2.12 Current utilization of Research Reactor on Radioisotopes production in China

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This paper describes the main technical parameters of the four research reactors and their current utilization status in radioisotope manufacture and labelling compounds preparation. The radioisotopes, such as Co-60 sealed source, Ir-192 sealed source, γ- knife source, I-131, I-125, Sm-153, P-32 series products, In-113m generator, Tc-99m gel generator, Re-188 gel generator, C-14, Ba-131, Sr-89, ^{90}Y, etc., and their labeling compounds prepared from the reactor produced radionuclides, such as I-131-MIBG, I-131-Hippure, I-131-capsul, Sm-153-EDTMP, Re-186-HEDP, Re-186-HA, C-14-urea, and radioimmunoassay kits etc. are presented as well. Future development plan of radioisotopes and labeling compounds in China is also given. Simultaneously, the possibility and methods of bilateral or multilateral co-operation in utilization of research reactor, personnel and technology exchange of radioisotope production and labeling compounds is also discussed in this paper.

Key words: Research reactor radioisotope production Radiopharmaceutical

1. Introduction

Many countries in Asia and Pacific area have the activity of research reactor operation and produce a great deal of radioisotopes in these reactors to meet the market demands. With the development of nuclear industry, more and more radioisotopes and their labeling compounds are produced and applied in the fields of scientific research, medicine, industry, agriculture and so on. As the developed countries, China has also made a great progress in

production and application of reactor produced radioisotopes and their labeling compounds There are two centers in China to produce most of primary radioisotopes from reactor. One is Nuclear Institute of China (NPIC, Chengdu); the other is China Institute of Atomic Energy (CIAE, Beijing). They respectively possess two research reactors and accessory facilities, which is requisite for radioisotope and labeling compounds production.

2.Facilities for isotopes production

Four research reactors are respectively possessed in NPIC and CIAE. They are for the purpose of irradiation testing of reactor material and elements, material performance modification and development and fabrication of radioisotopes. Their main technical parameters are listed in table 1:

Table 1 Reactors for radioisotopes production in China

Parameter \ Reactor	1	2	3	4
Name	High Flux Engineering Test Reactor	Ming Jiang Test Reactor	Heavy Water Research reactor	Swimming Pool Reactor
Abbreviated for:	HFETR	MJTR	HWRR	SPR
Designed power, MW	125	5	15	3.5
Operation power, MW	50~55	5	7.5~10	3.5
Max. thermal neutron flux, n/cm^{-2} ·s	6.2×10^{14}	8.03×10^{13}	2.4×10^{14}	5.2×10^{13}
Max. Fast neutron flux, n/cm^{-2} ·s	1.7×10^{15}	1.43×10^{14}		
Actual thermal neutron flux, n/cm^{-2} ·s	2.1×10^{14}	7.2×10^{13}	1.2×10^{14}	5.2×10^{13}

Two centers possess sufficient and qualified hot-cells, semi-hot-cells, radioisotope and labeling compounds production lines with suitable class clean rooms, well-equipped quality control laboratories, waste treatment center (include a national temporary storehouse of solid waste), and environment monitoring and evaluation center. Simultaneously, both NPIC and CIAE are building or rebuilding new facilities for radioisotope production and labeling compounds preparation to meet the requirements of increasing market (NPIC is rebuilding a chemical hot-cell for gel ^{188}W-^{188}Re generator trial production). For getting the GMP authentication, NPIC has upgraded the clean class of work areas of eight production lines (^{131}I, ^{125}I, ^{153}Sm-EDTMP, ^{89}Sr, ^{32}P series products, ^{131}I-MIBG, ^{131}I-hippuran). NPIC is applying to the national management bureau of pharmaceutical for GMP authentication of the above-mentioned production lines.

3. Current status of radioisotopes production

In 1960', China started radioisotope in CIAE. A few kinds radioisotopes were produced for scientific research. With the development of nuclear medicine and extending of application of radioisotope and their labeling compounds in the fields of industry, agriculture, and scientific research, the market demands increase rapidly. More and more radioisotopes and their labeling compounds were quickly developed. Particularly, with the complete of HFTER in 1970, the ability of radioisotopes production were greatly enlarged. Until now, almost all the primary radioisotopes can be produced in China. The installed capability, present batch size, and batches per month are listed in table 2:

Table 2 Current status of reactor produced main radioisotopes in China

Isotope	Installed capability	Actual production yield, Ci	remarks
^{60}Co	3,000,000	1,500,000	
^{192}Ir	1,500,000	1,200,000	
^{131}I*	3000Ci	2,500	
^{125}I	200Ci	60	
^{99}Mo	14000Ci	3,000	NPIC, gel-type
		3,000	CIAE, fission-type
^{113m}In	400Ci	50	For well logging
^{32}P***	400Ci	80	
^{89}Sr	10Ci	10	
^{153}Sm	1000Ci	300	
^{131}Ba	300	100	
^{186}Re	50Ci	nonscheduled	
^{90}Y		nonscheduled	For ^{90}Y applicator
^{14}C		nonscheduled	For labeling compounds

** Including ^{131}I oral solution and ^{131}I capsule.*

*** Half of parent ^{99m}Mo is imported abroad.*

*** Including phosphorus [^{32}P] glass microsphere, colloidal chromium phosphate [^{32}P] injection, sodium phosphate [^{32}P] oral solution, phosphate [^{32}P] injection*

Besides the above radioisotopes, we can also produce ^{198}Au, ^{51}Cr, ^{241}Am, etc. to meet the customer's temporary request.

^{60}Co: A large quantity of ^{60}Co is produced and applied in the fields of medicine, industry in China. It is for the manufacturing of tele-therapy source, industrial irradiation source, non-destructive testing (NTD) source, after-loading source, gamma-knife source, meter source, and non-standard source, etc (see table 3). For manufacturing of these Co-60 sources, five

cutting hot-cells are possessed in NPIC and CIAE, which have the shielding ability of one million Curies of Co-60 for each hot-cell. There are several hot-cells for sealed source welding as well. In NPIC, a new building for mini-sealed source manufacturing has been set up in October this year and the facilities are being debugged. It will be put into use at beginning of next year.

Table 3 Current status of ^{60}Co source production in China

Items \ Source	Teletherapy Source	Industrial source	Non-destructive source	After-loading source	γ -knife source	Non-standard source
Activity of each source, Ci	3,000~5,000	1,200~1,500	80~100	1.5~3	8,000~9,000	
Total activity, Ci	~350,000	~900,000	~100,000	~500	90,000	

Table 4 Current status of ^{192}Ir source production in China

Items \ Source	Therapy source	Industrial source	Non-destructive source
Activity of each source, Ci	80~120	3,000~10,000	1,200~1,500
Total activity, Ci	~80,000	300,000	800,000

^{131}I: Both NPIC and CIAE produce ^{131}I with dry distillation method as oral solution and raw materials of capsule and its labeling compounds. In the past, ^{131}I was produced with wet distillation method. This separation process is stopped and replaced by dry distillation in 1995 due to its low separation yield and liquid waste problem. Special filters are equipped in ventilation system of ^{131}I production line to remove escaping gaseous ^{131}I in exhaust for environment protection. The present installed capacity can not meet the increasing market demands in future, therefore, NPIC intend to construct a new facility for ^{131}I production.

^{125}I: Nature Xe sealed in Al container is irradiated in reactor batch by batch. ^{125}I is separated from cooled target by adsorption method. At present, the labeling of radioimmunoassay kit is the only use in China. However, with the development and application of ^{125}I seeds, which is used for prostate tumor treatment, the production scale of ^{125}I will be enlarged. A production line of ^{125}I seeds has been completed in Shanghai Xingke Pharmacy center. The current production process (batch-method) will be replaced by more advanced one (loop-method).

^{153}Sm: Both nature and enriched are used as target material depending on the power of

reactor and the quantity the users ordered. Both ^{153}Sm-EDTMP, ^{153}Sm raw material and cold EDTMP kits are provided in China.

^{99m}Tc generator: Both gel-type Tc-99m generator and fission-type Tc-99m generator are produced and supplied to y the market. NPIC produce gel-type Tc-99m generator twice a month based on zirconium molybdate gel and CIAE produce fission-type Tc-99m generator four time a month from fission ^{99}Mo. Because of the reactor operation program, half of the fission parent Mo-99 in CIAE is locally produced and the rest is imported from South Africa. Although the market is increasing, the total yield of ^{99m}Tc generator is steady, because of the establishment of six "milk station" in Beijing, Shanghai, Guangzhou, and Shaengyang.

^{32}P series products: Phosphorus and Sulfur are respectively used as targets of P-32 series products. At present, four types of ^{32}P series are produced and supply the market, including: phosphorus [^{32}P] glass microsphere, colloidal chromium phosphate [^{32}P] injection, sodium phosphate [^{32}P] oral solution, sodium phosphate [^{32}P] injection.

^{89}Sr: Because of the requirement of high flux for ^{89}Sr production, only NPIC can produce this radionuclide in HFETR. Its production yield is limited due to its high price. Approximate half of the product is locally produced and the rest is imported abroad.

^{113m}In generator: In the past, the ^{113}In was major nuclide for disease diagnosis and were produced on large scale. With the successful development of ^{99m}Tc generator, it was replaced by ^{99m}Tc and mainly used in industry (For oil-well logging). At present, It is almost stopped.

^{186}Re: A small amount of ^{186}Re is produced and provided the market in the form of NH_4ReO_4 and ^{186}Re-HEDP. We produce it on the customer's request.

^{131}Ba, ^{90}Y, ^{241}Am, ^{14}C: These radionuclides are non-periodically produced on small scale due to the limited market demand.

4. Current status of labeling compounds preparation

The labeling compounds using rector produced radioisotopes are mostly prepared in NPIC and CIAE and small quantity of labeling compounds are produced in other institutes, pharmacies and hospitals as well (see table 5). Sufficient facilities and quality control laboratories for labeling compounds preparation are possessed in these units.

Table 5 Radiopharmaceuticals prepared in China

Labeling compounds	Installed capacity, Ci	Actual yield, Ci	Produced by:
^{131}I-MIBG	50	10	NPIC, CIAE, Xingke company
^{131}I-Hippuran	100	30	NPIC and CIAE
^{131}I-capsule	500	20	NPIC and CIAE
^{153}Sm-EDTMP	1,000	200	NPIC and CIAE
^{153}Sm-citrate-HA	50	2	NPIC and CIAE
^{186}Re-HEDP	20	1	NPIC and CIAE
^{131}I-moncolone	200	5	The sixth hospital of Shanghai
^{99m}Tc kits*		1,000,000 kits	Hospitals and "milk stations"

**Before 1996, almost all the hospitals having nuclear medical center possess their own facilities and technique for ^{99m}Tc kits labeling by using eluted ^{99m}Tc from gel or fission ^{99m}Tc generator. After that, six "milk stations" were respectively established in Beijing, Shanghai, guangzhou, and Shengyang in succession. They prepare and provide ^{99m}Tc kits to hospitals. However, the other hospitals still prepare kits by themselves.*

5. Future planning on reactor produced radioisotopes development

For further utilization of HFETR, NPIC plans to enlarge the existing production scales and develop more new and potential radioisotopes by building new production facilities or rebuilding existing facilities to meet the requirement of growth nuclear medicine. Simultaneously, NPIC is improving the existing production facilities including the equipment, clean rooms, quality control laboratories, and quality management for GMP authentication.

---Continue to do more research work on development of gel ^{188}W-^{188}Re generator and to make it commercialized.

---Set up a new facility (using loop method) to produce high quality (low ^{126}I content) ^{125}I on large scale as raw material of ^{125}I seed source.

---Build a new ^{131}I production line to replace the old one, which can not meet the increasing market demands.

---Develop medical radioisotope ^{166}Ho and its labeling compounds.

---Develop ^{170}Tm mini-source.

6. International cooperation plan in radioisotope production

The High Flux Engineering Test Reactor (FHETR) with power of 125 MW is unique in Asia. It is valuable for radioisotope production. However, its potential is not completely exploited. In resent years, Many managers of famous radioisotope production companies in

the world (*Iordion, Dupont*, etc.) visited NPIC and showed their interests in the utilization of irradiation space of this reactor for radioisotope production. However, no substantive progress has been achieved.

Besides the two research reactors (HFETR and MJTR), NPIC also possesses numerous hot-cells, isotope production lines, quality control laboratory, waste disposal center, environment monitoring center and other accessory facilities which is requisite for radioisotope production. Any cooperative patterns are welcome.

In the coming years, the following fields and cooperative pattern we suggest may be acceptable:

---Confirm the cooperative project with Japan to produce ^{60}Co after-loading source for Japan to form a complete set of after-loading intracavitary therapy unit manufactured in Japan.

---Share the irradiation space for further exploitation and utilization of research reactors.

---Exchange technology and experience of GMP management of medical radioisotopes and radiopharmaceuticals through multipartite meeting or personnel training (or personnel exchange).

---Exchange production technology and experience of radioisotope and radiopharmaceuticals in which both sides can get their desired technologies.

---Jointly develops new radioisotopes or radiopharmaceuticals.