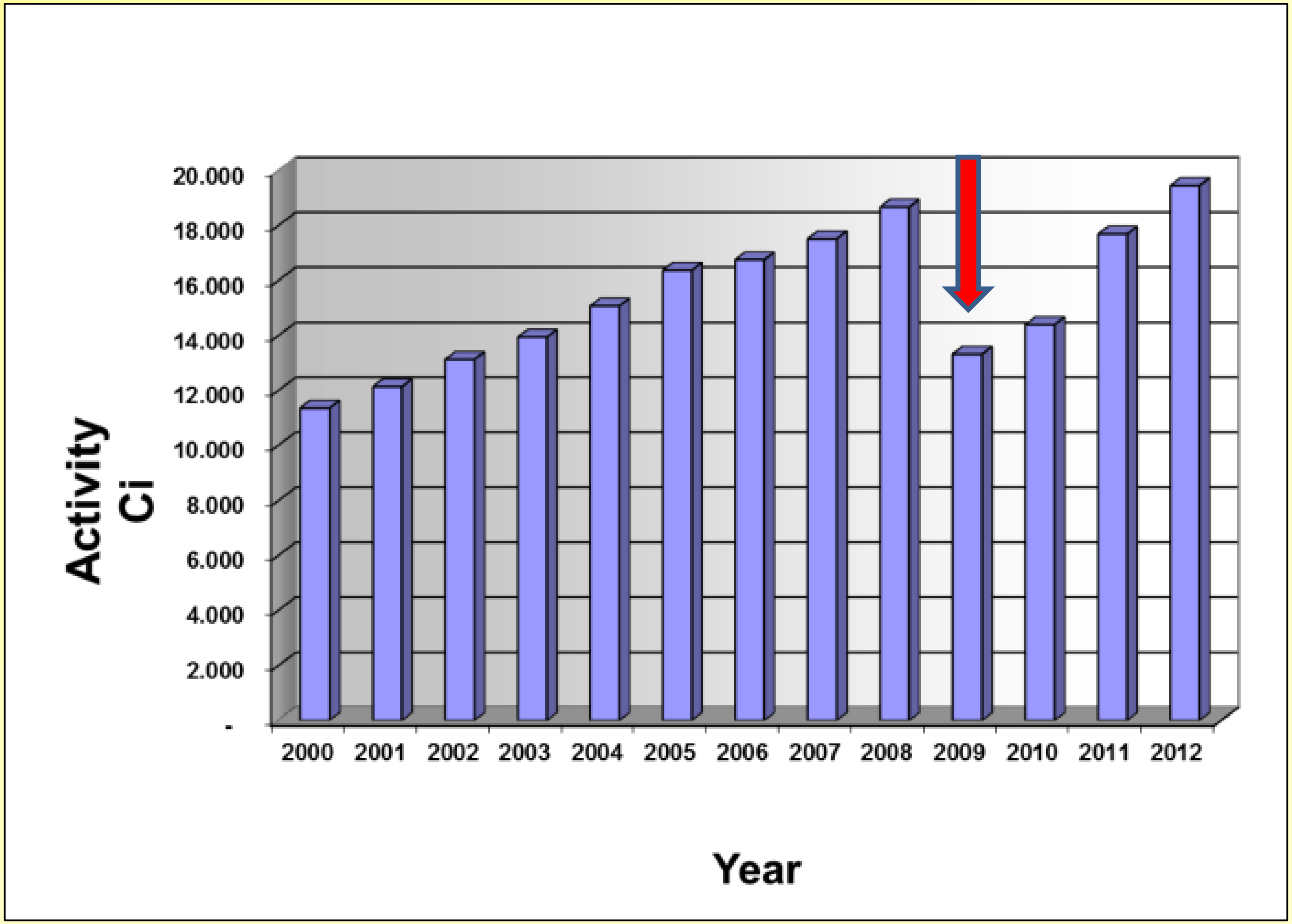
Kits for labelling with ^{99m}Tc	
MDP	Fitate
DTPA	SAH
Pyrophosphate	Dextran-500
ECD	Dextran-70
MAA	DISIDA
DMSA	GHA
Tin Coloidal Glucarate	EC MIBI

Strategies – ^{99}Mo Crisis

Short term:

- Before 2009 MDS Nordion Canada was the solo ^{99}Mo supplier to Brazil.
- The straight forward short term action included the purchase of ^{99}Mo from Argentina (LEU) and South Africa and also the distribution of ^{99}Mo/^{99m}Tc generators from Israel and Belgium (IBA).
- Nowadays administrative actions led to the purchase of ^{99}Mo from 3 suppliers: Argentina, South Africa and Canada.
- An adequacy of the Brazilian market (i.e., from 450 Ci ^{99}Mo/week to nearly 360 Ci/week) took place. A higher demand for low activity generators compared to the pre-crisis higher demand for high activity generators.
- The nuclear medicine physicians started to employ less ^{99m}Tc activity in the exams, leading to a better use of the generators

Country Demand – Generators - Brazil



2007-2008: +6.7%
2008-2009: -29.4%
2009-2010: +8.9%
2010-2011: +20.8%
2011-2012: +10.0%

Growing demand 5-10% per year

IMPORTED RADIOISOTOPES

- ***^{99}Mo:***
  - ***Argentine: 150 Ci (Saturday-Monday) LEU***
  - ***South Africa: 115 Ci (Tuesday-Sunday) LEU***
  - ***Nordion: 130 Ci (Thursday-Tuesday) HEU***
- ***^{131}I, ^{51}Cr, ^{111}In: Nordion***
- ***^{90}Y: Perkin Elmer***
- ***^{177}Lu: IDB, (Perkin Elmer)***

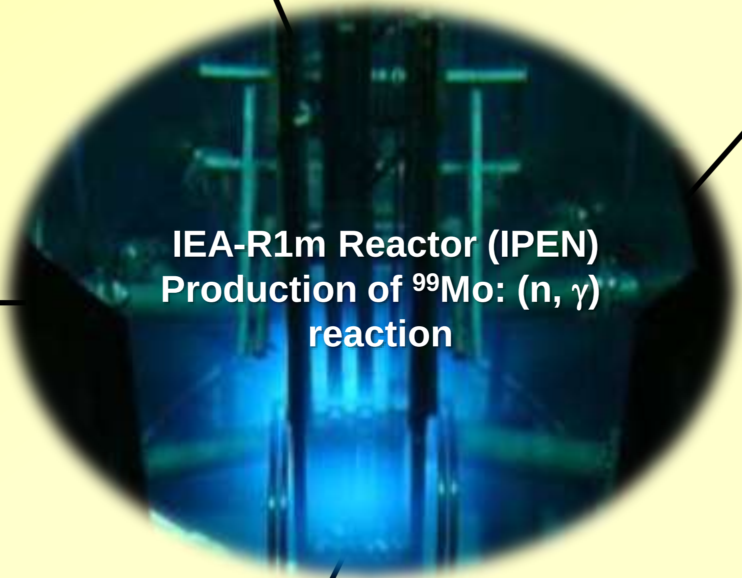
Strategies – ^{99}Mo Crisis

Medium term: To produce Mo-99 through the irradiation of MoO_3.

Natural or enriched ^{98}Mo target

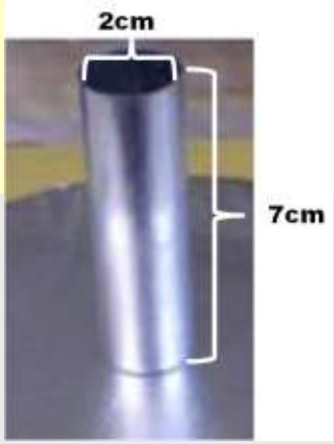
processing and separation of ^{99m}Tc: sell labeled kits or monodoses

Adequation of the Reactor operation



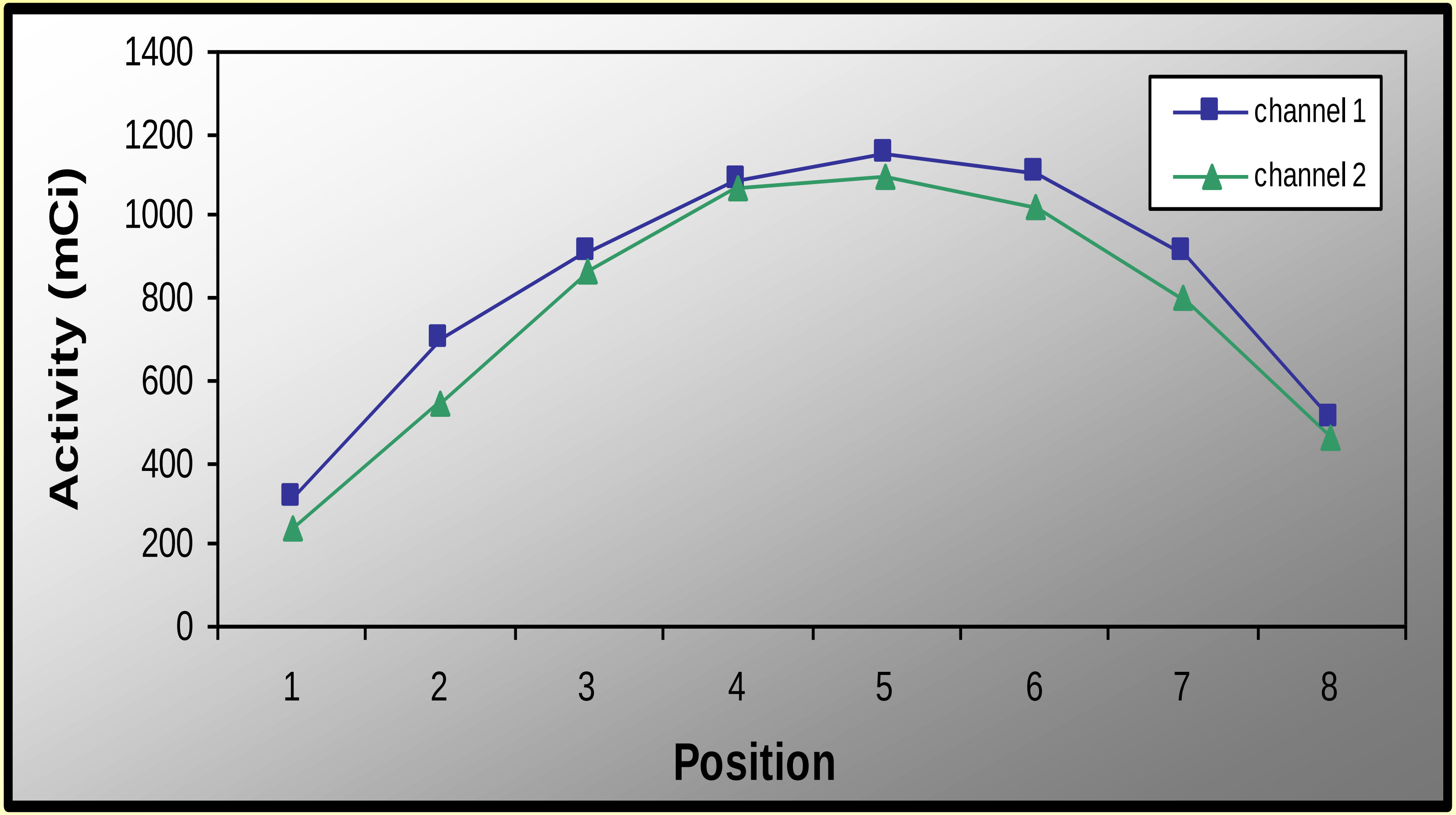
Distribution to clients in SP

Irradiations

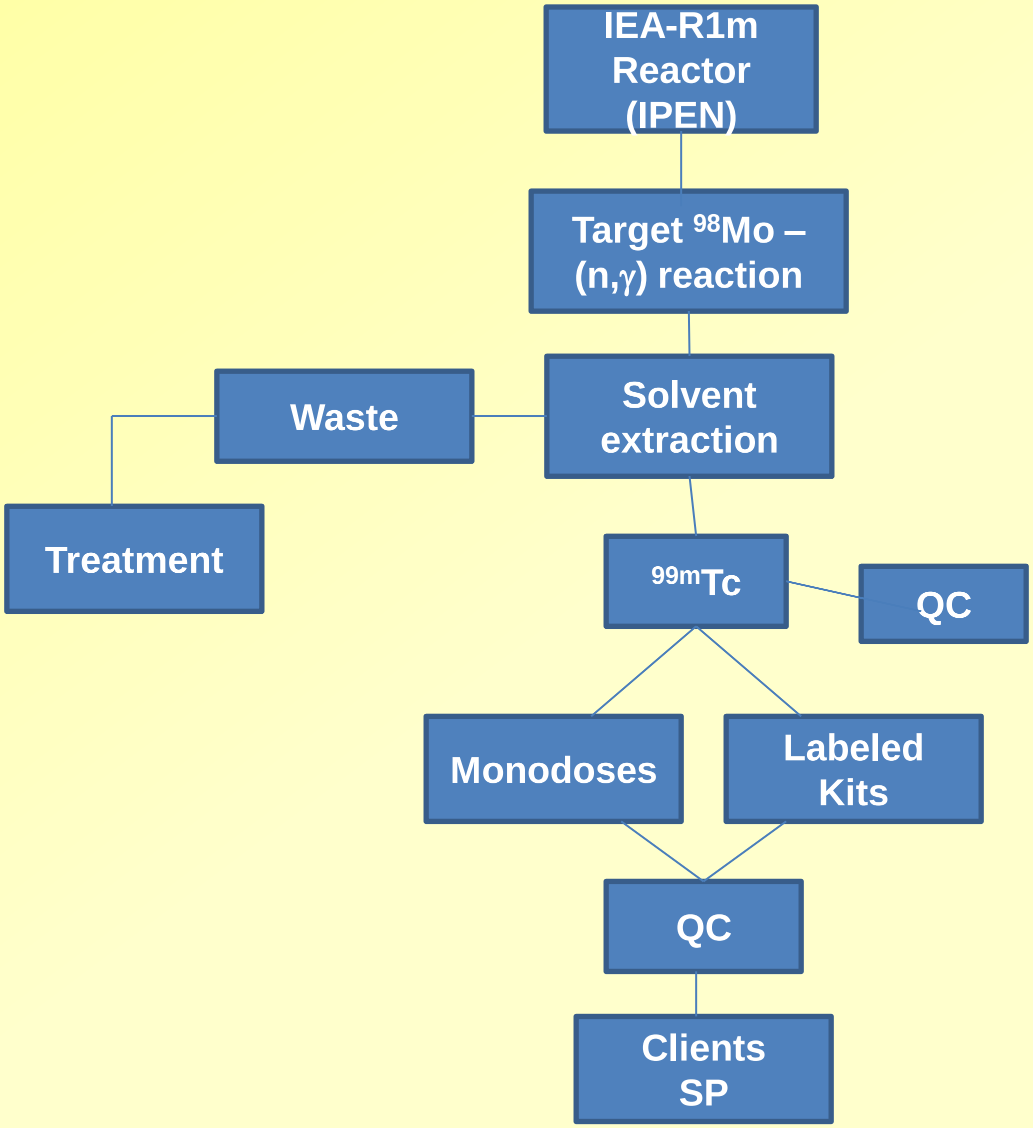


- **4.5 MW**
- **64 hours / week continous operation**
- **Al target holders – with or without quartz or poliethylene tubes**
- **Several irradiation positions**
- **Best positions: Be irradiator (2 channels, 8 positions each)**

Irradiation of MoO_3 inside the Be irradiator



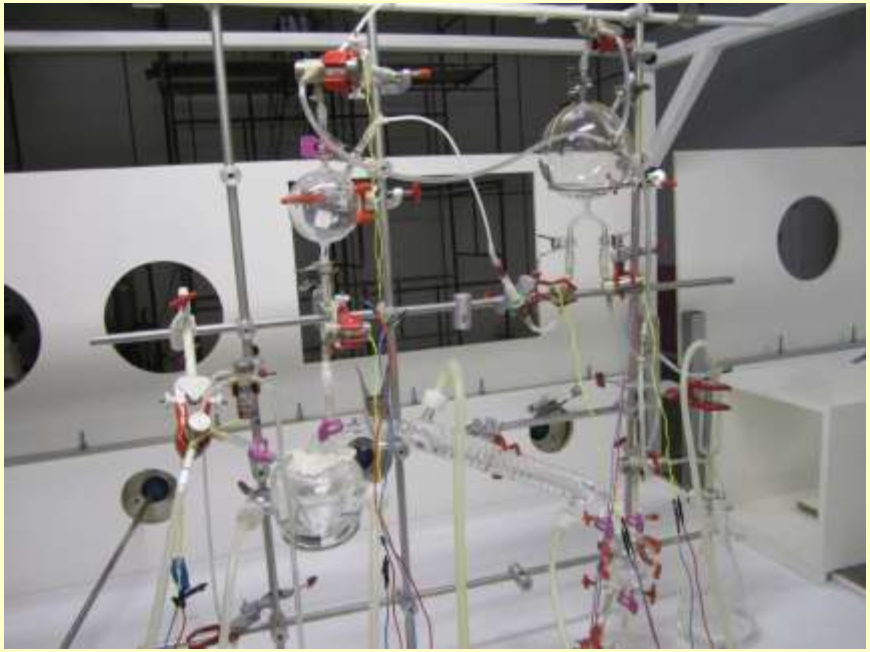
Production method of ^{99}Mo and distribution of ^{99m}Tc



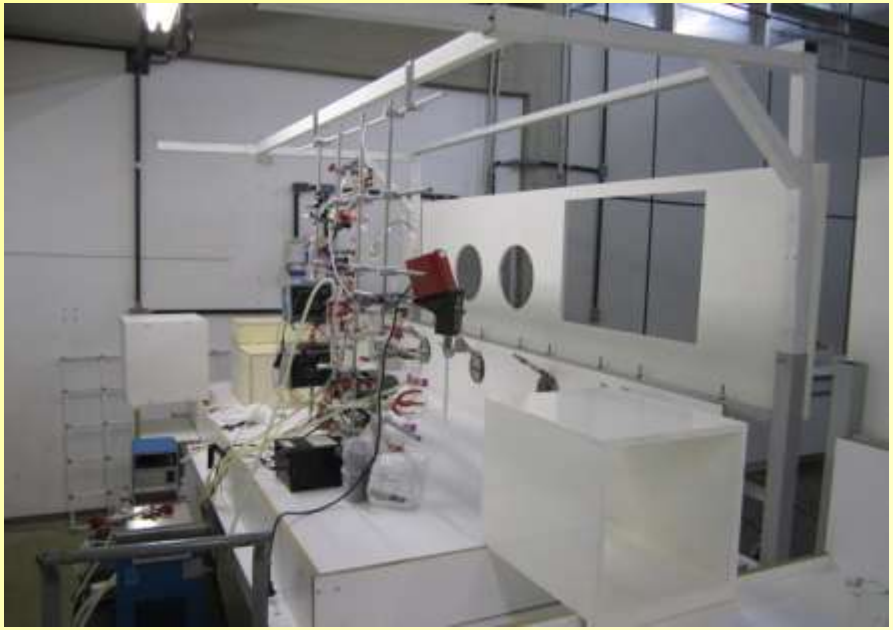
Strategies – ^{99}Mo Crisis

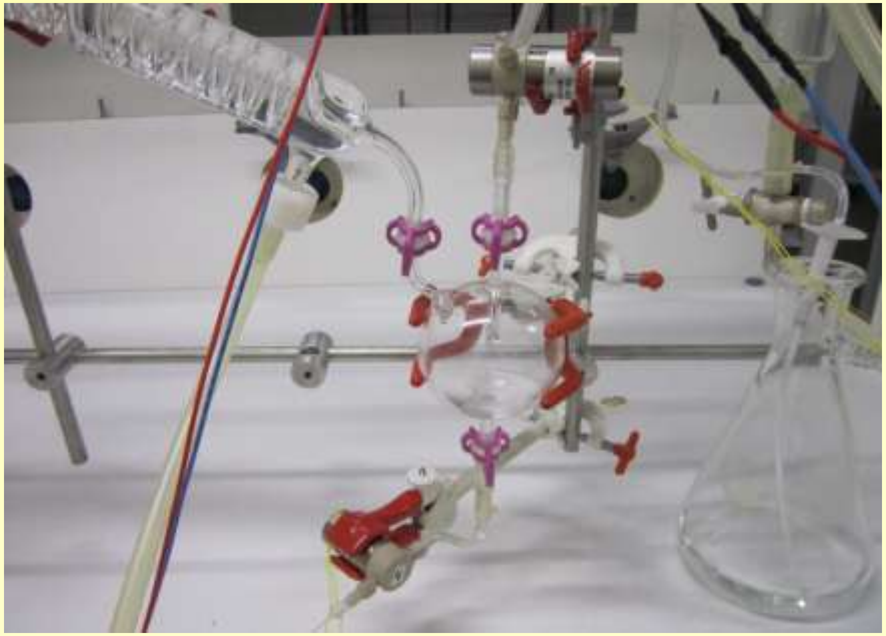
Medium term:

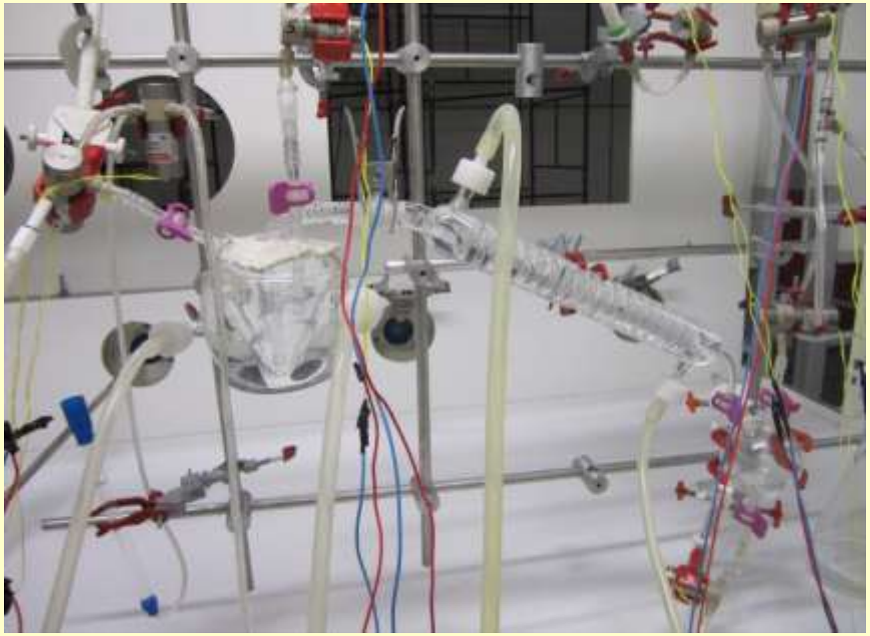
- Solvent extraction with MEK: 80% recovery yield of ^{99m}Tc. QC showed the adequate quality of ^{99m}Tc.
- 04 targets of MoO_3 (50 g each) irradiated for 64 hours finishing Wednesday 24:00 give 13% of Sao Paulo demand (Monday 08:00 – 75 Ci)
- Finishing Friday 24:00 → 50% of Sao Paulo demand
- Assembly of a new hot cell: July 2013



Project Mo-99 extraction







Strategies – ^{99}Mo Crisis

- **Long term project**: New Multipurpose Brazilian Reactor

- 30 MW– Located in Iperó, near São Paulo.

  - Aim – To support the nuclear medicine in Brazil through the radioisotope production for radiopharmaceuticals application that today is strongly dependent on international suppliers: in particular ^{99}Mo.

  - I-131, Lu-177, Y-90, Sm-153, Ho-166, P-32, W-188, Cr-51

  - Fission of LEU targets

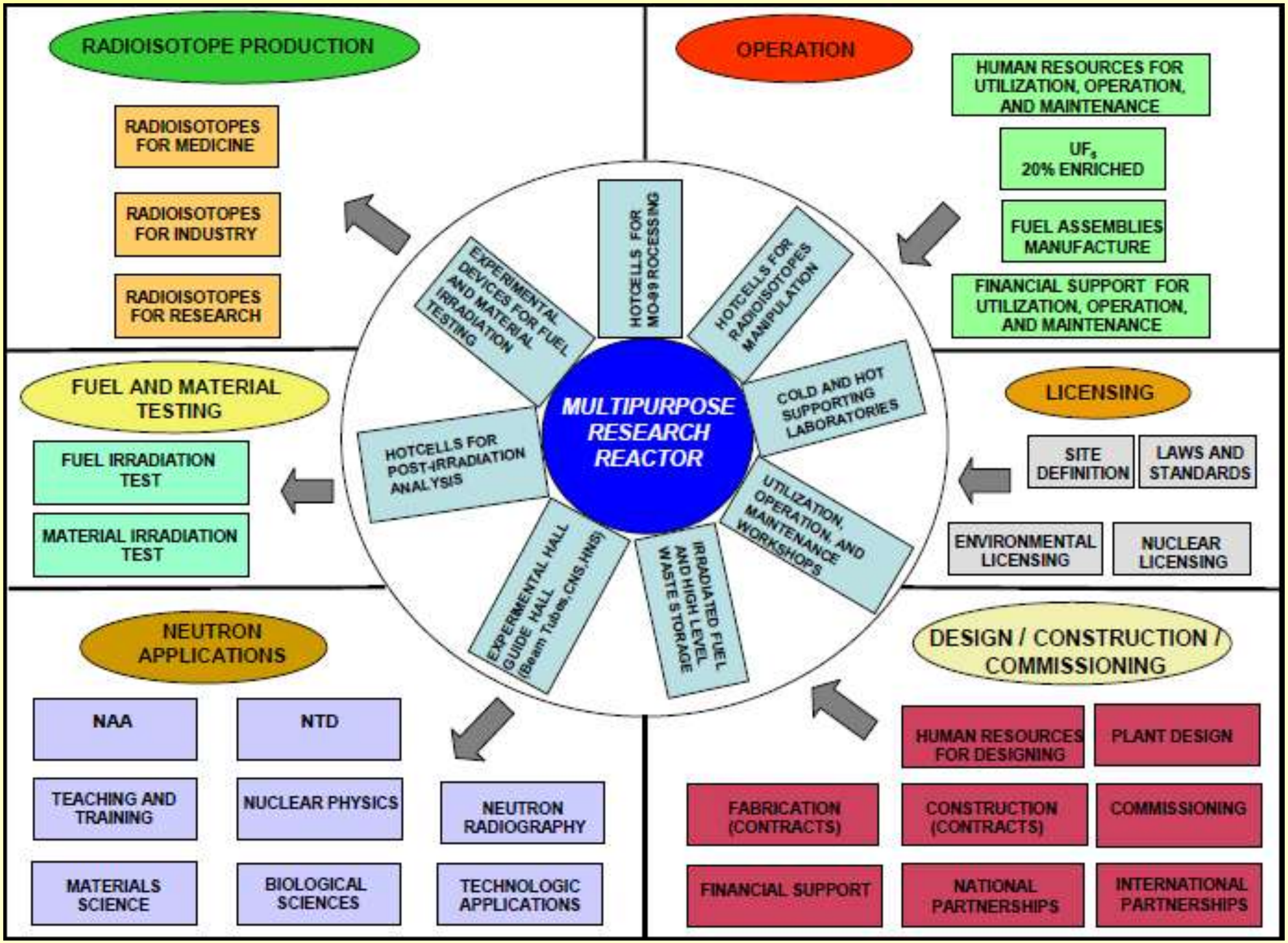
Brazilian Nuclear Program Review

- Electricity produced by nuclear power plants
  - Brazil will continue to use nuclear energy in its electrical power matrix.
- Nuclear Fuel
  - Brazil has a significant uranium ore reserve and domains the fuel cycle technology, including U enrichment.
  - Increase of industrial activities for supplying the nuclear power plants needs.
- Nuclear Techniques Utilization
  - **Increase of nuclear techniques applications and radioisotope utilization in the benefit of the society.**
  - Increase of autonomous technology development

Decision on the New Multipurpose Research Reactor!

- ✓ The Science Technology and Innovation Ministry has decided to support the new research reactor construction in accordance to the Brazilian Nuclear Program
- ✓ The Brazilian Nuclear Energy Commission (CNEN) is in charge of implementing the new research reactor.
- ✓ The State of São Paulo is giving support to the project.
- ✓ This new research reactor shall have neutron fluxes compatible to the multipurpose uses and application needs.

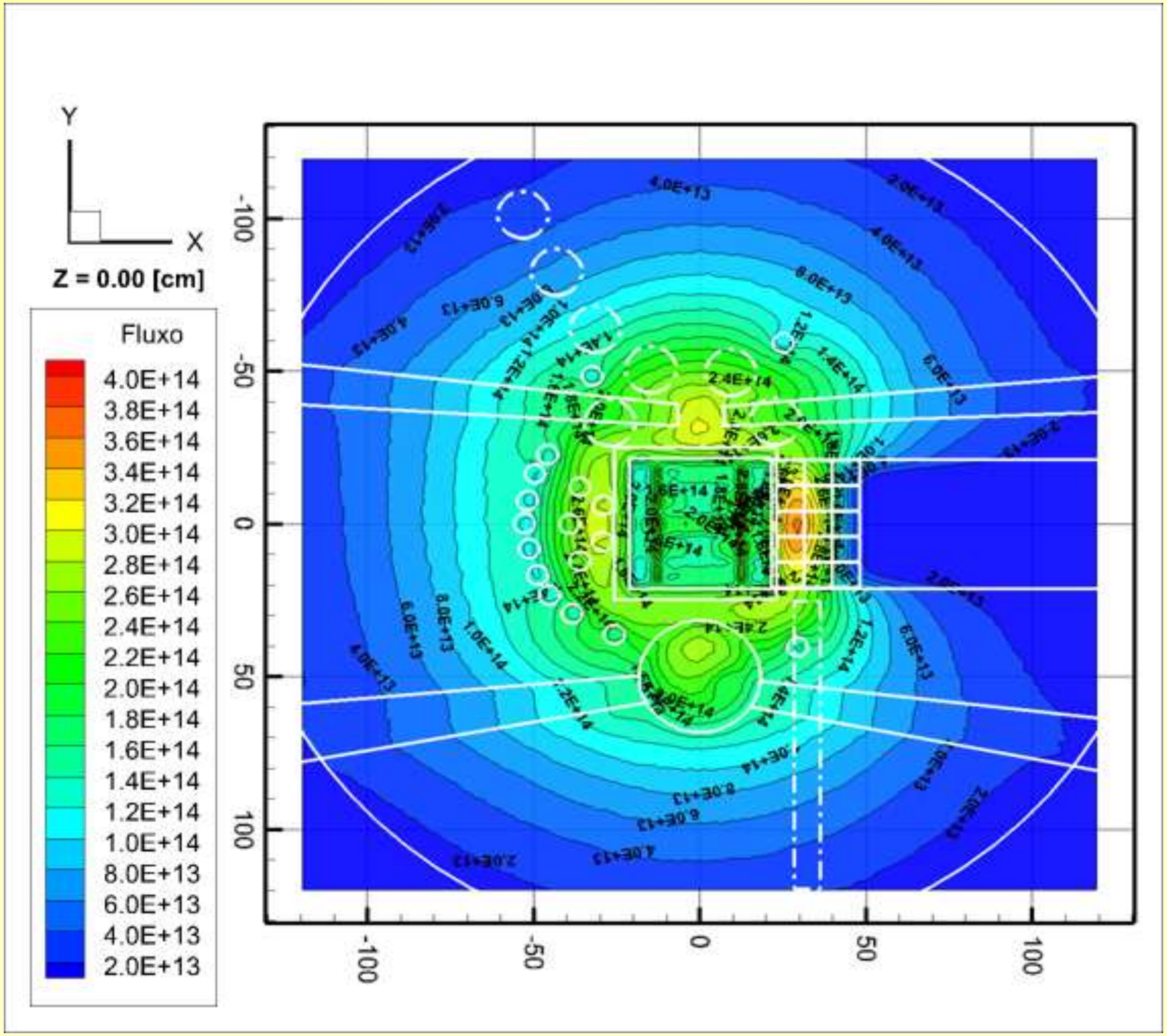
RMB Enterprise



Reactor Characteristics

- Open pool multipurpose research reactor with a primary cooling system through the core – OPAL RR as a reference model for conceptual design.
- The reactor core will be compact, using MTR fuel assembly type, with planar plates, U_3Si_2-Al dispersion fuel with maximum 4,8 gU/cm^3 density and 20 % U-235 enrichment.
- The reactor core will be cooled and moderated by light water, using heavy water as reflector and light water and/or beryllium in one side of the core .
- Neutron flux (thermal and fast) higher than $2x10^{14}$ $n/cm^2.s$.
- Maximum Thermal Power - 30 MW

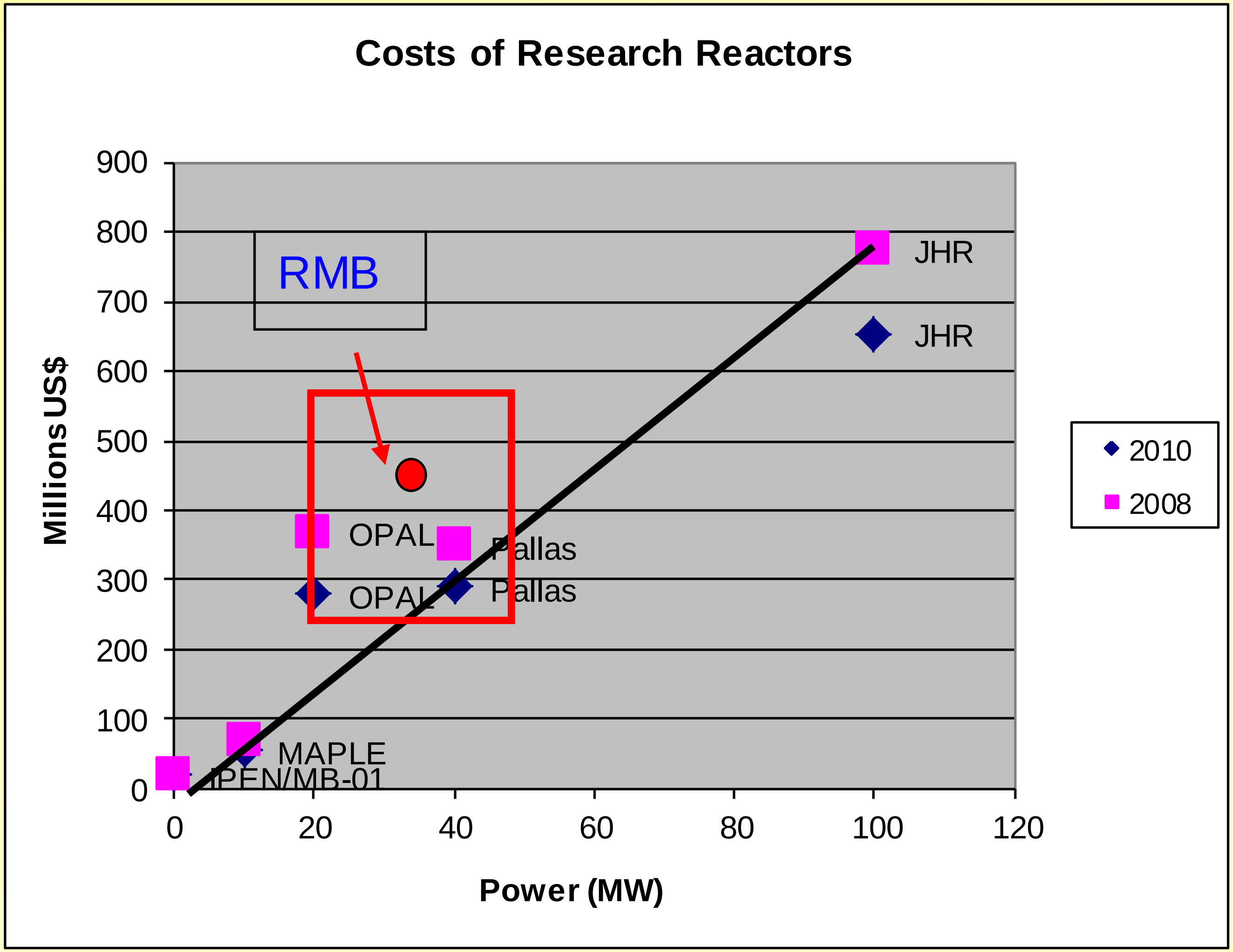
RMB Reactor


Y
X
Z = 0.00 [cm]
Fluxo
4.0E+14
3.8E+14
3.6E+14
3.4E+14
3.2E+14
3.0E+14
2.8E+14
2.6E+14
2.4E+14
2.2E+14
2.0E+14
1.8E+14
1.6E+14
1.4E+14
1.2E+14
1.0E+14
8.0E+13
6.0E+13
4.0E+13
2.0E+13
-100
-50
0
50
100

Project Management

- Project managed by the Research and Development Directorate of the CNEN (DPD-CNEN)
- Scope and preliminary design, licensing process managing and commissioning verification performed by the Research Institutes of CNEN: IPEN, CDTN, IEN, CRCN
- CNEN – CNEA (Argentina) Cooperation Agreement on Reactor Design of RMB and RA-10 based on INVAP / Opal design
- Basic and detailed design, manufacturing, construction, assembling and their management will be carried out by national and international companies.
- Project technically supported by Brazilian Academy
- Project Cost estimation of US$ 500 million (R$ 1000 million)
- Project time span of at least 6 years after the first contract signature and availability of funds. (2013)

Costs


Costs of Research Reactors
Millions US$
Power (MW)
900
800
700
600
500
400
300
200
100
0
0
20
40
60
80
100
120
RMB
JHR
JHR
OPAL
OPAL
Pallas
Pallas
MAPLE
IPEN/MB-01
2010
2008

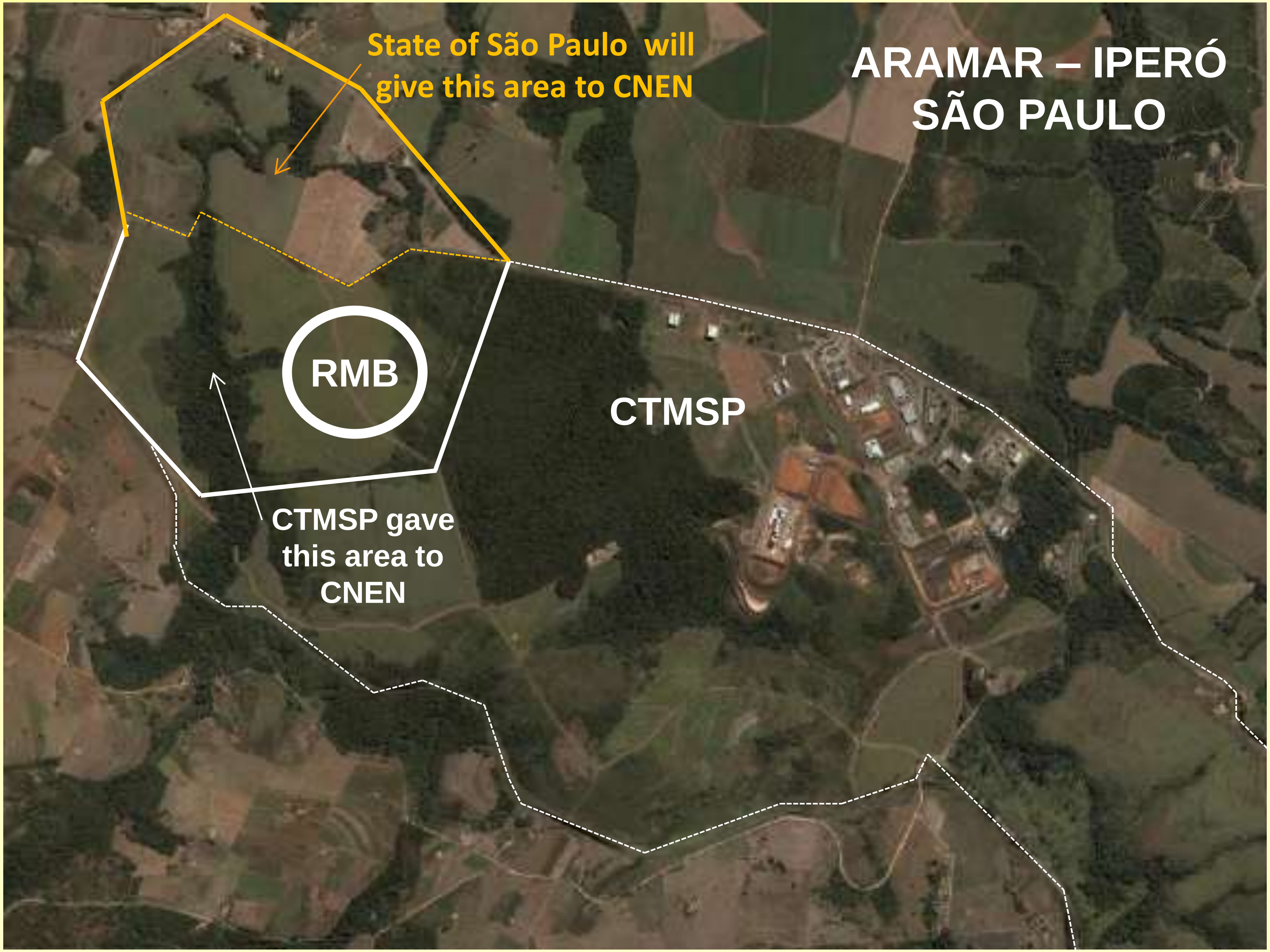
Project Status

- CNEN Institutes technicians are developing the conceptual engineering design of the reactor systems and main facilities.
- R$ 30 million allocated by the MCTI (FNDCT- FINEP) to contract the basic engineering design of systems, buildings and infrastructure of the RMB (except basic engineering design of pure nuclear systems and components). Work contract under development. Brazilian company INTERTECHNE
- Brazil-Argentina Agreement (CNEN-CNEA) for common basic engineering design of the RMB and RA-10 (pure nuclear part). OPAL reactor in Australia as a reference. (project of the Argentine company INVAP). R$ 20 million allocated by the MCTI (FNDCT- FINEP) in addition to the first application.
- Environmental licensing process started. Term of Reference for EIA/RIMA approved by IBAMA. Work contract under development. Brazilian Company MRS.
- Nuclear licensing started. Term of Reference for Local Licensing (first License) is under analysis by DRS/CNEN.

Site

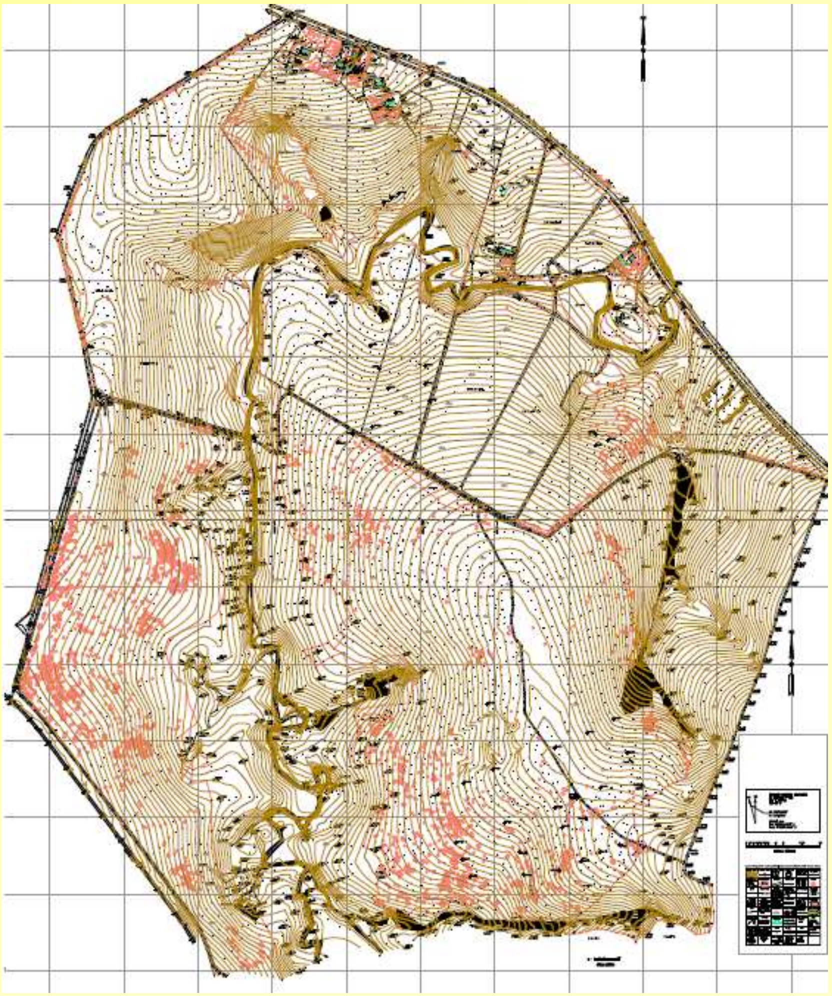
Iperó
State of São Paulo

Site


State of São Paulo will give this area to CNEN
ARAMAR – IPERÓ
SÃO PAULO
RMB
CTMSP
CTMSP gave this area to CNEN

Site works

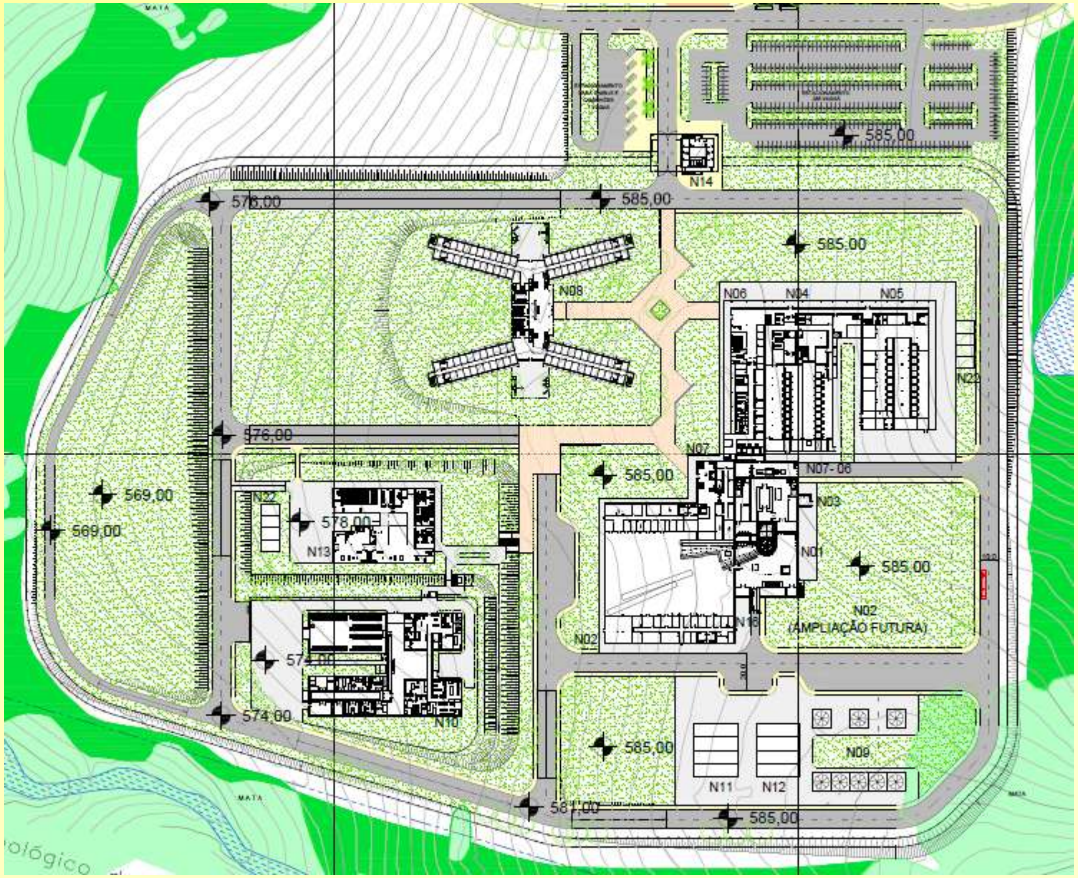
Topography survey



Ground Survey

Meteorological tower

RMB R&P Buildings

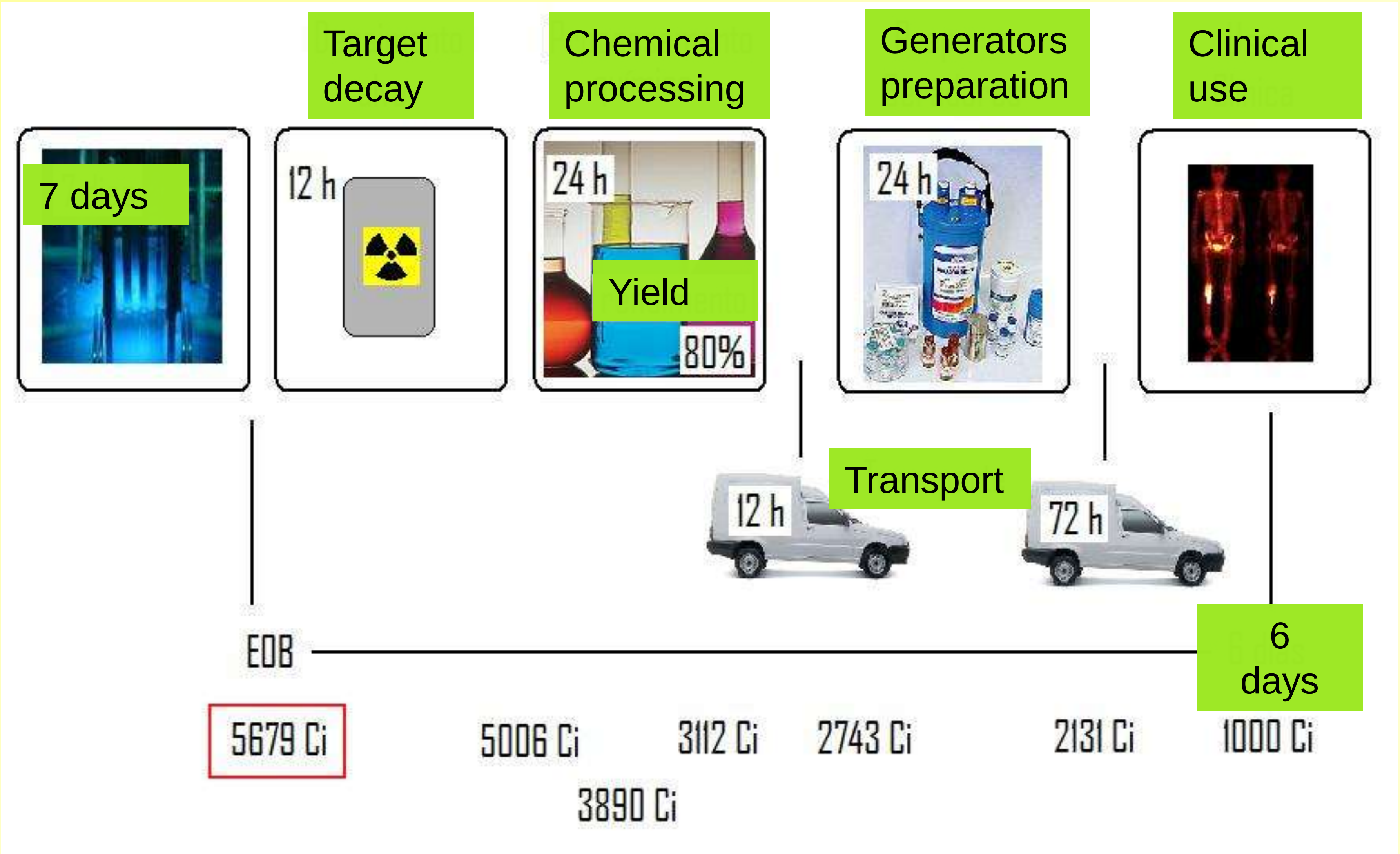


- **N01 – Reactor**
- **N02 – Neutron Beam Laboratory**
- **N03 – Spent Fuel and Material Handling**
- **N04 – Radioisotope Processing**
- **N05 – Post-Irradiation Laboratory**
- **N06 – Radiochemistry Laboratory**
- **N07 – Operation Office**
- **N08 – Researchers Offices**
- **N09 – Cooling Towers**
- **N10 – Waste Treatment and Storage**
- **N11,N12 – Electrical Cabins**
- **N13 – Workshop**
- **N14 – Access Control**

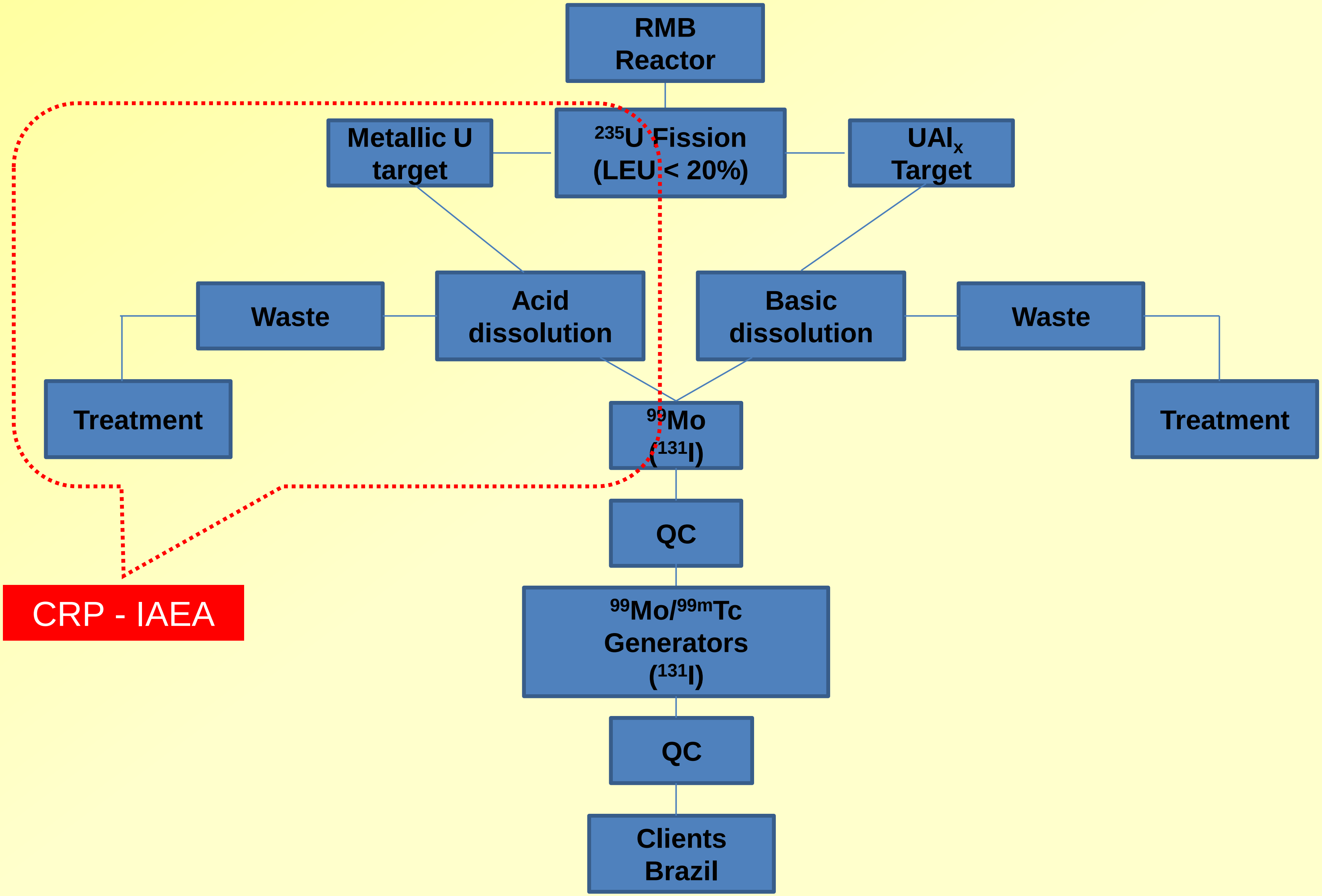
15100 – Radioisotope Production

- Project: Production of Mo-99 (and I-131)
  - Reaction:
    - ^{235}U fission (low enriched uranium – LEU)
- Groups:
  - Targets (CCN)
  - Neutronics (CEN)
  - Chemical separation (CQMA, CCCH, DIRF)
  - Waste managment (GRR)

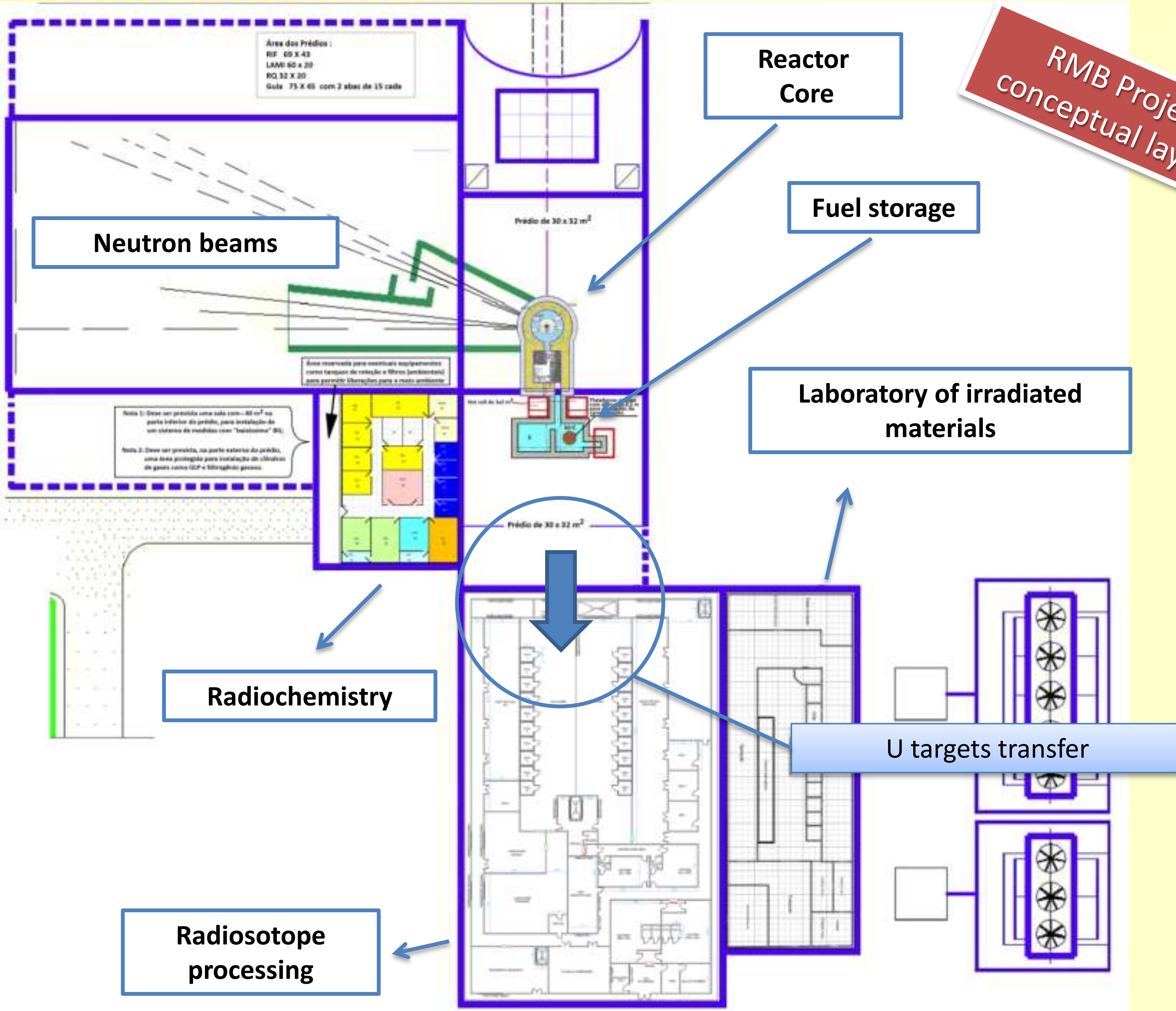
Projected total activity of Mo-99



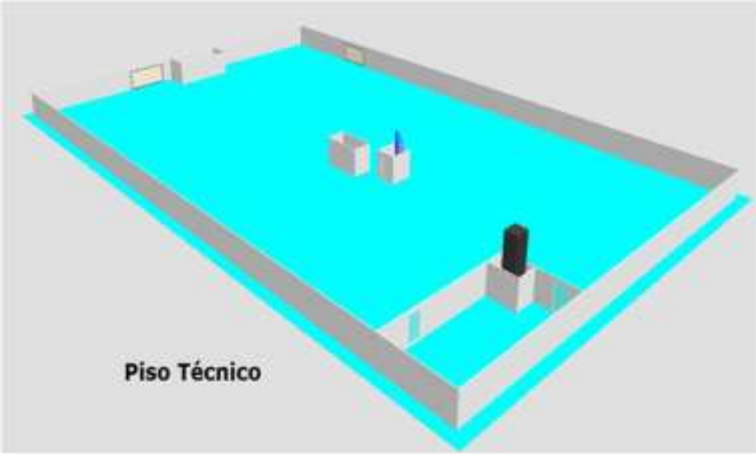
Production methods of ^{99}Mo and distribution of ^{99m}Tc

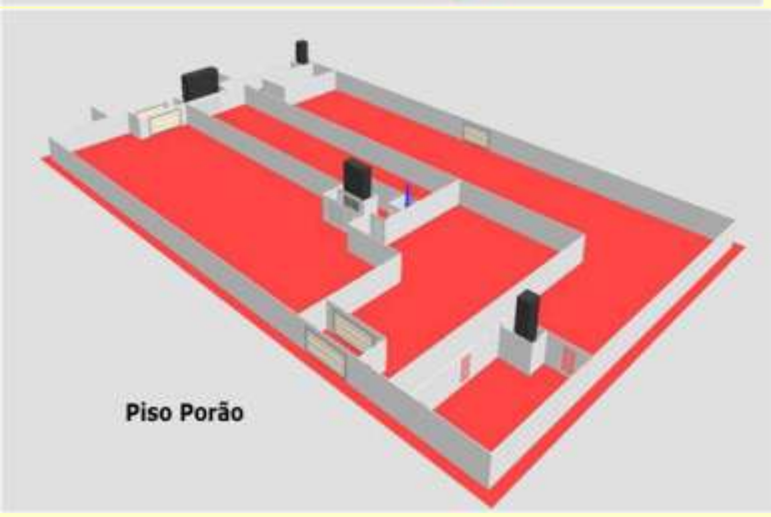


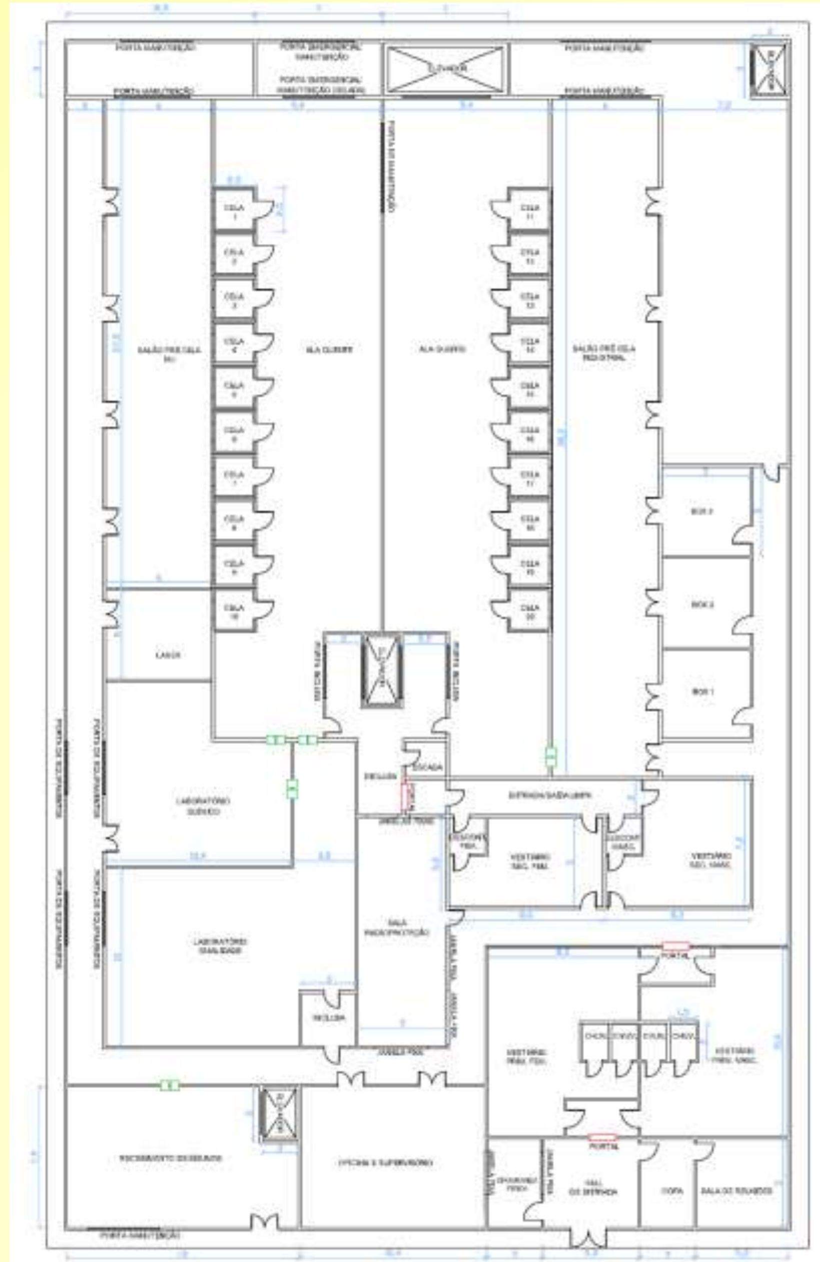
RMB Project: conceptual layout



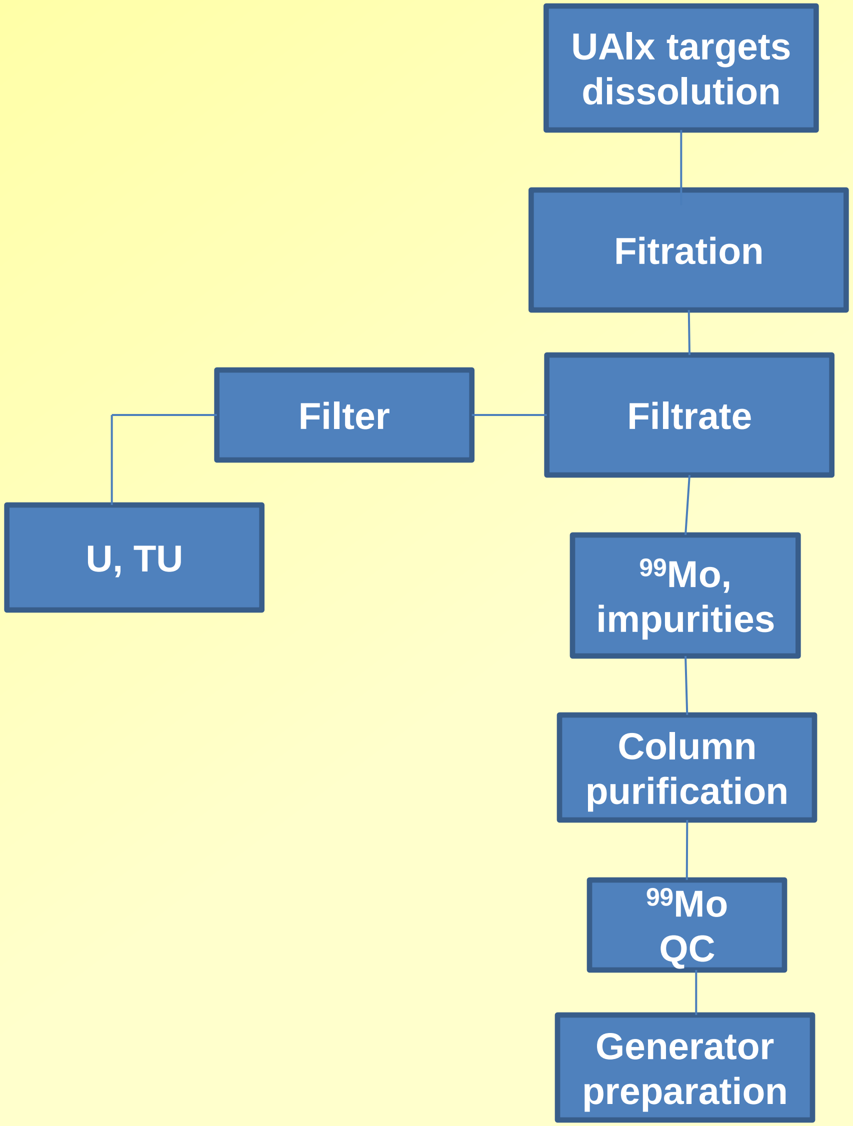
Conceptual Project







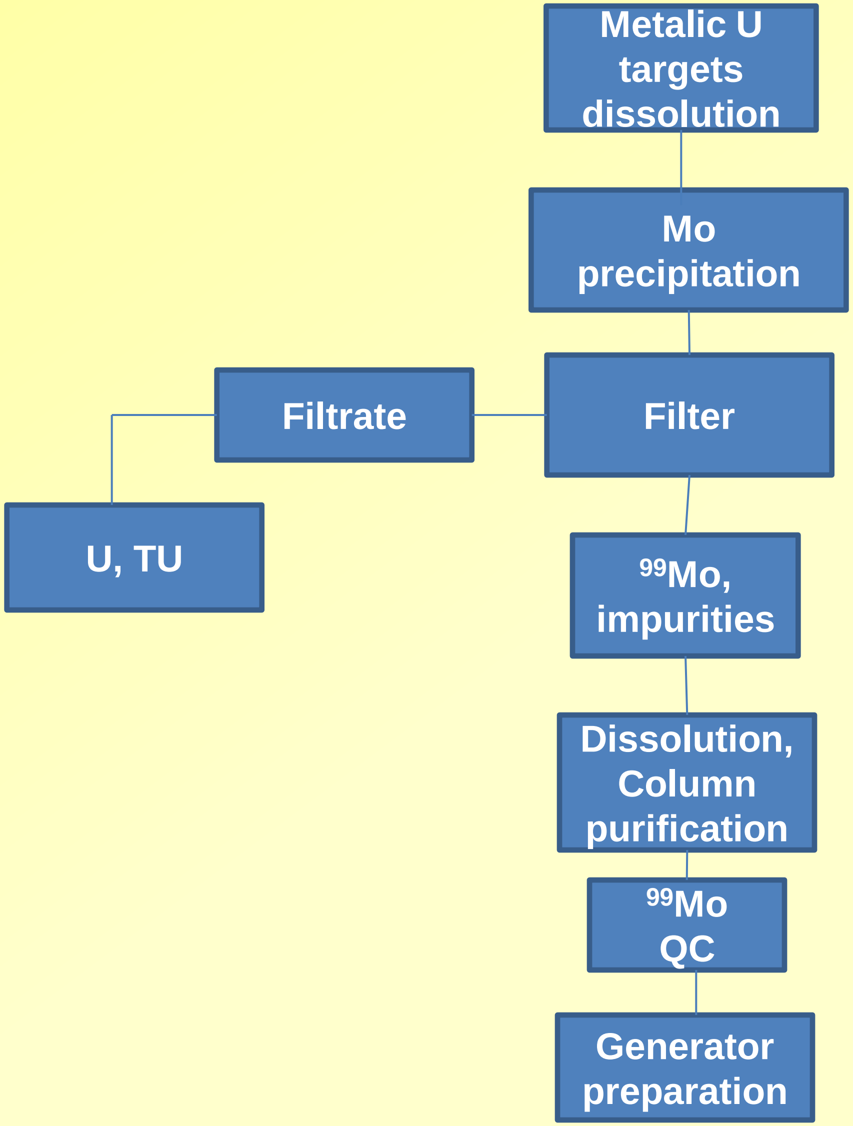
Alkaline dissolution



Alkaline dissolution

- First choice
- Project with IAEA and Argentina: 90´s
- Technology of producing UAlx targets
- New dissolution aproaches: use of nitrate and nitrite
- Column purification: anion exchange resin, chellex resin, alumina
- Waste management

CRP on Mo-99-Acid dissolution



Acid dissolution

- Dissolution of U foils
  - Crude foils of U were provided by the targetry group with a thickness of few mm and mass of 13 g
  - Dissolution solution used for few experiments with Mo-99 and I-131
- Mo precipitation with α-benzoinoxime (α-Bz) and phenanthroline (new)
- Column purification: Actvated charcoal (AC), AC with Ag, ZrO_2
- New: TiO_2
- Cold and tracer experiments: Mo-99, I-131, Te-123/121, Zr-95, Ru-103
- Waste management
- Major issue: LEU foil preparation

Conclusions

- **Short term strategies:** working well

- **Medium term strategies:** Tc-99m production starting in 2013

- **Long term strategies:** new project, new reactor schedule 2019-2020

Obrigado
Thank you
Gracias

jaosso@ipen.br

cnen ipen

Ministério da
Ciência, Tecnologia
e Inovação

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BRASIL
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