Appendix-2
Country Report on Isotope Production and Its Applications

Australia

Over the years the range of radioisotopes produced by ANSTO has decreased and now many of those produced are done so with commercial agreements in place for supply and distribution. The main radioisotopes currently produced are Mo-99, Tc-99m (generator), I-131, Cr-51, Y-90, Sm-153, Ho-16 and Lu-177.

The production of Mo-99 is a major activity at ANSTO and ANSTO has a long history of manufacturing this important radioisotope. Production commenced in the 1970s using a neutron activation process and MEK extraction of Tc-99m. In the 1980s production was moved to a simple fission process were UO2 targets enriched initially to 1.8% and then 2.2% U-235 were used. These processes were operated reliably and enabled nuclear medicine to develop in Australia.

The current Mo-99 process uses U/AL targets enriched to 19.75% and is a basic digestion process. Features of the process are:

- Target
  - -Al clad UAl dispersion flat plate target
  - -19.75% enriched U
  - -Irradiated at 9x1013 n/cm2/s for 3-10 days
- Process
  - -Plates dissolved in sodium hydroxide
  - -Uranium precipitates and captured in filter
  - -Dry filter cakes stored in non-critical array
- Separation
  - -ion exchange & successive purification steps

The process has now been operating since late 2008. Initial challenges have now been overcome and the current capacity is 1000 six day curies per week. This gives a large export capacity and ANSTO has exported Mo-99 to Japan, China, USA and Turkey. The Opal reactor has capacity to irradiate more Mo-99 and ANSTO is investigating options to utilise this capacity. ANSTO is also installing a Synroc process to encapsulate intermediate level waste from Mo-99 manufacture.

The Gentech Tc-99m generator is manufactured and distributed throughout Australia and New Zealand. In the past it ha been sold to Asian countries.

Iodine-131 is made from the neutron capture reaction ^{130}Te (n,γ) ^{131}Te --> b- + ^{131}I and sold as capsule, liquids or labelled to mIBG.

ANSTO has decommissioned its 30MeV cyclotron. Isotopes previously manufactured by this machine are no longer exported although ANSTO does distribute domestically from imported stock.

Bangladesh

"Current Status and Future Plan on Isotope Production in Bangladesh"

The aim of this report is to describe the current status and future plan on radioisotope production in Bangladesh. The main current radioisotope products are 1) Mo-99/Tc-99m, 2) I-131 NaI oral solution, and 3) I-131 Capsule. The Tc-99m is used for diagnostic purposes such as image of vital organs like thyroid, brain, lung, liver, kidney etc, and organ system like hepato-billiary, renal etc,. Since more than 80 % nuclear medical diagnostic procedures depend on Tc-99m radioisotope. On the other hand, I-131 is used for both diagnostic and therapeutic purposes. Such as, diagnostic studies of thyroid disorders, therapeutic application for treatment of thyrotoxicosis and thyroid cancer. Radioisotope production division of BAEC is able to fulfill the local demand of the above isotopes to substitute the import completely by indigeneous product. Besides, this division has established a kit production facility successfully for Tc-99m generator to fulfill the nuclear medicine demand locally. In future, this division has plans 1) to produce Lu-177 radioisotope locally using TRIGA reactor and 2) also generate Sr-90/Y-90 Generator like Tc-99m generator for therapy purpose.

Indonesia

The RSG-GAS reactor-BATAN, is designed as a multipurpose reactor with a nominal power of 30 MW, producing thermal neutron flux in the order within $2.0x10^{14}$ n.cm-2.s-1. As a multipurpose reactor, RSG-GAS provides facilities for utilization on material testing, radioisotope production, R&D using neutron irradiation as well as training. Since the year 1998, the reactor was operated at the power level of 15MW, up to max. 4

cores cycles annually, 540–600 MWD per cycle, based on optimization of the fuel availability, user requirement as well as efficiency. Starting the year 2004, the reactor is still operated at power level of 15 MW for 4 cycles a year, but each cycle is divided in 6 phases of operation. Each operation runs for 3 times of 11 days and 3 times 4 days. The shutdown times for maintenance are three times of 10 days and three times of 3 days. In the reactor grid there are 4 positions in the beryllium reflector, which consist of IR1, IR2, IR3, IR4; 4 positions in core (IP) and 1 central irradiation in the centre of the core (CIP), which has 4 IPs. All of IPs is intended for radioisotope production. A high neutron flux in the reactor core is potential to produce high quality radioisotopes by faster and more efficient irradiation. Various types of radioisotopes from fission and activation process have been produced in RSG-GAS reactor including for medical purpose: ^{125}I, ^{131}I, ^{99}Mo, ^{133}I; etc, for industrial purpose ^{192}Ir, ^{82}Br, ^{60}Co, etc, for tracer ^{14}C, ^{32}P, ^{35}S, etc. Irradiation of the FPM target is approximately done for 10 days and generates 1000 Ci of ^{131}I. Isotope irradiation facilities available in 4 IPs in beryllium reflector area and 5 hydraulics and pneumatic channels "Rabbit System". The Radioisotope production is also using Beam tube number 1 (S1) to produce ^{125}I. Rabbit system are mostly used for NAA in the field of industry, geology/mining, agriculture, health and environment. The radioisotopes potential customers in Indonesia, among others, hospitals, industries and universities. From outside Indonesia are Bangladesh, China, Japan, Malaysia, Korea and Singapore are noted as the regular customers. In cooperation with PT BATAN TEKNOLOGI, the RSG-GAS reactor is starting to develop the manufacturing process and infrastructures to increase the RI production fulfilling the present demands.

Kazakhstan

Radioisotope production. Development of isotope production technology at WWR-K was started after reactor re-commissioning in 1998. To date, the isotopes produced routinely: ^{99m}Tc, ^{131}I, ^{192}Ir. For Technetium-99m, so called "gel technology" is used. The column of portable generator is charged with particles of polymolybdate gel produced from irradiated molybdenum oxide (natural enrichment, 3-4 days of irradiation in central channel). The activity of gel generator is 18 GBq with 3 days precalibration. Iodine-131 is produced by traditional dry distillation from irradiated tellurium oxide, with iodine absorption in alkaline solution. Activity of bulk solution depends on irradiation time and amount of target material, defined by ordered quantity. Iridium-192, with specific activity of 200-300 Ci/g, is used for manufacturing of sealed sources for industrial radiography. Other types of sealed sources produced at WWR-K for local industry are cobalt-60 (low and medium activity), antimony-124 and thallium-204. For ecological and biological research tracers solutions of ^{134}Cs, ^{85}Sr, ^{60}Co, ^{3}H, ^{131}I are produced.

Korea

"Production and Development of Radioisotopes in HANARO"

Radioisotope production in Korea started in 1962 when the first research reactor, TRIGA Mark II, went into operation. The second landmark in the history of Korea's radioisotope production is the operation of Korea's second research reactor, TRIGA Mark III, in 1972. With this reactor, Korea Atomic Energy Research Institute could produce several radioisotopes on a practical scale sufficient to meet domestic demands. Based on such accumulated technologies and experiences, the production of radioisotopes in Korea became flourishing right after the construction of the multi-purpose high performance reactor, HANARO (30 MW power) and a new radioisotope production facility in 1997.

More than twenty radioisotopes are currently produced at KAERI and supplied to domestic users and international markets. Radioisotopes being produced on a regular basis are ^{131}I, ^{166}Ho, ^{192}Ir, ^{60}Co, ^{32}P, ^{51}Cr, etc. The main radioisotopes, which are supplied from HANARO, are ^{192}Ir, ^{131}I, and ^{166}Ho. Currently, KAERI produces about thirty curies of ^{131}I capsules and solutions every week, covering more than sixty percent of domestic demand. KAERI also produces more than 200, 000 curies of ^{192}Ir non-destructive testing sources, which is equivalent to about ten percent of the international market.

Current research topics are the development of the production technologies for therapeutic beta emitters, generator systems, and industrial gauge sources. Also, research activities to expand the applications of medical sealed sources are being actively undertaken such as the use of a ^{32}P sealed sources as an ophthalmic applicator. The key technologies for ^{188}Re generator and high dose rate brachytherapy ^{192}Ir source were transferred to a private company for their commercial production.

As the commercial supplies of radioisotopes and research activities expand, international relationships have been promoted. In addition, several units of these production systems were supplied to other countries.

Malaysia

Between 1988 and 2003, Reactor PUSPATI TRIGA (RTP) produced 14 types of radioisotopes especially for medical purposes. However, the production of Technetium-99m from Mo-99 with the specific activity of around 50 mCi per gram required 75 hours of continuous irradiation at the central thimble. With yield of about 4 Ci of Mo-99 for 80 g of natural Mo_2O_3 used as the target material, the MEK extraction technique requires delicate control of many parameters to obtain products with reasonable consistent quality. From 1991 to 1994, another radioisotope, Iodine-131 (I-131) was produced with maximum yield of about 2 Ci. However, due to many safety problems faced with the dry distillation production plant, it was later dismantled in 2003 and the hot-cell was decontaminated. Nuclear Malaysia replaced the production of Tc-99m and I-131 from the reactor with portable type chromatographic column generator, which could produce Tc-99m and I-131 on weekly basis and were more suitable for customers regardless of the distance. Due to economic as well as other reasons, Malaysian Nuclear Agency decided to import fission Mo-99 to produce Tc-99m generator from Indonesia, South Africa and Australia. Apart from that, an irradiated Ir-192 pellet with radioactivity of 50 Ci for each pellet were imported from abroad and final pigtail assembly was done at Nuclear Malaysia laboratory. Iodine-131 is going to be prepared inside a hot-cell with Grade C clean room environment. Such facility which includes processing, packaging and a certified GMP layout is in the progress of development. It is expected to be in operation in 2012.

The demand for radiopharmaceutical product has increased tremendously in Malaysia when many new nuclear medicine centers were operational. In the 1964 there was only one hospital using radiopharmaceutical but in 2009 the number has increased to 18 hospitals.

Other radioisotopes for industrial used were produced with limited quantity due to low demands. For example, there was no request for P-32 radioisotope from 1997 to 2006. From time to time, the reactor produced Iridium-glass, Au-198, Na-24, K-42 and some other radioisotopes by request and with limited quantity. The products are to serve non-destructive testing services as well as other users such as industry, agriculture, hydrology, sedimentology, scientific research, etc

Mongolia

Mongolia is a non-nuclear country, there are no nuclear power plant and research reactor. But radiation sources are used in the different fields such as medicine (radiotherapy, nuclear medicine and diagnostic radiology), industry, mining, geology, agriculture, education and R/D. Radioisotopes are using for the tele-therapy (^{60}Co), industrial gamma radiography (^{192}Ir), high/medium/low rate brachy-therapy (^{60}Co), borehole logging (Am/Be, ^{137}Cs), industrial fixed gauges with high activity sources (^{137}Cs), fill/thickness gauges, portable gauges (e.g. moisture/density) and XRF devices. All radiation sources including isotopes imported, do not produce isotopes.

Short-lived isotopes are using in medicine. Radiation diagnosis department, State Central Clinic Hospital is importing medical isotopes from China and Korea. In case of 2010, the hospital imported ^{99m}Tc of 500 mCi and ^{131}I of 200 mCi every 3 weeks and 2 months, respectively. 22% of total expenditure are used for transportations and custom tax. Price of isotopes is increasing year by year. Also need other isotopes such as ^{131}I, ^{125}I, ^{99}Te. ^{188}Re, ^{32}P, ^{198}Au for medical and other purposes. Thus Mongolia needs to produce some short-lived isotopes locally, obtaining research reactor.

The Philippines

The Philippine Research Reactor (PRR-1) has been shut down since 1988, so it has been over 25 years since radioisotope has been produced in the Philippines. The demand for radioisotopes however has remained and has been partially met expensively through importation. The local cost of imported ^{99m}Tc generator is higher than that of neighboring countries. Fortunately the Philippine Nuclear Research Institute (PNRI) has been able to get an IAEA TC Project namely PHI/6/021 “Setting-Up of a Facility for Molybdenum-99/Technetium-99m Generators”.

This project is basically the establishment of a radioisotope laboratory for the production of a technetium 99-m generator with the assistance of the IAEA. The laboratory is ready to receive the technetium 99-m generator production facility from the manufacturer and researchers have been trained in the various aspects of the production process. We envision the facility to bring down the costs of technetium 99-m based nuclear medicine procedures in the country. The Technetium 99-m Facility is expected to arrive by November 2011, the installation will follow and optimistic actual production start by first quarter of 2012

The general objective is to make available locally the technology for the preparation of the most commonly used ^{99mTc}-labelled radiopharmaceuticals. Specifically, the project aims to:

- To establish the local capability for the preparation of ^{99m}Tc generators, including the protocol for its production and associated quality control procedures,
- To develop protocols for the preparation and characterization of commonly used ^{99m}Tc radiopharmaceutical kits;

- To develop protocols for the preparation of ^{99m}Tc – biomolecules and radiolabelled compounds for medical research applications.

The plant will produce Mo99-Tc99m Generators for nuclear medicine and also produce the commonly used cold kit such as MDP for Bone scan and DTPA for renal scan. These kits are labelled with Tc99m and are collectively called Tc99m radiopharmaceuticals.

The end users and target beneficiaries are the Nuclear medicine centers in private and government hospitals and patients especially in government hospitals and Medical research institutions. Local Distributors will get the Tc99m from us and they will be the one to dispense in unit doses. The issues and challenges that we face are the following:

- Technological challenge would be the production itself of a generator with qualities at par with available Tc generators.
- This venture would be the first in the Philippines, so that labour pains in establishing such a facility are expected.
- The establishment of a steady supply of Mo-99 and logistics for obtaining from customs
- Supply system would be the Mo-99 which is imported and which is produced by few countries such as South Africa, Canada, Indonesia, Australia

Thailand

The radio-isotopes used in Thailand are partly produced by Thai Research Reactor and Radio-Isotope Production facilities available in TINT. The radio-isotope production is performed by irradiating targets in the high flux region of the reactor core. After the irradiation, the targets are removed and transferred from the reactor building to the radio-isotope processing building. The reactor produced radio-isotopes in Thailand include I-131 which is the derived from the irradiation of TeO_2 targets. Typical irradiation of TeO_2 targets is approximately 8 weeks. The irradiated targets are extracted for I-131 by dry distillation method. The total production capacity of I-131 production is 4 -5 Ci a week. Another radio-isotope produced by the Thai research reactor is Sm-153 which is derived from irradiation of Sm_2O_3 targets. The production capacity of Sm-153 is approximately 70 mCi/ batch taking 2 – 3 days of irradiation. The last type of radio-isotope produced by Thai Research Reactor is P-32. This is produced by one-week irradiation of $NH_4H_2PO_3$ target to obtain approximately 7 mCi / batch. The production of radio-isotopes in Thailand can serve approximately 40% – 50% of the current domestic I-131 demands. Other demands which are not produced in Thailand include Ir-192, Tc-99m, Co-60, Lu-177 and etc. Especially, the radio-isotopes for industrial applications are 100% imported.

1. Country Report on Possible Regional Cooperation

Thai Research Reactor has a number of irradiation positions. These include in-core irradiation positions, a pneumatic transfer irradiation position, out-core irradiation positions and beam ports. The maximum thermal neutron flux in the reactor core is approximately 2.9×10^{13} cm^{-2}/s. The current utilization of Thai Research Reactor includes radio-isotope production, gemstone coloration, neutron activation analysis, R&D activities, neutron radiography, public education and manpower training. The R&D activities utilizing the research reactor include mutation breeding and neutron activation analysis of toxic and nutrition analysis in food. The possible region cooperation in FNCA on RRN can be the sharing of neutron beam ports which are under utilized at the moment. In addition, the cooperation on study of irradiation technology and the sharing of research reactor design and operation can be realized.

Vietnam

"Status of radioisotope production and application in Vietnam"

After the reconstruction of Dalat Nuclear Research Reactor (DNRR) in late 1983, the production of radioisotopes and labeled compounds for medical use was started. Dalat Nuclear Research Reactor of nominal power of 500 KW is today the unique one in Vietnam. More than 90% of reactor operation time and over 80 % of reactor irradiation capacity have been exploited for radioisotope production. With one main irradiation channel of neutron flux of 2×10^{13} $n/cm^2.sec$ and some irradiation positions of lower neutron flux we have now routinely produced some important radioisotopes especially for medical purposes. The radioisotopes, radiolabeled compounds and radiopharmaceuticals produced in Dalat reactor have regularly been supplied to all nuclear medicine centres in Vietnam.

The radioactivity of more than 500 Ci of ^{131}I, ^{99}Mo- ^{99m}Tc, ^{32}P, ^{51}Cr, ^{153}Sm; ^{46}Sc; ^{192}Ir was annually produced. Radiopharmaceuticals such as ^{153}Sm-EDTMP. ^{131}I-Hippuran and in-vivo Kits for ^{99m}Tc labeling were also prepared routinely and regularly; More than 10 in-vivo Kits including modern radiopharmaceuticals such as HMPAO and MIBI kit were supplied to hospitals in Vietnam. RIA Kits such as T_3, T_4 Kit for in-vitro assay were prepared and ready to be supplied. In addition, the research in radiochemistry laid the basis for the development of technologies suitable for isotope production in low power research reactors always respected.

Beside these radioisotopes and radiopharmaceuticals for the healthcare sector, Nuclear Research Institute (NRI) has also produced radio-tracers such as Sc-46, Ir-192, Au-198 and La-140… for sediment studies, oil exploitation, evaluation of column efficacy in chemical industry, underwater and damp leakage evaluation studies, determination of liquid waste treatment station effectiveness.

"Radioisotope production laboratory"

An area of 600 sq.m is reserved for a rather limited programme of isotope production. The facilities available for the isotope production consist of one hot cell with master slave manipulator, one ^{131}I isotope production line equipped under Technical Cooperation Project No-VIE/0/002 of IAEA (1987) with 4 shielded cells, ball-joint manipulators and five shielded fume hoods for isotope labeling and γ-emitted isotope processing. One ^{99m}Tc generator production line (using fission ^{99}Mo solution and (n,γ) ^{99}Mo contained molybdate gel column) composed of two shielded cells and one multipurpose junior cave were put to use under Technical Cooperation Project №-VIE/6/016 of IAEA in 1990. All these facilities are connected with the existing ventilation system of the reactor.

Equipment for the production of Kits to be labeled with ^{99m}Tc isotope and for the quality control of radioisotopes and radiopharmaceuticals was also supplied by the IAEA.

"Use of local products in Medicine"

- Numbers of nuclear medicine centre in Vietnam: 23

  These centres are located in almost all parts of country.

- Numbers of gamma cameras (planar and SPECT): 20
- Radiopharmaceuticals used in these centres: $Na^{131}I$ solution, Sodium-(^{99m}Tc) pertechnetate, ^{131}I-Hippuran, Sodium-(^{32}P) orthophosphate, ^{32}P Applicator; in-vivo Kits (DTPA, DMSA, Phosphon, Glucon, Phytate , MAHSA, EHIDA, HMPAO, MIBI, MAG-3 etc.).
- Locally manufactured products takes 50% of total market. To get a higher market share in case of ^{99m}Tc generators we will increase the production by loading generations with imported ^{99}Mo solution.