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Alternative technologies for $^{99}Tc^{m}$ generators

Final report of a co-ordinated research programme 1990–1994

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FOREWORD

$^{99}Tc^{m}$ is the workhorse of nuclear medicine and currently accounts for over 80% of all in vivo diagnostic procedures. This radionuclide is made available to nuclear medicine centers in the form of a generator wherein the parent ^{99}Mo (generally produced by the fission of ^{235}U) is retained on a column of alumina and the daughter $^{99}Tc^{m}$ produced by the decay of ^{99}Mo is separated out by elution of the column with saline solution. The production of ^{99}Mo by the fission of uranium involves a complex and expensive technology; further large quantities of highly toxic radioactive wastes are produced in the fission process. The fission process is, therefore, not practicable for most developing countries. Fission ^{99}Mo is now routinely produced only in a few large production centers in the world and the short half-life of ^{99}Mo poses transportation problems. In view of the above, the need for developing alternative technologies for the production of $^{99}Tc^{m}$ generators using ^{99}Mo produced by non-fission routes has been keenly felt.

Recognizing the need to develop alternative technologies for the production of $^{99}Tc^{m}$ generators in developing Member States operating medium neutron flux research reactors, the IAEA initiated a co-ordinated research programme (CRP) in 1983. As a result of the work carried out under the auspices of this CRP (1983-1989), it became apparent that technologies based on low temperature sublimation processes and polymolibdate gels showed excellent potential for the preparation of reliable and economical $^{99}Tc^{m}$ generators.

With the aim of further developing the technological aspects and standardizing the production procedures for $^{99}Tc^{m}$ generators based on the above technologies, a follow-up CRP on "Alternative Technologies for $^{99}Tc^{m}$ Generators Based on Low-Temperature Sublimation and Gel Elution" was established in 1990.

Generators based on elution of polymolybdate gels have since been developed and evaluated. Further, based on their own research work and publication from other sources, the experts who participated in this CRP have made a detailed evaluation of other possible alternative technologies for the production of $^{99}Tc^{m}$ generators using ^{99}Mo produced by the non-fission route. The main objectives of these alternative technologies for production of $^{99}Tc^{m}$ generators are to minimize the production of long lived and toxic radioactive wastes and simplicity and convenience of operation, particularly for developing Member States.

The report includes detailed results obtained by all participants as well as an assessment of current alternative technologies.

The IAEA wishes to thank all the scientists who contributed to the success of the CRP.

EDITORIAL NOTE

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1. INTRODUCTION

$^{99}Tc^{m}$ is presently the most widely used radionuclide in diagnostic nuclear medicine accounting for over 80% of all diagnostic procedures. The prominent position of $^{99}Tc^{m}$ has been due to its near ideal nuclear properties, the ready availability of $^{99}Tc^{m}$ in the form of convenient generator systems and the rapid progress made in recent years in the development of a variety of $^{99}Tc^{m}$ radiopharmaceuticals for applications in cardiology, oncology and other fields. In the generator system the parent ^{99}Mo is retained and the daughter $^{99}Tc^{m}$ is separated out and obtained in the form of pure pertechnetate. Even though several methods are reported for separation of $^{99}Tc^{m}$ for use in nuclear medicine, the choice should be made very carefully to ensure pharmaceutical and radiological safety and absence of toxicity. The following four methods of separation of $^{99}Tc^{m}$ from ^{99}Mo are generally accepted as suitable for nuclear medicine applications and employed in regular use to some extent in different countries:

- Column chromatography over alumina.
- Solvent extraction using methyl ethyl ketone.
- Sublimation of technetium heptoxide.
- Elution of metallic molybdate gels.

Among these techniques the alumina column generators are the most widely used because of several advantages which include compact size, easy transportability, single step rapid operation, radiological and pharmaceutical safety and $^{99}Tc^{m}$ separation with high yield and purity. However, for preparing these generators high specific activity ^{99}Mo obtained most commonly by the fission of ^{235}U is required. Despite the operational advantages of alumina column generators the possibility of their routine preparation in many developing countries still appears remote due to various reasons, the most important being:

(a) complex and expensive technology involved in production of both fission ^{99}Mo and the generators themselves. At the level of $^{99}Tc^{m}$ generator required for utilization in nuclear medicine in most developing countries, operation of a fission ^{99}Mo plant may not be economical;

(b) non-availability of highly enriched ^{235}U essential for producing ^{99}Mo with a minimum risk of ^{239}Pu contamination;

(c) management of toxic fission product wastes generated.

Alternative technologies for $^{99}Tc^{m}$ generator using relatively low specific activity ^{99}Mo produced by the neutron activation of natural molybdenum would provide a less complex, less expensive, and more practical route for indigenous production and use of $^{99}Tc^{m}$ in most developing countries. In the long run this route would also be safe for the environment since it does not produce toxic long lived fission product wastes. In addition, the growing diversity in nuclear medicine studies using modern techniques such as single photon emission computerized tomography (SPECT) and the corresponding demands for producing well characterized high purity $^{99}Tc^{m}$ radiopharmaceuticals via a variety of synthetic routes may also require in the future $^{99}Tc^{m}$ of different specifications and purity requirements obtained from different generator systems as starting materials. For example, sublimation generators may provide $^{99}Tc^{m}$ more suitable for non aqueous labelling, for injections of very high biological and pharmaceutical purity and for applications requiring very high radioactive concentration. Similarly $^{99}Tc^{m}$ from gel generators can be eluted with water and may find

applications where NaCl is contraindicated. $^{99}Tc^{m}$ obtained by solvent extraction would be preferred in situations where trace inorganic chemicals and metals are not desired.

This report reviews the alternate technologies available for the production of $^{99}Tc^{m}$ with particular emphasis on recent work carried out under a co-ordinate research programme instituted by the IAEA.

Related IAEA publications include IAEA-TECDOC-515 - Fission Molybdenum for Medical Use (1989), IAEA-TECDOC-532 - Development of New Radiopharmaceuticals (1989) and IAEA-TECDOC-805 - Production of $^{99}Tc^{m}$ Radiopharmaceuticals for Brain, Heart and Kidney Imaging (1995). In addition, one new publication is planned in the field of $^{99}Tc^{m}$ labelled monoclonal antibodies for immunoscintigraphy.

2. PRODUCTION OF ^{99}Mo

^{99}Mo is generally produced by the direct (n, γ) activation of natural molybdenum or enriched ^{98}Mo or by the fission of uranium. Production of ^{99}Mo is also possible by the cyclotron irradiation of highly enriched ^{100}Mo, but this method of production may be very expensive and needs further research efforts to assess its feasibility. Direct (n, γ) activation of natural molybdenum yields ^{99}Mo of specific activity ranging from 4 to 40 GBq per gram for irradiation at neutron fluxes of 10^{13} to 10^{14} n/cm^2/s. The use of highly enriched ^{98}Mo (>98% ^{98}Mo) enhances the yield of ^{99}Mo and its specific activity by a factor of about 8. The fission yield of ^{99}Mo (for ^{235}U) is 6.1% and 1 g of 98% ^{235}U yields about 7500 GBq of ^{99}Mo for irradiation at a neutron flux of 10^{14} n/cm^2/s. The specific activity of fission produced ^{99}Mo exceeds 2×10^5 GBq\g.

The (n, γ) produced ^{99}Mo is of high radionuclidic purity if a pure target, generally MoO_3, is employed for irradiation. However significant quantities of ^{186}Re, ^{188}Re, ^{122}Sb, ^{124}Sb, ^{134}Cs, ^{60}Co, ^{65}Zn, ^{95}Zr, ^{95}Nb, $^{110}Ag^{m}$, ^{192}Ir, etc. have been detected in samples of (n, γ) produced ^{99}Mo; these impurities arise from activation of traces of Re, Sb, Cs, Co, Zn, Zr, Ag and Ir impurities which are likely to be present in MoO_3. In addition to these, traces of U may also be present in the MoO_3; the U impurity produces fission product radionuclides as well as ^{239}Pu.

For production of ^{99}Mo by the fission process, highly enriched ^{235}U is the favored target; however, recent trends favor the use of low enriched ^{235}U. An earlier IAEA report [1] describes the production of ^{99}Mo by the fission process.

3. ASSESSMENT OF ALTERNATIVE $^{99}Tc^{m}$ GENERATOR TECHNOLOGIES

During the last three decades, the following six types of generators using non-fission ^{99}Mo as the source have been developed and evaluated for $^{99}Tc^{m}$ [2, 3].

- Chromatographic alumina column generators using (n, γ) produced ^{99}Mo of medium specific activity.
- Solvent extraction based generators using (n, γ) produced ^{99}Mo of low and medium specific activity.

- Gel generators using zirconium molybdate(ZrMo)-^{99}Mo gels prepared from (n, γ) produced ^{99}Mo.

- Gel generators using titanium molybdate (TiMo)-^{99}Mo gels prepared by direct irradiation of preformed TiMo "gel" targets.

- Gel generators using zirconium molybdate (ZrMo)-^{99}Mo gels prepared by the irradiation of preformed ZrMo "gel" targets.

- Sublimation generators using neutron irradiated SiC-MoO_3-V_2O_5 targets.

3.1. CHROMATOGRAPHIC ALUMINA COLUMN GENERATORS USING (n, γ) PRODUCED ^{99}Mo OF MEDIUM SPECIFIC ACTIVITY

Column chromatography generators loaded with (n, γ) produced ^{99}Mo were in regular production before fission produced ^{99}Mo of the required purity became available in large quantities. This type of generator is still being produced and supplied from a small number of centers such as the Institute of Nuclear Research, Ulugbek near Tashkent. These generators contain a column of chromatographic grade alumina (10-15 g) on which the molybdate-^{99}Mo is firmly retained; the ^{99}Tc^m is eluted with saline solution. It is well known that the adsorption capacity of alumina and similar exchanger for molybdate is low (2-20 mg Mo per gram of Al_2O_3). Considering the specific activity of (n, γ) produced ^{99}Mo (4-40 GBq g) it is apparent that the maximum capacity of such generators will be limited to about 10 GBq of ^{99}Mo per generator. The radioactive concentration of the ^{99}Tc^m obtained by direct elution of such generators will not be adequate for large dose administrations. However, the development of practicable procedures [23] for concentrating the ^{99}Tc^m eluate (described in Annex III) will help to overcome the limitation of low concentration of the ^{99}Tc^m eluate. If enriched ^{98}Mo (>98% ^{98}Mo) is available for irradiation, the capacity of the generator may be upgraded to over 40 GBq of ^{99}Mo per generator. There are indications that highly enriched ^{98}Mo (>98% ^{98}Mo) will be available in good quantities and at a reasonable price. In this case, the use of enriched ^{98}Mo as the target for activation, followed by recovery of the expensive target will enable the production of higher activity (over 40 GBq) generators by the (n, γ) activation method. However, no information is thus far available in the open literature on the practicability and technological details of the production method.

3.2. SOLVENT EXTRACTION BASED GENERATORS USING (n, γ) PRODUCED ^{99}Mo OF LOW AND MEDIUM SPECIFIC ACTIVITY

Generators based on methyl ethyl ketone (MEK) extraction of TcO_4^- from alkaline molybdate solutions have been widely used for the production of ^{99}Tc^m [21, 22, 24]. The solvent extraction technology (SET) is currently in use in some countries and both centralized and hospital based generators are in operation. The solvent extraction procedure provides, under well controlled conditions, ^{99}Tc^m of high purity comparable to that from the alumina column generator [2]. The operation of the solvent extraction generator is, however, complicated and cumbersome and requires highly skilled and trained man-power. Such generators, provide an efficient mean of optimally using low and medium specific activity, (n, γ) produced ^{99}Mo. It is apparent that the solvent extraction method has a very useful and definite role for routine use in developing Member States. For the introduction and continuing use of this technology, however, adequate training programmes may have to be organized and the necessary facilities have to be established at hospital radiopharmacies.

3.3. GEL GENERATORS USING ZIRCONIUM MOLYBDATE (ZrMo)-^{99}Mo GELS

It is apparent that the essential elements of the ZrMo-^{99}Mo gel technology have been well standardized and established [4-7, 10, 12, 15, 17, 18, 19]. The procedures outlined in Annex I of this report may be used to produce about 30 generators per batch and containing about 20 GBq of ^{99}Mo per generator. The equipment and remote handling devices required for regular production of 30 generators per batch are not too elaborated and may be readily established in many developing Member States which have the necessary reactor irradiation facilities. For the production of 30 generators per batch a neutron flux exceeding 1×10^{13} n/cm^2/s with uninterrupted target irradiation for at least 3 days (72 hours) will be required.

This technology appears to be the ideal choice for a regular production programme on a scale of about 30 generators per week since the target is well known and stable, the processing operations are not too sophisticated and only the minimal quantity of wastes is produced. Further, the ZrMo gel is very stable, the column is rugged and very closely corresponds to the fission ^{99}Mo generator functionally. It is apparent that centers which have established ^{99}Tc^m production at the level of about 30 generators per week using imported fission ^{99}Mo may consider switching over to the ZrMo-^{99}Mo gel technology if they have the necessary reactor irradiation facilities. Such a transition would help eliminate or minimize the dependence on imports of fission ^{99}Mo.

3.4. GEL GENERATORS BASED ON DIRECT REACTOR IRRADIATIONS OF PREFORMED TITANIUM MOLYBDATE (TiMo) GEL TARGETS

The details of this procedure are given in Annex II. This technology appears to be the simplest for production on a relatively small scale (20 generators per week) [8, 9, 20]. The equipment and facilities required are modest and the production of wastes is the minimum. However, the target is sensitive to high temperature and will have to be irradiated with adequate cooling. At fluxes exceeding 10^{13} n/cm^2/s, a specially cooled irradiation container may be required. If the target cooling system in the reactor is efficient, as in the case of pool type reactors, normal irradiations would be possible. Considering the relatively low apparent density of the target in the irradiation container such irradiations however do not ensure optimum use of the irradiation volume of the reactor.

It is apparent that this technology would be quite appropriate for centers which have a modest production programme (not exceeding 20 generators per week). The necessary reactor irradiation facilities include a neutron flux of about 10^{13} n/cm^2/s and target loading into the wet irradiation channel. The temperature of the TiMo gel during irradiations should not exceed 100°C. The possible use of highly enriched ^{98}Mo [16] in this technology may be considered. Though no studies have been done in this direction it appears that the use of enriched target and its recycling will be very attractive for scale up of the production levels. It appears that the used target may be recovered by simple washing procedure to remove salts. It will be a logical follow up of the work done under this CRP to undertake a detailed study of target conversion to gel, irradiation, generator production, elution and target recycling, using about 2-3 g of 99% ^{98}Mo.

3.5. GEL GENERATORS BASED ON DIRECT REACTOR IRRADIATION OF PREFORMED ZrMo GEL TARGETS

The details of this method are included in Annex I. Irradiation of ZrMo gel appears to have certain attractive features [8, 13]. The ZrMo gels are more stable than TiMo gels

with respect to ^{99}Mo breakthrough and the mechanical properties of the gel. However, the work done in this field has been limited and conditions of gel preparation for irradiation may have to be optimized. Co-production of radionuclides of Zr and Hf (present as an impurity in the Zr) would pose problems in the generator shielding and may limit the possible use of this technology for regular production.

3.6. SUBLIMATION GENERATORS USING NEUTRON IRRADIATED SiC-MoO_3-V_2O_5 TARGETS

Details of this method are given in Annex IV. It is apparent that sublimation separation of $^{99}Tc^m$ from irradiated SiC-MoO_3-V_2O_5 targets has the attractive features of high yields of very pure $^{99}Tc^m$ free of sodium chlorine and others salts. The product is practically free of many impurities which are likely to be present in trace quantities, as may be the case in $^{99}Tc^m$ prepared from other generator systems. This method would therefore be an ideal route for the preparation of very pure $^{99}Tc^m$ for radiochemical studies. However, the methodology suffers from several disadvantages for use in a hospital based medical generator system. The SiC-MoO_3-V_2O_5 eutectic is highly corrosive and expensive quartz apparatus is required for the sublimation. Such a generator system will have to be recycled to save on the costs of the equipment. As such, the potential of this system for a medical $^{99}Tc^m$ generator is somewhat limited. However, a centralized generator based on sublimation separation would be an attractive and practicable proposition where there is a need for $^{99}Tc^m$ of very high purity and in a form free of sodium chloride and others salts.

4. TECHNOLOGIES DEVELOPED UNDER THE CRP

4.1. $^{99}Tc^m$ COLUMN GENERATORS BASED ON CONVERSION OF ^{99}Mo TO ZIRCONIUM MOLYBDATE

This method has a distinct advantage in that it uses a time tested and well proven target, namely MoO_3, which can be readily irradiated in the reactor. The general procedure followed by various groups in the CRP consists of the following steps:

(a) Irradiation of MoO_3 in a nuclear reactor to produce ^{99}Mo. The irradiation period has varied from several hours to a week in neutron fluxes ranging from 10^{12} to 7×10^{13} n/cm^2/s. Samples have also been irradiated in a power reactor.

(b) Dissolution of the irradiated MoO_3 in alkali. Both sodium hydroxide and potassium hydroxide have been used.

(c) Preparation of Zr(IV) solution in water by dissolving zirconium nitrate or zirconium oxychloride.

(d) Mixing the Zr(IV) solution and ^{99}Mo solution with continuous stirring to form zirconium molybdate precipitate.

(e) Filtering and drying of the precipitate followed by powdering and sieving, if necessary, to get a free flowing ZrMo gel powder. Work carried out during the present CRP has shown that by properly controlling the drying conditions, a readily disintegrated ZrMo gel can be obtained thus avoiding the grinding and sieving steps.

(f) Elution of the ZrMo-^{99}Mo powder with water or saline to get $^{99}Tc^m$. The $^{99}Tc^m$ solution usually has a higher ^{99}Mo and stable Mo breakthrough than acceptable. These are removed by passing the $^{99}Tc^m$ through a purification bed of alumina or hydrous zirconium oxide.

When the radioactive concentration of $^{99}Tc^m$ is low, a concentration step is proposed to increase the same. This is achieved by reduction of $^{99}Tc^mO_4^-$ using Sn(II) ions, adsorption of the reduced $^{99}Tc^m$ on an alumina column, followed by its oxidation using H_2O_2 or NO_3^-, heating and elution of $^{99}Tc^m$ in a small volume [23]. The details of the concentration procedure are given in Annex III. Alternately, $^{99}Tc^mO_4^-$ can also be adsorbed on acid alumina or hydrous zirconia from water solution and re-eluted using 0.9% NaCl solutions.

The yield of $^{99}Tc^m$ from ZrMo gel generators has been found to be good by various groups. But it has also been found to depend critically on precipitation conditions, i.e. pH and mole ratio, and more particularly on drying conditions. These aspects have been investigated by various groups in this CRP.

The procedures for conversion of ^{99}Mo to ZrMo gel have been optimized by different groups which, though differing somewhat in technical details, have been found to result in ZrMo gels of acceptable performance. The procedures are described in more detail in Annex I. The quality of $^{99}Tc^m$ obtained from ZrMo generators have been found to be acceptable by different groups. $^{99}Tc^m$ obtained from ZrMo gel generators have been tested for compliance with physicochemical limits as well as in animal distribution studies and found to be satisfactory.

The technological aspects of designing practical and transportable generator systems for use in hospitals and handling conversion of high activity ^{99}Mo to ZrMo in shielded facilities using remote handling devices which are important for regular use of this generator system have also been tackled as a part of this CRP. Prototype designs for shielded plant facilities and generator systems have also been developed.

4.2. $^{99}Tc^m$ COLUMN GENERATORS BASED ON NEUTRON IRRADIATION OF TITANIUM MOLYBDATE

For the preparation of TiMo based $^{99}Tc^m$ generators the following are the essential steps:

(a) An aqueous solution of $TiCl_4$ is carefully mixed with a solution of ammonium molybdate or ammonium heptamolybdate with stirring to form a precipitate of TiMo.

(b) TiMo precipitate is filtered, washed and dried. If necessary, dried TiMo is ground and sieved to get a free flowing material of appropriate particle size.

(c) The TiMo gel is subjected to a few essential quality control tests like water content, X ray powder diffraction, pH of aqueous suspension, dispersability in water and Mo leachability.

(d) TiMo is irradiated in the nuclear reactor to produce sufficient quantity of ^{99}Mo. Since a threshold water content for TiMo has been found essential for good $^{99}Tc^m$ yields, the irradiation conditions such as target temperature and neutron flux characteristics can be expected to have a crucial role. The experience of participating groups in this CRP

has shown that good yields of $^{99}Tc^{m}$ can be obtained from TiMo targets irradiated in different types of reactors available in their countries. However, care has to be exercised in target preparation to avoid excess moisture content which may lead to pressure build up in target and rupture of the can during irradiation.

(e) Use of an alumina purification bed has been found necessary to avoid ^{99}Mo breakthrough in the final product. The preparation of TiMo gel is a crucial step particularly when bulk production for regular irradiations are planned. The experience of the participating groups in this CRP has shown that this methodology has been fairly well standardized to obtain a reproducible product. Different groups in the CRP have used modifications of the basic procedure in choice of Ti source, Mo salt, precipitation conditions and drying procedure which are described in Annex II. The yields of $^{99}Tc^{m}$ obtained in different groups with good quality TiMo have been generally $>80\%$. Poor yields obtained in a few exceptional cases are probably attributable to less than optimal reactor irradiation conditions. The purity of $^{99}Tc^{m}$ obtained in different groups using this generator system has been found comparable to $^{99}Tc^{m}$ from fission ^{99}Mo generator.

4.3. $^{99}Tc^{m}$ SUBLIMATION GENERATOR BASED ON SiC-MoO_3-V_2O_5 EUTECTIC MIXTURE

The sublimation generator based on SiC-MoO_3-V_2O_5 has overcome some of the disadvantages of earlier sublimation systems based on MoO_3 and titanium molybdate, particularly poor and irreproducible yields of $^{99}Tc^{m}$. At the same time the major advantages of the sublimation system, namely, very high chemical and pharmaceutical purity and radioactive concentration have been retained.

The SiC-MoO_3-V_2O_5 eutectic target has been developed by the Hungarian team and the experience of other participating teams with this system is very limited. This eutectic target is reported to give high percentage yields of $^{99}Tc^{m}$ by subliming it from a melt of MoO_3-VO_5 mixture which is retained in an inert SiC solid grid thus rendering the irradiated target also transportable. A transportable generator system and an electronic control system for the operation has also been developed. The details of target preparation and generator system are given in Annex IV. The $^{99}Tc^{m}$ separation efficiency has been found to critically depend on the sublimation temperature which should be higher than the melting point of the eutectic i.e. 640°C. In practice the sublimation temperature is maintained at 700°C. At this temperature the sublimation efficiency of $^{99}Tc^{m}$ is reported to exceed 90%. Sublimed $^{99}Tc^{m}$ is carried by passing air through the heated target and passed through a filter containing layers of quartz wool, alumina, again quartz wool and fine powder of MoO_3. The $^{99}Tc^{m}$ retained on alumina is eluted with minimum volume of solution. The total $^{99}Tc^{m}$ recovery reported is 80% and total run time is ~25 minutes. Sterility and pyrogen tests carried out on 240 samples from eight generators have given satisfactory results. The system, however, has been tested only with ^{99}Mo activities of the order of 10 MBq and testing with its designed capacity of 11 to 22 GBq of ^{99}Mo in 5 g of target is planned.

ANNEXES

In the four annexes of this report, details of the laboratory procedures followed by each participating scientist are given. For convenience, these procedures are classified in accordance to the type of the technological process.

Annexes I and II include procedures for the preparation of generators based on the polymolybdate gel systems. Annex III give suggestions to concentrate $^{99}Tc^{m}$ solutions from large alumina and gel column generators obtained from low specific activity ^{99}Mo and Annex IV provides details on the procedures to prepare generators based on the sublimation technique.

Annex I

PROCEDURES FOR PRODUCTION OF $^{99}Tc^{m}$ GENERATORS BASED ON ^{99}Mo CONVERSION TO ZIRCONIUM MOLYBDATE

I-1. ARGENTINA

(R.O. Marques, R.H. Riozo National Atomic Energy Commission, Buenos Aires)

I-1.1. $^{99}Tc^{m}$ generator based on irradiation of preformed ZrMo

Preparation of ZrMo:

4 g MoO_3 are dissolved in 27 cm^3 of 2N NH_4OH with gentle warming. The pH of the resulting solution is 4.5-5. Then 8.78 g of $ZrOCl_2.8H_2O$ are dissolved in 110 cm^3 water (pH of this solution ~1). The first solution is added to the second solution drop wise. The gel formed is filtered through a Buchner funnel under vacuum and dried overnight at 50°C. The dry gel is ground in agate mortar.

I-1.2. Irradiation conditions

Reactor	:	RA-3 Swimming pool type reactor
Amount	:	0.4 to 2.3 g gel
Container	:	Direct in cold welded Aluminium can
Neutron flux	:	1.8 to 2.2 $\times$ 10^{13} $n/cm^2/s$
Duration	:	20 - 24 h
Max. ^{99}Mo sp. act.	:	1.85 GBq/g
Post-irradiation treatment	:	1 drop of H_2O_2 in 3 cm^3 H_2O contacted for 18 hours
Elution with	:	saline solution
Purification column	:	0.7 cm height alumina (internal) glass column with sintered disc

I-1.3. Generator performance

$^{99}Tc^{m}$ yield	:	~60%
^{99}Mo in $^{99}Tc^{m}$ (%)	:	~0.05% (1^{st} elution excluded)

I-2. BELARUS

(I.A. Savushkin, Institute of Power Engineering Problems, Minsk)

I-2.1. Irradiation conditions

Reactor	:	RBMK power reactor
Amount of target	:	12 g MoO_3
Container	:	Quartz vial, dia: 10 mm, height: 140 mm
Flux	:	2 to 5 $\times$ 10^{13} $n/cm^2/s$
Duration	:	100-200 hours
Sp. act. ^{99}Mo	:	12-22 GBq/g

I-2.2. ZrMo preparation procedure

(a) 12 g of MoO_3 was dissolved in 36 cm^3 of 5M NaOH with stirring.

(b) 4.0 cm^3 of 6M HCl was added to above solution and kept stirring for 10 min. pH was adjusted to 7.5-7.6.

(c) 34 g $ZrOCl_2.8H_2O$ was dissolved in 76 cm^3 H_2O with heating to 60-70°C.

(d) At temperature 60-70°C the zirconium solution was added slowly to polymolybdate solution from step (b).

(e) Gel obtained was incubated for about 10 min.

(f) Gel suspension was poured on filter and filtered under suction.

(g) The gel was washed successively with:
- 150 cm^3 H_2O
- 50 cm^3 H_2O
- 40 cm^3 0.0015 M HCl
- 50 cm^3 0.8 percent NaCl in 0.015 M HCl.

(h) The gel was then dried under vacuum for 30 min.

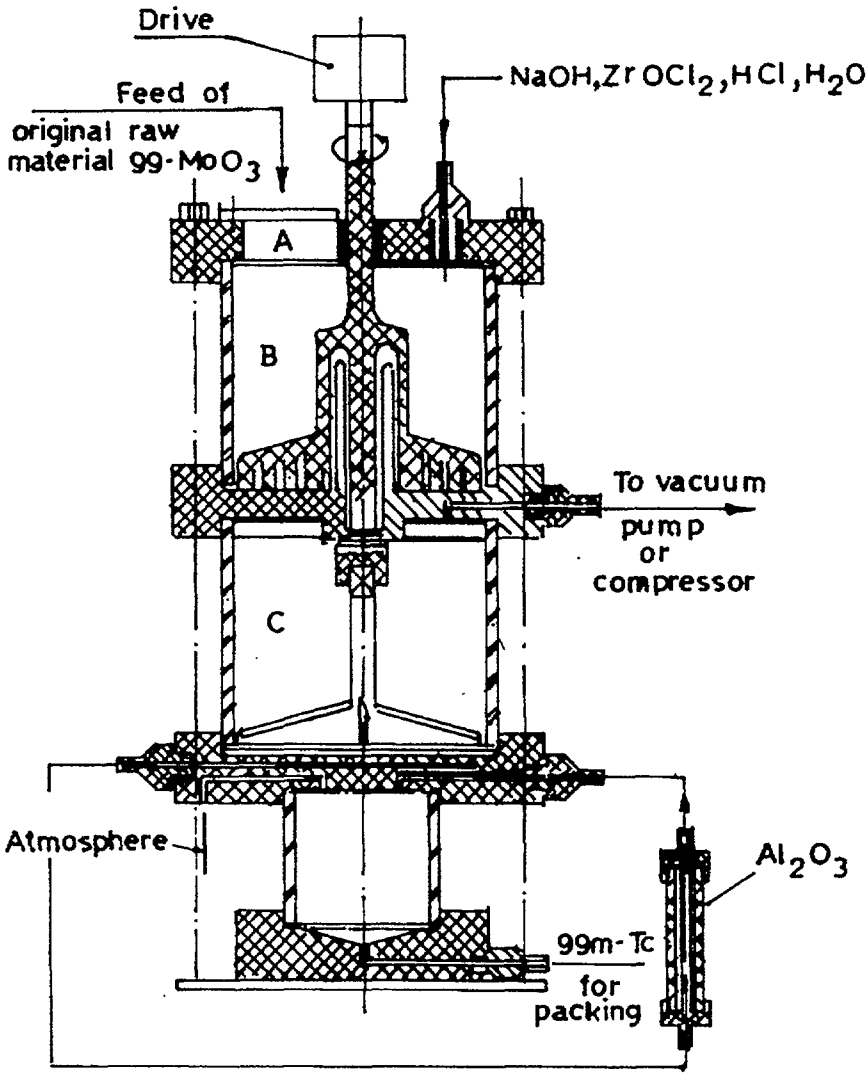
I-2.3. Generator performance

Generator elution	:	for 10 days using 50 cm^3 0.8% NaCl solution
Purification column	:	Chromatographic aluminium oxide (2.5 g)
$^{99}Tc^m$ yield	:	70-88%
^{99}Mo breakthrough (%)	:	not more than 2×10^{-2}%
Chemical impurities	:	Al <2 ppm, Zr <5 ppm Mo <0.1 ppm

I-2.4. Description of apparatus

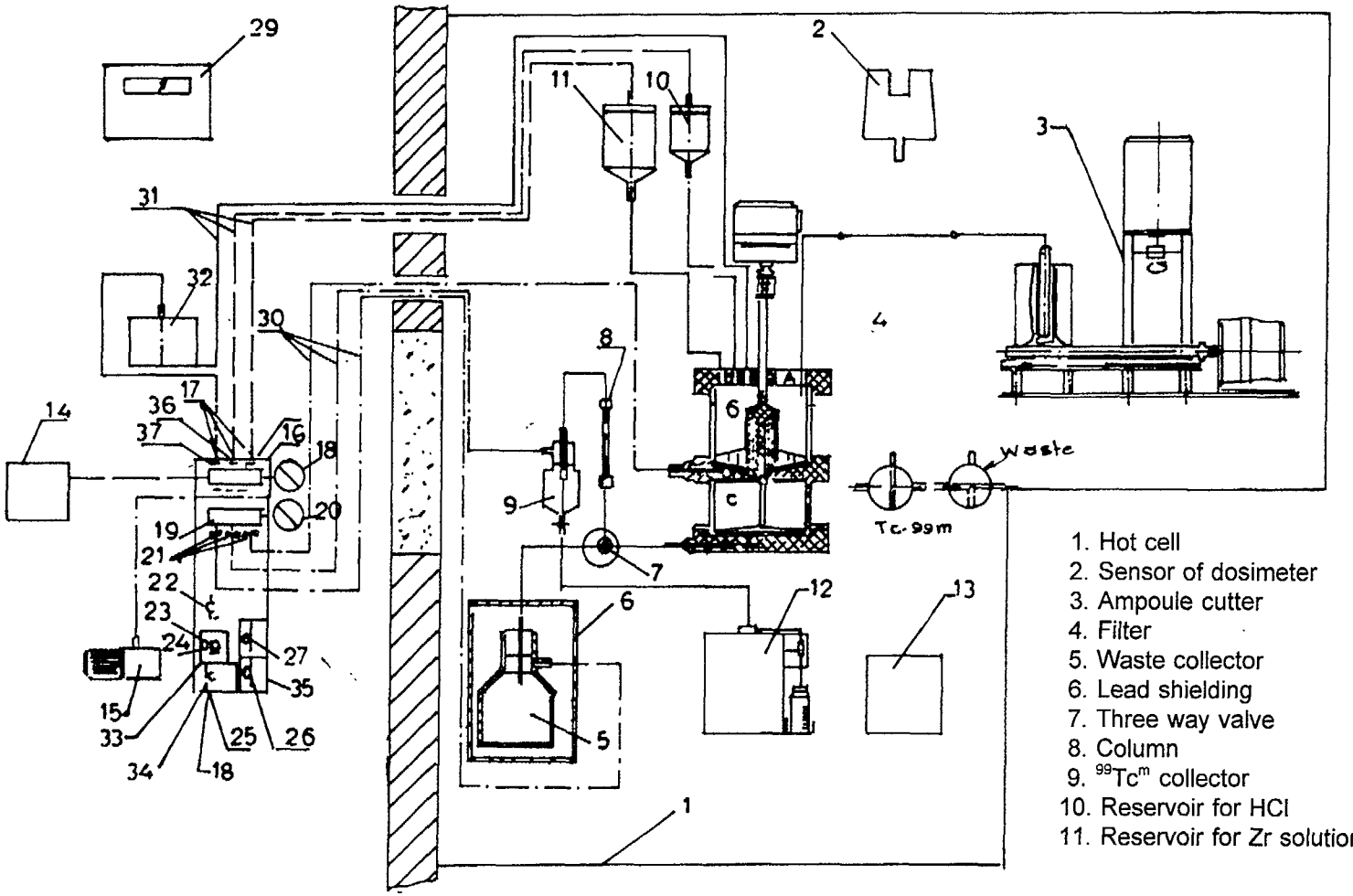
(a) Centralized generator for $^{99}Tc^m$:
It consists of an apparatus (Fig. 1) having an upper compartment provided with a hydro-shutter and blade mixer and a lower compartment with a filtration system and outlet for $^{99}Tc^m$ pertechnetate.

(b) Remote handling facility:
The centralized $^{99}Tc^m$ generator is housed in a hot cell fitted with other handling accessories (Fig. 2) such as ampoule cutter.



A - Feed port for $^{99}MoO_3$; B - Precipitation chamber; C - Filtration chamber

FIG. 1. ZrMo-based $^{99}Tc^m$ generator at centralised production facility (Belarus).



1. Hot cell
2. Sensor of dosimeter
3. Ampoule cutter
4. Filter
5. Waste collector
6. Lead shielding
7. Three way valve
8. Column
9. $^{99}Tc^{m}$ collector
10. Reservoir for HCl
11. Reservoir for Zr solution
12. Packaging system
13. Sterilizer
14. Compressor
15. Pump
16. Receiver
17. Air vent
18. Manometer
19. Receiver
20. Vacuum gauge
21. Vent
22. to 27. Switches
28. Control panel
29. Dosimeter
30. Vacuum tube
31. Tube
32. Reservoir
33. Control panel for cutter
34. Control of filter mixer
35. Electromagnetic switch for packaging system
36. Vent for HCl
37. Vent for washing

FIG. 2. Diagrammatic view of hot cell facility for centralised production of ZrMo-based $^{99}Tc^{m}$ generator (Belarus).

I-3. CZECH REPUBLIC

(F. Melichar, K. Svoboda, Nuclear Physics Institute)

I-3.1. Irradiation conditions

Reactor	:	LWR-15 research reactor
Flux	:	5-7 × 10^{13} n/cm^2/s
Target	:	Zr-Mo matrix (0.1-0.2 g) in cold quarts tubes of various shapes

- The irradiation ampoules serving after irradiation as elution columns.
- The ampoules were irradiated in special holders allowing independent washing on each ampoule wall by cooling water.
- The ampoules with holder was placed in aluminium open cases, to ensure better heat transfer.

Duration	:	12-72 hours
Specific activity	:	5-7 GBq/g Zr-Mo matrix

I-3.2. Zirconium molybdate gel matrix preparation

(a) Gradually mixing 1 molar solutions of ammonium molybdate and Zr oxychloride.

(b) Before mixing, acidity of the Zr oxychloride solution was adjusted with HCl to pH 1.8-2.5.

(c) After the solidification of the solution mixture, Zr molybdate sol. was adjusted to pH = 5 with aqueous ammonia solution.

(d) The hydrogel was kept in gelatinous solution for 24 hours decanted gradually with deionized water and filtered.

(e) Spherical particles were dried in air at 20°C. Polydisperse xerogel was classified into 3 grain size fractions.

(d) For further experiments and for preparation of the gel generator matrix, a fraction mean grain size X2 = 0.175 was used.

I-3.3. Characteristics of the gel

Appearance	:	yellowish white polydisperse xerogel
Chem. composition	:	sample (1) Zr 15.8; Mo 24.8; H_2O 23.8; Mo/Zr1.57
(wt%)	:	sample (2) Zr 15.9; Mo 27.9; H_2O 18.5; Mo/Zr 1.75
Summary formula	:	$Zr_2Mo_7O_{28}(HO)_2$
X ray structure	:	type Zr $(MoO_4)_3^{-2}$
Lattice parameters	:	D = 3.53100; 10.980; 3.6170

Infrared spectroscopic analysis:

The change of infrared spectra absorption bands corresponding to the OH^- vibrations of water molecules is in dependence on the drying temperature. Asymmetric vibration band in the region of MoO_4^{-2} vibrations is split into additional bands and the vibration frequencies are shifted, indicating the presence of polymolybdates in the matrix. In the spectra, a very wide absorption band with several flat maxima was also observed.

Radiation stability:

The irradiated samples were studied by EPR spectral analysis which revealed the presence of paramagnetic centers (pentavalent molybdenum), the concentration of which was growing with the drying temperature of samples and with the gamma radiation dose.

Paramagnetic centre concentration in dependence on the xerogel drying temperature and the gamma-radiation dose received.

xerogel drying temperature [°C]	gamma-radiation dose [MGy]	paramagnetic centre concentration
60	0-3	0
80	0-3	0
160	0-3	3.0×10^{17}
60	3-6	7.6×10^{18}

I-3.4. Generator preparation

Silica-glass columns with internal diameter 3 and length of 10 mm were packed with 100 mg Zr-molybdate Ti-molybdate and plugged at the ends with silica wool. Before irradiation samples were sealed. The columns were used for percolation experiments, i.e. determination of the elution profile and the kinetics of $^{99}Tc^m$ elution into the solution. The elution was always performed with 1 ml 0.2 M HCl at 20°C.

I-3.5. Generator performance

$^{99}Tc^m$ yield	:	variation with conditions obtainable values up to 90%
^{99}Mo content	:	without purification column <0.5%
Radiochemical purity	:	$^{99}Tc^m$ in form of pertechnetate 98%
Biodistribution	:	results identical with compounds labelled by $^{99}Tc^m$ from "classical" commercial sorption generators

I-4. INDIA

(D.V.S. Narasimhan, P. Saraswathy, L.N. Singh, R.R. Patel, S.K. Sarkar, Board of Radiation and Isotope Technology, Bombay)

I-4.1. Irradiation conditions

Reactors	:	CIRUS and DHRUVA research reactors
Target	:	MoO_3 in cold welded Al can (up to 15 g per can)
Duration	:	one week
Flux	:	3-7 $\times$ 10^{13} n/cm^2/s
Specific Activity	:	9-18 GBq per g Mo

I-4.2. Procedure for conversion of ^{99}Mo to ZrMo

(a) 15 g of MoO_3 irradiated in the reactor for 1 week is dissolved in 100 cm^3 2 M NaOH with warming. The solution is filtered through a G 3 filter.

(b) 2.5 g of $ZrOCl_2.8H_2O$ are dissolved in 400 cm^3 of double distilled water. The pH of the solution is about 1. The solution is warmed to about 45°C.

(c) The ^{99}Mo solution is added drop wise to the zirconium solution with continuous stirring on a magnetic stirrer. Sometimes the precipitate formed is too thick and the magnet does not move. Some more water may be added till it starts rotating again and the addition of ^{99}Mo continued. After complete addition of ^{99}Mo the stirring is continued for 3-5 min.

(d) The pH of the slurry is checked by paper and it should be slightly acidic (4-5).

(e) The precipitate is filtered over Whatman 41 filter paper in a Buchner funnel or glass G1 sintered disc filter of about 500 cm^3 capacity. Smaller capacity funnels can be used for smaller quantity of precipitates. The filtration is done slowly applying continuous suction, over half an hour period to allow the precipitate to settle gradually. The suction is continued till the precipitate develops cracks.

(f) Air from a compressed air line is heated to about 70°C using an electric heater and passed continuously from below the filter. The presence of Whatman filter does not interfere with the process. The air flow is regulated carefully. The temperature of the outgoing air is measured occasionally using a thermometer.

(g) The drying is continued till the precipitate dried completely as visually judged from color change and shape of the material. Under our conditions 10 g of Mo was found to take about 20 hours. 1 and 2 g of Mo were found to take about 3-5 hours respectively.

(h) 50-100 cm^3 of saline is added to the dried material. On addition of saline the material disintegrates making a cracking noise. The disintegration gives a fairly good indication of the quality of the gel. The saline solution is sucked away and the material is dried to a free flowing material by continuing the suction. No further processing of the material is found necessary.

(i) The disintegrated ZrMo gel is transferred to a beaker and dispensed into glass generator columns to pre-calibrated heights (7-8 g each) for subsequent use as $^{99}Tc^{m}$ generators.

I-4.3. Characteristics of the gel

Appearance	:	yellowish white granular power
X ray powder diffraction analysis(simulated sample)	:	amorphous (Fig. 3)
pH of aqueous suspension	:	4.5-6

I-4.4. Generator performance

^{99}Mo activity used for conversion	:	0.75-13 GBq
Amount of Mo per batch	:	1-10 g
$^{99}Tc^{m}$ yield	:	70-90%
^{99}Mo breakthrough	:	<0.01% with 5 g acidic alumina purification column

I-4.5. Design of plant and generator

Schematic diagram of ^{99}Mo conversion to ZrMo gel, cutaway view of the shielded plant for ^{99}Mo conversion and schematic diagram of the generator are shown in Figs 4-6.

I-5. THAILAND

(S. Charoen, W. Sukontpradit, S. Laohawilai, G. Aungurarat, S. Jingjit, Office of Atomic Energy for Peace, Bangkok)

I-5.1. Irradiation conditions

8.76 g of MoO_3 were irradiated in tightly closed aluminium container at thermal neutron flux of 2×10^{13} n/cm^2/s for 39 hours (Tue. = 12 h, Wed. = 6 h, Thu. = 6 h, and Fri. = 15 h)

I-5.2. Zirconium molybdate gel preparation

Zirconium oxychloride solution, 0.1 M, pH 1.6 was prepared by dissolving 19.35 g of $ZrOCl_2.8H_2O$ in 600 cm^3 of distilled water.

Ammonium molybdate solution, 0.2 M, pH 4, was prepared by dissolving 8.76 g of MoO_3 in 3 M NH_4OH, adjusting pH to 4 with 5 M HNO_3 and making to 300 cm^3.

The zirconium oxychloride solution was stirred vigorously at room temperature and the molybdate solution was slowly added drop wise to it. After leaving overnight the precipitate was filtered by vacuum sucking and dried at 80°C for 6 hours. The dried product was crushed and sieved to obtain grain size between 150 to 500 μm.

I-5.3. Gel characteristics

Appearance	:	translucent yellow glassy solid
Water content	:	7-8% (wt. loss at 100°C for 24 hours)

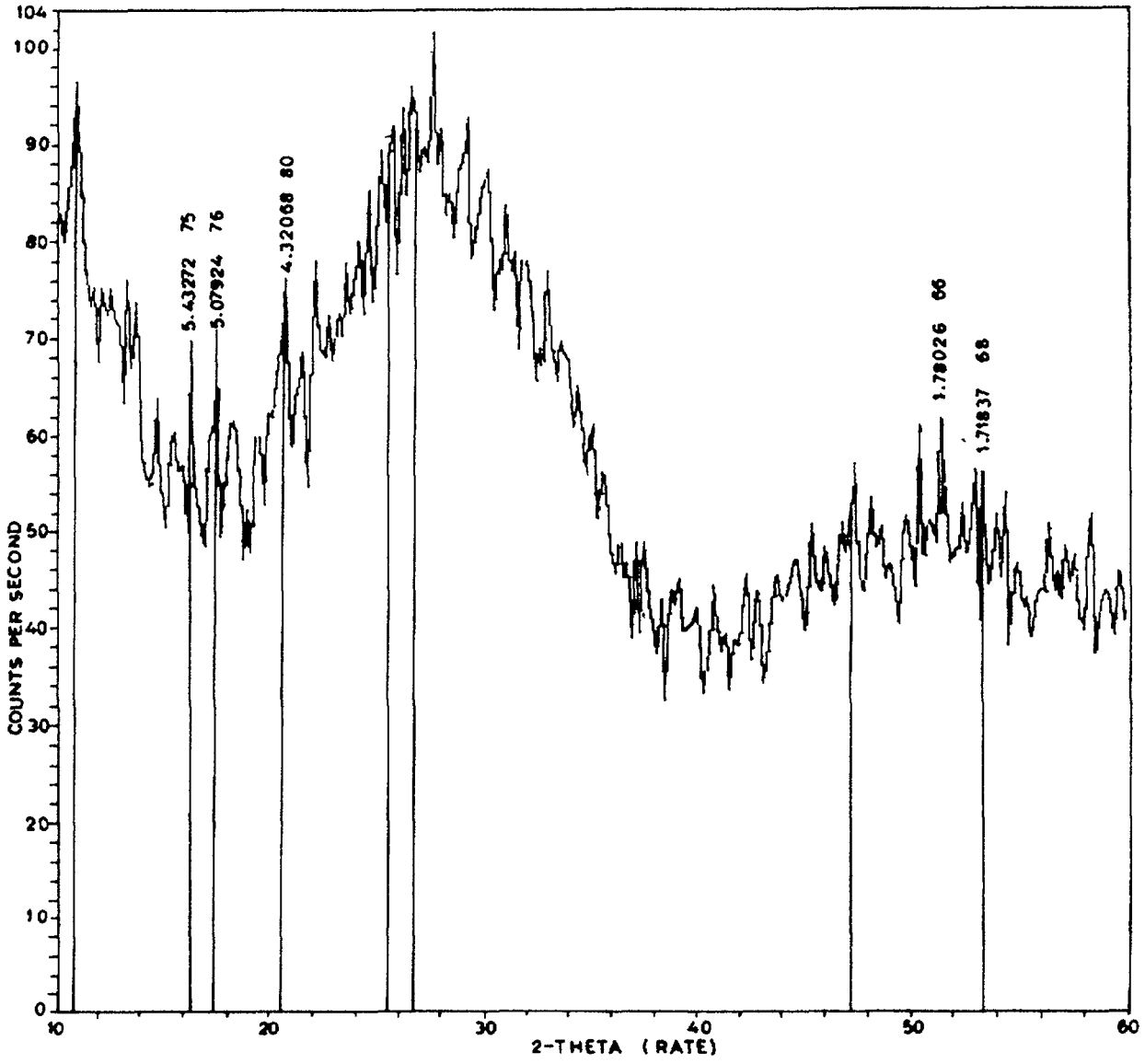


FIG. 3. X ray diffraction pattern of ZrMo gel (India).

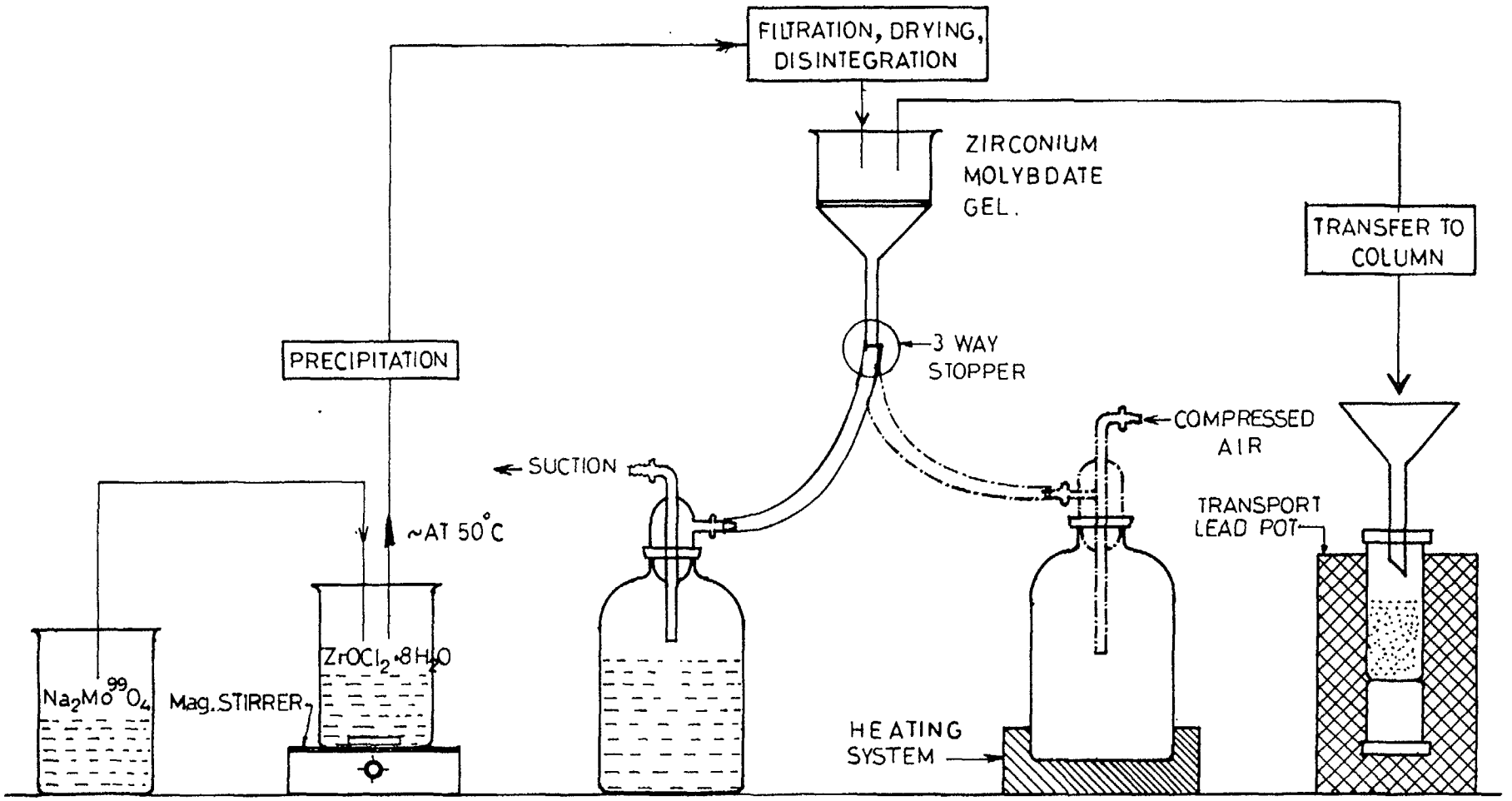
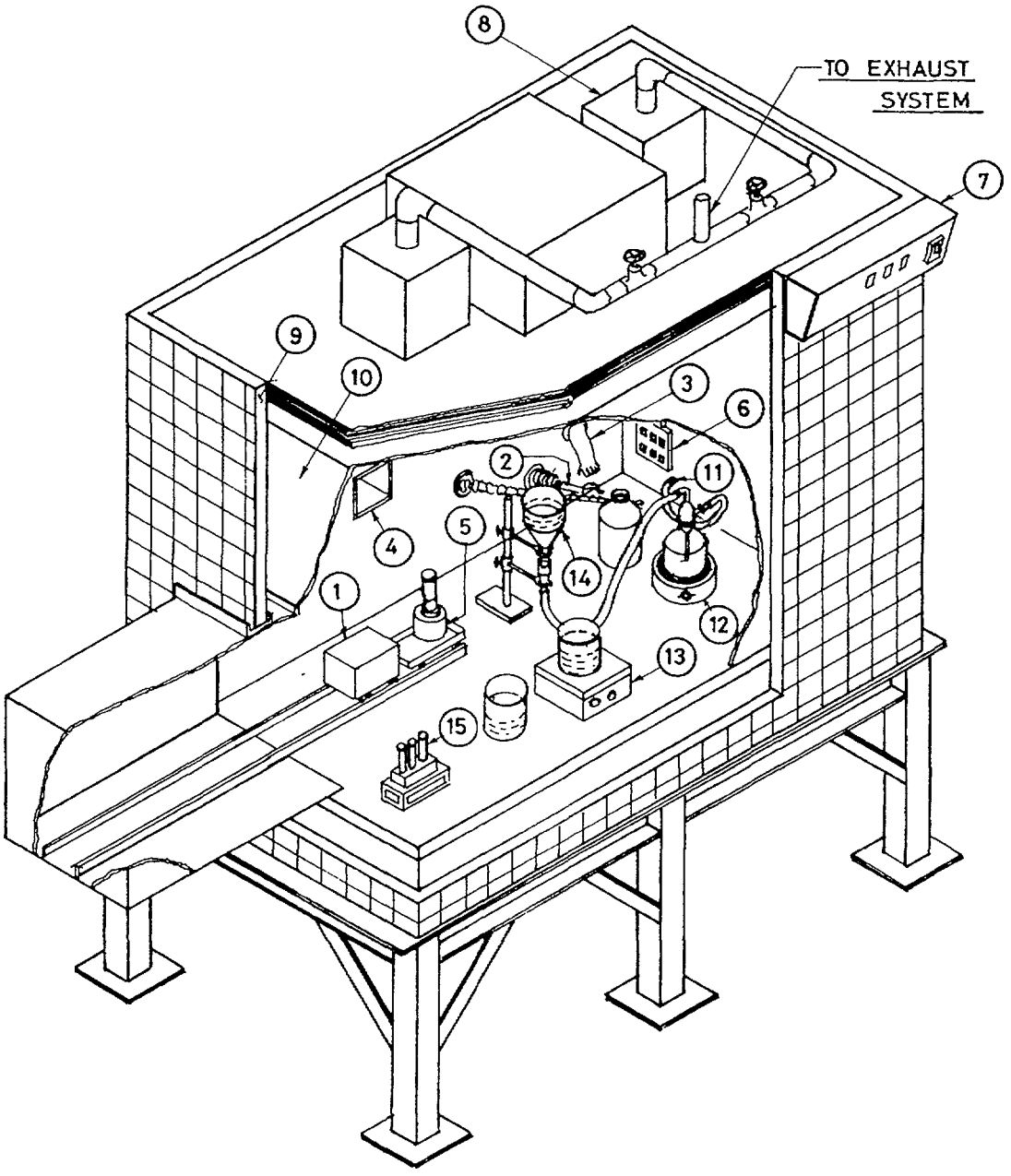


FIG. 4. Schematic diagram of ^{99}Mo conversion to ZrMo gel (India).



1. Remotely operated trolley
2. Remote tongs
3. Rubber gauntlet
4. Lead glass viewing window
5. Lead holder for glass column
6. Electrical panel inside the box
7. External electrical panel
8. Absolute filter assembly
9. Lead wall of production box
10. Containment box
11. Suction/compressed air line
12. Heater
13. Magnetic stirrer cum heater
14. Filtration/drying assembly
15. Glass column

FIG. 5. Cutaway view of shielded plant for processing ZrMo gel generator (India).

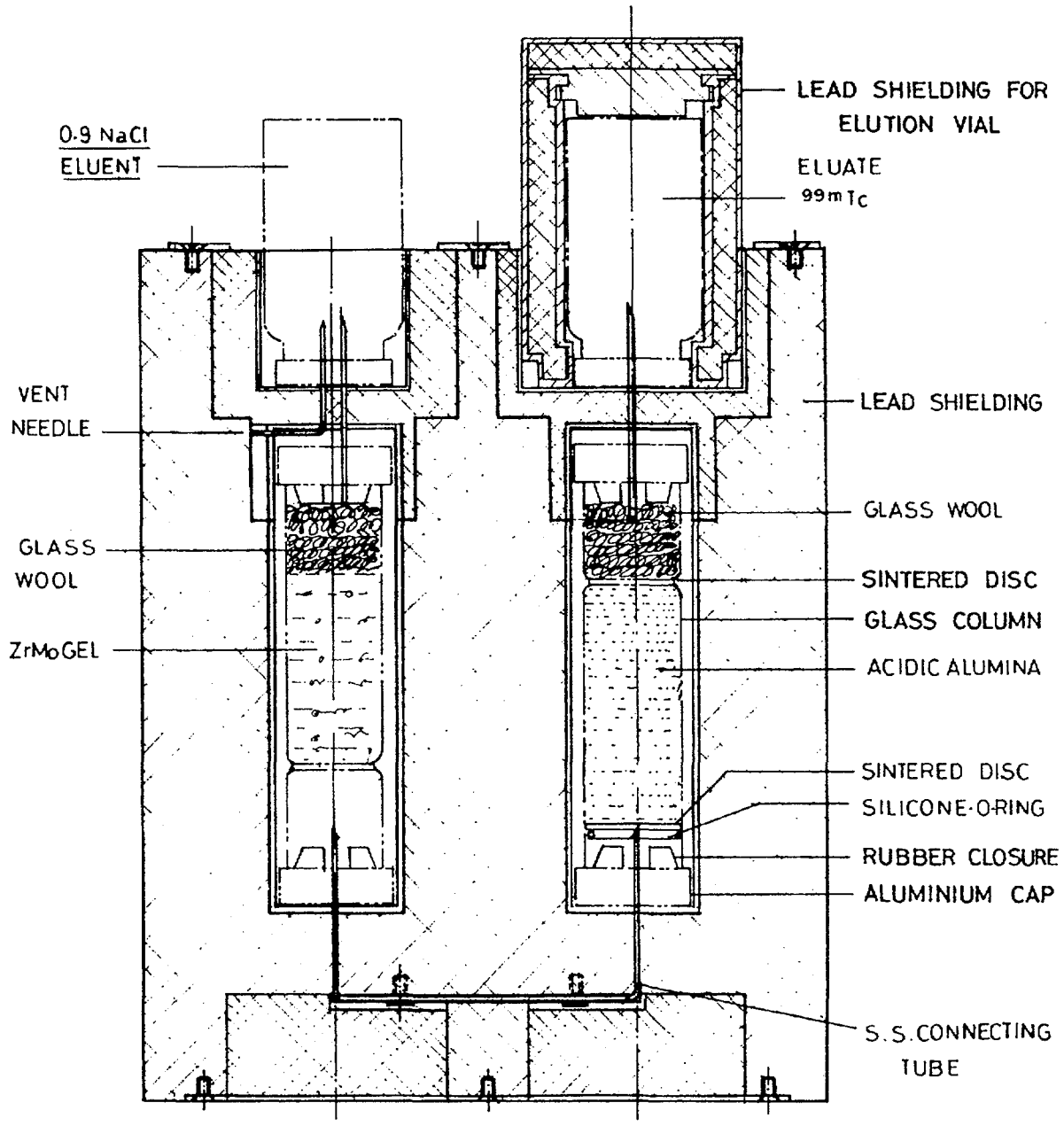


FIG. 6. Schematic diagram of ZrMo gel generator (India) (125mm length × 80 mm width × 156 mm height).

I-5.4. Generator preparation and evaluation

The $^{99}Tc^{m}$ generator was prepared by adding 10 g of zirconium molybdate gel to a glass column (1.5 cm in diameter and 10 cm height) with sintered glass frit (G-4) and glass microfiber filter at the bottom end of the column. The column was washed with 50 cm^3 of saline solution. The gel column was connected to Al_2O_3 safety column (2 g Al_2O_3 in glass column 0.8 × 5 cm with G-3 sintered glass frit).

Eluent	:	0.9% NaCl (10 cm^3)
$^{99}Tc^{m}$ yield	:	77.4 ± 5.5%
^{99}Mo breakthrough	:	<0.01%
Chemical purity	:	<5 ppm of Zr and Mo
Max.^{99}Mo activity	:	3.7 GBq
Labelling of kits	:	good

I-6. VIET NAM

(Le Van So, Nuclear Research Institute, Dalat)

I-6.1. Gel preparation

^{99}Mo conversion to ZrMo gel was carried out in hot cell. 15 g MoO_3 was irradiated in the Dalat reactor at neutron flux 2 × 10^{13} $n/cm^2/s$ and dissolved in 100 cm^3 5 M NaOH and suitably diluted with water. The gel was synthesized using specially designed automatic apparatus similar to the one used for TiMo gel preparation (TIMOGEL). The details of the apparatus are given in Annex II.

For bulk preparation of gel using a set of standardized factors was installed and put to routine use. Mo content of gel was >340 mg Mo per gram gel. The following preset precipitation conditions have been standardized for production of ZrMo gels.

Concentration of $ZrOCl_2$ and molybdate solution	:	0.25 M
Acidity of reaction solution	:	pH = 3
Temperature of reaction	:	60°C

After precipitation, ZrMo precipitate was allowed to stand for 2 hours in mother liquor. Following this step, the supernatant solution was decanted. The precipitate was filtered by vacuum sucking through Whatman filter paper, washed with distilled water, dried first at 60°C for 2 hours, then at 80°C for one hour. Afterwards the dried ZrMo gel particles were reduced to the size of less than 1 mm in diameter by treating with distilled water when the dried gel spontaneously disintegrates. It was washed with water further to eliminate Cl^- and NH^+_4 ions. Then the gel was dried at 60°C for one hour before column packing. 31.5 g of ZrMo gel was obtained. Generators containing 5 g gel each were prepared.

I-6.2. Characteristics of ZrMo gel

(Methods are described in Annex II under TiMo gel preparation. These parameters may be checked using simulated inactive ZrMo preparation obtained by the standardized procedure.)

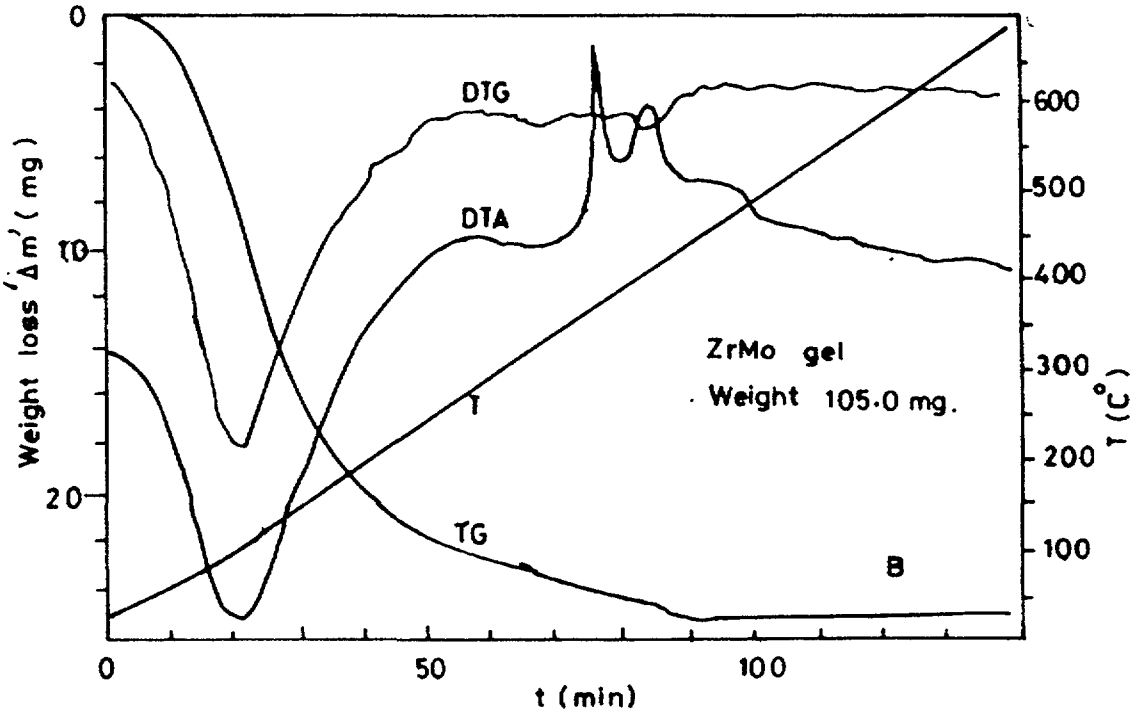


FIG. 7. Thermogram of ZrMo gel (Viet Nam).

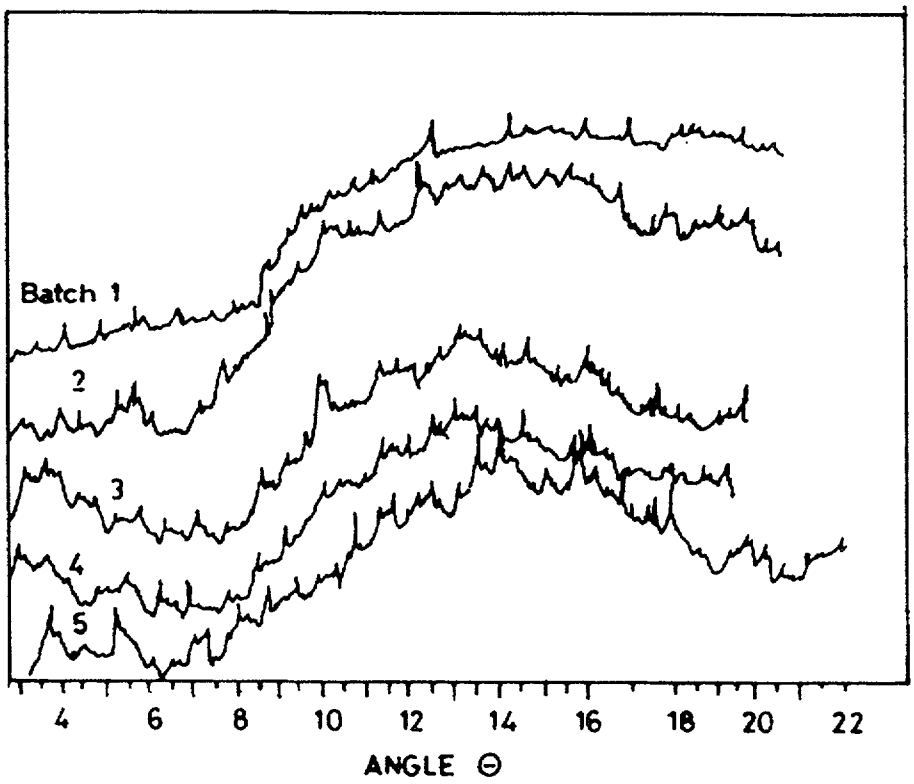


FIG. 8. X ray diffraction pattern of ZrMo gel (Viet Nam).

Molybdenum content	:	320 mg per g of gel
Mo:Zr molar ratio	:	1.17
Crystal water content	:	7.26%
Total water content	:	19.8% (thermogram in Fig. 7)
Gel structure	:	Amorphous (Fig. 8)
Gel particle size	:	0.1-0.2 mm 10%
		0.2-0.4 mm 20%
		0.4-0.6 mm 40%
		0.6-0.8 mm 19%
		0.8-1.1 mm 11%

The X ray diffraction pattern of an optimized preparation of ZrMo gel is given in Fig. 8.

I-6.3. Elution performance of generators

Wt. of gel	:	5 g
^{99}Mo activity	:	7.5 GBq
Avg. $^{99}Tc^{m}$ yield	:	83%
Mo content of eluate	:	$<5\mu$g Mo/cm^3
RN purity	:	>99.99%
RC purity	:	>99%
Labelling efficiency	:	>98% with kits
Biodistribution (studies in rats)	:	satisfactory

Annex II

PROCEDURES FOR PRODUCTION OF $^{99}Tc^{m}$ GENERATORS BASED ON NEUTRON ACTIVATION OF TITANIUM MOLYBDATE

II-1. ARGENTINA

(R.O. Marques, R.H. Riozo National Atomic Energy Commission, Buenos Aires)

II-1.1 Preparation of titanium molybdate

Ti metal (4.8 g) was dissolved in a mixture of NaOH and HF acid, in a precipitation beaker with gentle warming. The final volume was 50 cm^3 at pH of 1 (water was added).

7.5 g of MoO_3, were dissolved in 48 cm^3 of 2 N NH_4OH.

From the first solution 25 cm^3 were used (0.06 mol), and the second solution (0.05 mol) was added drop by drop to it, with continuous stirring.

The gel thus obtained was filtered with a Buchner funnel under vacuum, and dried in an oven for 5 hours at 50°C.

II-1.2. Irradiation conditions

Reactor	:	RA-3 swimming pool type reactor.
Amount	:	0.4 to 2.3 g gel.
Container	:	direct in cold welded Aluminium can.
Neutron Flux	:	1.8 to 2.2 $\times$ 10^{13} $n/cm^2/s$
Duration	:	20 - 24 hours
Max. ^{99}Mo sp. act.	:	1.85 GBq/g
Post irradiation treatment		1 drop of H_2O_2 in 3 ml H_2O contacted for 18 hours
Elution with	:	saline solution
Purification column	:	0.7 cm height alumina (internal) glass column with sintered disc glass
$^{99}Tc^{m}$ yield	:	65%
^{99}Mo breakthrough (%)	:	0.05 (first two elution excluded)

II-2. CZECH REPUBLIC

(F. Melichar, P. Švihla, Nuclear Physics Institute)

II-2.1. Irradiation conditions

Reactor	:	LWR-15 research reactor
Flux	:	5 - 7 $\times$ 10^{13} $n/cm^2/s$
Target	:	Ti-Mo matrix 0.1 - 0.2 g in cold quarts tubes (Identical as Zr-Mo matrix)
Duration	:	12-48 hours
Specific activity	:	max. 2.0 GBq per g Ti-Mo matrix

II-2.2. Titanium molybdate gel matrix preparation

Ammonium molybdate solution was prepared by dissolving 78.3 g of molybdenum trioxide and 129 g of urea. For the second solution, 57.8 g titanium tetrachloride was added to 500 ml of distilled water drop-wise under continuous stirring.

The titanium oxychloride solution was mixed with ammonium molybdate solution (3.16 g SPAN in 25 ml xylene). The precipitate was filtered off, washed with distilled water and dried at 60°C for 8 hours till the moisture content was near to 10%.

II-2.3. Characteristics of the gel

Appearance	:	white polydisperse xerogel
Chem. composition [wt %]	:	sample (1) Ti 6.23, Mo 27.9, H_2O > 10, Mo/Ti 4.48
		(2) Ti 12.16, Mo 29.6, H_2O > 10, Mo/Ti 2.43

II-2.4. Generator preparation

Silica-glass columns with internal diameter 3 and length of 10 mm were packed with 190 mg Ti-molybdate and plugged at the ends with silica wool. Before irradiation samples were sealed. The columns were used for percolation experiments, i.e. determination of the elution and the kinetics of $^{99}Tc^m$ elution into the solution. The elution was performed with 0.9% sodium chloride solution at 20°C.

II-2.5. Elution performance

$^{99}Tc^m$ yield	:	variation with conditions obtainable values up to 20%
Radiochemical purity	:	$^{99}Tc^m$ in form of pertechnetate 98%. ^{99}Mo content without purification column < 0.5%

II-3. INDIA

(D.V.S. Narasimhan, P. Saraswathy, L.N. Singh, R.R. Patel, S.K. Sarkar, Board of Radiation and Isotope Technology, Bombay)

II-3.1. TiMo gel preparation

- 1.1 cm^3 $TiCl_4$ is dissolved in 9 cm^3 double distilled water by warming at ~50°C.
- 1.4 g MoO_3 is dissolved in 10 cm^3 of a 1:1 ammonia and double distilled water solution.
- The molybdate solution is added drop wise with continuous stirring to the titanium solution and stirring continued for 3-5 minutes till a thick gel is formed.
- The gel is vacuum filtered through Buchner funnel and air dried at room temperature for ~30 m.
- Drying is carried out by heating in an electric oven at 80°C for 5-6 hours till the material appears dry. This is followed by grinding for particle size reduction and sieving to select particles between 50-150 μm.

II-3.2. Gel characterization

Water content	:	>8% (average 11%) determined by loss on drying at 105°C till constant wt. is recorded in two consecutive weighing
pH of suspension	:	2-3 (250 mg of gel suspended in 2 cm^3 water, vortexed, centrifuged and supernatant pH checked)
Gel structure	:	Crystalline (Fig. 9). Examined by X ray diffraction using Diano X ray diffractometer and Cu X ray tube/graphite monochromator

II-3.3. Irradiation

0.25-3 g titanium molybdate were irradiated in aluminium cans for 3-7 days at neutron fluxes of 1 to 1.4 $\times$ 10^{13} $n/cm^2/s$ in the self serve position of CIRUS reactor. Irradiations were also performed at neutron flux of 3 $\times$ 10^{13} $n/cm^2/s$ in the tray rod position of DHRUVA reactor operating at a power level of 45 MW.

II-3.4. Column processing and elution

Radioactive TiMo gel was transferred to glass columns (13 mm $\times$ 77 mm) with fused G-2 sintered glass frit. They were washed with 2-4 cm^3 1% K_2CrO_4 solution followed by appropriate volume of 0.9% sodium chloride solution.

$^{99}Tc^m$ yield	:	>75% for optimized gel
Purification bed	:	4 g acid alumina
Maximum ^{99}Mo activity	:	1.6 GBq
^{99}Mo breakthrough (%)	:	<0.05% with purification column

II-4. PERU

(M. Castro, Instituto Peruano de Energía Nuclear, Lima)

II-4.1. Preparation of titanium molybdate

- Titanium molybdate was prepared by precipitation carried out by mixing aqueous ammonium heptamolybdate solution (7.80 g of MoO_3 dissolved by adding slowly to 50 cm^3 of 25% NH_4OH) with titanium oxychloride solution (for experiments, 5 cm^3 of $TiCl_4$ were added to 44.5 cm^3 of water drop wise with continuous stirring).
- The precipitate obtained was filtered through a Whatman paper washed several times with double distilled water and dried at 80°C for 6 hours till the moisture content was near to 10%.
- The samples thus obtained were manually crushed and sieved to 100-150 mesh. Finally the titanium molybdate was stored air tight in dry atmosphere at room temperature.

II-4.2. Irradiation conditions and sample preparation

TiMo was irradiated in the RP-10 Reactor (Nuclear Center RACSO-Lima) at a neutron flux of 1 to 2 $\times$ 10^{13} $n/cm^2/s$ for 8 hours, every Friday. The average power level of the reactor during all irradiations was 7 MW. Water temperature was 34°C.

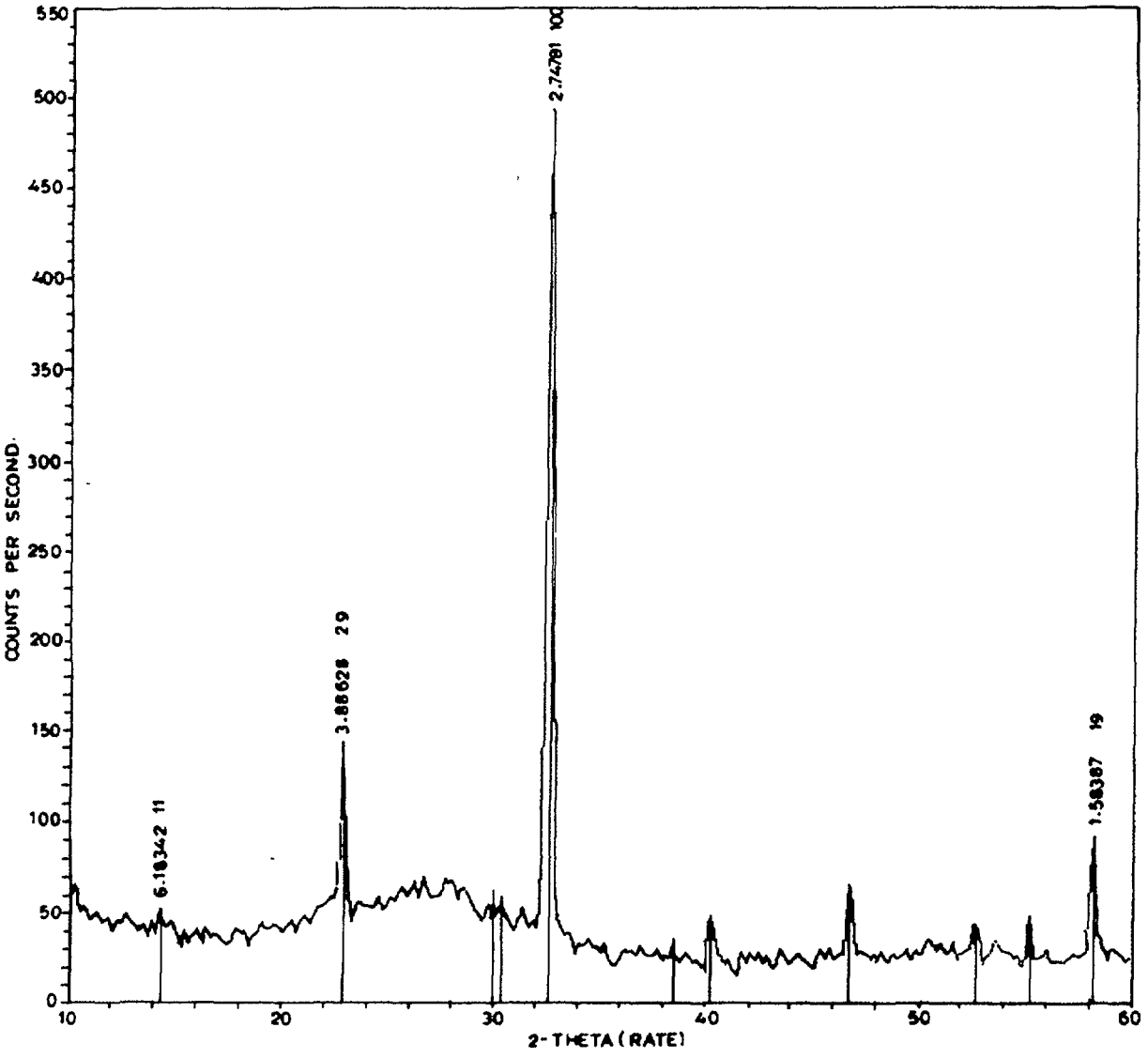
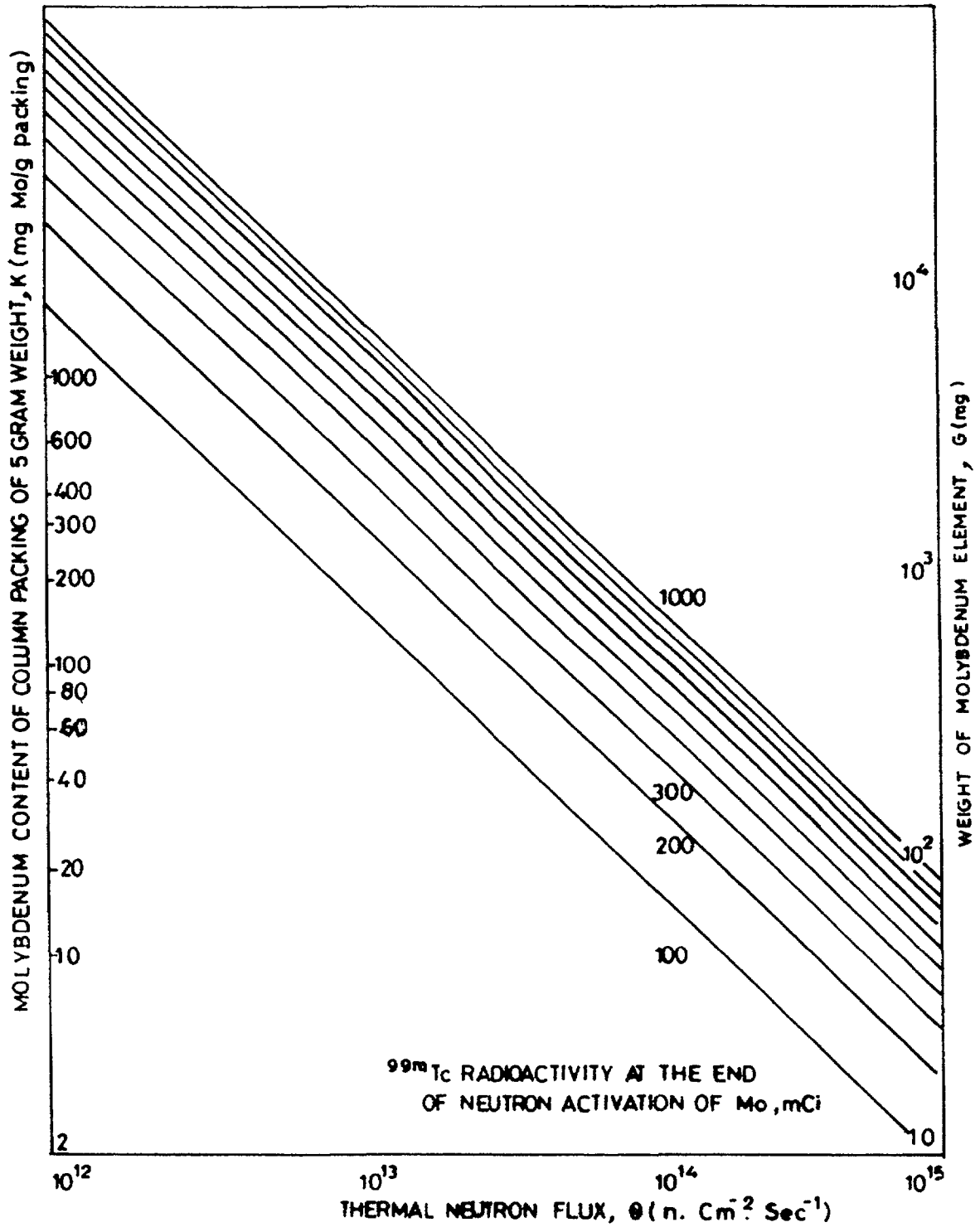


FIG. 9. X ray diffraction pattern of optimal TiMo gel (India).



Standardization conditions: Activation duration: 100 hours
Column packing weight (gel): 5 g
Data related to irradiation channel: R cd (Au) = 2.17, α = -0.02

FIG. 10. Neutron activation of natural molybdenum for preparation of SCG (Viet Nam).

4 g TiMo targets were closed airtight in aluminium container and also TiMo sealed in quartz ampoules placed inside Al cans with holes in caps to permit cooling with reactor coolant.

II-4.3. Column preparation and elution of generator

The TiMo after irradiation is transferred over 2 grams of acid alumina (sieved and selected and previously treated with 0.01 N HCl) in a generator column with sintered glass disc at the bottom. TiMo was kept in contact with $K_2Cr_2O_7$ 0.001 M solution for 1 hour. It was washed with 150 cm^3 saline solution. Purification column of 3 g acidic alumina was used to contain ^{99}Mo breakthrough to reasonable limits. Before elution the column is sealed with a rubber closure and aluminium cap. $^{99}Tc^m$ elutions are done with 10 cm^3 of saline solution.

$^{99}Tc^m$ yield	:	70% (in samples containing 10% water content, irradiated in quartz ampoules placed inside aluminium cans with drilled holes on the caps)
pH	:	6.5
R.C. purity	:	>99.9%
^{99}Mo content (%)	:	0.02%
Labelling efficiency	:	>95% with kits (MDP, sulphur colloid, MAA)
Chemical purity	:	Al <10 ppm, Cr <0.05 ppm, Mo <20 ppm
Toxicity	:	negative

II-5. VIET NAM

(Le Van So, Nuclear Research Institute, Dalat)

II-5.1. Considerations of irradiation and Mo content requirements for practical generator systems

By suitably substituting in standard activation equation the following expression has been arrived at correlating neutron flux (F), time of irradiation (t), target weight (M) and the Mo content per gram (K) in TiMo target:

$$K = 5.56 \times 10^{13} (A_{Tc})\{(M^{-1})(1-e^{-0.0104t})\}^{-1} (F^{-1})$$

A standard chromatographic generator (SCG) has been defined for practical use in clinical diagnosis so that minimum requirements of neutron flux and Mo content of TiMo gel can be arrived at. SCG is defined to have 18.5 GBq $^{99}Tc^m$ at the end of irradiation equivalent to about 7.4 GBq $^{99}Tc^m$ at first elution in a target mass of 5 g so that the elution volume is 10 cm^3. In such a case the above equation (for natural Mo containing targets and for irradiation time 100 hours) can be simplified as follows:

$$K = 1.72 \times 10^{13}\{(A_{Tc})F^{-1}\}$$

The requirements of Mo content and neutron flux for different activities at time of unloading is given in Fig. 10. For SCG i.e. 18.5 GBq $^{99}Tc^m$ activity at unloading, a minimum flux of 2.5×10^{13} n/cm^2/s and a Mo content of 344 mg per gram of gel is required. Incidentally it may be mentioned that the maximum Mo content reported for TiMo

gels suitable for irradiation is 344 mg per gram of gel. It can be also seen from Fig. 10, that for neutron flux of 5×10^{13} n/cm^2/s Mo content of about 180 mg per gram of target would be adequate to get a SCG.

II-5.2. TiMo gel preparation

An automatic apparatus for bulk preparation of gel using a set of standardized factors was installed and put to routine use for bulk preparation of gel. The schematic flow diagram of the apparatus is given in Fig. 11. The apparatus TIMOGEL has a production capacity of 1 kg TiMo every 24 hours of operation. Mo content of gel was >340 mg Mo per gram gel. The precipitation conditions can be preset. The following conditions have been standardized for production of TiMo gels:

Concentration of $TiCl_4$ and molybdate solution	:	0.25 M
Acidity of reaction solution	:	pH = 3
Temperature of reaction	:	retained at 60°C
Flow rate of solution addition for precipitation (with continuous stirring)	:	50 cm^3 per min

After precipitation, TiMo precipitate was allowed to stand for 2 hours in mother liquor. Following this step, the supernatant solution was decanted. The precipitate was vacuum filtered through Whatman filter paper, washed with distilled water, dried first at 60°C for 2 hours, then at 80°C for one hour. Afterwards the dried TiMo gel particles were reduced to the size of less than 1 mm in diameter and washed with distilled water to eliminate Cl^- and NH^+_4 ions. Then the gel was dried at 60°C for one hour before reactor activation.

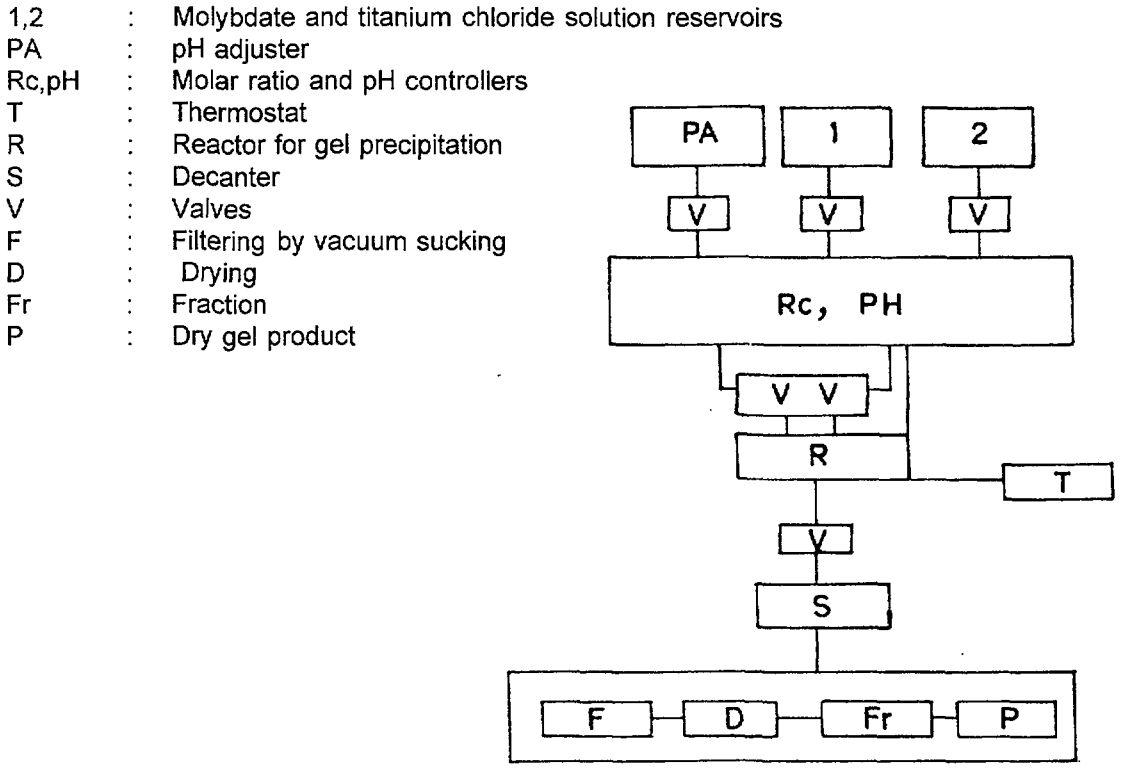


FIG. 11. Schematic flow diagram of TiMo gel apparatus (Viet Nam).

II-5.3. Gel characterization

Molybdenum content and molar ratio:
Average 345.6 mg per g of gel and 1.29 (Mo:Ti) determined by neutron activation analysis.

Water content:
6.2% average; crystal water content determined by drying at 105°C for 2 hours. Total water content (18%) determined by thermoanalysis using Mettler TA-HE-20 derivatograph (Fig. 12).

Gel structure:
Amorphous (Fig. 13); investigated using TUR-M-62 diffractometer with a CuKα (Ni-filter) radiation.

Gel particle size, determined using optical microscope:

0.1-0.2 mm	8%
0.2-0.4 mm	24%
0.4-0.6 mm	35%
0.6-0.8 mm	20%
0.8-1.2 mm	13%

Ion exchange property:
5 meq at pH 5; and 3 meq at pH 4.5 (per g of gel); determined by titrating 0.10 TiMo in 60 cm^3 0.1 M NaCl with 0.1 M NaOH.

II-5.4. TiMo irradiation and generator evaluation

Neutron activation of TiMo gel in reactors with thermal neutron flux in the range 2 to 5 $\times$ 10^{13} $n/cm^2/s$ were carried out for investigation of radiation stability and $^{99}Tc^m$ elution performance.

Reactor	:	NRI (Viet Nam), ANSTO (Australia) and OAEP (Thailand)
Neutron flux	:	2 $\times$ 10^{13}n/cm^2/s; 5 $\times$ 10^{13}n/cm^2/s and 2.6 $\times$ 10^{13}n/cm^2/s respectively
Duration	:	100 hours, 100 hours and 50 hours respectively
Wt of TiM target	:	1 g
Container	:	Al can specially designed (Fig. 14) to ensure better heat transfer and economic reactor space requirement
^{99}Mo activity	:	1.12, 2.61 and 0.74 GBq respectively
Purification column	:	1 g alumina/zirconia
Elution volume	:	2.5 cm^3
99Tc^m yield	:	82-88%
^{99}Mo breakthrough	:	<0.001%

II-5.5. Performance of generators

Wt. of gel	:	5 g TiMo
^{99}Mo in gel	:	7.5 GBq
Clean up column	:	1.0 g ZrO_2
Average $^{99}Tc^m$ yield	:	~80%
Elution volume	:	10 cm^3 0.9% NaCl
Mo content of eluate	:	<5 μg Mo/cm^3

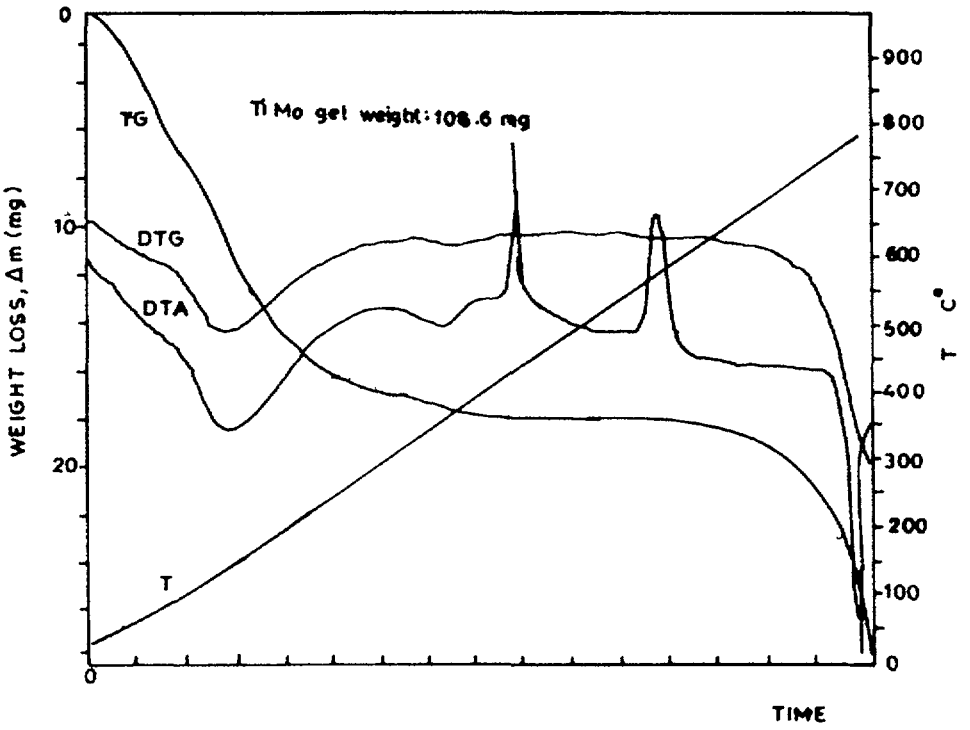


FIG. 12. Thermogram of TiMo gel (Viet Nam).

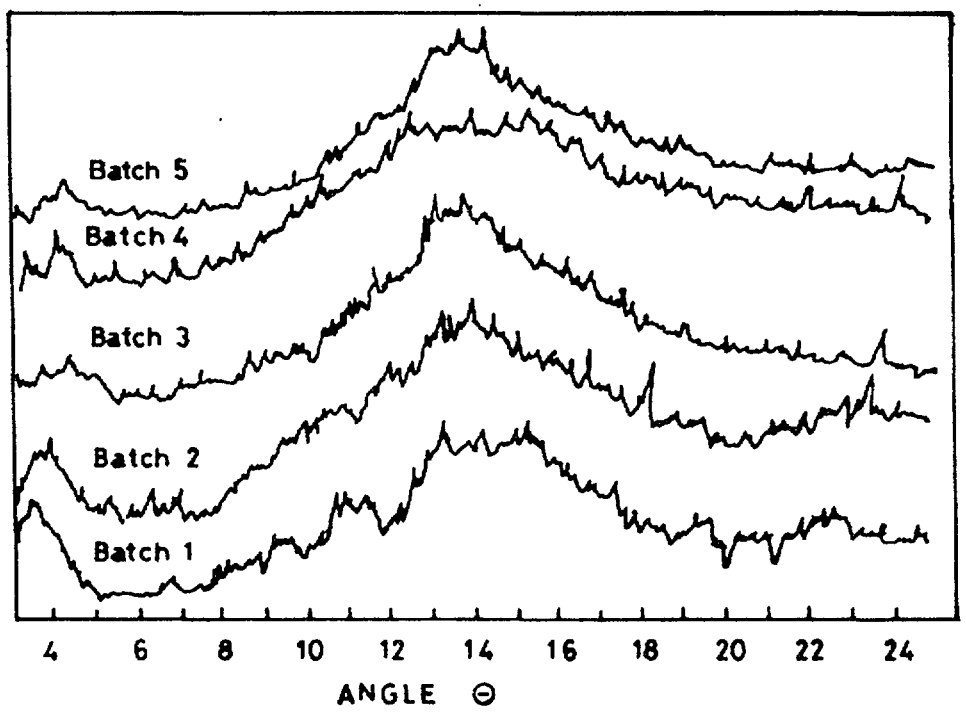


FIG. 13. X ray diffraction pattern of TiMo gels (Viet Nam).

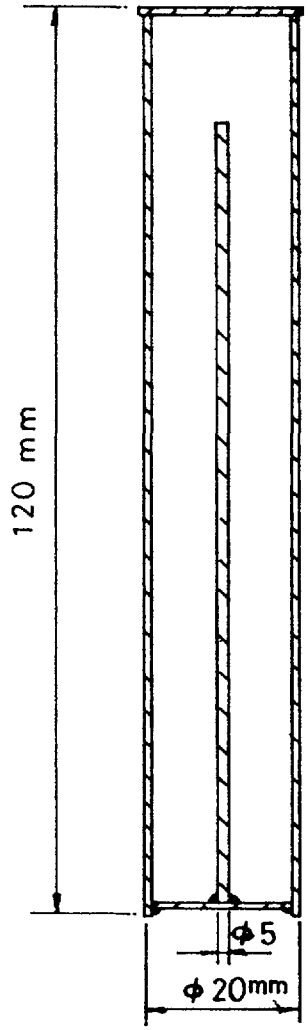


FIG. 14. Irradiation aluminium container for neutron activation of TiMo gel (Viet Nam).

RN purity	:	>99.99%
RC purity	:	>99%
Labelling efficiency	:	>98% with kits (phytate, gluconate, phosphonate, HSA, DMSA, HIDA, DTPA citrate and pyrophosphate)
Biodistribution (studies in rats)	:	satisfactory

Based on the above results a generator Gelutec-A was designed and evaluated. Gelutec-A is a gel-type portable, simple chromatographic $^{99}Tc^{m}$ generator system using pre-formed, reactor activated TiMo gel column containing 7.5 GBq ^{99}Mo at first elution for application (equivalent to 18.5 GBq ^{99}Mo at EOB).

Annex III

PROCEDURE FOR CONCENTRATION OF $^{99}Tc^{m}$ SOLUTIONS FROM ALUMINA COLUMN GENERATORS USING (n, γ) ^{99}Mo AND GEL GENERATORS

III-1. GERMANY

(S. Seifert, G. Wagner, A. Eckardt, Institute of Bioorganic and Radiopharmaceutical Chemistry, Rossendorf)

This procedure is suggested for concentrating $^{99}Tc^{m}$ solutions from large alumina column generators loaded with (n, γ) ^{99}Mo or old fission ^{99}Mo generators or gel generators [23].

III-1.1. Principle

- elution of the generator with an appreciable volume of NaCl.
- reduction of Tc (VII) to Tc (IV) with $SnCl_2$.
- Tc (IV) is adsorbed quantitatively in a second column (concentration column) loaded with 2.5-3.0 g of alumina.
- reoxidation of Tc (IV) to Tc (VII).
- elution of pertechnetate with 3-4 cm^3 of saline solution.

III-1.2. Concentration procedure

(a) The generator is eluted in any volume (up to 100 cm^3) of 0.9% $NaNO_3$ solution of pH 3.0 into an evacuated vial containing 0.05 mg of stannous chloride in freeze dried form.

(b) This reduced hydrolysed $^{99}Tc^{m}$ is loaded onto alumina column (80 $\times$ 8 mm i.d. 2 g acidic alumina) for concentration.

(c) After adsorption the column is heated to >300°C to oxidise the reduced $^{99}Tc^{m}$ (in presence of nitrate ions).

(d) After cooling the reoxidised $^{99}Tc^{m}$ in pertechnetate form is eluted in 2 to 3 cm^3 saline. More than 95% $^{99}Tc^{m}$ is recovered under these conditions.

(e) The column can be used repeatedly up to 20 times.

III-1.3. Quality of $^{99}Tc^{m}$ from concentration columns

Al and Sn	:	<detectable limits
RC purity	:	>95%
Labelling efficiency	:	>95% with MAG_3 and HMPAO
$^{99}Tc^{m}$ activity tested	:	37 GBq

III-2. PERU

(M. Castro, Instituto Peruano de Energía Nuclear, Lima)

III-2.1. Procedure for use with gel generators

- A glass column (hereafter called primary column or TiMo bed column) containing 6 g of alumina is charged with 10 g of irradiated titanium molybdate pre soaked with $K_2Cr_2O_7$ for 30 min.
- The column is washed with 150 cm^3 of saline solution. Immediately after each elution the $^{99}Tc^m$ present as Tc (VII) is reduced to Tc (IV) adding stannous chloride.
- Tc (IV) is adsorbed in a concentrator column also called second column which is previously charged with 2 g of alumina.
- This alumina must be washed with 0.09% $NaNO_3$ solution. The concentrator column is at the same time a purification column to reduce ^{99}Mo content to reasonable limits.
- The alumina column is kept in contact with 1.5 cm^3 of an oxidising solution consisting of 3 drops of 25% H_2O_2, 3 drops of 25% NH_4OH and double distilled water.
- The second column is heated at temperature >90°C for a short time. After elimination of liquids and condensate vapours the column is sealed and sterilized at 120°C for 15 min.
- Finally the concentrator column is eluted with 2.5 cm^3 of saline solution. The yield is 78% and time taken is 1 hour.

The end product has the following characteristics:

pH	:	7.0
R.C. purity	:	>99.9%
Concentration	:	200 MBq/cm^3
^{99}Mo	:	not detected
Chemical purity	:	Mo <5 ppm, Al <5 ppm, Cr <0.04 ppm

Annex IV

PROCEDURE FOR PRODUCTION OF $^{99}Tc^{m}$ SUBLIMATION GENERATORS BASED ON EUTECTIC SiC-MoO_3-V_2O_5

IV-1. HUNGARY

(J. Miller, Institute of Isotopes Co. Ltd., Budapest)

IV-1.1. Preparation of target

(a) The SICCATEC target material consists of the following dry components (wt.per cent): 51.4% eutectic mixture of MoO_3 and V_2O_5, 16.4% fine SiC powder (1200 mesh), 25.7% coarse SiC powder (180 mesh), 6.5% dextrine.

(b) The eutectic component is produced from 63.3% wt% of MoO_3 and 36.7% wt% of V_2O_5. These two powders are thoroughly mixed, melted and kept 3 hours at a temperature slightly exceeding its melting point (660°C). After solidification and cooling down, the melt is ground into finely divided powder.

(c) The dry SICCATEC target mixture is moistened with bi-distilled water to get a dense and very sticky mass (due to the presence of dextrine). The mass is then formed into ~5 mm balls.

(d) The balls are dried under an infrared lamp. The dry and hardened balls are heated at about 360°C for 150 min. The dextrine as a carbohydrate, loses its chemically bound water (carbonization). Then the temperature is elevated to 650°C in a quartz tube at a slow current of air. The carbon gets removed from the balls in the form of CO_2 leaving behind a very porous structure.

(e) The recovery experiments have shown that after about 100 days decay after a one-week use as $^{99}Tc^{m}$ generator, the balls can be encapsulated and irradiated again. Such a production run can be repeated with the same balls four times. The further use is prevented by the accumulation of traces of different "parasitic" radioisotopes in the SiC particles such as ^{51}Cr, ^{60}Co,^{124}Sb, ^{76}As.

(f) In case enriched $^{98}MoO_3$ target is used it should be recycled with minimum loss. For this purpose the balls are dissolved overnight in the aqueous solution of 2 M NH_4OH with slow stirring. All the parasitic radioactivity is concentrated in the heavy precipitate of SiC particles. The solution is then evaporated to dryness and the dry residue can be used as an eutectic mixture. The ^{98}Mo loss does not exceed 1.5% in one recovery run.

IV-1.2. Design of generator and $^{99}Tc^{m}$ elution

The generator concept is shown in the scheme (Fig. 15). The generator body is a vertical bifurcated quartz tube.

A horizontal quartz support finely perforated with laser beam holds a thin and dense layer of quartz wool on which another layer of activated alumina is placed (Tc-filter). Another layer (Mo-filter) supported by quartz wool and consisting of especially milled finely

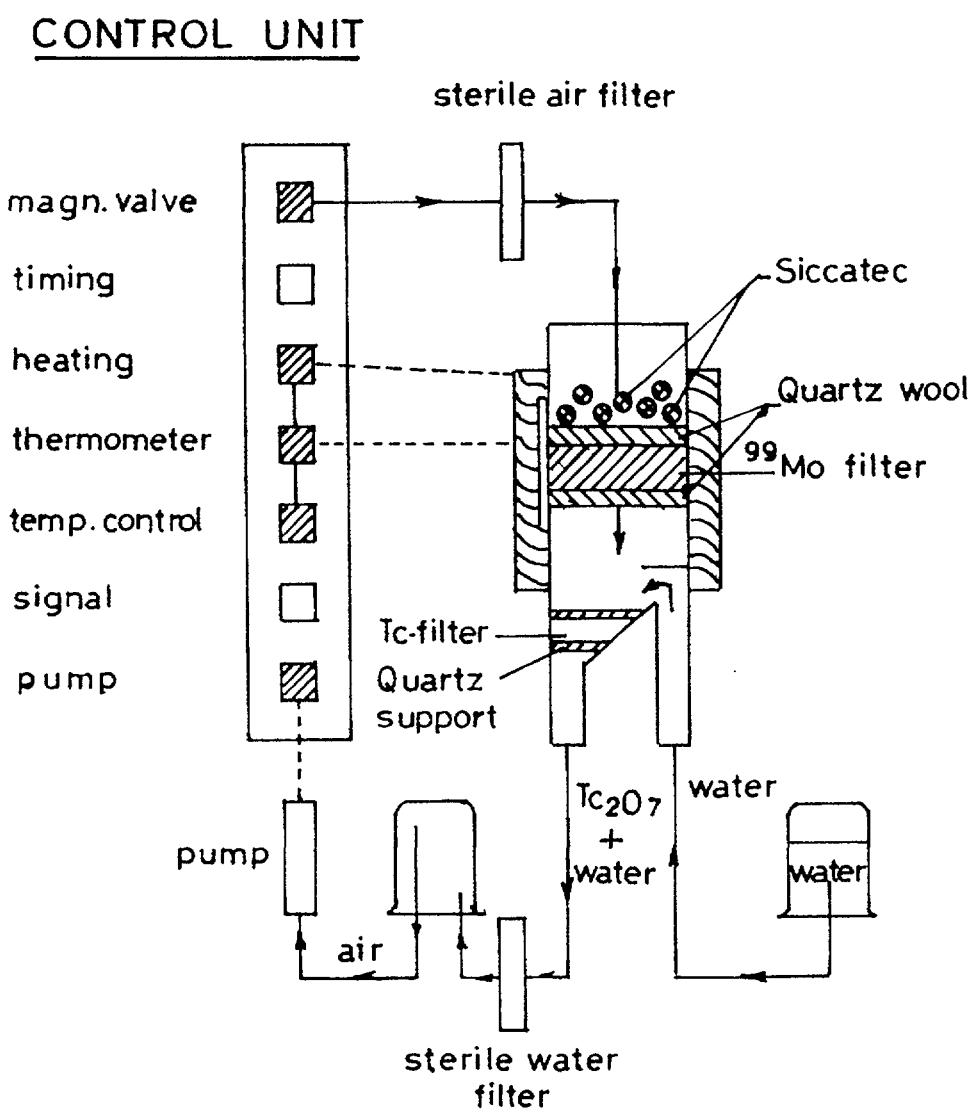


FIG. 15. Concept of sublimation generator (Sicca Tec Hungary).

divided non-radioactive MoO_3 powder is put above the Tc-filter and has double function. One, it traps the traces of radioactive ^{99}Mo by an ion exchange process. Second, it promotes the oxidation of TcO_2 to Tc_2O_7 in gaseous phase being an essential condition of high separation efficiency. The upper layer is formed by the SICCATEC target itself. The generator body is heated during the $^{99}Tc^m$ separation process by a so called thermocoaxial heating coil controlled by a platinum resistance thermometer attached to it.

The windings of the heating coil are distributed along the axis of the quartz tube in such a way that the temperatures were at the target 705 ± 20°C, at the Mo-filter 570 ± 20°C and at the Tc-filter 390 ± 20°C. A slow airflow is maintained from top to bottom in the tube by exhausting with a pump through the branch where the Tc-filter is located. The other branch of the tube is coupled to a vessel containing the washing saline or distilled water. All

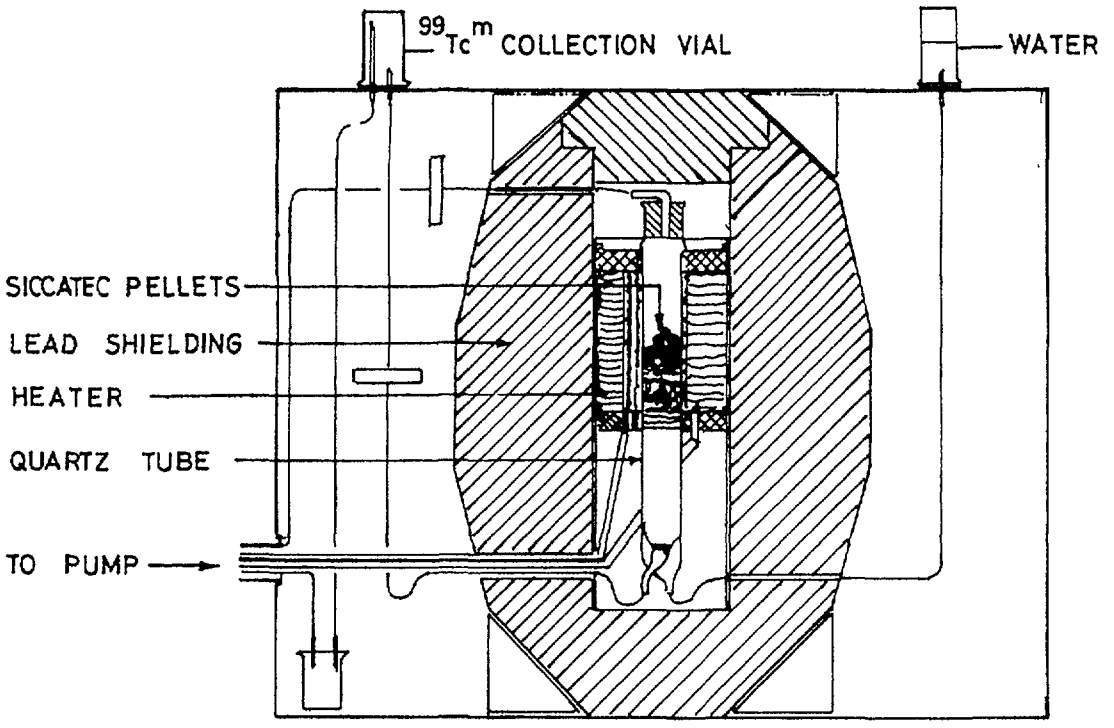


FIG. 16. Design of sublimation generator (Sicca Tec Hungary).

the gaseous $^{99}Tc^{m}$, after volatilization, is collected on the Tc-filter and the latter is cooled down to 100°C or less, the upper end of the tube is closed and the washing solution is sucked into the vessel for the end-product.

The generator operates automatically via an on line electronic control unit. Its operation is simple; 25 minutes after pushing the button START the sterile pertechnetate solution is ready for medical diagnostic use. During this time the generator can be left unattended. The design of the SICCATEC generator weighing 15 kg is depicted in Fig. 16.

$^{99}Tc^{m}$ yield	:	80% (cumulative), 90% (sublimation)
^{99}Mo content	:	5×10^{-4}%

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PARTICIPANTS IN THE CO-ORDINATED RESEARCH PROGRAMME

Castro, M.	Gerenica de Radioisotopos, Centro Nuclear "Rasco", Instituto Peruano de Energía Nuclear, Avenida Canada # 1470, Lima 41, Peru
Charoen, S.	Isotope Prod. Division, Office of Atomic Energy for Peace, Vibhavadi Rangsit Road, Chatuchak, Bangkok 10900, Thailand
Marqués, R.	Comisión Nacional de Energía Atómica, Producción de Radioisotopos, Avenida del Libertador 8250, Buenos Aires - 1429, Argentina
Miller, J.	Department of Radiochemistry, Institute of Isotopes of the Hungarian Academy of Sciences, P.O. Box 77, H-1525 Budapest, Hungary
Narasimhan, D.	Board of Radiation and Isotope Technology (BRIT) - Radiopharmaceuticals Operations, V.N. Purav Marg, Deonar - Bombay 400 094, India
Savishkin, I.	Institute of Power Engineering Problems, Academy of Sciences, Department of Physical and Technical Problems and Safety of Power Plants, Sosny, 220109 Minsk, Belarus
Seifert, S.	Central Institute of Nuclear Research, P.O. Box 19, D-8101 Rossendorf b. Dresden, Germany
Sukontpradit, W.	Isotope Prod. Division, Office of Atomic Energy for Peace, Vibhavadi Rangsit Road, Chatuchak, Bangkok 10900, Thailand
Van So, L.	Radioisotope Department, Nuclear Research Institute, Dalat, Viet Nam
Vera-Ruiz, H.	International Atomic Energy Agency, Wagramerstrasse 5, P.O. Box 100, A-1400 Vienna, Austria
Wagner, G.	Central Institute of Nuclear Research, P.O. Box 19, D-8101 Rossendorf b. Dresden, Germany

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