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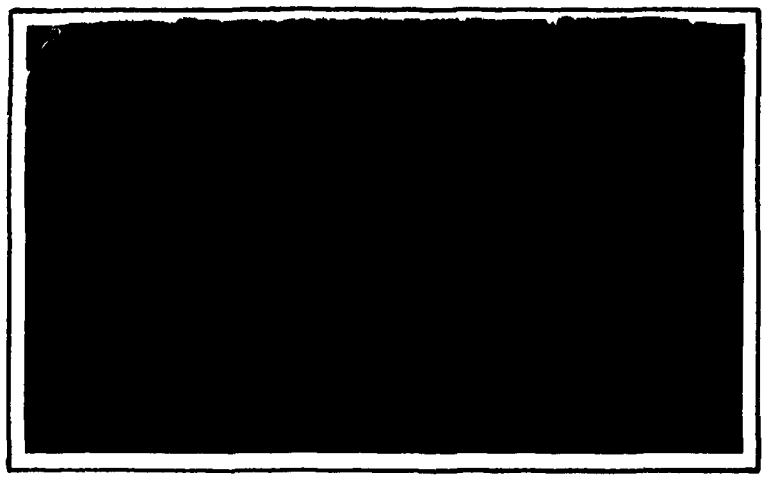
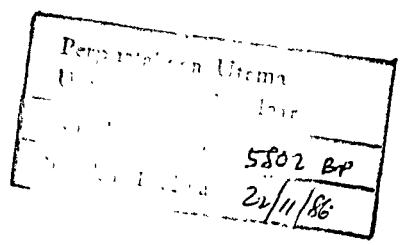


SEMINAR PENGELUARAN DAN BEKALAN RADIOISOTOP UNTUK PENGGUNA-PENGGUNA DI MALAYSIA

KOMPLEKS PUSPATI, BANGI,
22HB. OKTOBER, 1986.



anjuran:
UNIT TENAGA NUKLEAR
JABATAN PERDANA MENTERI

SEMINAR PENGELUARAN DAN BEKALAN RADIO-
ISOTOP UNTUK PENGGUNA-PENGGUNA DI MALAYSIA

PROGRAM SEMINAR

8.30 pagi - Pendaftaran peserta

9.00 pagi - Ucapan Pengerusi Seminar dan pembukaannya oleh Y. Bhg. Datuk Prof. Mohd. Ghazali b. Hj. Abdul Rahman (Ketua Pengarah UTN)

9.30 pagi - Sessi pembentangan kertas kerja
Pengerusi : En. Nahrul b. A.M. Rashid

- Kertaskerja I : Radioisotope Production for Medical and Non-medical Applications at The Nuclear Energy Unit
Pembentang : En. Mohamed b. Awang

10.00 pagi - Jamuan ringan

10.20 pagi - Kertaskerja II : Integrated Approach to Quality Control Procedures of Radioisotopes and Radiopharmaceuticals
Pembentang : Cik Rohani bt. Mohammad

10.50 pagi - Kertaskerja III : Radioisotope Production and Distribution in Australia.
Pembentang : Mr. Jim Brough

11.20 pagi - Kertaskerja IV : Radioisotope Distribution Center of the Nuclear Energy Unit
Pembentang : En. Razali Hamzah

11.50 pagi - Sessi perbincangan
Pengerusi : En. Razali b. Hamzah

12.30 tgh. - Tayangan video

1.00 tgh. - Makan Tengahari

2.15 ptg. - Lawatan ke makmal

3.45 ptg. - Ucapan Penutup

4.00 ptg. - Jamuan ringan

4.15 ptg. - Bersurai.

Radioisotope Production For Medical and Non-medical Application at the Nuclear Energy Unit (UTN)

Mohamed b. Awang, Zulkifli Mohd. Hashim & Yusof Azuddin b. Ali

1. Introduction

Producing radioisotopes which are within the capabilities of TRIGA MK II reactor, importing in bulk those which cannot be produced and dispensing them for local distribution are among the tasks being carried out by the Nuclear Energy Unit (UTN). Isotope production basically involves several stages i.e. target preparation, irradiation and chemical processing to extract and purify the radioisotope.

Before irradiation of any target material can be started, the following tasks have to be considered carefully :-

1. Preparation of target
2. Calculation of final activity
3. Preparation of safe target handling after irradiation.

The irradiation container are mostly cold-welded aluminium cans. Some targets are sealed in cylindrical quartz ampoules or plastic ampoules. The chemical processing of radioisotopes are normally carried-out in ventilated facilities like hot-cells, glove boxes or front shielded fumehoods. Examples of chemical processing used at UTN are solvent extraction, separation using ion-exchange resin, distillation, etc.

The products intended for medical use have to undergo a more stringent precaution so that the final products will not only be radiochemically and chemically pure but also micro-biologically pure (sterile and apyrogenic). In order to meet this requirement we have installed mini-clean work stations (laminar flow cabinets), a clean room, autoclaving apparatus and use of γ -irradiation for terminal sterilisation whenever applicable.

...2/-

2. Contents

The production programme at PTN could be classified under two general classes i.e. medical products and non-medical products.

2.1. Medical Products

a) Production of ^{99m}Tc - pertechnetate ($^{99m}TcO_4^-$)

Neutron activation of molybdenum trioxide (MoO_3) produces parent radioisotope ^{99}Mo. The parent ^{99}Mo will emit β^- - particle and decay to form daughter ^{99m}Tc (see fig. 1). The specific activity of ^{99}Mo obtained at a neutron flux of 2.255×10^{12} $n/cm^2,s$ ranges from 1.75 mCi $^{99}Mo/g$ MoO_3 for 24 hours on/off (staggered) irradiation to 6.25 mCi $^{99}Mo/g$ MoO_3 for 72 hours continous irradiation. However, increasing the neutron flux to 1×10^{13} n/cm^2 s i.e by using the central thimble facility of the reactor will approximately increase the specific activity of ^{99}Mo by a factor of 6.

Chemical Processing

Solvent extraction technique is used to separate ^{99m}Tc from the radioactive alkaline solution of Potassium Molybdate(K_2 $^{99}MoO_4$). The solvent used is Methyl Ethyl Ketone (MEK). Pertechnetate (^{99m}Tc) is extracted into MEK from molybdate solution.

The compact solvent extraction plant is illustrated in Fig. 2. The whole processing steps in Figure 3 can be completed within 50 minutes. It will be possible to achieve an activity concentration of 16 mCi ^{99m}Tc/ml from the 72 hours irradiation and a total activity of about 200 mCi ^{99m}Tc per batch (80 g MoO_3 target). An overall efficiency of the plant is 65%. This is found to be constant for over 200 runs.

...3/-

b) Production of Cold Kits For ^{99m}Tc Labelling

Depending on the nature of formulation, these cold kits could be dispensed either as a -sterilised, freeze dried products or aseptically produced cold kits in the liquid form.
Currently, freeze drying is done in the clean room. This method is suitable for the preparation of Sn-containing radiopharmaceuticals. Here, we produce Sn-Methylene Diphosphonate (MDP) by freeze-drying. It involves several stages like pre-freezing to lock up the compound in a solid matrix. A controlled heating applied at the later stage of freeze-drying will cause the frozen compound to sublime and leave a dried, hydroscopic residue as a product. This preparation is done under an aseptic condition and terminally sterilised at the γ -irradiation cell available. Reconstitution with ^{99m}Tc pertechnetate will produce a multi-dose ^{99m}Tc-MDP.
Apart from this mode of preparation, the Sulphur Colloid Kit is formulated and dispensed in the liquid form into three separate vials i.e. reaction solution, acid solution and a buffer solution. This three components when needed will be easily mixed with ^{99m}Tc-pertechnetate to produce the desired ^{99m}Tc-Sulphur Colloid for scanning.

Pre-Clinical test on Medical products

It was mention earlier in the introduction that medical products have to undergo a more stringent precaution to ascertain their purity not only chemically, radiochemically and radionuclidically but also biologically and microbiologically. At the preclinical stage, normally biological tests are done on Sprague-Dawley rats. Dissection of these laboratory animals at a certain time post-injection will verify the uptake in a selected target organ.

...4/-

In case of ^{99m}Tc - SC, the target organs are the reticulo-endothelial tissues predominantly found in the liver and spleen. The usuall liver uptake is approximately 85% to 90% and the spleen uptake is about 3% to 5%. On the other hand, the skeleton is the target organ for ^{99m}Tc-SN-MDP. Studies on laboratory animals indicate an uptake of more than 2% per gram (femur).

After it has satisfied all the requirements, the last test of purity that it has to fullfill is the microbiological purity. The products must be sterile and pyrogen free before it could be accepted as a pharmaceutical aid.

2.2. Non-Medical Products

Some useful radioisotopes currently being produced at UTN are listed in Table 1. Generally, they are relatively easier to produce compared to medical products. A few examples of the production are briefly described.

a) Production of ^{32}P

Non-carrier-free radioisotope ^{32}P can be produced through (n,γ) reaction of red phosphorus. The irradiated red phosphorus is dissolved in 70% HNO_3 and the solution is boiled to reduce the volume. An average yield of 80% is obtained. For each gram of red phosphorus irradiated (72 hours irradiation at a flux of $2.255 \times 10^{12} n/cm^2.s$) 25 mCi ^{32}P is produced. It is possible to produce an activity concentration of 5 - 10 mCi ^{32}P/ml. and total activity of 200 mCi.

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b) Production of ^{82}Br

The production of ^{82}Br is based on the $^{81}Br(n,\gamma)$ ^{82}Br nuclear reaction. Potassium Bromide, KBr, is used as the target material. Irradiated KBr is dissolved in distilled water and passed through a column containing resin Dowex 50. Radioisotope ^{42}K will be retained in the column. The ^{82}Br ($K^{82}Br$) solution can be concentrated by boiling the eluate. Usually, the activity concentration of the product is adjusted to 1 mCi/ml.)

c) Production of miscellaneous radioisotopes

Usually, these radioisotopes (see Table 1) are produced on customer's request. Radioisotope like ^{64}Cu, ^{42}K, ^{24}Na, ^{86}Rb, ^{110m}Ag and ^{192}Au are produced without any diffulcuties.

In the case of ^{59}Fe and ^{46}Sc, enriched targets could be used in order to increase the specific activity of the products. At present, natural Fe_2O_3 and Scandium Glass are used as target materials. The long-lived radioisotope Tritium (^{3}H) is prepared by dissolution of irradiated Li_2Co_3 in concentrated HCl and distillation of this solution will produce ^{3}H as $^{3}H_2O$ (Triated water). Other potential radioisotopes which could be produced using the reactor are ^{140}La, ^{204}Tl, ^{72}Ga, ^{71}Ge, ^{63}Ni and ^{131}I.

3. Future Programme of Radioisotope Production at UTN.

Table 2 shows a production programme for beginning 1987 until 1990. This projection was based on the current demand and future predicted demand of radioisotopes (this will be elaborated in the last paper). Emphasis will be given to both industrial and medical radioisotopes. Short and medium half-life radioisotopes will be mostly produced at UTN and those of longer half-lives will be imported in the form of 'raw irradiated targets' and processed locally. Example of the later case is ^{192}Ir. The reason for this is the limitations imposed by the reactor which has insufficient neutron flux density.

To cater for the new radioisotopes and the increase in the amount of radioisotopes in the future, new facilities have to be acquired. Most of these facilities were requested through the submission for the Fifth Malaysian Plan. Table 3 shows some of the major equipments needed.

Apart from the equipment, irradiation facility at the TRIGA Reactor will also be upgraded to meet some of the requirement in the future. An irradiation pipe is expected to be installed in the core position early next year. The flux at the pipe will be approximately 5 to 6 times more than that of the Lazy Susan (i.e. the present irradiation facility for production).

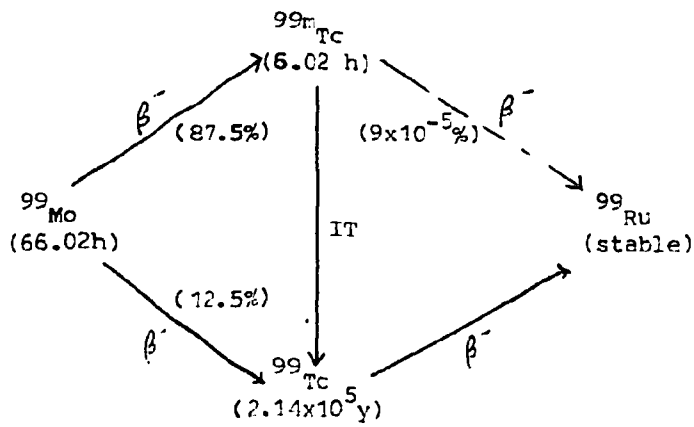
4. Conclusion

Basic experience and expertise in the production and quality control of radioisotopes has been achieved at UTN. Eventhough the production and supply of radioisotopes is still at its early stages, the production personnel is capable and ready to increase and diversify the production. This could be done because of the availability of expertise, instruments and good logistics support.

Lastly but not least, we would like to call upon our guests to suggest any other new radioisotopes which should be produced at UTN to fullfill the local demand or if not possible because of technical constraints, locally processed fror imported bulk supplies.

Fig. 1

The decay sequence of ^{99}Mo to ^{99}Ru



Schematic diagram of compact solvent extraction ^{99m}Tc plant

Explanation of symbols

1. Beaker with ^{99}Mo solution
2. 2 to 5 reservoirs
5. Extraction flask
7. Overhead stirrer machine
8. Alumina column
9. Evaporator and heating element
10. Condenser
11. MEK collector container
12. Drop counter
13. Three way valve
14. Vacuum generator
15. Control panel
16. Hot-plate stirrer

▨ Valves

Fig. 2 : Schematic diagram of compact solvent extraction ^{99m}Tc plant.

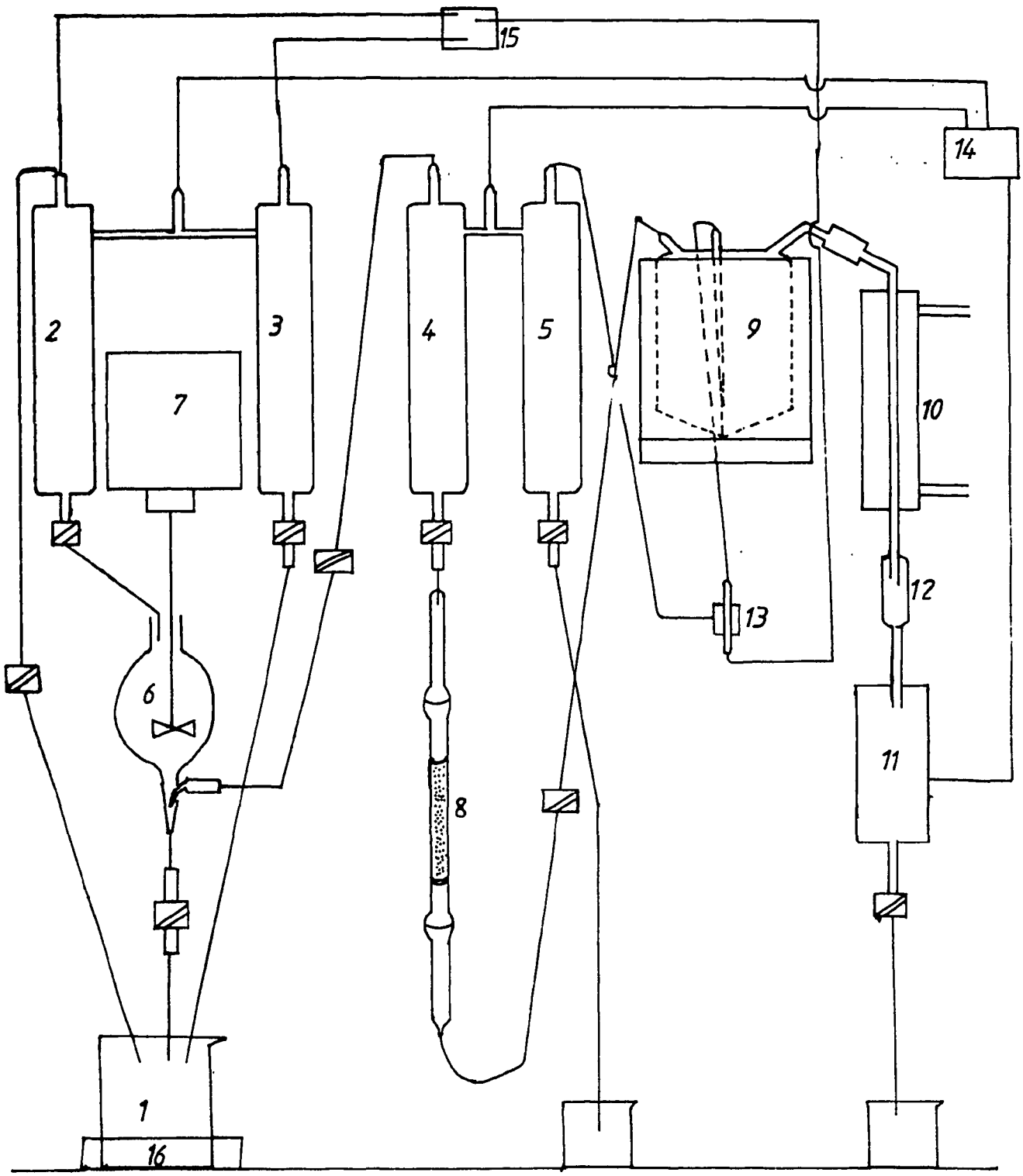


Fig. 3

A simplified scheme for ^{99m}Tc production using solvent extraction technique

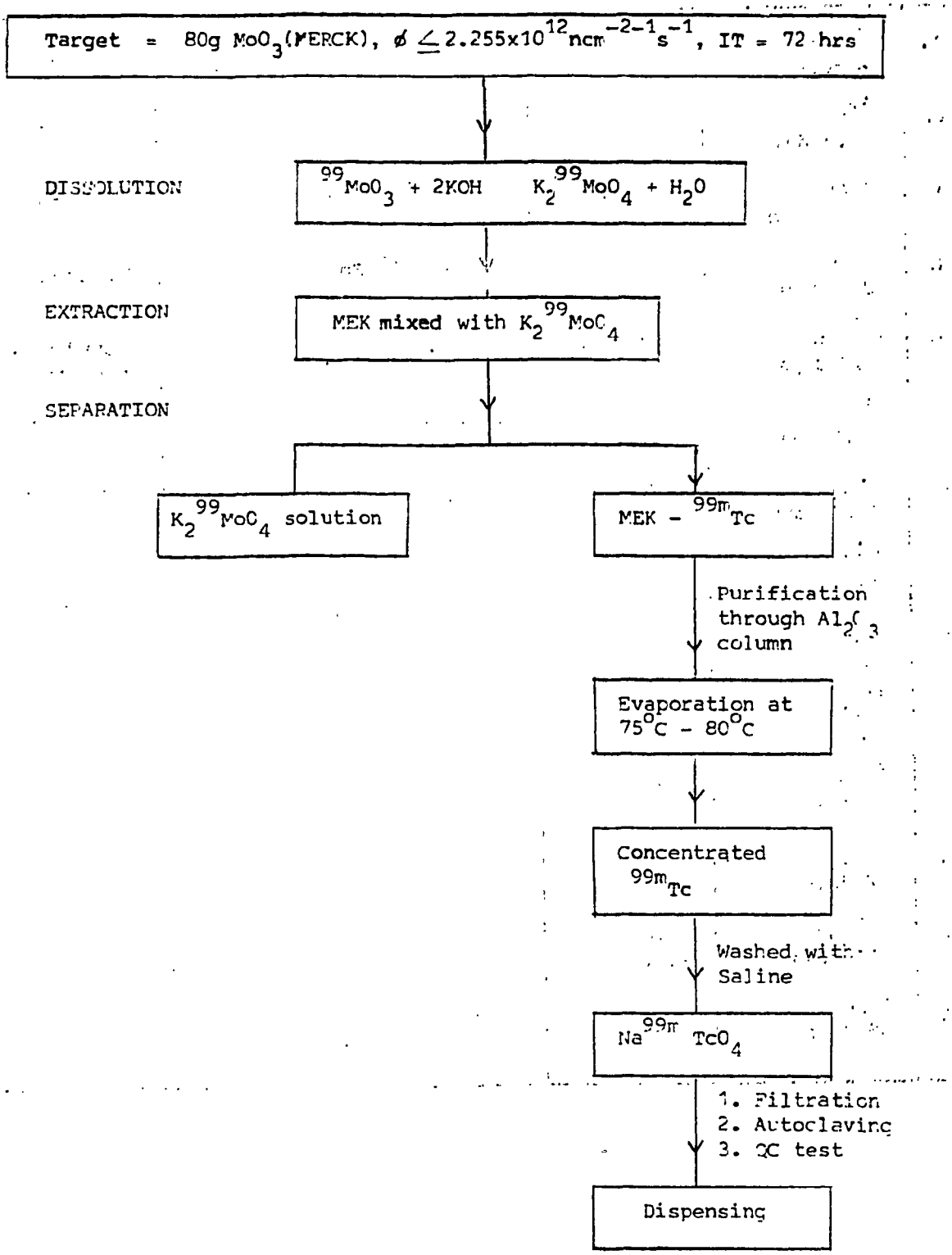


Table 1

Radioisotopes produced using TRIGA MK II reactor at Nuclear Energy Unit

No.	Radioisotope & half life	Target Material	Nuclear Reaction	Average yield/batch	Application
1.	^{99m}Tc 6 hours	MoO_3	$^{98}Mo(n,\gamma)^{99}Mo$	200 mCi	Medicals
2.	^{32}P 14.3 days	Red Phosphorus	$^{31}P(n,\gamma)^{32}P$	200 mCi	Fertilizer placement
3.	^{64}Cu 12.8 hours	$Cu_2SO_4.5H_2O$ CuO	$^{63}Cu(n,\gamma)^{64}Cu$	100 mCi	Plant nutrition
4.	^{65}Zn 245 days	ZnO	$^{64}Zn(n,\gamma)^{65}Zn$	60 mCi	Sendiment transport
5.	^{198}Au 2.7 days	Gold Foil	$^{197}Au(n,\gamma)^{198}Au$	50 mCi	Ground water velocity
6.	^{3}H 12.3 years	Li_2CO_3	$^{6}Li(n,\alpha)^{3}H$	25 mCi	Gauging
7.	^{42}K 12.4 hours	K_2CO_3	$^{41}K(n,\gamma)^{42}K$	10 mCi	Soil nutriton
8.	^{24}Na 15 hours	Na_2CO_3	$^{23}Na(n,\gamma)^{24}Na$	10 mCi	Water strear gauging
9.	^{86}Rb 18.7 days	Rb_2CO_3	$^{85}Rb(n,\gamma)^{86}Rb$	10 mCi	Tracing
10.	^{82}Br 35.4 days	KBr	$^{81}Br(n,\gamma)^{82}Br$	10 mCi	Ground water tracing
11.	^{51}Cr 27.7 days	$K_2Cr_2O_7$	$^{50}Cr(n,\gamma)^{51}Cr$	10 mCi	Water stream gauging
12.	^{46}Sc 84 days	Sc-glass	$^{45}Sc(n,\gamma)^{46}Sc$	10 mCi	Sendiment transport
13.	^{110m}Ag 253 days	Silver metal	$^{109}Ag(n,\gamma)^{110}Ag$	5 mCi	ground water direction
14.	^{59}Fe 45 days	Fe_2O_3	$^{58}Fe(n,\gamma)^{59}Fe$	100 uCi	Entomology

Table 2

Radioisotopes / Radiopharmaceutical Products To Be Produced by UTN in Future.

No.	Radioisotopes/Radiopharmaceutical Product (Kit)	Expected year of Production	Applications
1.	New Radiopharmaceutical kits :		
	Glucoheptonate & HIDA	1987	Kidney Scan & Hepatobiliary imaging
	DTPA and MAA	1988	Kidney scan & lung scan
	DMSA	1989	kidney scan
2.	^{131}I production	1988	Thyroid diagnosis and theraphy.
3.	RIA-kits (T3, T4, TSH)	1988	In-vitro applications.
4.	^{192}Ir (assembling sources)	1989	Radiography (Industrial)
5.	Gel generator (^{99m}Tc)	1989	Medical (Brain scan and others)

Table 3

New Equipment / Facilities For Future Production

No.	Equipment/Facility	Purpose	Quantity
1.	Miscellaneous hot-cell (from IAEA)	Production of miscellaneous radioisotopes (γ-emitters) in the range of 100 s mCi to a few Cis ^{46}Sc, ^{24}Na, ^{82}Br, ^{140}La, etc.	1
2.	Hot-cells and in-cell equipment) for ^{192}Ir.	^{192}Ir sources assembly and quality control.	2 in-series
3.	Fume-cupboards	For handling low-level radioactive materials.	2
4.	Laminar Flow Cabinet	Production and dispensing of new radiopharmaceutical kits.	2
5.	Freeze-drying unit.	Freeze-drying cold kits.	1
6.	Automatic -counter	RIA and other radioactive samples counting.	1
7.	Refrigerated centrifuge	For RIA development works.	1
8.	In-cell equipment for ^{131}I.	Routine production of ^{131}I for kidney diagnosis and therapy	1

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INTEGRATEG APPROACH TO QUALITY CONTROL PROCEDURES OF RADIOISOTOPES AND RADIOPHARMACEUTICALS

ROHANI MOHAMAD
UNIT TENAGA NUKLEAR

INTERGRATED APPROACH TO QUALITY CONTROL PROCEDURES OF RADIOISOTOPES AND RADIOPHARMACEUTICALS

By: Rohani Mohammad

INTRODUCTION

Quality control procedures are those procedures essential for the determination of the purity and integrity of radioisotopes and radiopharmaceuticals. It is part of Good Manufacturing Practice (GMP) mainly concerned with sampling and analytical testing, and with the establishment of specifications and documentation which form the basis for release of raw materials and finished products.

Radioisotopes which are not used for medical purposes undergo tests involving the identification of radionuclides present and radioactivity measurement.

Radiopharmaceuticals are pharmaceuticals containing radionuclides and are used for the diagnosis and therapy of human diseases. Since they are intended for human administration, it is imperative that they undergo strict quality control measures. All quality control procedures that are applied to non-radioactive pharmaceuticals are applicable to radiopharmaceuticals; in addition, tests for radionuclidic and radiochemical purity have to be carried out. Thus, this paper mainly describes the various quality control procedures that are carried out at UTN for radiopharmaceutical products.

Radiopharmaceutical kits referred to in this paper pertain to preparation kit also known as 'cold kit'. They are non-radioactive preparation used as scanning agent after the addition of radionuclides, most often Tc-99m. Therefore, these kits can be prepared well in advance of use and their quality ascertain.

Due to the number and different types of tests to be performed, the Quality Control (QC) Section of Isotope Department is subdivided into three separate units which are Chemical/Radiochemical, Biological and Microbiological QC. These units complement each other in our efforts towards the production of high quality products. Subsequent discussions will be focused on the various types of QC procedures performed by the different units.

Chemical/Radiochemical QC

This unit deals not only with the finished products but also the raw materials. For the preparation of cold kits the starting materials undergo all the tests specified in either the BP or USP which usually includes, identification, limit tests and assay. For those materials of plant or animal origin, additional microbiological tests have to be done. Only those chemicals that pass these rigorous tests will be used in the manufacture of the kits.

Finished products are tested for the following:-

1) **Physical characteristics and pH**
2) **Radionuclidic purity**
3) **Radioactive concentration (radioassay)**
4) **Radichemical purity**
5) **Chemical purity**

The first step in quality control is the physical examination of the product. A particular preparation should exhibit the correct physical appearance, such as colour of the solution or powder. A true solution should not contain any particulate matter and colloidal or aggregate preparation must have a proper size range of particles for a given purpose. The same goes for freeze-dried preparation which should not show any sign of wetness. On satisfactory completion of visual inspection, the pH of the product can be ascertained. This is usually done by using a narrow range pH paper. For radiopharmaceuticals the pH usually falls within the range of 5 to 7.

Radionuclidic purity and radioactive concentration are usually performed on radioisotopes . Radionuclidic purity test will enable the amount of radionuclidic impurities present to be determined. For this purpose a multichannel analyser coupled to a lithium-drifted-germanium detector [Ge(Li)] is used to analyse the gamma-spectrum. In order to hasten the analysis, the analyser is interfaced to a micro-computer. A Basic86 program is written to enable the analysis to be made. The program is able to identify and quaantify the amount of radionuclidic impurities present in the eluates. Some of the impurities limits for Tc-99m pertechnetate are:

	USP Limits	BP Limits
Mo-99	0.15 uCi/mCi	0.1 %
I-131	0.05 uCi/mCi	0.005 %
Ru-103	0.05 uCi/mCi	0.005 %
Sr-89	0.0006 uCi/mCi	0.00006 %
Sr-90	0.00006 uCi/mCi	0.000006 %
Others	0.1 uCi/mCi	0.01 %

All radioisotopes and radiopharmaceuticals produced must be assayed for activity. This can be carried out by means of a dose calibrator which is a well-type air or gas-filled ionisation chamber coupled with an electrometer, which reads the activity of a radioactive sample in Curies or Becquerel.

Radiochemical purity is the fraction of total radioactivity in the desired form. Some example of radiochemical impurities are free pertechnetate and hydrolysed Tc in many Tc-99m labelled complexes, free I-131 in I-131 labelled protein and so on. The presence of radiochemical impurities in a radiopharmaceutical results in poor-quality scans due to its poor localisation in the organ of interest and the high background from the surrounding tissues.

A number of analytical methods are used to detect and determine radiochemical impurities in a given radiopharmaceutical. Chromatography is one of the more popular method and paper chromatography or ITLC (Instant Thin Layer Chromatography) is mostly used. ITLC strips are made of glass fibre

Biological QC

Biological quality control includes the biodistribution of radiopharmaceuticals in rats and pyrogen testing of radiopharmaceuticals using the rabbit method.

Biodistribution Studies

Biological studies is important in ensuring that radiopharmaceuticals localise in organs of interest. The test is carried out by injecting a suitable amount of the preparation (usually less than 0.2 ml) into the tail vein of Sprague-Dawley rats. The animal is sacrificed a certain period post injection depending on the radiopharmaceutical understudy. Various organs such as liver; spleen; kidney; heart; blood; bone; skin; muscles; lungs; stomach; etc are sampled and later counter in an automatic gamma-counter. Analysis of the results are done with the help of a computer program called BIODIST. The results obtained are expressed in per cent per injected dose and per cent injected dose per gram tissue as follows:

$$\% \text{ Injected Dose (ID)} = \frac{\text{Counts/Total organ counts}}{\text{Standard Counts}}$$

$$\% \text{ ID / g Tissue} = \frac{\% \text{ ID}}{\text{Total Organ Weight}}$$

If the % ID or % ID/g tissue obtained is within the specified limits for that particular radiopharmaceutical, then the preparation complies with the test and can be approved.

Pyrogens Test

Pyrogens are either polysaccharides or proteins produced by the metabolism of microorganisms. They are 0.05 - 1 um in size and in general they are soluble and heat stable. The bacterial products, the so-called endotoxins are the prime examples of pyrogens, but various chemicals also can add pyrogens to a radiopharmaceutical solution.

Sterility of a solution does not guarantee its apyrogenicity nor does sterilisation destroy the pyrogens in a radiopharmaceutical. Since pyrogens arise mainly from the metabolism of bacteria, the best recourse to prevent pyrogenic contamination is to use sterile glassware, solutions and equipment under aseptic conditions in any prepartion procedure.

The USP XX bases the pyrogen test on the febrile response in rabbits within 3 hours after injection of the material. Three mature normal rabbits are chosen for the test, and their temperature are controlled by keeping them in an area of uniform temperature. The test sample is injected into the ear vein of each of the three rabbits. The rectal temperature of the animals are measured 1, 2 and 3 hous after injection. If the rise in individual animal is less than 0.6 oC and if the sum of the temperature rise in all 3 animals does not exceed 1.4 oC, then the test sample is considered apyrogenic.

impregnated with silica or poly-silicic acid. A small aliquot of the radiopharmaceutical preparation is spotted on the strip and then chromatographed using 85 % methanol, acetone, MEK or saline as solvent. The strip when dried is usually cut into two halves and counted. The activity found in the two portions will indicate the purity of the product. The required purity is usually 95 %.

In the case of chemical purity, it is the fraction in the desired chemical form, whether or not all of it is in the labelled form. Chemical impurities arise from the breakdown of the material either before or after labelling eg. aluminium is a chemical impurity in the Tc-99m eluate. The presence of chemical impurities prior to radiolabelling can result in undesirable labelled molecules that may or may not interfere with the diagnostic test. Undue chemical impurities may also cause toxic effect. Identification of these impurities should be performed, usually by calorimetric methods.

The limits for chemical impurities determined routinely in Tc-99m pertechnetate generator eluate are:

Lead	< 40 ppm
Molybdenum	< 50 ppm
Aluminium	< 10 ppm
Ketone	< 1 % (from solvent extraction method)

Microbiological QC

Microbiology QC unit is responsible for the environmental control test and also the sterility test of medical radioisotopes and kit preparations.

Sterility indicates the absence of any viable bacteria or other microorganisms in a radiopharmaceutical preparation. Sterilisation can be done using suitable methods, such as autoclaving, gamma-irradiation or membrane filtration. The method chosen will depend on the nature of the product, the solvent and various additives. Whatever the methods of sterilisation used, the products had to be tested for sterility.

These test must be performed aseptically so that external bacteria are not added to the test samples during the procedure. According to USP XX, sterility tests are performed by incubating the radipharmaceutical samples in fluid thioglycollate medium at 30-35 oC for 7 to 14 days for the detection of bacteria and soya bean casein digest medium incubated at 20-25 oC for 7 to 14 days for the detection of fungi contamination. These methods are adopted at UTM. If growth is observed in either media ,the radiopharmaceutical is considered not sterile.

Recently a rapid method has been introduced for the detection of pyrogens. This method utilizes the lysate of amebocytes from the blood of the horsecrab, Limulus polyphemus. The principle of the test based on the formation of an opaque gel by pyrogens upon heating at 37 oC with the Limulus amebocyte lysate (LAL). The reaction takes place within 15 - 60 minutes after mixing and depends on the presence of pyrogens. The thicker the gel, the greater the concentration of pyrogens in the sample. The test has not yet replaced the rabbit test.

CONCLUSION

Various aspects of the quality control procedures for radioisotopes and radiopharmaceuticals have been discussed. It is by no means exhaustive. The paper highlighted those procedures that are important in ensuring the efficacy of the product. It also gives a general idea of the various procedures that are actually carried out by the QC Section. However, quality cannot be established by testing alone, it must be built into the product during the whole manufacturing process and maintained during transportation and storage.

RADIOISOTOPE PRODUCTION AND DISTRIBUTION IN AUSTRALIA

The Commercial Products Unit of the Australian Atomic Energy Commission provides Australian and Overseas customers with a comprehensive range of high quality radioactive products and associated services.

The Commission has been producing radioisotopes since 1960 and the growth in the sales of radioactive products between 1961 and 1986 is shown in Fig. I. In the early 60's most of the radioisotopes produced were for industrial applications but by 1968 half were being used in medicine and from that time on growth has been primarily for use in medical applications. At the present time only 11% of sales are in industrial users, even though the demand for these products is still growing.

The rapid growth in the use of radioisotopes in medicine was encouraged by the fact that they were supplied to Australian users free of charge up until 1978. At that time Government policy was changed. New legislation required that all products and services provided to hospitals should in future be paid for at regular commercial rates. This policy change encouraged overseas manufacturers to enter the Australian market and this resulted in a wider range of products being available but it also meant that the AAEC had to face strong competition in the marketplace for its products. The competition has been met and the AAEC is once again the primary supplier of radiopharmaceutical products to the Nuclear Medicine Centres of Australia.

The Commission manufactures approximately 100 different products using about 20 different radioisotopes. Some 50 batches of radiopharmaceuticals are manufactured and about 600 shipments made each week to centres throughout Australia and the South East Asian region.

The emphasis of our production program has changed from being research driven to being market driven, which means that what we do and when we do it is now determined primarily by the needs of the customer. We

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place great importance on establishing the present and future needs of our customers on a regular basis, and use this information for making all our key decisions with respect to production scheduling and new product development.

The Australian experience is in many ways unique because we offer on the one hand a very personalised service through our ability to dispense our various products to exact customer requirements whilst at the same time offering a range of products which can be matched only by the largest of the multi-national companies who compete with us. This ability has grown largely from the fact that not only do we manufacture radioisotopes and radiopharmaceuticals but we also provide a centralised dispensing service for products which we source in bulk from overseas manufacturers. The provision of such a centralised service is of great National advantage because it ensures that users are not totally dependent upon overseas supply and can obtain a personalised service which at the same time has created a National centre of expertise and excellence from which future new products will originate.

In addition to distributing the radioisotopes which it produces, the AAEC imports bulk radioisotope supplies for redispensing and other radioactive products such as radioimmunoassay kits and labelled compounds for resale. These imports come primarily from the USA, Japan, Canada, France, Belgium and Italy. These products are imported either because no production facilities exist in Australia and the demand for the isotopes does not justify the expenditure necessary to set up such facilities, or because the radioisotopes can only be produced using a cyclotron.

The most significant cyclotron produced radioisotopes are Gallium-67, Thallium-201, Indium-111 and Xenon-127. The isotope which has a great deal of future potential is Iodine-123, but because of a short half-life of 13 hours importation is extremely difficult and the product unacceptably expensive for routine use.

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The Australian government has now approved funding for the construction of a cyclotron for medical use and we anticipate that a 40 MEV machine will be in operation in Sydney within five years.

The AAEC has found that there are many advantages associated with centralised distribution.

- There is a simplified coordination between production and delivery/despatch schedules.
- Shipments can be lodged with carriers in consolidated form and the higher level of business attracts more favourable freight rates.
- The existence of routine delivery sequences to both customer and carriers means that all personnel involved within the Commission and outside, become thoroughly familiar with the shipment routines. This level of competence is very important and enables deliveries to be made reliably and with the minimum of delay between the time of despatch and the receipt of the products by customers. The follow-up of any mislaid shipments is also made much easier and faster.
- Finally, it is possible to employ a small team of officers who specialise in the packaging and despatch of radioactive products and who are thoroughly familiar with the complex and exacting regulations for the shipment of radioactive goods.

These advantages can combine to give a better overall customer service than would otherwise be available.

The Commission arranges for its products to be delivered by road, rail, sea and air, but the primary methods are by road and by air.

Nearly all the the Commission's products leave Despatch in its own fleet of special purpose vehicles, which deliver the products

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directly to customers within the Sydney metropolitan area or to the depots of road transport companies for delivery to regional country areas or to the airport for most of the products which have to travel interstate. Onforwarding from other airports is mainly by road but occasionally rail transportation is used.

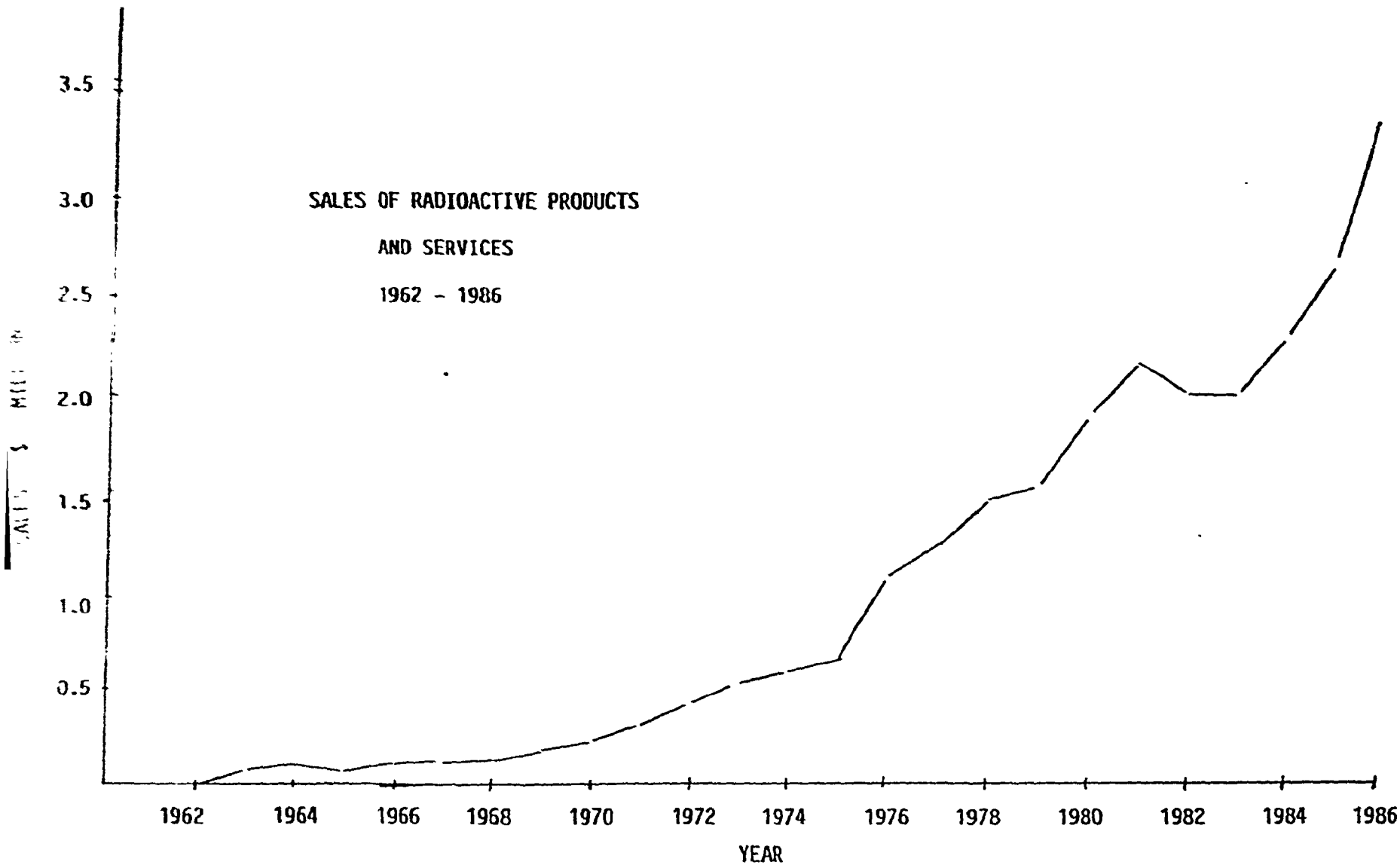
All shippers of radioactive products which use the airlines have problems with delivery reliability, which can arise from such things as:

- flights cancelled without notice,
- shipments offloaded at intermediate airports,
- flights booked out with other freight,
- livestock in cargo hold which cannot travel with radioactive shipments,
- products put on the wrong plane,
- the use of an aircraft which cannot carry the required amount of radioactivity.

No doubt many customers have first hand experience of the above problems, however, it is our experience that as a major distributor having direct and influential contact with airline operating staff, we have far less incidence of failed or delayed delivery than do other organisations. We have been able over the years to establish a close and successful working relationship with all our carriers and we would expect that PUSPATI staff would, over a period of time, achieve a similar relationship with Malaysian transport companies.

For many years now Australia has been providing advice and assistance to the Unit Tenaga Nuklear at PUSPATI. Under this program many PUSPATI staff have been attached to the Commission for extended periods to study our facilities and to receive advice on how best to design and build the facilities which now exist here, at PUSPATI. There have also been many visits by Commission staff to PUSPATI to assist in the commissioning of the facilities and to round-off the

training of PUSPATI staff using these new facilities. As a consequence we are confident that the staff at PUSPATI will be able to provide Malaysia and some of the surrounding countries with the type of service, albeit on a smaller scale, that the Commission has been able to supply within Australia. In particular we see considerable potential for PUSPATI to provide high quality products and services utilising the radioisotopes Technetium-99m, Iodine-131 and Iridium-192; to this end we will be making available to PUSPATI supplies of these key radioisotopes.


SALES OF RADIOACTIVE PRODUCTS
AND SERVICES
1962 - 1986
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1962
1964
1966
1968
1970
1972
1974
1976
1978
1980
1982
1984
1986
YEAR

SEMINAR PENGELUARAN DAN BEKALAN
RADIOISOTOP UNTUK PENGGUNA-PENGGUNA
DI MALAYSIA
KOMPLEKS PUSPATI, BANGI,
22HB. OKTOBER, 1986.

RADIOISOTOPE DISTRIBUTION CENTRE OF THE NUCLEAR ENERGY UNIT

ROSNAH JANOR
UNIT TENAGA NUKLEAR

Radioisotope Distribution Centre of The Nuclear Energy Unit

(Rosnah Mohd. Janor)

This short paper attempts to explain to customers as well as potential clients what the radioisotope distribution centre is, its role and it's relation to the Customer Services Unit, UTN.

A. INTRODUCTION

In January 1983 a survey was conducted on the use of radioisotopes in the country. It was then discovered that there was a need to upgrade the supply service sector. It was also found out then that prices of radioisotopes were rather expensive compared to prices other countries.

Based on the finding of the Survey, in 1984 it was proposed that a Distribution Centre be set up in the Isotope Department to coordinate sales of radioisotopes in Malaysia. With the setting up of this centre, those isotopes imported in bulk from overseas suppliers will be redispensed in UTN and redistributed in the region, together with those locally produced by UTN.

In 1985 a working paper on this Distribution Centre was submitted to the Cabinet for discussion and approval. Comments from various relevant Government agencies were sought and found favourable. In principle, the proposal was approved by the cabinet ministers.

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Currently, the centre is placed under the Customer Service Unit, a unit responsible for coordinating the operations of services oriented projects in UTN.

The idea concerning this distribution centre is not a new one. Such centres are already in existence in Australia, Greece, Denmark, Hungary and many other countries. It has been shown that in these countries the distribution centres have contributed a lot to the extensive use of nuclear technology through providing reliable radioisotope supply services as well as other services associated with it.

It is emphasised here that in no way will the centre act as a regulatory body. Also, other private agents can continue provide the radioisotope supply services as long as they abide by the rules outlined in the Radioactive Substance Act 1984, Which is enforced by the Atomic Energy Licensing Board.

B. OBJECTIVES

The distribution centre aims to achieve certain objectives, the main ones being :-

1) to promote and distribute UTN produced radioactive and non radioactive products in Malaysia and in neighbouring countries.

2) to establish direct contacts with overseas suppliers and engage in commercial activities with them in order to :

   (a) import radioactive products from these suppliers to be redispensed and/or redistributed in the region.

(b) help other institutions in Malaysia and other departments in UTN in acquiring their supplies of radioisotopes in the safest, easiest and most reliable ways.

(c) Introduce and supply informations to users on availability of new products and new techniques.

3) to provide and coordinate after sales services to customers in the region, and also provide other services associated with the use of radioisotopes. This may include quality control checks, package contamination checks, consultations etc.

These objectives are in line with one of the objectives of UTN ie to introduce,promote and encourage the use of nuclear technique in the country.

C. RATIONALE

There are a number of rationale to support the setting up of this centre in UTN. They are :-

1) to maximise usage of resources such as equipment and expertise which are already available in UTN.

Equipment, expertise and logistic support are what is needed in order to operate this distribution centre. These are already available in UTN since UTN will also be distributing its products to the customers. So if

...4/-

UTN embarks on the activity of importation and distribution of radioisotopes, this will not incur a great investment on our part, as far as procurement of staff and equipment is concern. Instead, we will be maximising the use of our present resources.

2) to promote and speed up the use of nuclear technology in Malaysia by providing reliable radioisotopes supply services to customers.

To a large extent, the growth of nuclear technology in the country will depend on supply of radioisotopes used. Reliable supplies at a reasonable cost is of utmost important to support the needs of industries using nuclear techniques. By having this centre we are providing another alternative to users for supply of radioisotopes. This indirectly will help stabilise prices and also introduce competition in the market. This will benefit customers in the sense that they can get better quality of supply and services.

3) to help customers obtain quality products and services from overseas manufacturers.

This may be achieved by offering quality control services on products imported in bulk and also by doing inspections on packages for any radioactive contaminations, before the packages are delivered to customers.

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4) to encourage technology transfer

By having a close collaboration / relation with overseas manufacturers, UTN can benefit in ways such as training of its staff, experts visits and consultation services from overseas manufacturers. This in turn will benefit customers because UTN will be conducting seminars and courses from time to time, to introduce users to new products and new techniques. Hence both parties will gain from this technology transfer.

D. PRODUCTS AVAILABLE

1) Locally Produced Products

At present UTN can produce 14 types of non medical products. They are :-

Phosphorus - 32	Technetium - 99
Sodium - 42	Iron - 59
Potassium - 42	Zinc - 65
Silver - 110 m	Sc - 46
Hydrogen - 3	Au - 198
Copper - 64	Br - 82
Rubidium - 86	Cr - 51

Specifications of each of these products are available in our products catalogue. There will be a few more radioisotopes added to the list in the near future. They are I -131, Ga-72, La-140 and Tl-204, Ni-63.
Users are invited to give suggestion and / or recommendation on what products they wish us to try and produce. We are happy to evaluate such requests.

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For medical products, we are well on the way to produce MDP (Methylene Diphosphonate) and Sulphur Colloid Technetium kits. Currently we are in the process of submitting the application for registration of drugs / cosmetics for approval to market these products. Submission is made to The National Pharmaceutical Control Laboratory.

2) Imported Products

Radioisotopes that can be imported in bulk and redispensed at UTN are :

a) I - 131 (medical and non medical)

b) I - 125

c) Tc - 99m (medical)

d) Kits not produced in UTN including Tc-99m labelled kits and RIA kits.

e) Labelled compounds.

Users are welcome to enquire about any products they wish to purchase. Our ordering informations and general conditions of sales are clearly laid out in our product catalogue. We will try to help users in the best way we can.