VIETNAM ATOMIC ENERGY INSTITUTE
DA LAT NUCLEAR RESEARCH INSTITUTE

FNCA 2024 STUDY PANEL

# Production of radioisotopes for medical use and demand in Vietnam

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Japan- 3.2024

# 1. Production of radiopharmaceuticals in Vietnam

❖ In Vietnam, Dalat Nuclear Reactor is the only reactor that apply to production and supply radiopharmaceuticals in cancer diagnosis and treatment for 25 hospitals in Vietnam, and we also exported radiopharmaceuticals to Cambodia.

❖ We have 5 cyclotron for production F-18, 7 PET/CT, 17 SPECT/CT and 28 SPECT

❖ Reactor:

✓Produce I-131 solution and capsule for the diagnostic and treatment of thyroid disease (thyroid cancer, hyperthyroidism, basedow);

✓Produce lyophilized KITs and labelling with Tc-99m (generator Mo-99/Tc-99m) on SPECT/CT for cancer diagnostic (MDP (bone scan), DTPA (kidney scan), MIBI (heart scan);

✓ Produce P-32 applicator: Treatment of skin diseases

✓ Produce P-32 solution: Treatment of metastatic bone pain

❖ Cyclotron:

✓ Produce F-18 FDG for diagnostic of cancer, cardiovascular and neurological diseases (PET/CT).

# 1. Production of radiopharmaceuticals in Vietnam

- 1960: Construction of Da Lat nuclear reactor with the TRIGA Mark II reactor with a small capacity of 250 kW and using low enrichment fuel (19.75%) with 3 main goals:
  - Training
  - Research
  - Production of radioisotopes
- March 20, 1984: The reactor officially operated at a capacity of 500 kW

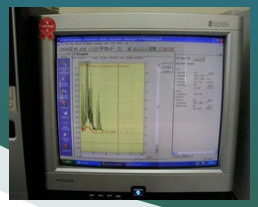
# 1. Production of radiopharmaceuticals in Vietnam

## Production process of radioisotopes in Dalat Nuclear Reactor

1. Prepare irradiation target

2. Thermal neutron irradiation

3. Radiochemical treatment



4. Quality Control

5. Transportation

6. Hospital

# 1. Production of radiopharmaceuticals in Vietnam

## 1. Prepare irradiation target

Choose target according to requirements:

Non-explosive, non-flammable, non-volatile substance.

The target material must be durable in radiation conditions.

Target must have high purity and appropriate enrichment.

The target must be chemically stable and easy to handle after irradiation.

If the target has hygroscopic properties, it must be heat treated to dry completely before irradiation.

You should choose in Oxide or metal form.

Aluminum container (2.6 x 23.6 cm) and glass ampoule containing target sample

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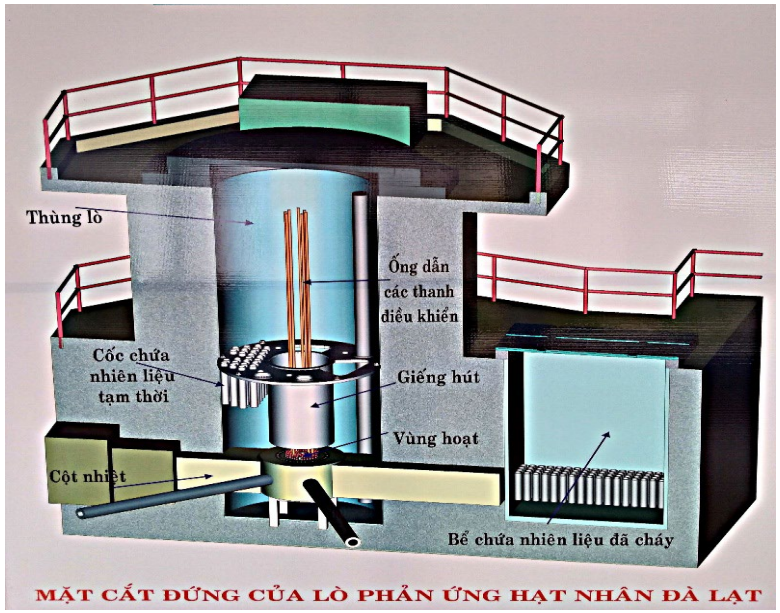
## 2. Thermal neutron irradiation

Irradiation conditions:

- Thermal neutron flux: $2.3.10^{13}$ n/cm$^2$/s
- Irradiation time: 85-180 continuous hours
- Temperature: 40 – 60$^o$C



MẶT CẮT ĐỨNG CỦA LÒ PHẢN ỨNG HẠT NHÂN ĐÀ LẠT

## 3. Radiochemical treatment

Depends on the material we choose reasonable procedures such as:

- High temperature distillation
- Dissolve and separation
- Exchange, isotope labeling
- No radioactive treatment

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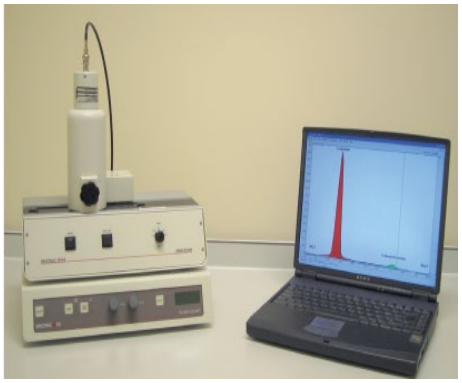
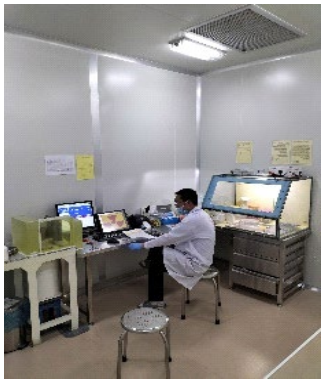
## 4. Quality Control

| No. | Criteria | Method |
|---|---|---|
| 1 | pH value | pH meter/pH paper |
| 2 | Radionuclide purity | Multichannel gamma ray spectrometer (ORTEC) |
| 3 | Radiochemical purity | Thin layer chromatography, column chromatography, electrophoresis chromatography |
| 4 | Radioactivity | Calibrator ISOMED-2000 |
| 5 | Endotoxin | Method of making gel on Endosafe PTS |
| 6 | Sterility | Incubation in Fluid Thioglycollate Medium (FTM) and Soybean-cascein digest medium (SCDM). The FTM is for the detection of anaerobic and aerobic bacteria. SCDM for the detection of aerobic bacteria and mold. |





# 1. Production of radiopharmaceuticals in Vietnam

## 5. PACKAGE AND TRANSPORTATION

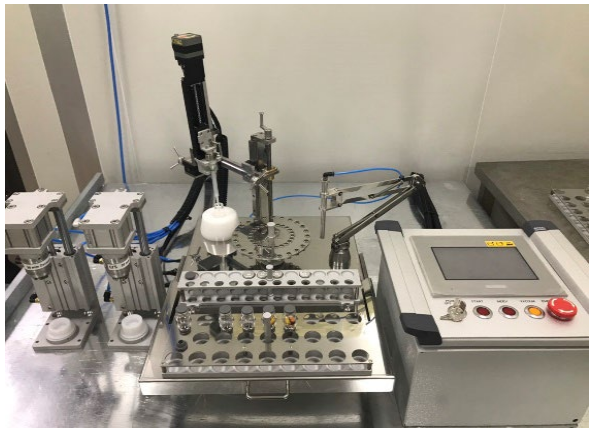
Transportation



# 1. Production of radiopharmaceuticals in Vietnam

## EQUIPMENTS FOR PRODUCTION (GMP-WHO)

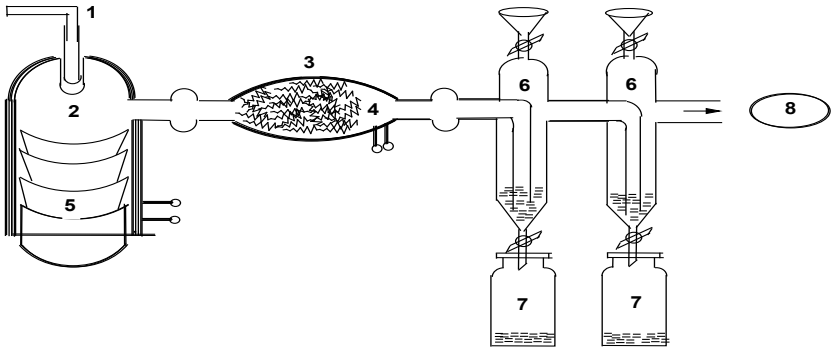





# 1. Production of radiopharmaceuticals in Vietnam

## Production process of Iodine-131 solution

$$^{130}TeO_2 \ (n,\gamma) \ ^{131}TeO_2 \xrightarrow{\beta^-} {}^{131}I \xrightarrow{NaOH} Na^{131}I$$

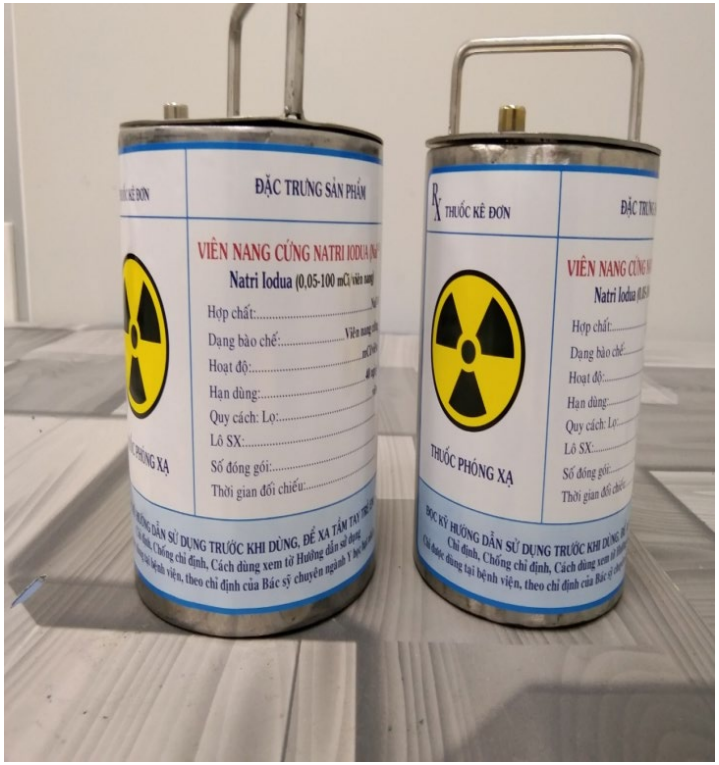



- The energy of gamma rays I-131 is 364 keV and beta rays are 606 keV. The radioactive half-life is 8.02 days.
- Production process meets GMP-WHO standard with lead-shielded boxes to ensure radiation safety for operators

# 1. Production of radiopharmaceuticals in Vietnam

## Production process of Iodine-131 capsule

- Using the micropipette to suck and drop of I-131 solution according to the calculated activity into the capsule containing the excipients (Natri biphosphat ($Na_2HPO_4$) + Natri thiosulfat ($Na_2S_2O_3$))
- Measuring the radioactivity on the dose calibrator.
- Quality control, package, and supply.



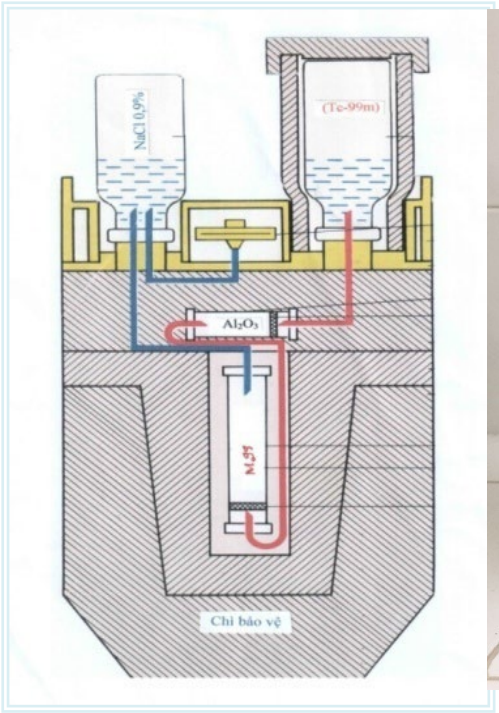
# 1. Production of radiopharmaceuticals in Vietnam

Production process of generator 99Mo/99mTc

$$^{235}U(n,f) \text{ -------> } Na_2{}^{99}MoO_4 \xrightarrow{\beta^-} \text{-------> } Na^{99m}TcO_4$$

❖ The gamma ray energy of 99mTc is 140 keV. The radioactive half-life is 6.02 hours.

❖Generator 99Mo/99mTc: Tc99m labelling with lyophilized KIT to diagnostic of organs such as MDP (bone), DTPA (kidney), Phytec (liver)….





# 1. Production of radiopharmaceuticals in Vietnam

Production process of lyophilized KITs (KITs for radiopharmaceuticals preparation)

❖ Excipients ingredients ⟶ Lyophilize in Freeze-dryer ILShinBioBase (24h, -65$^{o}$C, 5 Torr) ⟶ Sterilize products by irradiating gamma rays on a $^{60}$Co source, dose rate 2.5 Mrad ⟶ Lyophilized KITs.



➢ We have 3 lyophilized KITs: MDP (bone scan), DTPA (kidney scan) and Phytec (liver scan)

# 1. Production of radiopharmaceuticals in Vietnam

## Production process of P-32

$$^{31}P_2O_5\ (n, \gamma)\ ^{32}P_2O_5 \text{ ----> } H_3{}^{32}PO_4 \text{ ----> } NaH_2{}^{32}PO_4$$

Half-life 14.3 days.
Maximum beta radiation energy 1.71 MeV.

**P-32 have 2 types of products:**

+ P-32 applicator: Treatment of skin diseases by direct application.

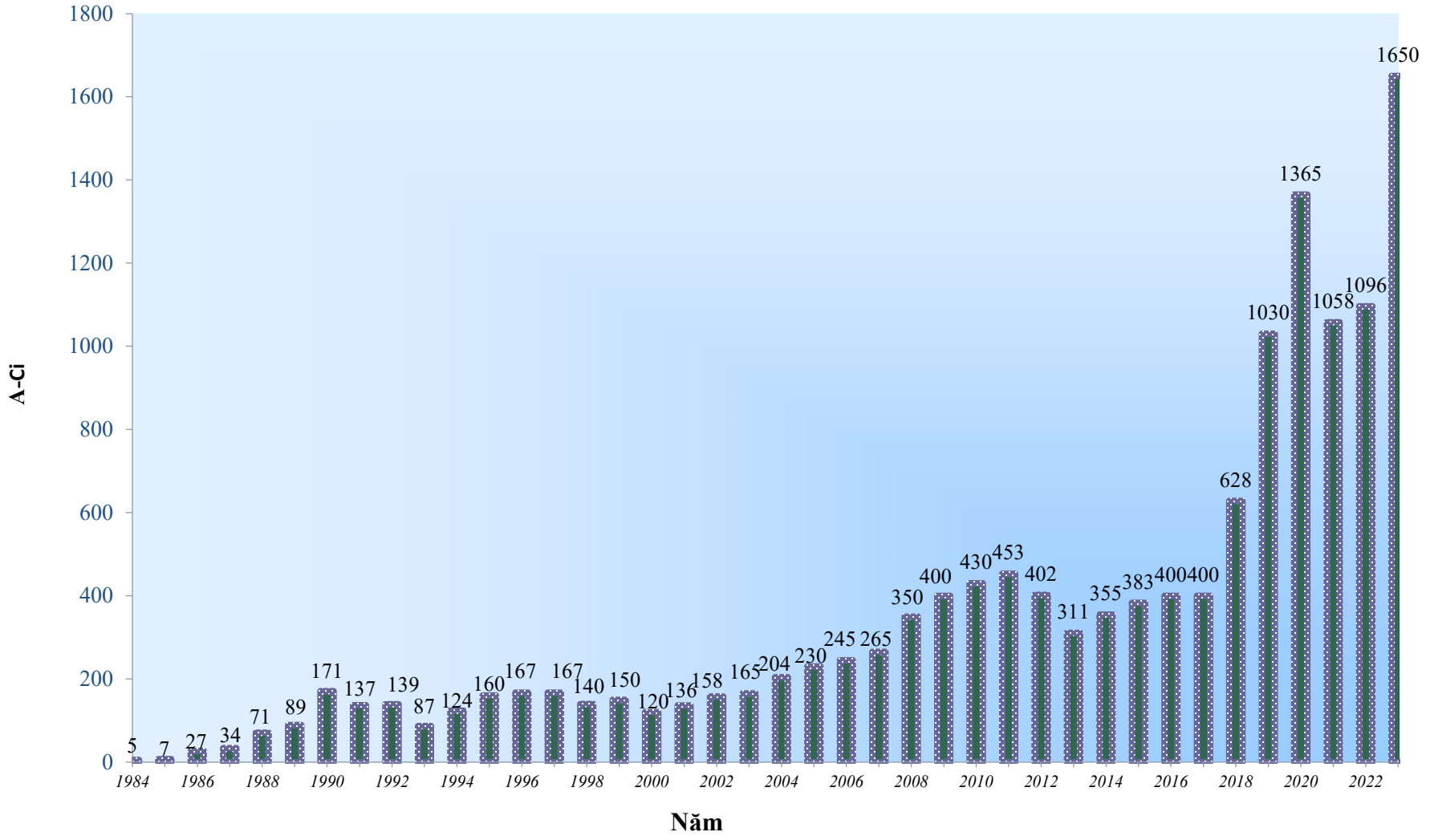
+ P-32 orthophosphate oral solution: Treatment of metastatic bone pain

# 2. Current results

| Product | Radiopharmaceutical | Activity/year |
|---|---|---|
| 06 commercial radiopharmaceuticals meet GMP-WHO standards | $^{131}$I solution | 300 Ci |
| | $^{131}$I capsule | 1300 Ci |
| | Generator $^{99}$Mo/$^{99m}$Tc | 50 Ci |
| | MDP (bone scan) | 2000 vials |
| | DTPA (kidney scan) | 500 vials |
| | Phytec (liver scan) | 50 vials |


# 2. Current results

## Total radioactivity of produced in medicine annually



# 2. Current results

| Researched products | |
|---|---|
| **Radiopharmaceuticals** | **Application** |
| $^{99m}$Tc-MIBI | Diagnose of heart disease |
| $^{177}$Lu-DOTATATE | Treatment of neuroendocrine tumors |
| $^{90}$Y-Microspheres | Treatment of primary and secondary liver cancer |
| $^{131}$I-Rituximab | Treatment of non-Hodgkin lymphoma |
| $^{177}$Lu -DOTA-J591 | Treatment of metastatic prostate cancer |
| $^{166}$Ho-Chitosan | Treatment of liver cancer |
| Ninotuzumad I-131, Y-90 | Treatment of head and neck cancer |
| Nano $Fe_3O_4$@lapatinib – $^{153}$Sm | Treatment of breast cancer |

- These products are very necessary for nuclear medicine in Vietnam

# 3. Demand in Vietnam

| Demand of using radiopharmaceuticals until 2030 | | | |
|---|---|---|---|
| **No.** | **Radiopharmaceuticals** | **Applications** | **Quantity (Ci/year)** |
| 1 | Generator Mo-99/Tc-99m | Cancer diagnostic | 500 |
| 2 | I-131 (solution and capsule) | Diagnostic and treatment of thyroid disease | 5.000 |
| 3 | Lu-177, Sm-153, Y-90, Ho-166, I-125 | Diagnostic and treatment of cancer | 4.500 |
| 4 | KITs for radiopharmaceuticals preparation | Diagnostic: MDP (bone scan), DTPA (kidney scan), MIBI (heart scan)… | 10.000 (vials) |
| 5 | $^{131}$I-MIBG | Treatment of neuroblastoma | 500 |
| 6 | $^{153}$Sm-EDTMP | Treatment of metastatic bone pain | 1.000 |
| 7 | $^{177}$Lu-PSMA | Treatment of metastatic castration-resistant prostate cancer | 1.000 |
| 8 | $^{177}$Lu - DOTATATE | Treatment of neuroendocrine tumors | 1.000 |
| 9 | $^{18}$F-FDG | Cancer diagnostic | 500 |

# 3. Demand in Vietnam

## Challenges

- Nuclear reactor in Vietnam has a small capacity of 500kW;
- Demand of using radioisotopes is increasing;
- Import radioisotopes is difficult because the Ministry of Health in Vietnam needs complex documents from the facility for exporting:
  - GMP certificate of manufactures.
  - Certificate of Analysis of Active Pharmaceutical Ingredients (APIs)
  - Drug substance (*S.1. General information; S2. Manufacture; S3. Characterization; S4. Control of drug substance; S5. Reference standards or materials; S6. Container close system; S7. Stability*)
- Domestic research and commercialization of new radioisotopes.

# 4. Future Radiopharmaceuticals

1

**Research radiopharmaceuticals that have been commercialized in the world:**

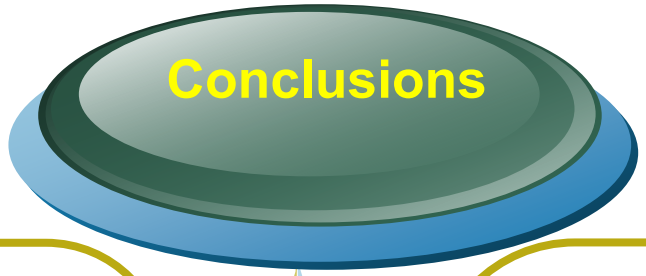
1. $^{153}$Sm-EDTMP: Treatment of metastatic bone pain
2. $^{131}$I-MIBG: Treatment of neuroblastoma
3. $^{177}$Lu-DOTATATE: Treatment of neuroendocrine tumors
4. $^{177}$Lu-PSMA: Treatment of prostate cancer

2

**Research on radiopharmaceuticals that have not been commercialized in the world :**

**Small molecules, monoclonal antibodies, nano radiopharmaceuticals, alpha particles (At-211, Ac-225...)**

# 5. Conclusions




- By the 2023, the reactor has operated about 5,650 hours/year with a total activity of 1,650 Ci, and exported to Cambodia with small capacity of 500 kW.
- We have 06 commercial radiopharmaceuticals meeting GMP-WHO standards.
- Radioisotopes at the Dalat nuclear reactor are irreplaceable production for diagnostic and treatment of thyroid cancer in Vietnam

- The demand for radiopharmaceuticals in Vietnam is increasing, so:
  - It is necessary to import radioisotopes.
  - In Vietnam will build a Center for Nuclear Science and Technology Research with a high-capacity research reactor 10 MW.

# Thank you so much!