The current status and challenge for radioisotopes production by JRR-3

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Japan Atomic Energy Agency（JAEA）
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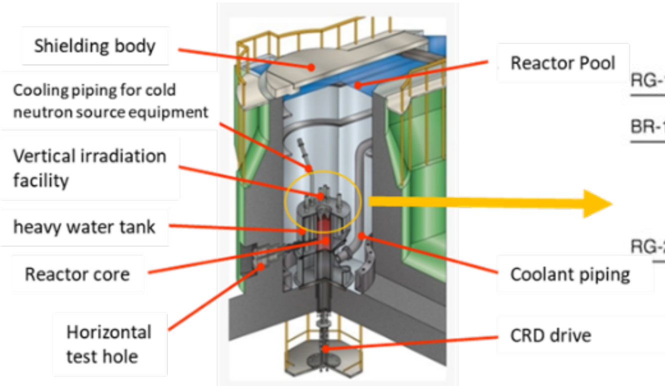
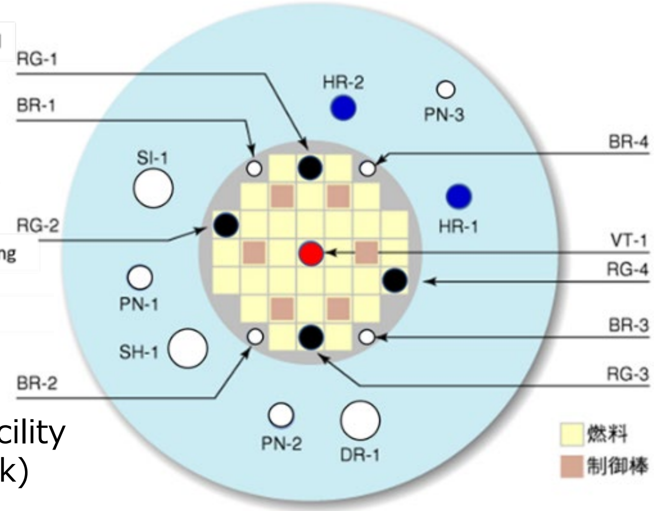
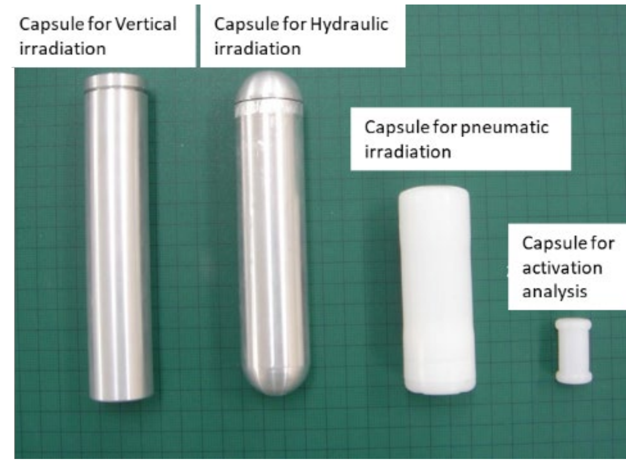
About the research reactor JRR-3

JRR-3 specifications	
Purpose	Beam experiments, Irradiation experiments of fuels and materials etc.
Reactor type	Light water moderated and cooled, pool type reactor that uses low-enriched uranium
Maximum thermal power	20 MW
Reactor core geometry	Cylindrical (Diameter:60 cm) (Height:75 cm)
Operation	26 days continuous operation/cycle, 6~7 cycle/year

Overview of irradiation facilities in JRR-3







● Hydraulic Irradiation facility (in Heavy water tank)

● ● Vertical irradiation facility (in reactor core)

Facility name		Irradiation time	Φ_{th} (n/cm²/s)	Purposes
Hydraulic irradiation facility	**HR-1** **HR-2**	10 min ～ 1 Cycle	9.5×10^{13}	**RI Prodcution** Activation analysis
Pneumatic irradiation facility	PN-1 PN-2 PN-3	5second ～ 20min	5.0×10^{13}	Activation analysis
Vertical irradiation facility	**VT** **RG-1～4** BR-1～4	1Cycle～	2.0～3.0×10^{14}	Irradiation for material **RI Production**
Rotating irradiation facility	DR-1	1Cycle～	3.0×10^{13}	Irradiation for material

VT/RG have about twice the flux of thermal neutrons and about 10 times the flux of epithermal neutrons compared to HR.

Irradiated capsules in VT/RG can only be loaded and unloaded after the reactor is shut down.

History of radioisotopes production in JAEA

The following nuclides had been manufactured and sold with the research reactors (JRR-3,JRR-4,JMTR) until around 2000.

- Unsealed Source
  - ^{24}Na,^{42}K,^{56}Mn,^{64}Cu,^{72}Ga,^{82}Br,^{90}Y,^{99}Mo, ^{140}La,^{153}Sm,^{177}Lu,^{186}Re,^{198}Au etc…
- Sealed Sources
  - ^{192}Ir,^{198}Au,^{153}Gd (for medical use)
  - ^{192}Ir,^{169}Yb, ^{60}Co (for industrial use) etc…

JRR-3

JRR-4

JMTR

However, JAEA discontinued the production and distribution of radioisotope sources, except for shot-lived radioisotopes for research use.

History of radioisotopes production at JAEA

These reactors used for radioisotope production were shut down since 2011 due to the need to comply with new regulatory standards for research reactors introduced after the Tohoku earthquake.

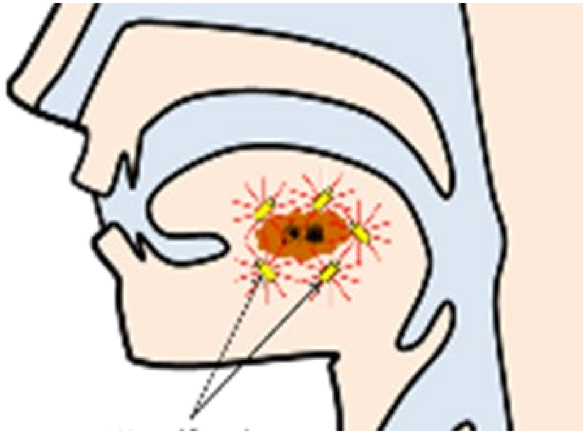
	JRR-3	JRR-4	JMTR
First criticality	1962.9	1965.1	1968.3
Reactor shutdown	2010.12～	2010.12～	2006～
Decision on decommissioning	―	2013.9	2017.4

But JRR-3 was restarted in 2022.2 after taking measures related to novelty standards.

As part of that, the radioisotope production were resumed

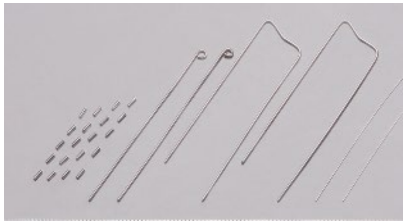
1. The production of sealed sources (^{198}Au, ^{192}Ir)
2. Research and Development of RI Production(^{99}Mo, ^{177}Lu)

The production of sealed sources (^{198}Au, ^{192}Ir)



Brachytherapy image using ^{198}Au seeds

Sealed sources(^{198}Au)



Sealed sources(^{192}Ir)

At the JRR-3, we irradiate ^{198}Au and ^{192}Ir for use in brachytherapy .

Brachytherapy is commonly used as an effective treatment for cervical, prostate, breast, and skin cancer and can also be used to treat tumors.

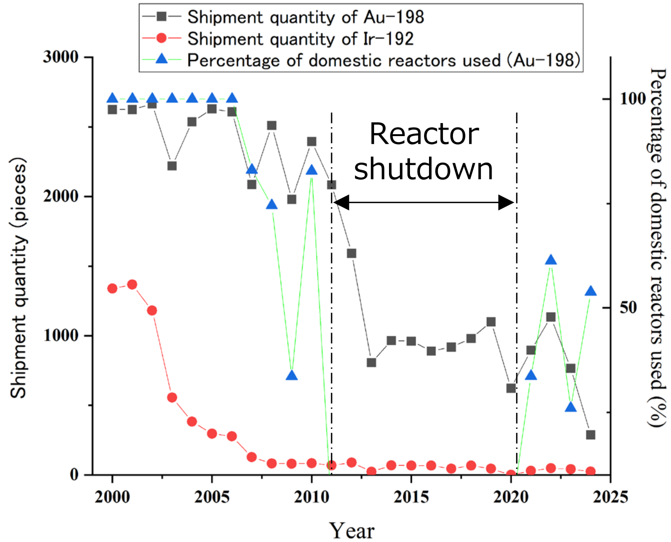


Fig.1 Shipment quantity of sealed sources for brachytherapy

After 2011,domestic production was discontinued and replaced by overseas producing.

After restart of JRR-3, ^{198}Au 30~60% ,^{192}Ir 100%
(Domestic production rate)

Research and Development of RI Production （^{99}Mo)

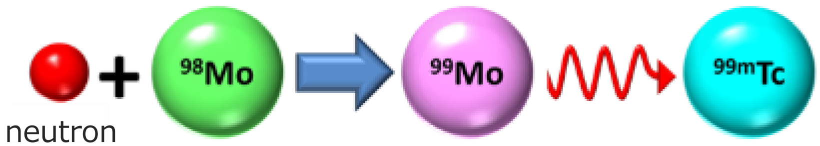
^{99}Mo is one of the most used RI for medical use. However,
<u>it is dependent on overseas imports, and there is concern that international conditions and other factors may affect its distribution.</u>

Therefore, Japan's policy is to try to produce some of it domestically.
As part of that, <u>JAEA is considering the production of ^{99}Mo by the neutron capture reaction with JRR-3.</u>

Comparison of manufacturing methods

	Fission	(n,γ)
Using U	Yes	No
Pu buildup	Yes	No
Proliferation resistance	Low	High
Specific activity	High	Low

Neutron Capture Reaction that Production ^{99}Mo



【Production target】

Specific activity : 1 Ci/g.Mo ~

^{99}Mo activity : 1,000 Ci/week ~

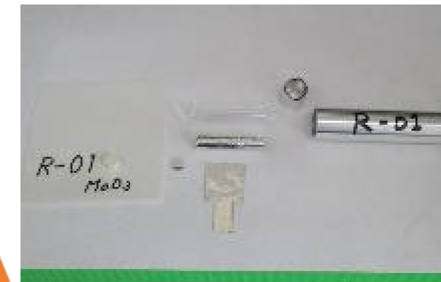
Frequency : weekly or biweekly

Production process of sample for irradiation (^{99}Mo)

MoO_3 powder
(Natural ratio)

Physical pressure
and
Sintered at 750℃

Pellet size:φ10×5 mm
Mass : 1.2 g
Theoretical density:70%
Solubility: Dissolved in NaOH



Put pellet into the capsules

Capsule welding and helium gas leak testing

Evaluation of the amount of Mo-99 produced

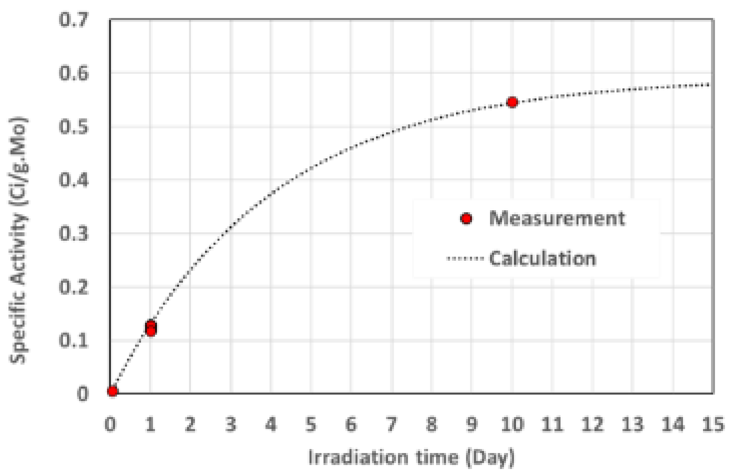


Fig.1 Evaluation of the amount of Mo-99 produced with HR

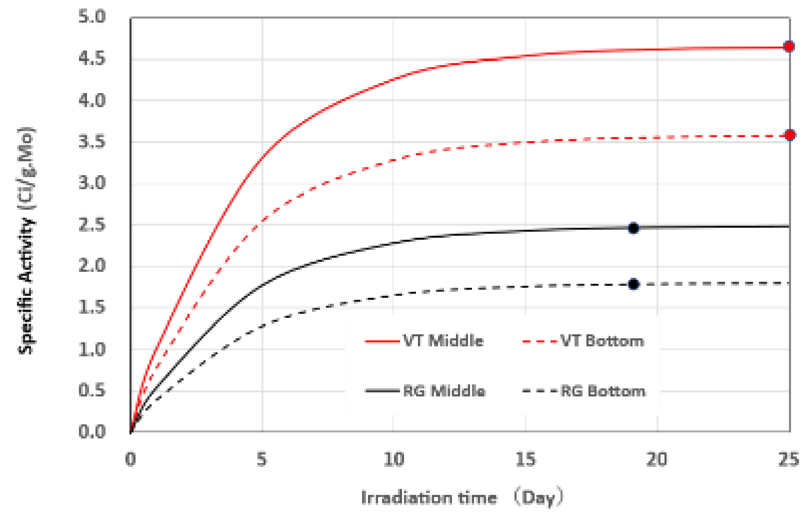


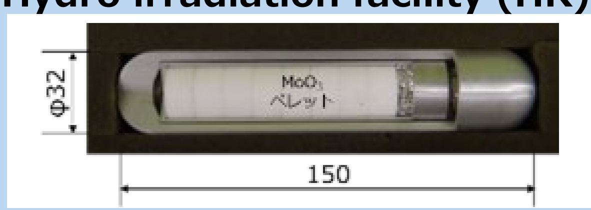
Fig.2 Evaluation of the amount of Mo-99 produced with VT/RG

Specific radioactivity :

about 0.5 Ci/g Mo
(irradiated for 7 days in HR)

3.5～4.6 Ci/g Mo (irradiated for 1Cycle in VT)
1.8～2.5 Ci/g Mo (irradiated for 1Cycle in RG)

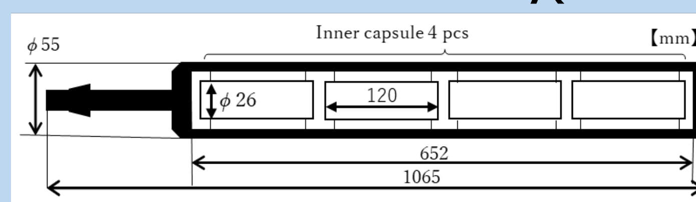
Hydro irradiation facility (HR)



MoO_3 150g (per inner capsule) x 3
irradiated with HR for 7 cycle

About 135 Ci (5 TBq)

Vertical irradiation facility(VT･RG)



MoO_3 230g (per inner capsule) x 4
irradiated with RG for 1 cycle (26 day)

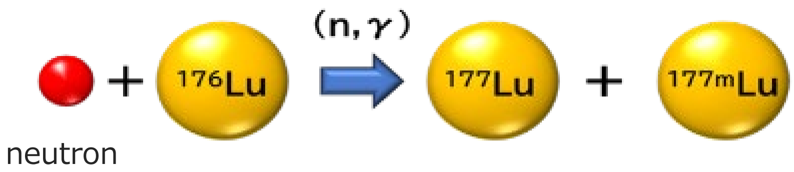
About 1300 Ci (48 TBq)

Research and Development of RI Production （^{177}Lu）

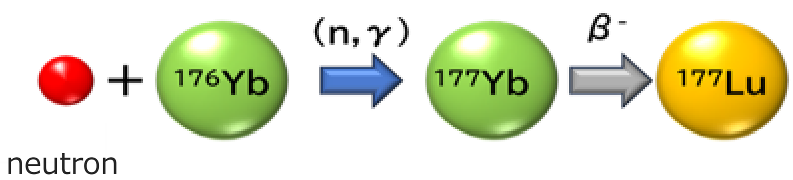
^{177}Lu is one of the RI for medical use. However, it is dependent on overseas imports, and there is concern that.

Lu-177 Production Method with the reactor

・Direct Production Route



・Indirect Production Route



	Direct Production Route	Indirect Production Route
Target	$^{176}Lu_2O_3$	$^{176}Yb_2O_3$
Catalytic support	With	Without
^{177m}Lu	With	Without
Production	Many	Few
Separation process	Unnecessary	Necessary

JAEA conducted test production of Lu-177 using JRR-3 by means of the both these methods and evaluated the amount of Lu-177 produced.

Production process of sample for irradiation (^{177}Lu)

$^{176}Lu_2O_3$ powder
(64.3%,enriched)
or

$^{176}Yb_2O_3$ powder
(99.9%,enriched)
ISOFLEX USA

(If the irradiation target weight is 0.1mg)
Dissolve in HNO_3aq and Evaporate to dryness in a quartz ampoule

(If the irradiation target weight is 5mg)
Place powder sample in a quartz ampoule

Quartz ampoule
(Atmospherically sealed)
Mass：Lu_2O_3: 0.1mg
Yb_2O_3:0.1mg /5mg

Put pellet into the capsules

Capsule welding and Ethylene glycol testing

Evaluation of the amount of Lu-177 produced by direct Route

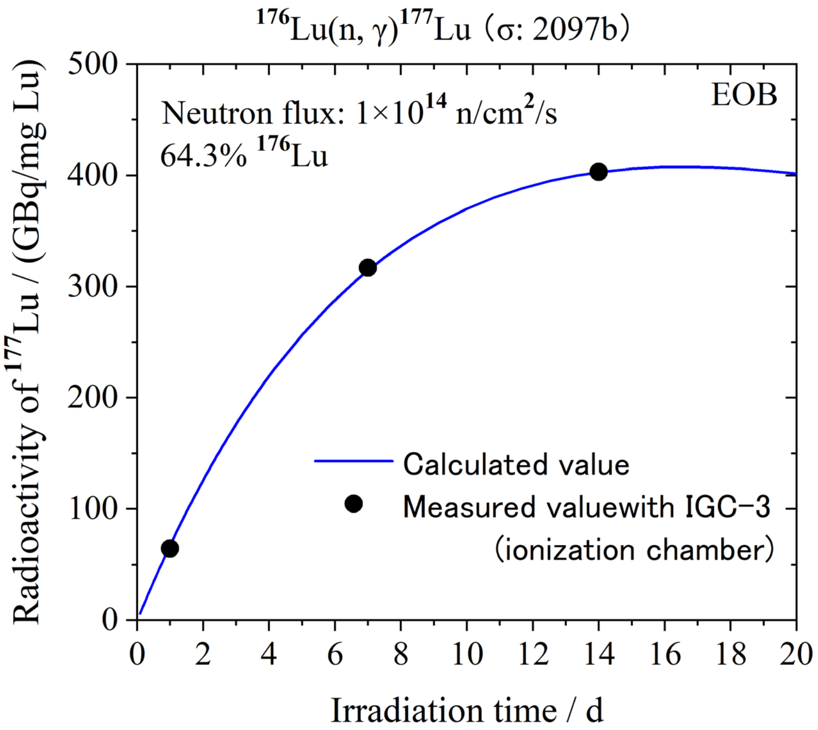


Fig.4 Evaluation of the amount of Lu-177 produced by the direct method with HR-1

Specific radioactivity :
about 400GBq/mg Lu
(irradiated for 14 days in HR-1)

⇒Irradiation of 1 g of Lu for 14 days yields ^{177}Lu equivalent to about 7,000 persons.

(Assume 1 week for manufacturing, pharmaceuticals, and dosing, Calculating one dose of Lutathera® as four doses of 7.4 GBq for one person.)

Although lower than the specific activity of the overseas ^{177}Lu product.
But it was confirmed that JRR-3 could produce for nonclinical testing purposes.

Evaluation of the amount of Lu-177 produced by indirect Route

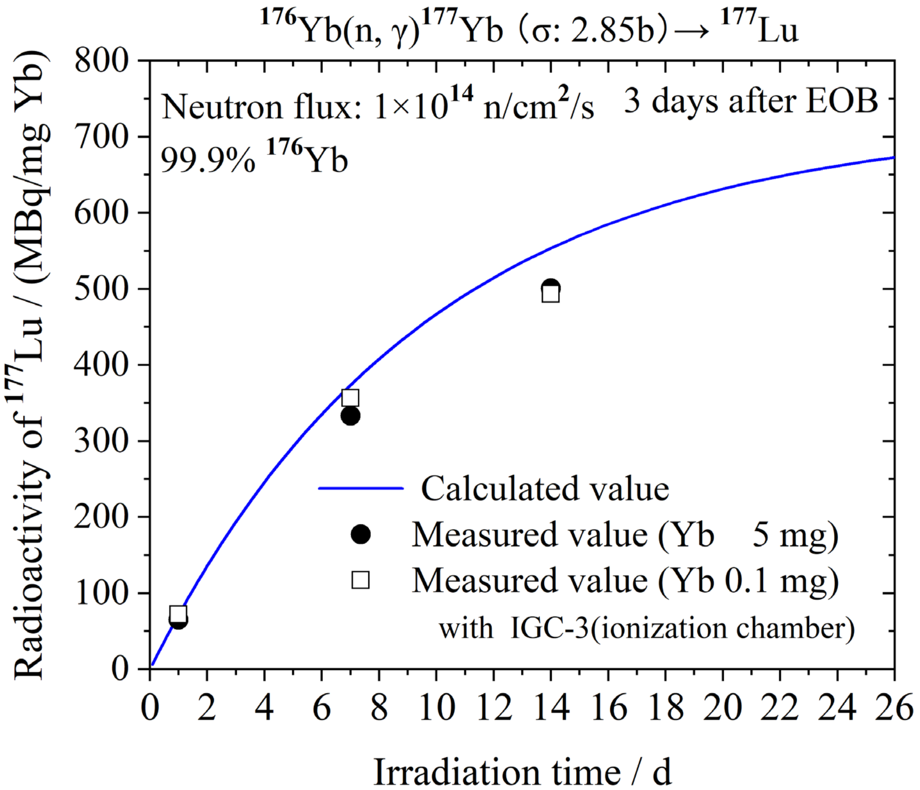


Fig.5 Evaluation of the amount of Lu-177 produced by the indirect method with HR-1

Specific radioactivity :

about 500MBq/mg Yb

(irradiated for 14 days in HR-1)

⇒Irradiation of several grams of Yb could generally meet the demand.

The current JRR-3 permit does not allow for the irradiation of the samples containing RI.

⇒ It is difficult to supply the product from a cost perspective.

In Conclusion and Future prospects

・JAEA had previously worked on RI production using research reactors. However, concerns about the shutdown of research reactors in Japan prevented its implementation. With the resumption of operations at JRR-3 in 2022, RI production for medical and industrial use has been restarted.

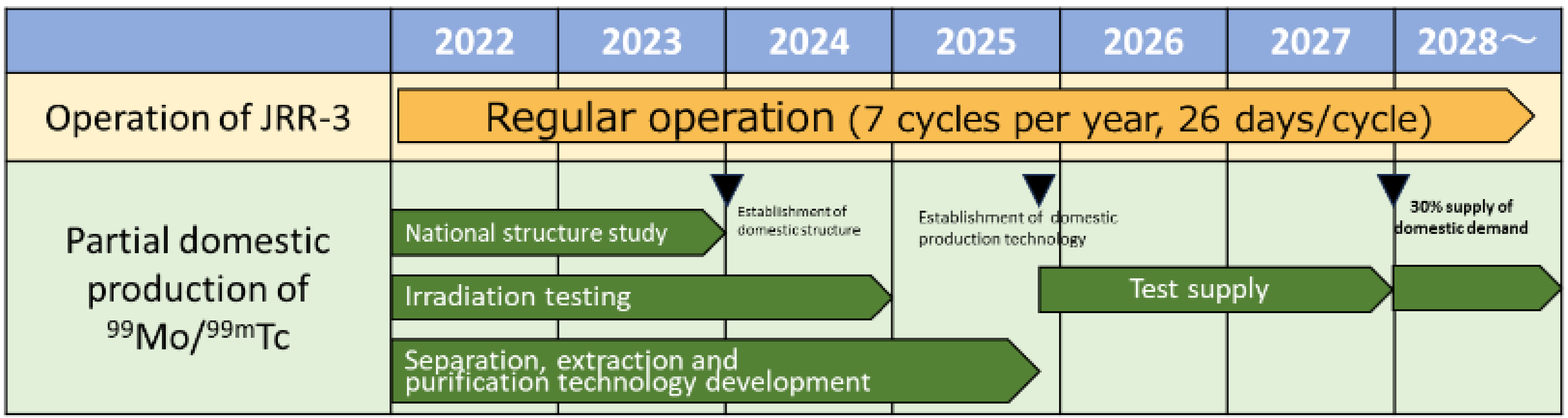
・ In addition, research and development of RI production are being conducted.

・Regardless of these, we plan to proceed with radioisotope production and separation development to meet user needs.

Thank you very much for your kind attention.

JAEA's commitment to the Action Plan

" Action Plan for Promotion of Production and Utilization of Radioisotopes for Medical Use" (decided by Japan Atomic Energy Commission in May 2022) was formulated to realize domestic production of radioisotopes for medical use, etc.



【Activities as JAEA: Medium- to long-term plan for FY2022 - 2028】

・JAEA will strengthen efforts to foster innovation through collaborative partnerships with industry, academia, and government.

・To secure a stable domestic supply of Mo-99 for nuclear medicine diagnostic reagents, JAEA will promote the development and social implementation of irradiation production technology, utilizing the capabilities of JRR-3."