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Manual of Radioisotope Production

INTERNATIONAL ATOMIC ENERGY AGENCY, VIENNA, 1966

MANUAL OF RADIOISOTOPE PRODUCTION

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FOREWORD

Many countries now possess research reactors. Since the radioisotopes from these reactors bring benefits in many different spheres, such as agriculture, medicine, biology, hydrology and engineering, the first step taken at any new reactor centre is usually the establishment of a sound isotope production programme.

The International Atomic Energy Agency organized a series of regional study-group meetings, the aim of which was to stress the importance of isotope production and encourage the efficient use of these research reactors. Actual production processes differ, depending on the scale of production and prevailing local conditions, so each reactor centre has of necessity to adapt itself to the processes most appropriate to it.

This Manual is a first attempt to collect information on isotope production processes for the use of isotope producers. The dissemination of such information may enable appropriate isotope production programmes to be established at new centres and, at the same time, contribute to the improvement of those production processes already in operation.

The Agency is grateful to the consultants who offered invaluable assistance in the preparation of this Manual and to the national atomic energy authorities who have provided up-to-date information on their radioisotope production processes.

CONTENTS

PART I

GENERAL

INTRODUCTION

The Manual of Radioisotope Production has been compiled primarily to help small reactor establishments which need a modest programme of radioisotope production for local requirements. It is not comprehensive, but gives guidance on essential preliminary considerations and problems that may be met in the early stages of production. References are included as an aid to the reader who wishes to seek further in the extensive literature on the subject.

In preparing the Manual, which is in two parts, the Agency consulted several Member States which already have long experience in radioisotope production. An attempt has been made to condense this experience, firstly, by setting out the technical and economic considerations which govern the planning and execution of an isotope programme and, secondly, by providing experimental details of isotope production processes. Part I covers topics common to all radioisotope processing, namely, laboratory design, handling and dispensing of radioactive solutions, quality control, measurement and radiological safety. Part II contains information on the fifteen radioisotopes in most common use. These are bromine-82, cobalt-58, chromium-51, copper-64, fluorine-18, gold-198, iodine-131, iron-59, magnesium-28, sodium-24, phosphorus-32, sulphur-35, yttrium-90 and zinc-65. Their nuclear properties are described, references to typical applications are given and published methods of production are reviewed; also included are descriptions in detail of the production processes used at several national atomic energy organizations.

No attempt has been made to distinguish the best values for nuclear data or to comment on the relative merits of production processes. Each process is presented essentially as it was described by the contributor on the understanding that critical comparisons are not necessary for processes which have been well tried in practical production for many years. The information is presented as a guide to enable the reader to select processes most suitable to his local conditions.

1. PRODUCTION AND UTILIZATION OF RADIOISOTOPES: SOME GENERAL ASPECTS

The immense variety of radioisotopes and their derived products is illustrated by the large number of suppliers' catalogues and directories that exist. The latest edition of the International Directory of Isotopes published by the International Atomic Energy Agency in 1964 [1] lists some 80 distributors and several thousand different products. The uses to which these materials are put are equally numerous and diverse but, broadly speaking, they can be regarded as falling within three categories.

In medicine, the ionizing radiation from radioisotopes has long been used for purposes of therapy, but in recent years techniques in which radioactive materials are used as tracers in diagnosis has dominated medical application [2-6].

In industrial applications [7-12] the amounts of radioactivity used are generally higher and there is a greater need for radiological protection and for some measure of legal control. Even so, many techniques, such as gamma radiography, thickness gauging and other methods of process control, are already in established use. However, it is probable that the potential for industrial applications is much greater than is indicated by their present use.

The third category, applications in research, is so diverse as to make it difficult to appreciate its full extent. Several Agency publications [7-8, 13] provide examples of research uses in special fields of application but, in general terms, the radioisotope has become an accepted tool of the research scientist and one with which great progress has been made, especially in biochemistry, agriculture and related sciences.

After twenty years of effective existence radioisotopes have become established as an important element of progress in three major fields of human activity: medicine, industry and research.

The major beneficiary of radioisotopes is undoubtedly medicine; it accounts for more than 50% of the total radioisotope consumption. The utilization of isotopes for medical purposes stands in a class by itself and the diversity of radioactive materials in use for such purposes is briefly illustrated in Table I.

In industrial applications radioisotopes contained in sealed capsules are used as sources of radiation. For example, alpha particle emitters, such as polonium-210, americium-241, plutonium-239 or radium-226, are used for ionization, or, in conjunction with beryllium, for the production of neutrons. Beta particle emitters, such as strontium-90, thallium-204, promethium-147, tritium and krypton-85, are used as radiation sources for gauging, ionization, X-ray production and for self-luminous paints. Gamma emitters, such as caesium-137, cobalt-60, iridium-192 and thulium-170, are used for radiography, for sterilization and for the initiation of chemical reactions. The use of radioactive tracers has also been applied extensively in engineering and metallurgy, and in the investigation of industrial plant processes.

Some typical examples of the isotopes used in industrial processes are given in Table II.

Industrial uses of radioisotopes are receiving increasing attention and a comprehensive survey has been carried out recently by the Agency [10]. The survey shows some of the savings which can be achieved from the application of radioisotopes to industry. The findings are summarized in Table III.

Finally, the application of radioisotopes to problems in agriculture and hydrology well illustrate the use of radioactive material as a tool of research and its value to countries where an increasing population demands the proper development of food and water resources [14-19]. Some examples of the isotopes used in agriculture and hydrology are given in Table IV.

The extent of radioisotope consumption

Generally speaking, the more a country is industrialized the greater is the extent of its consumption of radioisotopes. In 1963, for example, isotope consumption per capita was twice as high in the United States of America

TABLE I

SUMMARY OF MEDICAL APPLICATIONS OF RADIOISOTOPES

Blood cell labelling	Chromium-51 DFP-^{32}P
Bone scanning	Calcium-47 Strontium-85
Brain scanning	Arsenic-74 Bismuth-206 Copper-64 Chlormerodrin-^{197}Hg and ^{203}Hg 131-Radioiodinated Human Serum Albumin Iodinated polyvinyl pyrrolidone-^{125}I and ^{131}I Technetium-99m
Cardiac output	131-Radioiodinated Human Serum Albumin Sodium-24
Cardiac shunts (diagnosis)	Krypton-85
Cerebral blood flow	Iodoantipyrine-^{125}I and ^{131}I Krypton-85 Xenon-133
Chondrosarcoma (radiotherapy)	Sulphur-35
Circulatory studies	Chromium-51 131-Radioiodinated Human Serum Albumin Sodium-24
Copper metabolism	Copper-64
Fluid volume – (extracellular)	Bromine-82 Sodium-24 Sulphur-35
– (total)	Iodoantipyrine-^{125}I and ^{131}I Tritiated water
Gastro-intestinal tract studies –	
Blood loss	Chromium-51
Fat absorption	Iodinated oleic acid-^{125}I and ^{131}I Iodinated triolein-^{125}I and ^{131}I
Protein loss	Iodinated P.V.P.-^{125}I and ^{131}I
Vitamin B_{12} uptake	Cyanocobalamin-^{57}Co and ^{58}Co Hydroxocobalamin-^{57}Co and ^{58}Co
Intraocular tumours (diagnosis)	Phosphorus-32
Iron metabolism	Iron-55 and 59
Kidney function	o-iodohippuric acid-^{125}I and ^{131}I Sodium diatrizoate-^{125}I and ^{131}I Rubidium-86
Kidney scanning	Chlormerodrin-^{197}Hg and ^{203}Hg

TABLE I (cont'd)

Leukaemia (radiotherapy)	Bismuth-206 Phosphorus-32
Liver function	Gold-198 Rose Bengal-^{125}I and ^{131}I
Liver scanning	Rose Bengal-^{125}I and ^{131}I Technetium-99m
Lung function	Xenon-133
Lymphatic irradiation	Iodinated triolein in 'Lipiodol'
Osteomyelitis (diagnosis)	Calcium-47
Paget's disease (diagnosis)	Calcium-47
Pancreas scanning	L-Selenomethionine-^{75}Se
Peritoneal effusions (radiotherapy)	Gold-198 colloid Yttrium-90 colloid Zirconium phosphate-^{32}P colloid
Pernicious anaemia (diagnosis)	Cyanocobalamin-^{57}Co and ^{58}Co
Pleural effusions (radiotherapy)	See peritoneal effusions
Polycythemia vera (radiotherapy)	Phosphorus-32
Potassium metabolism	Potassium-42
Sodium metabolism	Sodium-24
Thyroid disorders (radiotherapy)	Sodium iodide (^{131}I) injection and Solution
Thyroid function	Sodium Iodide (^{131}I) injection and Solution Iodine-^{131}I Diagnostic Capsules
Thyroid function (in vitro tests)	L-Thyroxine-^{125}I and ^{131}I L-Triiodothyronine-^{125}I and ^{131}I
Thyroid scanning	Sodium Iodide (^{131}I) Injection and Solution Technetium-99m
Wilson's disease (diagnosis)	Copper-64

as in the United Kingdom, and in the latter it was twice as high as in France. The pattern of isotope use is similar in all countries and always shows that the greatest use is in medicine, with research and industrial applications making their appearance later and in smaller amounts. The utilization of isotopes in a country which is undergoing development generally tends to be lower: this can readily be understood since the use of radioisotopes in medicine, in industry and in research requires a basic minimum of industrial attainment. At a symposium organized by the Agency in October 1961 on the Programming and Utilization of Research Reactors [23], figures were presented for the average consumption of isotopes by a country with a population of 10 million inhabitants. The figures are reproduced in Table V.

The radioisotopes cited are used almost entirely for medical purposes and their value at the international prices prevailing in 1961 is estimated

TABLE II

ISOTOPES USED IN INDUSTRIAL PROCESSES

Radioisotope	Industrial applications
^{14}C, ^{144}Ce, ^{90}Sr, ^{192}Ir, ^{137}Cs ^{60}Co, ^{170}Tm, ^{204}Tl, ^{106}Ru, ^{85}Kr	Thickness gauging
^{137}Cs, ^{60}Co, ^{85}Kr, ^{90}Sr, ^{204}Tl, ^{144}Ce	Density gauging
^{60}Co, ^{137}Cs, ^{90}Sr, ^{85}Kr	Level gauging
Ra-Be, ^{241}Am, ^{210}Po, ^{137}Cs, ^{239}Pu, ^{60}Co, Ra	Logging devices
^{137}Cs, ^{60}Co, ^{192}Ir	Radiography
^{3}H, ^{14}C, ^{24}Na, ^{32}P, ^{82}Br, ^{35}S, ^{45}Ca, ^{51}Cr, ^{46}Sc, ^{55}Fe, ^{58}Co, ^{65}Zn, ^{85}Kr, ^{86}Rb, ^{131}I, ^{110m}Ag, ^{198}Au, ^{203}Hg, ^{210}Po, ^{147}Pm, ^{124}Sb	Tracing

at $10 000. This level of consumption can be taken as a useful guide for developing reactor centres.

The utilization of radioisotopes requires not only well-developed medical institutions but some auxiliary services such as electronics and health physics. These services are essential before significant progress can be made in the use of isotopes for both medical and other purposes. Although international suppliers offer a large choice of appropriate electronic equipment it can only be used if adequate servicing and repair facilities are available within the country. A new reactor centre commonly provides such services and therefore acts as a nucleus for radioisotope development.

The legal control of health and safety, when using radioisotopes and radiation, is a matter which sometimes restricts the initial development of the use of radioactive materials. It is advisable to establish some form of legislation at an early stage since risks can go undetected in the absence of special training and the use of special instruments. In this context, the Agency has already published much of the necessary information [24–26].

Finally, it is essential that those handling radioactive materials, whether in the form of sealed or unsealed sources, should have the necessary training: this can most readily be acquired in one of the many countries which now organize radioisotope courses in Isotope Schools.

TABLE III

SOME SAVINGS FROM THE APPLICATION OF RADIOISOTOPES TO INDUSTRY
($ million)

	24 countries (1961-1963)	USA (1963)	USSR (1961)	Total
Gauging	26.7 - 43.4	35.2 - 50.4	100 [a]	162 - 194
Radiography	12.1 - 28.9	4.0 - 7.6	22	38 - 58
Ionization	1 - 2	- [b]	- [b]	1 - 2
Tracing	~10 - 40	27.0 - 48 [c]	58 [a]	95 - 146
TOTAL	~49 - 104	66 - 106	180	296-400

a) The exact distribution of savings in gauging and tracing is not known.

b) Included in other groups.

c) Includes also certain gauging and ionization applications.

Some problems of the local production of radioisotopes

Although small amounts of radioactive materials can be produced with neutron generators or with other types of accelerators, a local radioisotope production programme depends essentially on the availability of a nuclear reactor. This Manual considers only those radioisotopes which can be prepared by means of a reactor. Clearly, although important, radioisotope production by itself does not justify the construction and operation of a reactor: this function can only be part of an integrated research programme. The multi-purpose use of reactors is typical of the actual situation in most nuclear centres. It is also clear that the type of reactor will determine to a large extent the possibilities for radioisotope production. A report by the Agency [27] includes a review of reactor-based isotope production and comments on the suitability of different facilities. Generally speaking, the swimming-pool type of reactor, used mainly for research purposes, is the most suitable type of reactor for isotope production. Its main advantages are the ability to introduce samples into the reactor core for high-flux irradiation, and the ability to load hot samples under water. The ease with which pneumatic tubes can be introduced is of value for short irradiations.

The availability of a reactor for isotope production is usually governed by the extent to which it is used for other research projects. Further, it should be recognized that one type of reactor is not ideal for the production of all radioisotopes: the large production of cobalt-60 or tritium will present difficulties for the small reactor centre. In practice, except in unusual circumstances, it is unreasonable for a small reactor centre to try to make all types of radioisotope with a research reactor.

TABLE IV

EXAMPLES OF ISOTOPES USED IN AGRICULTURE AND HYDROLOGY

Isotope	Agriculture
^{14}C, ^{27}Mg, ^{32}P, ^{35}S, ^{42}K, ^{45}Ca, ^{52}Mn, ^{54}Mn, ^{56}Mn, ^{55}Fe, ^{59}Fe, ^{60}Co, ^{64}Cu, ^{65}Zn, ^{89}Sr, ^{90}Sr, ^{99}Mo, ^{137}Cs	Soil, plant and animal nutrition
^{15}N, ^{32}P	Fertilizer placement
^{3}H, ^{36}Cl, ^{38}Cl	Water movement
Ra-Be, Po-Be, Am-Be neutron sources	Percentage soil moisture determination
^{22}Na, ^{24}Na	Soil and animal water volume determination
^{131}I	Animal pathology and nutrition
^{3}H, ^{14}C, ^{22}Na, ^{24}Na, ^{32}P, ^{35}S, ^{36}Cl, ^{38}Cl, ^{42}K, ^{45}Ca, ^{46}Sc, ^{52}Mn, ^{54}Mn, ^{56}Mn, ^{55}Fe, ^{59}Fe, etc.	Entomology
^{74}As, ^{76}As, ^{14}C	Weed control
	Hydrology
	Surface water
^{131}I, ^{82}Br, ^{198}Au, ^{3}H, ^{24}Na	Water stream gauging (discharge measurement)
^{82}Br, ^{131}I	Effluents from waste disposal
^{86}Rb, ^{140}Ba, ^{140}La, ^{46}Sc, ^{198}Au	Sediment transport; bed load sediment by tagged particles

TABLE IV (cont'd)

	Ground water
Be-Ra, Be-Po, Be-^{241}Am neutron sources	Percentage soil moisture
^{3}H, ^{51}Cr (complexed), ^{60}Co (complexed), ^{58}Co (complexed), ^{82}Br, ^{35}S (as sulphate)	Ground water tracing
^{82}Br, ^{131}I, ^{3}H	Ground water velocity
^{131}I, ^{110m}Ag	Ground water direction

A comment should be made here about the running of the reactor. It is unusual to keep a research reactor in operation without some interruptions. Radioisotope production, on the other hand, requires a certain degree of continuous running and regularity of reactor cycle. It is therefore essential when a production programme is drawn up to be able to rely on some

TABLE V

AVERAGE CONSUMPTION OF ISOTOPES
(Population of 10 million inhabitants)

Radioisotope	Annual consumption (Ci)
^{131}I	5 - 10
^{198}Au (colloidal)	5 - 10
^{32}P	1 - 2
	(mCi)
^{51}Cr	100 - 150
^{24}Na	100
^{59}Fe	2 - 5
^{35}S	up to 200
^{14}C	up to 50

measure of regularity of reactor operation and also to allow for the inevitable occasional interruption in the reactor schedule.

Apart from the reactor, it is also essential to have sufficient in the way of ancillary services, such as health physics, nuclear electronics, workshops, analytical services and counting rooms, etc. A minimum of processing laboratory space will also have to be provided.

It is also useful at this point to consider, before an essentially localized isotope production programme is started, the possible advantages of establishing a larger regional centre for isotope production and distribution or one in which several centres embark on a co-ordinated programme, each carrying out that part to which its facilities are best suited. Either of these schemes can of course only exist where efficient communications allow. A regional centre undoubtedly leads to a great saving in money, facilities and manpower and should be more efficient than a national centre due both to the larger market it can supply and to the larger pool of scientific experience available to it. The extra degree of specialization which each part of the region can then achieve also has some advantages.

There is undoubtedly much to be gained in establishing a national isotope production programme. As has been shown in many countries already, it stimulates a more rapid growth in the use of radioisotopes. It provides a good training ground for scientists who, once qualified in these techniques, can give advice to new customers and assist them in their projects. Radioisotope production acts as a stimulus to other research activities.

Some of the difficulties of establishing a local isotope production programme must, however, be recognized. From the economic point of view, local production will always cost more than importation from large suppliers who have the means and volume of production to operate more economically. A research reactor will never produce all the isotopes needed, and such products as cobalt-60 for cobalt therapy, carbon-14 and tritium, which represent a large proportion of the demand, require irradiation conditions which cannot be met in a conventional research reactor. Similarly, the labelled compounds required in research are so varied that it is impossible to make reasonable provision for the production of all that may be needed in a particular country. It is therefore usual for new reactor centres to embark first on the production of short-lived radioisotopes where transport from a distant producer is relatively costly and inconvenient. However, in view of the speed of air transport, even this comment is valid only for isotopes with a half-life of about 30 h or less.

All things considered, the local production of radioisotopes will be able to satisfy only a fraction of the national demand, say about half, since it has often been observed that the commencement of domestic production stimulates the demand for more, and less accessible, radioactive materials. Thus, if national production is considered necessary for short-lived radioisotopes, or valuable in promoting the use of radioactive methods, its limitations and cost must be appreciated. The decision to start should only be the result of a deliberate choice, though it may be influenced by political and other considerations. Scientific prestige, lack of foreign currency, independence from foreign supply and other such considerations must be carefully weighed against cost in terms of money and scientific manpower requirements.

The extent to which radioisotope production can be undertaken at a particular reactor centre depends very much on the general policy at that centre and the size of the total effort available to the whole programme. Isotope production will usually be only one of the many projects based on the reactor and the choice of which radioisotopes to produce will to some extent depend on the nature of the other work undertaken. If it is planned to start with a laboratory which produces only the short-lived radioisotopes, this can be a relatively simple and inexpensive operation. The next stage of development, involving a larger range of isotopes, particularly those used in medicine, needs a larger and much more costly facility.

It is an advantage to prepare the way for local production by importing radioisotopes from other reactor centres a long time in advance of local production. In this way the users can be made familiar with the problems of radioisotope handling and experience can be gained by health physicists, technicians and others who will eventually be concerned with production. At this stage elementary safety regulations can be worked out and forms of control can be practised. When local isotope consumption reaches a level where several customers are importing the same materials routinely and frequently, the point is reached where some form of central distribution becomes possible and economic. According to the Agency Report (Technical Reports Series No. 19 [28]), considerable savings can be made by grouping orders together. If there are at least three establishments receiving deliveries at the same time, savings can achieve as much as 50% of the separate cost. Any central dispensing and distribution developed at this stage can later be incorporated into the local production programme. The creation of such a distribution centre has other advantages. It enables those concerned directly with the work to keep up-to-date on the exact state of the radioisotope demand and to forecast its development through the contacts established with users. It also makes for greater efficiency in the supervision of protection and all matters of safety, since all users within the country will be known.

Finally, the training of scientific and technical personnel is a problem which must be faced at an early stage. Visits to overseas laboratories, visiting fellowships to organizations using radioisotopes and consultation with the Agency are some of the ways in which this can be done. Sufficiently long training periods should be allowed for each individual, say one year, and it is important to arrange training not only for those staff directly in charge of radiochemical work but also for those responsible for the design and construction of laboratories and equipment.

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2. ANALYSIS OF A RADIOISOTOPE PRODUCTION PROGRAMME

Once it has been decided to establish a reactor centre and a positive decision has been made to produce radioisotopes locally, the immediate subsequent step is to carry out a detailed analysis of the aims of the programme; to survey the local needs for radioisotopes, and to study the prospects for their utilization at various stages as the programme develops. These preliminary steps are of great importance, since they will form the basis for a working plan, and, where possible, the survey should be carried out with the aid of experts.

The rate of development of a radioisotope production programme will depend primarily on the extent of urgency and support that it is given by the controlling authorities. A prerequisite for the proper implementation of such a programme, if it is to be a positive factor in the economy and technical progress of a country, is the preparation and timely execution of a master plan along the following lines:

(a) Training to be carried out of skilled personnel, especially chemists, who are capable of carrying out a production programme and correlating it with a research and development programme.
(b) Radioisotope techniques and basic nuclear concepts to be introduced into the curricula of higher educational institutes. Courses in radioisotope techniques to be organized for students, teachers, physicians, scientists and engineers, and a cadre of scientists capable of using radioisotopes for industrial, agricultural, hydrological and other applications, to be formed.
(c) Departments of medical institutions to be organized for the use of radioisotopes for therapy and diagnosis.
(d) A broad radioisotopes promotion programme to be started among other potential users in industry and research.
(e) Radioisotope production and development facilities to be constructed near the reactor and the necessary equipment acquired.

The direction which the radioisotope production and development programme will take, its rate of progress and its goals will be different for each country, depending on local conditions such as the nature of the economy, its state of development, the availability of scientists, engineers and technicians, and the potential needs and capacity for utilizing isotopes in medicine, industry, agriculture and other branches of applied and pure science.

The shortage of skilled manpower is a major problem in all developing countries. The main obstacle to realizing a scientific and engineering project, such as a radioisotope production programme, is the acute lack of personnel firstly during the early planning stages and later for the execution of the programme. A first step must therefore be the selection and training of suitable people. Two types of personnel are necessary for the production of radioisotopes. The first is the radiochemical engineer who carries out the production and the processing of isotopes on a routine basis. His background is preferably chemistry, or chemical engineering with some basic knowledge of radiochemistry. A period of six months to one year training in radioisotope production and processing with an overseas group operating in the isotope field should be sufficient to prepare him to carry out his duties.

The other type of person needed, especially in the development stages of a radioisotope programme, is a skilled radiochemist. His education should be more thorough, both in chemistry and nuclear physics. A man with a postgraduate degree is to be preferred. Six months to one year of additional training in a radioisotope development and production group, or with a nuclear chemistry group, is usually sufficient to provide him with the necessary practical experience. Such a person should be in control of the radioisotope production and development team. The training of skilled supporting technicians can usually be done locally on the job. The close association of an engineer concerned with the problems of remote control operations, shielding and other specialized equipment design, is of great assistance; he will also require appropriate training.

The size of the radioisotope team depends on whether it is closely connected to a nuclear and radiochemistry research group, in which case the number of people providing services can be kept to a minimum, or whether the team operates independently and has to be large enough to deal with routine services, with development with research, and trouble-shooting. The presence of an analytical chemistry group is helpful in this context, otherwise the radioisotope group will need to carry out analytical control operations as well as its other duties. As a general rule it is advisable to start with a group of about four chemists, two employed on routine production, assisted by two technicians, one on development and one on quality control measurement and standardization. To a certain extent, it is also advisable to interchange the people doing different types of work to make them more familiar with and competent in all aspects of the team's function. As the programme expands more people may be added to the team, but overstaffing should naturally be avoided. This interrelation of staff functions is referred to again later.

The use of radioisotopes always begins in medical institutions, which do not depend on local supplies alone. Many of the common radiopharmaceutical preparations are relatively long-lived and their importation is common. This may remain the case even after a local programme is effective. Commencement of the local production and distribution of radioisotopes will only alter in degree the need for further facilities and equipment. Some additional training and experience for the medical staff might be needed, but this can be supplemented locally by a visiting expert and by topical courses.

The situation with regard to the industrial applications of isotopes is different from that in medicine. The use of sealed sources for industrial applications will generally be independent of a local radioisotope production programme for a long time. Though it is important to develop such industrial uses, it should be recognized that they are fairly specialized and call for advanced types of radiation sources, which are usually supplied by specialized manufacturers. The situation is different for industrial tracer applications which are of an investigatory nature, the tracer technique usually being employed to determine process parameters or plant dynamics. Such tracer applications require experienced staff equipped with the necessary monitors and measurement equipment and who are familiar with the

particular system under investigation. The training in different industrial applications of several such persons for about a year is desirable.

In general terms, the greatest benefit from the applications of radioisotopes is achieved when local production is supplemented by a broad educational and promotional programme.

Stages in the development of a production programme

Construction of the radioisotope handling and processing facilities can be undertaken in stages according to the production and development programme decided on and according to the levels of radioactivity to be handled. A modest programme of isotope production will obviously require only a limited amount of equipment whilst an ambitious programme will require a hot laboratory with versatile facilities and a stockpile of equipment. It is difficult to make specific recommendations in this connection but guidance for a stage-wise development of a radioisotope programme is outlined in what follows.

Stage 1

The programme should start with custom irradiations and the supply of unprocessed isotopes, such as sodium-24, potassium-42, bromine-82 and gold-198 seeds. The operations involved consist mainly of irradiation, in a pneumatic "rabbit" or in sealed aluminium or quartz vials, inside the reactor core, and occasionally subsequent dissolution of the irradiated target, or some similar simple chemical operation such as precipitation or electroplating. At times it may be necessary to prepare an isotope as a radiation source.

Calibration of the preparation to a required precision is of special importance. The supply of standard and reference sources might form an additional useful service and could be extended to include the calibration of imported radioisotopes. At this stage, the aim should be to achieve confidence and experience in the basic radiochemical procedures. Most operations could be carried out with simple equipment such as gloves, tongs and a few lead bricks in a fume hood – possibly the occasional use of a glove box. The levels of radioactivity should not exceed a few millicuries of short-lived isotopes ($T_{\frac{1}{2}} < 3$ d). This stage of progress will meet some of the needs for sources and tracers in research and for industrial studies, while the medical uses will be quite limited to preparations which can be further treated at the hospital's own laboratory (e.g. sterilization) or used mainly for external purposes and for oral administration.

Stage 2

Production involving the simple processing of short-lived isotopes (< 3 d) should generally follow after six months' to one year's experience of the first stage. In some instances this stage can overlap the first, especially in centres which are interested in launching an accelerated programme, or in countries which have a low demand for isotopes other than for medical use. It should be emphasized that such a short cut requires well-trained

and experienced personnel and the assistance of experts. Additional operations to those mentioned previously consist of simple chemical treatment, the increase of radioactivity levels to a few tens of millicuries, or the sterilization of preparations and their supply in readily usable forms, such as in multi-dose vials for medical use. Products for injection, which fall in this category are, for example, isotonic and sterile solutions of sodium-24, potassium-42, copper-64, arsenic-76, gallium-72, fluorine-18 and bromine-82. Although this stage provides some isotopes for medical use, the more commonly-used isotopes in medicine are not included, since their preparation is more complicated and a substantial amount of experience must be gained before their inclusion in a routine supply programme. It is advisable to concentrate at this stage on studying simple labelling, Szilard-Chalmers separations and other processing procedures for later possible introduction into routine production. Of special importance is the study of procedures for preparing isotopes of high specific activity. Attempts should be made to promote industrial and research uses of short-lived isotopes, especially for tracing purposes.

Although the demand for these short-lived isotopes only amounts to a small proportion of the total demand, its importance must not be underestimated; these products often serve to stimulate the introduction of radioisotope techniques. The manipulation of unsealed sources and the use of short-lived isotopes is an excellent apprenticeship since the risks associated with them are obviously small by comparison with those arising from long-lived materials.

The facilities necessary for this stage of production consist of semi-hot laboratory rooms with sufficient space for several 5 to 10-cm lead-shielded benches, fume hoods and one or two glove boxes. Most operations can be carried out with tongs and beakers but some will require through-the-wall tongs and remote viewing through lead glass bricks or mirrors. Standard procedures of bottling, sterilization and standardization must be practised. Only after sufficient experience and confidence is achieved in proper execution of this stage can the operation be scaled up to the third stage.

Stage 3

This stage is concerned with the production of processed radioisotopes of relatively short half-lives, and with the special preparations of longer-lived isotopes. The recommendation to include long-lived isotopes refers to such products for which either their specifications and availability from other sources are not satisfactory, or local demand is high and the production effort is justified. Processing fission products, or the production of isotopes of high toxicity which require special precautions, should still be avoided.

Radiopharmaceutical preparations of special importance at this stage are, for example, colloidal gold-198, Neohydrin mercury-197 and technetium-99m. The production of special forms of phosphorus-32, sulphur-35, chromium-51, cobalt-58 and cobalt-60 might also be worth while. A greater demand for such preparations might arise from special interests

in medicine, agriculture, hydrology or industry. In this connection, simple labelled compounds might also be considered but preparation should be limited to special needs which justify the effort.

Another kind of activity to be included in the programme at this stage is the establishment of a central dispensary for imported isotopes which are in frequent and widespread demand. This function could result in a substantial saving in the cost of shipments from outside the country as well as minimize inefficient use and waste. Isotopes such as iodine-131, iodine-125, phosphorus-32, and sulphur-35 are examples of those which might be included in the central import and dispensary service of a radioisotope production programme at this time. A careful economic appraisal should always be made before such an additional function is included in the programme.

At this stage the production group can no longer be housed in simple temporary accommodation and a special hot laboratory is likely to be required. The different facilities and equipment needed for such a programme are discussed in detail in Section 3.

The stages of development and the scale of each stage proposed for developing a radioisotope programme are based on experience gained in several small reactor centres during the last decade. The recommendations have attempted to be objective and have taken account of such factors as the economics of maintaining a limited and balanced programme versus an extensive one. Due consideration should be taken of the cost of putting scientific personnel, usually in short supply in developing countries, on to routine production and services rather than directing them to more important functions. Limited scientific manpower needs to be carefully conserved. Considerable expenditure may be involved in constructing and operating a hot radiochemical facility for producing isotopes, the purchase and import of which is competitive and satisfactory. Iodine-131, carbon-14, cobalt-60, tritium and caesium-137 are isotopes which may be mentioned in this context. This is especially true for long-lived isotopes or fission products. These criteria are flexible to a certain extent and have to be considered together with local policies and circumstances before a decision on their production is made.

Further expansion of radioisotope production to include a wider spectrum of isotopes than those recommended above, at higher levels of activity, will require specially designed hot facilities and a larger staff. This may be practical for countries which are very active in agricultural and industrial studies and have to meet the supply of isotopes to advanced medical institutions serving a population of more than 20 to 30 million people. The production of substantial amounts of iodine-131 or cobalt-60 on a routine basis or the large-scale separation of fission products requires very advanced equipment, such as hermetically-sealed cells, lead or heavy concrete shielding, and active waste-disposal problems become serious. These special facilities become necessary where the levels of radioactivity handled and processed exceed the curie level. The facilities require skilled engineering and maintenance personnel and the support of a large reactor centre with an advanced nuclear research and engineering programme. This scale is beyond the scope of this Manual.

The aim should be to maintain a balanced and restrained production programme and each new extension of the programme should be given careful consideration.

Some mention should be made here of the research and development work associated with a production programme. Two major motives should be considered: first, the need to find new or more suitable methods for producing the required radioactive preparations; and second, the need to maintain an atmosphere of scientific satisfaction and to encourage new ideas and radioisotope application. Such an attitude avoids stagnancy of existing personnel and will also serve to attract good people. A positive and long-term view should be taken of the balance between research and development on the one hand and the need for production services on the other. Considerable emphasis should be given to research and development activities, and in this connection mention should also be made of the advantage of seeking co-operation from other regional centres in developing new methods and new applications. Co-operation and co-ordination between closely-located centres is of great value and might make the production programme more efficient and economical as well as providing more momentum for development.

3. HANDLING AND PROCESSING FACILITIES

When planning an isotope production programme at a newly established reactor centre, some of the first questions that arise are: What kind of equipment and facilities are really needed? Which of the types commercially available are best suited to the desired production range? What do they cost?

It is assumed that the final goal of planning is to establish a routine production of radioisotopes mainly for medical and agricultural use on a scale sufficient to cover the demand of a country where radioisotope methods are in current use. A considerable fraction of any future requirements of industry, and for the physical and technical sciences, for instrumentation and radiography sources, etc., could be met by minor additional investment.

A programme like this can be gradually developed along the lines described in Section 2, and the first stage, the preparation of short-lived unprocessed isotopes or targets dissolved in water or mineral acid solutions, can be established at relatively modest cost. The second stage of the programme can usually be achieved by putting up some additional equipment within the existing chemical laboratory. Such a laboratory will in most cases be provided at the various reactor centres.

The third stage, the production of radioisotopes most commonly used in medicine and agriculture, involves considerably more investment, as this production level requires a laboratory facility specially constructed for the purpose. However, this does not mean that the erection of a completely new building is unavoidable; often good conventional chemical laboratories can prove very useful as accommodation for a smaller plant. If plans are to proceed to the third stage, and sufficient money can be raised, it is strongly recommended that the question of laboratory design be looked into at an early opportunity. This can be done by utilizing the experience of centres which

have already developed their isotope production facilities following schemes similar to those sketched in the previous chapter. If detailed plans for the isotope laboratory are decided upon before the programme is started, the training and development through the introductory stages can be undertaken during laboratory construction, with the equipment that later will be part of the completed facility. In this way much time and money can be saved.

Irradiation facilities

The necessary irradiations are assumed to be carried out in a medium-sized research reactor. It is preferable that the needs for radioisotope production should be considered during the design of the reactor, thus avoiding problems that might arise later. Usually irradiation containers, transfer systems, etc., must be specially designed to fit both the reactor irradiation facilities and the processing equipment, and it is of great advantage to be able to plan the entire concept at one time.

For the range of isotope production as envisaged in this Manual, an effective irradiation volume of about 5 litres, with an average thermal neutron flux of 10^2 n/cm^{2}s will be necessary. If the average neutron flux available for target irradiation is higher than 10^{12} n/cm^{2}s, this volume can be reduced. In addition, irradiation positions with a lower flux should be provided, e.g. in a thermal column. The neutron flux distribution within the irradiation facilities should be carefully plotted.

For irradiation in moderate and low neutron fluxes no special equipment will be required beyond that necessary to locate the targets in their proper position. For fluxes around 10^{13} n/cm^{2}s and higher, however, the problem of nuclear heating becomes significant. The attenuation of gamma rays may cause the temperature of targets to rise to several hundreds of degrees centigrade. This will, to some extent, restrict the selection of chemicals to be irradiated, and in some cases cooling of the targets must be provided. The heat evolution may also be reduced by fixing the target cans to a firm support during irradiation, to improve the heat conductivity conditions.

If the reactor is of the tank type, the irradiation facilities usually consist of air-filled horizontal or vertical tubes penetrating the reactor core or the reflector. To secure the best possible utilization of the available channels the effective diameter should be from 30 to 50 mm. Arrangements should be made to be able to unload the reactor frequently, preferably every day.

Most reactors have to be shut down during the loading and unloading of target materials and, to avoid waste of time, care should be taken in planning the handling equipment to secure rapid and convenient manipulation. Special equipment for loading and unloading a reactor without shut-down, the so-called "irradiation machines", are available commercially, but the cost is considerable, and to use such a device fully requires a large production programme.

Irradiation containers are made of aluminium, preferably with a low content of sodium, manganese and copper. For most applications in reactors with "dry" channels, ordinary cans with screw-caps, wall thickness 0.4-0.7 mm, are sufficient. Most of the materials irradiated for radioisotope

production can be placed directly into the aluminium cans. In some cases, however, an inner container is necessary, for example if the target material is likely to react with aluminium during irradiation, or if the target is a very small amount of powder, which may be difficult to manipulate. Sealed quartz tubes or, for shorter irradiation periods (up to one week with a flux of 10^{12} n/cm^2 s), sealed polyethylene can be used as an inner container. Standard irradiation containers may be purchased commercially; approximate prices are $0.10–0.30 per unit.

In reactors of the "swimming-pool" type irradiations may be performed by lowering the target containers down into the water pool near the reactor core in some sort of basket. This type of reactor is usually more easily adaptable for irradiation work and is more easily modified at a later stage than the tank type. On the other hand, immersing the target containers in water produces additional technological problems. The irradiation containers must be sealed by welding and must also have heavier walls, otherwise they will float to the surface of the water. Such target containers will also require more complicated equipment for decanning.

To meet the requirements for short-time irradiations without shutting down the reactor too often, a pneumatic irradiation facility ("rabbit" channel) will prove very useful. A "rabbit" facility is commonly provided for research purposes and can be used for radioisotope production during unoccupied periods. The installation costs for a pneumatic irradiation facility are approximately $20 000.

The transport of irradiated target cans from the reactor hall to the isotope production laboratory should take place in shielded containers. The type to be chosen for this purpose will depend upon the distance between the irradiation and processing facilities. If the distance is short, up to a few hundred metres, a small lead-shielded carriage, housing four to eight irradiated cans simultaneously, is recommended. Such a carriage can be purchased for $1500. If the distance is of the order of several kilometres, shielded containers carried by a truck, with lifting cranes for handling, are preferable. When irradiated materials are to be transported outside the premises in which they are produced, the containers should, of course, comply with the requirements for the safe transport of radioactive materials [1].

Production equipment

The constituent parts of an isotope production facility are described later in this Section. Equipment of this kind is necessary to maintain a production programme whether it is decided to proceed to stage 3 or not. The introductory stages in the development of a programme are also discussed.

(a) Process enclosures and supports

To prevent the uncontrolled spread of radioactive contamination, the processing of radioactive materials requires a specially ventilated enclosure for each apparatus, the required volume per enclosure being about one cubic metre. This basic idea of containment should be applied in planning all types of radioisotope production laboratories, but the system may vary, both in

the enclosures used and in the manner in which they are arranged to form the whole plant.

The types of enclosures are:

Open fume hoods
Ventilated boxes with a limited opening for hand access ("slit boxes")
Sealed glove boxes working at reduced pressure
Sealed reduced-pressure boxes with remote handling equipment
"Master-slave" manipulator cells

Equipment that is as expensive as manipulator cells is not necessary for the type of work proposed in this Manual, but the other four types are all suitable.

Generally, 0.5 m/s is adopted as the minimum linear air velocity through openings in a process enclosure of this kind. An open fume hood may consume as much as 1500 m^3 air per hour to fulfil this requirement. If the air has to be heated or cooled, the operation of a number of such hoods will be rather expensive and troublesome. Uncertainty in the laboratory air balance conditions is also introduced, since the extent of the opening of the hood may vary from time to time. However, fume hoods are ideal for many types of inactive and low-activity chemistry and will always be preferred by the laboratory personnel, since operations can be performed more easily and rapidly than in glove or slit boxes. They should therefore not be omitted; a limited number of hoods should be provided in locations where air balance conditions allow them.

Ventilated boxes with small hand openings are convenient, especially for process development work on the microcurie scale. It is also preferable to perform the cleaning of contaminated glassware and laboratory apparatus in a container of the slit box type.

Glove boxes may be used as enclosures for work with low-energy beta emitters like carbon-14 and sulphur-35, although efficiently ventilated fume cupboards are usually adequate for such low-toxicity isotopes. However, in the production of radioisotopes emitting gamma rays, the radiation level will be too high for hand access. Sealed boxes under reduced pressure, with remote handling tongs, are the most widely used enclosures in radioisotope production. The same type is well suited to dispensing work.

Some of the boxes in the laboratory will probably have to be shielded with a lead wall. Usually 5 cm thickness is sufficient for millicurie quantities, but for the preparation of sodium-24, and perhaps also iodine-131 in large quantities, 10-cm lead thickness is advisable. Boxes for the production of pure beta emitters like phosphorus-32 and calcium-45 do not normally need any shielding beyond that provided by the box wall. For large quantities of high-energy beta emitters, however, about 1 cm of lead is required as a shield against the brehmsstrahlung. Local shielding may be necessary to reduce the intense β dose in dose proximity to the apparatus.

Enclosures may be constructed in several ways, and the choice of materials may also vary widely. As a general principle, the main parts of the side walls and roof should be made of transparent material, methyl methacrylate sheet (Perspex, Plexiglas) being ideal for this purpose. A cheap but very suitable type of production enclosure consists of a rectangular box made of ordinary mild steel, 2 mm thick, which is covered by a good quality epoxy

resin paint. Suitable dimensions are 1200 × 700 mm, with a height of 900 or 1000 mm. The side walls and roof of the box are cut away, leaving just a ledge which serves as support for 8-mm Plexiglas windows. The windows are pressed against air-tight rubber seals by means of a frame with screws or spring clips, and may easily be removed, permitting access for the maintenance of box equipment. Operations are carried out through one of the larger faces. Connections for services and effluent lines are welded into the bottom of the box, or service lines may be brought in through a panel in the top face.

Many isotope producers prefer process boxes made entirely of plastic materials, the main structure being made of polyvinyl chloride or resin-bonded glass fibre. Many kinds of such boxes are available commercially, but prices are higher than those for steel boxes.

One drawback to the use of steel boxes is the possibility of corrosion. If the epoxy painted surface is broken by impact, the steel plates will become exposed to attack from acid vapours which are usually present. By careful operation, however, abrasion of the epoxy surface is avoided.

Stainless steel is an alternative to epoxy-painted mild steel as a construction material for process enclosures; the price is somewhat higher. However, since hydrochloric acid vapour will also attack stainless steel to a considerable extent, the gain in using it is small.

Since some of the boxes have to be shielded with lead, a rigid support has to be provided. If this support is made in the form of a thick concrete platform (300 mm), on which the box stands, and supported on either concrete blocks or a steel construction, base shielding is simultaneously taken care of. The supporting table should preferably be designed as a steel container, into which concrete can be poured. Between the platform and the box a thin sheet of rubber is placed.

Figure 1 shows a complete box unit, commercially available, constructed according to the principles outlined above. Illumination of the box equipment is provided by fluorescent tubes mounted in a frame on top of the box and shining in through the roof window.

(b) Shielding

To obtain the most economical result, shielding walls should always be placed as close to the source of radiation as is practically possible. The usual way to protect production personnel against the radiation from gamma-emitters is to erect a lead wall surrounding all sides of the production enclosure. The thickness of such a wall will generally be 5 cm or, in special cases, 10 cm. For the production of limited amounts of soft gamma-emitters, however, a sufficient degree of shielding can often be obtained by just shielding locally some of the glass equipment in the box, thus saving money and improving convenience in handling.

A lead shield is easily made of bricks, such as the one shown in Fig. 2. Such bricks can be cast to a sufficient accuracy and are better when made of lead containing 4-7% antimony to increase their mechanical strength.

Some sort of interlock between the bricks should be provided. The leakage of radiation between plain bricks is in fact negligible, but the inter-

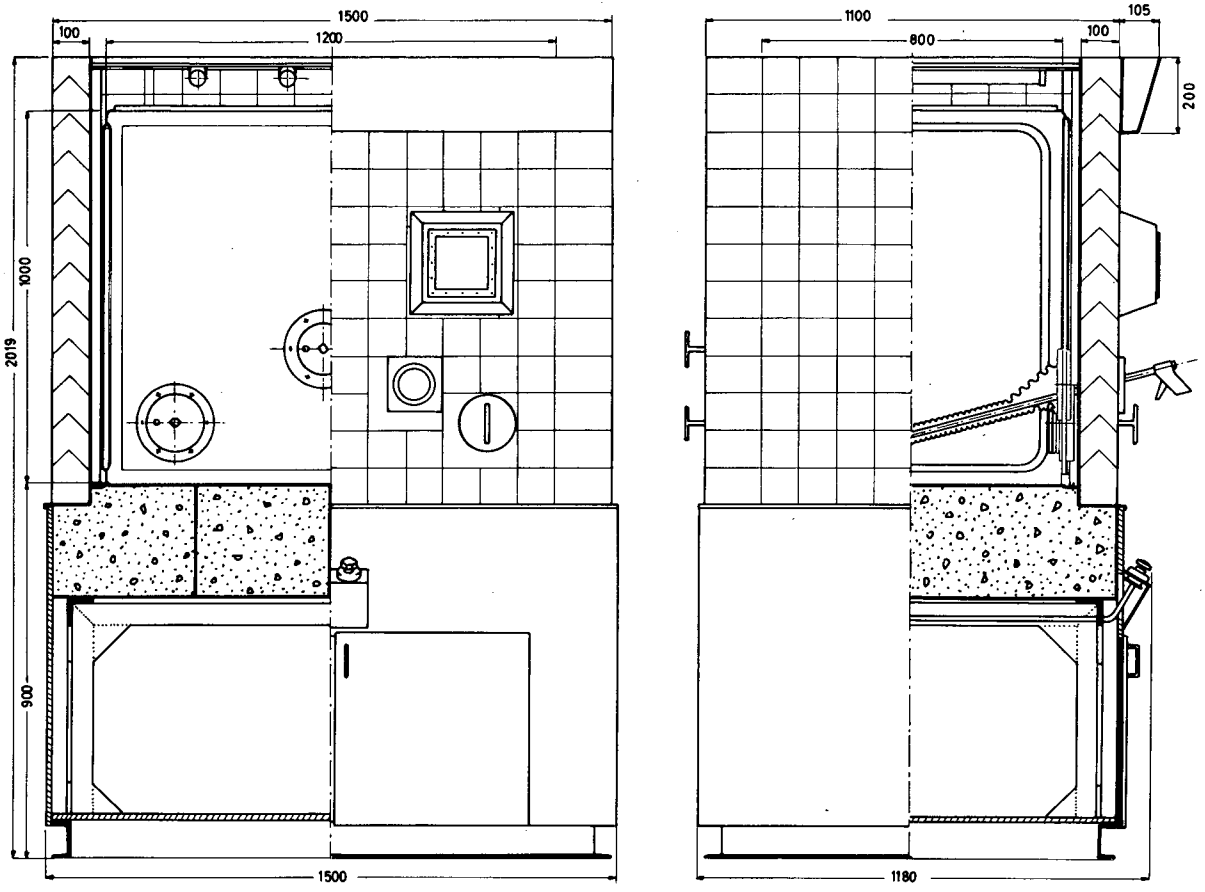

FIG. 1. Typical shielded cell for isotope production

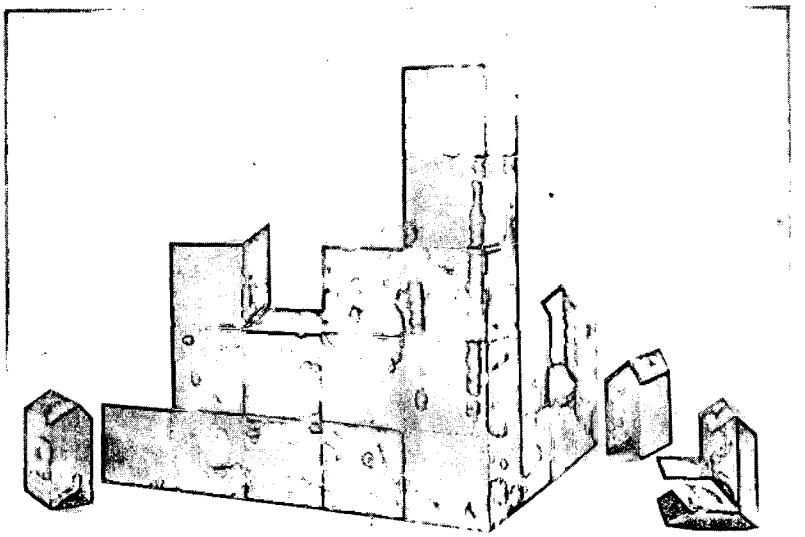

FIG.2. Interlocking lead bricks for shielding walls (10×10 cm, 5 cm thick)

locks will contribute considerably to the stability of the complete lead wall, and this is important. In addition, the wall should be held in place by some sort of rigid steel framework, conveniently placed between box and shield.

The price for a lead shield of this type is estimated to be \$300 to \$400/m^2 if it is 5 cm thick, a 10 cm-thick wall costing double. Provision also has to be made for viewing windows, transfer port plugs and sphere joints for the handling tongs.

Viewing windows are made of lead glass and may be obtained in several qualities and forms. For a 5-cm-thick lead wall a window 10 cm thick, of a standard density of 4.2 is appropriate. A 10-cm-thick lead shield requires twice the window thickness. The windows should be mounted in frames fitting the interlocking lead brick system, and the space between the glass and the lead frame should be packed with lead yarn. The protection given by such a window is a little less than equivalent to the lead wall, but if it is mounted in a line with the inside of the wall and with a frame like those shown in Fig. 1, the extra distance from the source adds to the protection. Practically, no deficiency of shielding at the windows can be measured with such a wall.

Lead glass windows with densities of up to 6.2 are available, as also are glasses specially resistant to radiation, but the prices are higher and the colour darker compared to standard windows. They are also more easily scratched. The price of a standard lead glass, 10 cm thick, with window area 15 × 15 cm, is about \$75.

Because of the helpful effect of refraction, just one or two windows of the type mentioned will be sufficient to see the whole area of the operations in one cell.

(c) Tongs and related equipment

Remote-handling tongs of various types and at different prices may be obtained from commercial suppliers. This equipment is normally satisfactory, but as a general guide the more rigid type of tongs should be chosen. Some isotope producers use tongs with detachable heads to enable them to change the types of jaws without removing the tong from the box. However, it is not difficult to find one type of head among those available commercially that will suit almost all the operations that have to be carried out. This seems to be the most practical solution, with the addition of a few special tools for opening screw-cap cans, cutting polyethylene tubes, etc.

Flexible plastic sleeves should be attached to the tong shafts to prevent contamination being carried into the laboratory when the tongs are drawn outwards. Several types of such sleeves are on the market, but special care should be taken to select a rather rigid type, preferably bellow-shaped and as narrow as possible; the price is higher, but it is well worth it. A wide, clumsy sleeve is easily torn and will prevent the operator from seeing much of the cell equipment.

Sphere joints are used for tong handling through the lead walls to prevent binding. The spheres and seating should not both be made of lead unless the sphere is coated with brass or stainless steel. Another method is to have the seatings cast in brass. The whole joint should be put together as a single removable unit; it will then be possible to replace a damaged PVC sleeve from outside the lead wall. The sphere joint principle is also used conveniently in beta boxes, a small sphere made of plastic or hardwood being used.

Many types of gloves for use in glove boxes are available commercially. It is useful to provide a glove port in most production boxes for making adjustments with the hand while the radiation level in the box is low. Neoprene gloves will last longer than those made of ordinary latex rubber and are to be preferred in spite of the higher cost. The standard type of glove fits a glove port of 15-cm diam. Plastic plugs should be available in the boxes to seal the glove ports when they are not in use.

(d) Chemical processing equipment

Most of the chemical processing equipment, dissolution and reaction vessels, transfer tubes, evaporation and distillation facilities, filters, etc., should be made of ordinary borosilicate glass, with standard stop-cocks, socket-cone joints and ball joints. Only in special operations do materials other than glass have to be introduced. For introducing inactive reagents into the box during the operation, glass tubes may be used, but more flexibility is achieved by the use of plastic or silicon rubber tubes, with a glass connection penetrating the shielding wall; a funnel may be attached to the outer end. When not in use, the glass connection socket should be blocked by a stopper fitted with a safety clip.

As all sense of touch is lost when the fingers are replaced by a remote-handling tong, the stop-cocks used should always be of the type with a re-

taining ring to hold the key in place. In most cases vacuum quality stop-cocks are necessary.

An opening station for screw-cap cans should be provided in each production box and, if inner irradiation containers are to be used, a cutter for the silica ampoules or polyethylene tubes must also be at hand.

Some sort of rigid support frame should always be provided for the glass equipment; this is specially important since the handling is to be carried out by means of tongs. Several materials are suitable for supporting frames, but the possibility of corrosion should be kept in mind. Aluminium, preferably anodized, is quite suitable for this purpose. When mounting processing equipment in a box it is important to allow sufficient distance between the operation face and the equipment to be handled, otherwise the useful area covered by tongs will be significantly reduced. The glass apparatus should be placed as close to the back wall of the box as possible, leaving at least 35 to 40 cm open space at the front.

Liquids are commonly transferred from one production stage to the next by suction. Vacuum is provided by a rotary vacuum pump, conveniently mounted in the supporting table and serving three or four production boxes. Electromagnetic valves can be used for connecting the pump to the various equipment sections. Autopipette filler bulbs made of rubber are very useful for transfers of this sort when only a slightly reduced pressure is required. Where heating is needed a convenient source is the electric "Isomantle" type, which can be purchased in several sizes to fit various sizes of reaction vessel. For the gentle heating of liquids an infrared heating lamp will be found convenient. A variable transformer, mounted outside the process box, controls the heating rate. As a general rule, heating by gas flame should be avoided and indeed is dangerous in any sealed enclosure which has little or no ventilation.

(e) Dispensing, packing and control facilities

Organization of the dispensation of radioisotopes is discussed in detail in Section 4, but a few comments on the equipment needed are given here. When dealing with isotopes for medical use, dispensing should always take place in special boxes, preferably, though not essentially, isolated in a dispensing room. Boxes, shielding, remote handling tongs and transfer ports, etc., for dispensing are identical to the equipment used for production. Dispensing boxes should be installed in such a way that the operator can perform the filling, reading and emptying of pipettes in a seated position. To read a pipette at some distance through a lead glass window may be difficult, therefore care should be taken to select pipettes with very distinct graduations. Only top quality pipettes should be used notwithstanding the higher cost.

The main equipment to be placed inside a dispensing box is a remotely operated rack of pipettes, a sealing machine for bottles and an autoclave for sterilization. Beside these, it is useful to have a device for the storage of production batch bottles. Bottles standing about loose on the floor of the box should be avoided.

A relatively large room should be left for packing shipments of radioisotopes. The bottles containing the radioisotope solutions are placed in

lead pots within the dispensing unit. Such containers can then be handled with very short, rigid tongs, and no lead-shielding packing cell will then be necessary.

It will be necessary to check the activity in the shipment to detect any possible mistakes in calculation or volumetric measurement which may occur. Such a check can be performed within the dispensing unit or in the packing room. An ionization chamber suitable for this check together with the necessary lead for shielding can be purchased for about $1000.

Another item of equipment necessary in the packing room is a sealing device for tin cans. The bottles should be enclosed in sealed cans to meet the requirements for the safe transport of radioactive materials [1]. Ordinary tin cans with a volume of 1 litre are suitable for most shipments of radioactive solutions. The price of an electrically operated sealing machine for such cans is between $200 and $300.

The packing room should also be provided with a well for the temporary storage of radioisotope packages. Packing materials, i.e. lead pots, tin cans, cardboard boxes, etc., also need a lot of space for storage, and it should be kept in mind that such materials will be cheaper if purchased in bulk.

Figure 3 shows a typical lead container used for the shipment of radioisotopes. The construction should be noted. With a lead pot like this the upper part of the bottle stands above the top of the container after lifting off the lid. As the bottle will never be filled to the neck with radioactive solution, this will cause no radiation problem, but the removal of the bottle with tongs is thus facilitated.

Instruments to measure the radiation dose-rate must be available in the packing room for the measurement of surface radiation of the packages ready for transport. Many types of battery-operated instruments are available which are very suitable for this purpose. Prices range from $200 to $800.

Facilities for a limited programme

A radioisotope production programme limited to the supply of short-lived isotopes in an unprocessed form, or in simple solution, (the proposed first stage referred to in Section 2), can be carried out at relatively modest cost. The space required might be found within the laboratory facilities already present at the reactor centre. A radioisotope service on this scale should be organized in connection with a nuclear chemistry group, if one exists.

This first-stage production programme will probably satisfy only a small fraction of the country's demand; for the rest, importation must be depended on. In such a case it may prove practical and economical to operate a dispensary for imported isotopes in conjunction with the production group.

An example of an isotope laboratory intended for production on the first stage scale, together with the dispensing of imported stock solutions of other radioisotopes, is sketched in Fig. 4. The space required is 75 m^2, and it is assumed that the isotope laboratory will occupy part of an established laboratory installation. If the programme is limited to production only, the

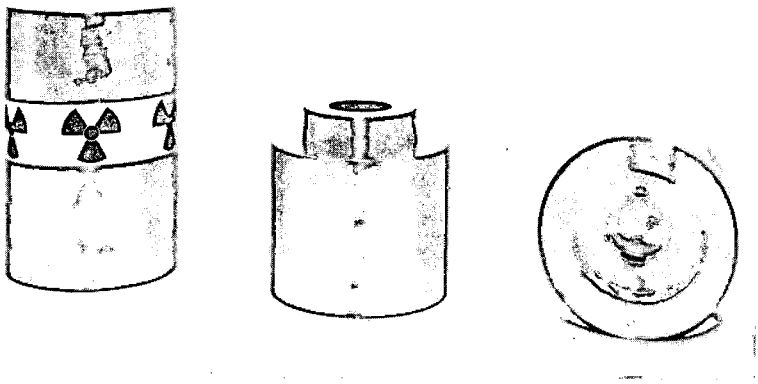

FIG.3. Lead pot for shipment of bottles containing radioactive solutions

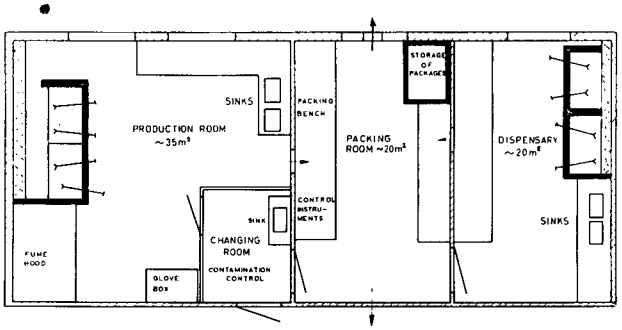

FIG.4. A small isotope production laboratory

dispensary can be omitted, bringing the space requirement down to 55 m^2, but this should be considered an absolute minimum. Additional space for counting, analytical control, offices, etc., will of course be necessary, but these facilities could be located elsewhere.

The rooms should be arranged together in such a way that only one entrance will normally be used. At this entrance a small area should be left for change of clothing and contamination control. A sink for hand washing is necessary. The production laboratory should be fitted out with a few lead-shielded remote handling tong boxes, a glove box (or slit box) and a fume hood. The fume hood should be used as a multi-purpose unit, and extra lead bricks should be provided for temporary shielding. Typical examples of the use of this equipment are the transfer of radioactive material from one type of container to another, the dissolution of irradiated materials in water, and the preparation of radiation sources of various kinds. Ventilators and filters for the enclosures may be placed on the top of the boxes. The production laboratory should also have sinks for cleaning glassware, etc., and a supply of medical-grade water must be provided. Bench space will be required for preparing targets for irradiation and for handling dilute solutions for

measurement and standardization. The dispensing and sealing of bottles may be performed within the production boxes.

The packing room should have plenty of bench space, a suitable instrument for the measurement of surface radiation from the packages and preferably also an ionization chamber for checking the shipments. Packing materials need a lot of space for storage, and a shielded storage area should be provided for imported shipments and packages ready for dispatch.

The dispensing room is intended for the treatment of imported stock solutions and should have one or two shielded boxes equipped with opening and sealing devices for penicillin bottles, remotely operated pipettes and autoclaves. The room should have sinks for cleaning of glass ware, and laboratory benches with lockers and drawers. It is useful to provide small openings in the walls of the laboratories for the transport of units between adjacent rooms; the same can be done for passing packages into the packing room.

The special equipment needed for a laboratory like this, such as boxes, tongs, processing equipment, lead bricks, instruments, etc., should be purchased with a view to using it later in a more comprehensive plant.

With a laboratory like this, or a similar one, it should be possible to proceed to the second stage of a radioisotope programme without any major additional investment. Most of the isotopes produced are in small demand, and a production service can be maintained with just a few production boxes, changing the glass equipment for each new isotope. It is assumed that a counting room, instruments for physical measurement and analytical services are available in other parts of the reactor site. Some additional office space will be necessary for record keeping.

Laboratory layout and structure

The production of the radioisotopes described in Section 2 as coming within the third stage of development require a laboratory facility of more specialized construction. The size of such a laboratory will vary within wide limits depending on the size of the population to be served. Apart from a few special items, a laboratory for isotope production can be constructed very similarly to, and should cost little more than a conventional chemical laboratory of high standard. If the processing of high-toxicity isotopes is to be included in the programme the laboratory, or at least part of it, must be classified as a Type A [2], which means that the laboratory design and construction should not be undertaken without the aid of experts. An important question is of course, whether a new building is to be erected for housing the plant, or if an existing building is to be converted.

It is better for a new building to be constructed as a single storey, as this removes any doubt about the ability of the top floor to carry the weight of shielding and saves the expense of a top shield on the production cells. This also makes access for maintenance of the cell equipment much easier. The scattered radiation reaching the operator area from the top of the cells will not be negligible. Services like water, electricity and compressed air lines may then be brought into the production cells through the box roof.

If the laboratory is to be erected in a cold-climate area, it will prove most practical to provide a basement under the laboratory floor in which to place water and sewage pipes to prevent freezing. In such a case the area covered by the building may be reduced significantly, as service equipment, ventilation plant, stores and a laboratory waste system can also be placed in this basement.

Where a building of more than one storey is to be used for the plant, it should be noted that bottom shielding for the production cells is cheaper and more convenient to provide than top shielding, since some sort of support for the side shielding will be necessary in any case. For this reason the location of the gamma-emitter production rooms on the top floor of a building is preferred if the floor is strong enough. Such an arrangement will, however, necessitate a lift arrangement for the transport of shielded radioactive materials to and from the plant. Fitting an existing building to a radioisotope production plant will often give rise to practical problems. If the building to be used was originally constructed for non-laboratory purposes, the cost of conversion will probably be very high. Generally it is recommended that such a conversion should be avoided if possible. In either case it is good practice to keep all radiochemical laboratories and related rooms together as one area to which access is restricted and completely separated from the offices. A new building should consist basically of two main wings, one for administration and other office work and the other for active work such as production, dispensing, research and development. Between the two should be a section for cloakrooms, washing rooms and equipment for contamination control. The need for sufficient space both for cloakrooms and offices should not be underestimated.

A few practical solutions to problems of layout, taken from existing radioisotope plants in the small- and medium-size class, are shown in Figs. 5, 6 and 7. Figure 5 shows a relatively small plant in Risø, Denmark, of one storey, with a total floor area of 990 m^2. Production laboratories and related rooms occupy about one half of the total area [3].

A production laboratory of the "one storey with basement" type in Kjeller, Norway, is shown in Fig. 6. The sizes of the various sections are:

	(m^2)
Laboratories and related rooms	700
Cloakrooms, contamination control section and lobby	220
Offices (two storeys)	430
Basement (ventilation, waste-room, stores, stokehold, etc.)	500
Total area	1850

This laboratory was built and equipped during the period 1958-1960 for about $400 000 [4]. The radioisotope production programme has been combined with research work in the field of production methods development, measurement techniques and radioisotope applications. As mentioned in Section 2, such a programme extension is generally advantageous, and the extra space required will not cause more than a small addition to the total plant investment.

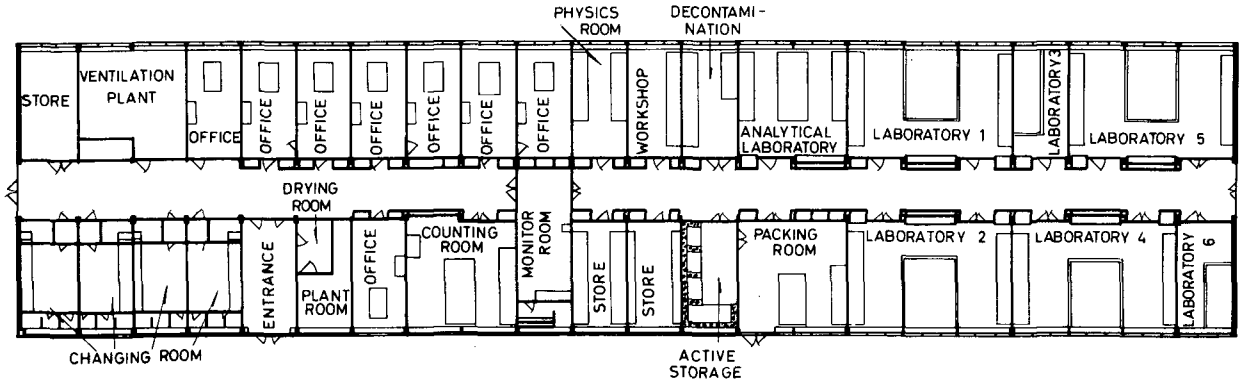

FIG. 5. Laboratory ground plan (Isotope Production Plant, Risø, Denmark)

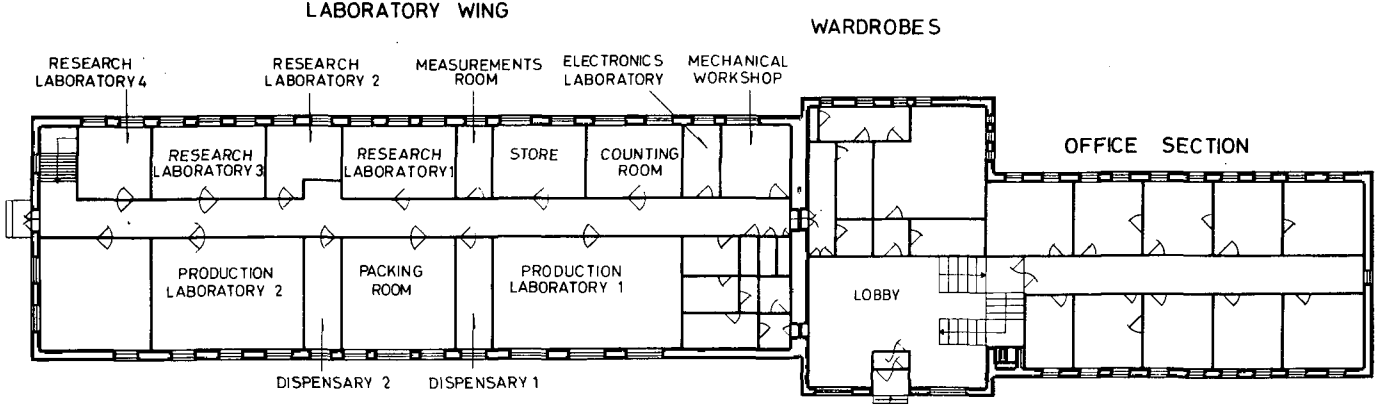

FIG. 6. Laboratory ground plan (Isotope Production Plant, Kjeller, Norway)

Figure 7 shows a plant in Inchas, United Arab Republic, intended for a more extensive programme, with a staff of about 35 persons [5]. The design closely resembles that of the Norwegian laboratory (Fig. 6), with a basement under a part of the laboratory wing and a second storey on top of the inactive wing. The approximate costs for this laboratory are as follows:

	$
Building costs	250 000
Fixed inventory, waste collection, ventilation monitoring systems	180 000
Production equipment	120 000
Mobile instruments, tools, etc.	150 000
Total cost	700 000

It may be noted that all these laboratories are constructed with complete separation between the offices and the active section. Choice of the best form structure will, of course, depend upon the terrain and the climate. All rooms should be arranged together as simply as possible and the windows permanently sealed to maintain the ventilation balance.

Gamma shielding is usually 5 to 10-cm-thick lead, and the laboratory floors must be designed to carry this load. A reasonable figure is 5 tons/m^2. All radiochemical laboratories should preferably have swinging doors without thresholds and transparent glass panels should be provided in the doors, to prevent collisions and to enable inspection of a room from outside in the case of a contamination accident. The rooms should not be unnecessarily high, as the amount of air to be supplied increases directly with the height of the room once the number of air changes per hour is decided. A suitable ceiling height is 2.5 to 3 m.

The general finish of the laboratories should be clean and smooth. Corners between walls, ceilings and benches should be rounded by means of plastic strip, and laminated plastic is a good cover material for working benches. Plastic asbestos tiles are ideal for the floors; they are easily cleaned and decontaminated. The joints represent no problem provided the floors are carefully waxed from time to time. The greatest advantages of tiles compared to linoleum is their mechanical strength and the fact that the tiles can be replaced one by one should they be damaged or seriously contaminated. Welded polyvinyl chloride is also a good material for floors but it is somewhat more expensive than tiles if the rooms are not large.

Conventional equipment can be used for illumination, window frames, etc., and a good quality paint is sufficient for walls and ceilings finish. Walls between adjacent rooms should preferably be of a light structure since there is no advantage in making the walls very heavy for shielding purposes. The principle of shielding the radioactive sources and not the rooms in which the radioactive work is carried out, should always be applied. In general, the recommendations for a high-standard conventional chemical laboratory are directly applicable to the planning of a moderate-size isotope production plant.

The production and dispensing cells within the rooms may be arranged in several ways. Some isotope producers prefer one separate room for the production of each isotope, while others use a single production laboratory

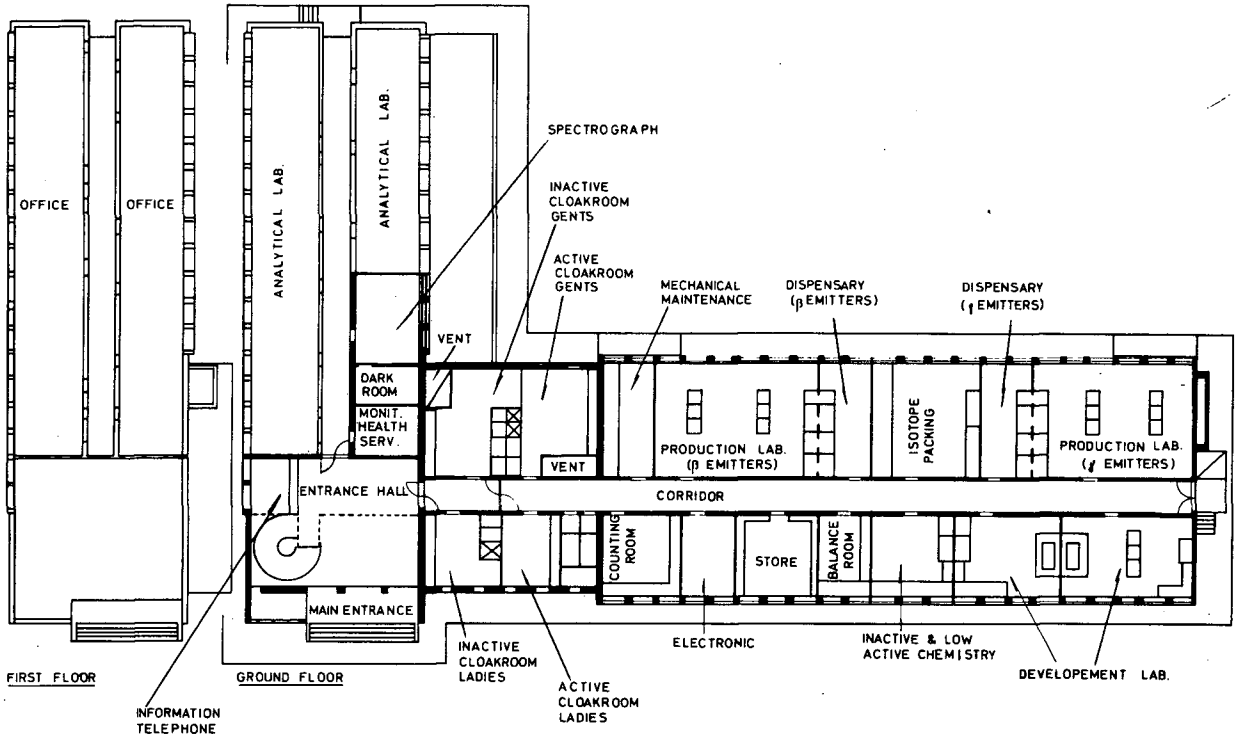

FIG. 7. Laboratory ground plan (Isotope Production Laboratory, Inchas, United Arab Republic)

for all the processing equipment. The main advantage of the first case is that the chance of cross-contamination is reduced and, if an accident occurs, it will be limited to a small part of the plant. On the other hand a single large production laboratory secures the best space utilization and is, of course, cheaper to build. Something between these two extremes seems to be the best solution. When designing a laboratory of this kind it is advisable to reserve at least two rooms for production and two for dispensing, in which the various cells can be grouped together according to the type of shielding. If processing of high-toxicity isotopes, e.g. ^{131}I, is to be included in the production programme, it might be advantageous to isolate this production equipment in a special room.

The number of tong boxes to be allowed for should be about ten to fifteen. In addition to these, dispensing might further occupy a minimum of three boxes. The number of dispensing units should not be too small as this equipment will need service and maintenance from time to time. It should be possible always to take about half the equipment out of regular operation and still be able to make the necessary shipments with the rest of the boxes. All dispensing boxes should preferably be equipped identically. At some isotope-production centres it is the practice to link dispensing equipment to the processing equipment in a combined production-dispensing unit. In this way a few boxes may be saved, but on the other hand the boxes must have larger dimensions and additional difficulties arise when maintenance work is being carried out. Also, during normal operation complete separation between production work and dispensing work is preferable.

If the production boxes are placed together, three to four per row, better economy of laboratory space is achieved. In addition, considerable shielding may be saved and the layout of benches, services and effluent systems simplified. Figure 8 shows a set-up of three production units for beta emitters,

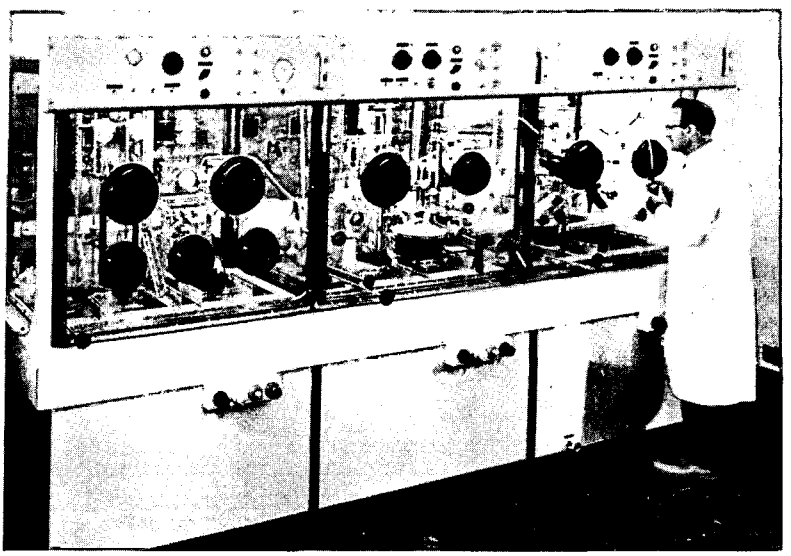

FIG. 8. Production boxes for beta emitters (Kjeller, Norway)

constructed according to this principle. The boxes are made of stainless steel with 8-mm Plexiglas windows.

In connection with the arrangement of production boxes the following question must be answered: To what extent will the programme include the production of the less frequently used radioisotopes, such as bromine-82, cobalt-60, mercury-197 and -203, and silver-110 m? The production methods for such isotopes usually consist of simple dissolution of the target material in water or the transformation of a carbonate, metal or oxide to a chloride solution with the subsequent need to evaporate the hydrochloric acid. It is by no means necessary to keep one production box fully equipped for each radioisotope. A better approach is to keep one or two boxes for this type of operation and simply change the glass equipment within the boxes. By careful operation this arrangement should cause no radiation or cross-contamination problems.

For major products, such as iodine-131, phosphorus-32, gold-198, sulphur-35, etc., it will of course be necessary to reserve one box for each process. For countries with sufficient demand it is recommended that a reserve production box be set aside for isotopes where continuity of production is important (Fig. 9).

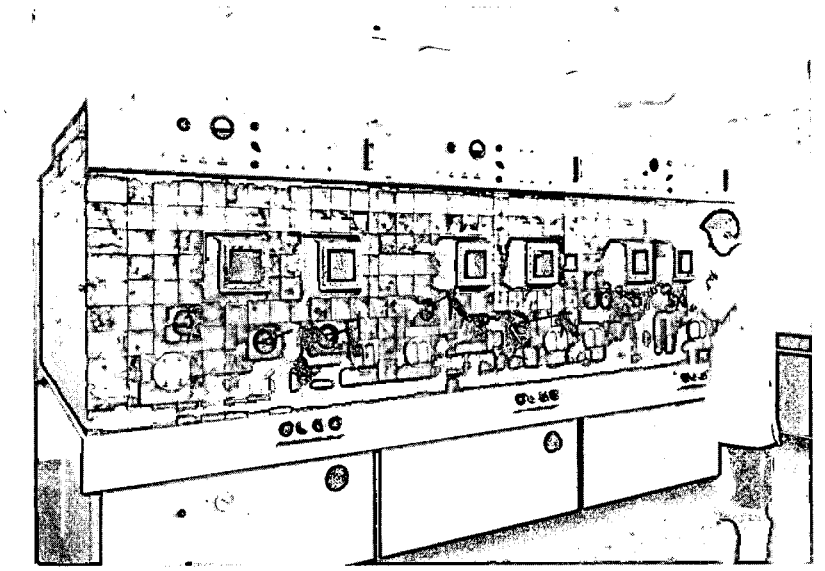

FIG. 9. Shielded production cell for gamma emitters (Kjeller, Norway)

A few comments should be made on the placing of production units within the laboratory. Beta boxes do not need additional shielding beyond the Perspex windows and can be placed anywhere in the laboratory, preferably at some distance from the walls, giving access from all sides. Gamma boxes are conveniently arranged so that they have lead shielding at the front and sides whilst the back shielding is made of a cheaper material, e.g. heavy concrete blocks. Space should be left between the boxes and the back

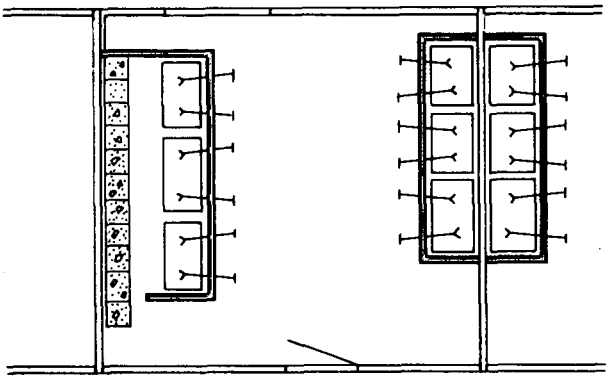

FIG.10. Arrangement of shielded production cells

shielding to allow access for maintenance work when the radiation level is low. The principle is illustrated on the left of Fig.10.

Another form of arrangement is shown in the right hand part of Fig.10. This method is suitable when dealing with a number of gamma boxes in adjacent rooms. Much lead shielding can be saved but access to the interior of the boxes for repairs must be provided through the box roof, or through a removable side wall. A system used at some centres is shown in Fig.11. The production cells are grouped together within a large shielding wall with their operating faces outside and a maintenance and transport oven between the two rows of cells. The transport can also be arranged with a conveyor belt system. An advantage of this system is that the operation hall can be regarded as a semi-active area, but the arrangement is expensive and is suited to a larger programme than the one considered here.

Transfer of radioactive materials within the laboratory

The system for transferring radioactive materials between laboratories and cells should be planned carefully, since it will always represent a weak point in the containment system. The majority of contamination accidents in radiochemical laboratories are caused by some weakness in the transfer system. Transfer of highly radioactive sources within the laboratory should be done in a shielded transport container which should be constructed to fit the transfer ports of the various production and dispensing cells. Figure 12 shows a typical transport container of this kind. It consists of a drawer designed to hold either target cans or product bottles. The drawer can be pushed into a production box or drawn back into the lead container, which is carried on a small four-wheeled carriage. The container is closed by means of a sliding door. For carriages of this type to be fully effective, it is important that the working height above the floor is standard throughout the laboratory.

The simplest method for transfer operations of this kind is to use a lead pot on a wheeled table. The whole pot is placed inside the cell and emptied by means of the cell handling tongs. This method is best suited to small

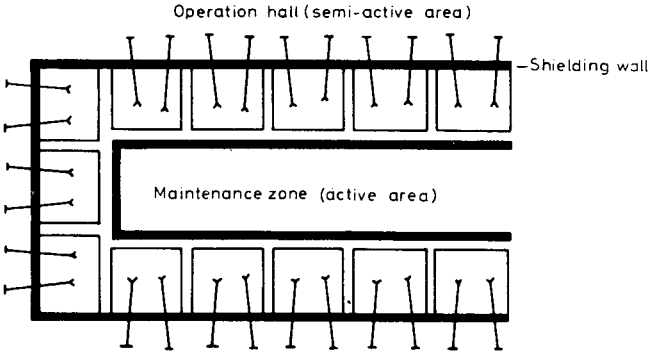

FIG. 11. Arrangement of shielded production cells

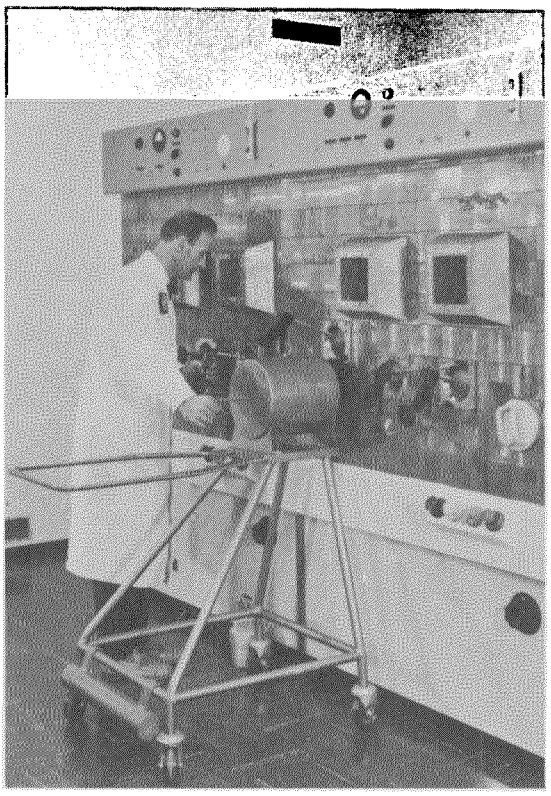

FIG. 12. Transfer unit for radioactive materials

amounts of radioactive material, e.g. transport of bottles for shipment from dispensary to packing room, since the shielding pot must be small to be handled in this way.

If production and dispensing boxes are arranged together in adjacent rooms, as outlined in Fig. 9, transport is most conveniently arranged by

connecting two boxes with a tube through the wall. The transfer of bottles is then easily performed with the cell tongs or, if greater distances are involved, by the use of a suitable conveyor belt. Transport of this kind should be limited to certain areas within a laboratory, thus minimizing the background radiation in counting rooms, etc., and possibility of the spread of contamination to areas intended for low-activity work. The principle is illustrated in Fig. 13. The rooms to the right are used for counting, research and development, and will not be affected if a transport accident should occur. During a transfer operation the box containment has to be broken. Opinion is divided about the best way to solve this problem of transfer ports. Some centres use double-sealed transfer ports in the boxes, giving full air-lock conditions: others prefer a system with a completely air-tight outer door and a slide door inside to prevent the escape of loose solid contamination when the outer door is opened. The first method with a complete air-lock cannot guarantee no transfer of solid contamination into the laboratory and air-borne contamination may be trapped inside the air-lock to be released

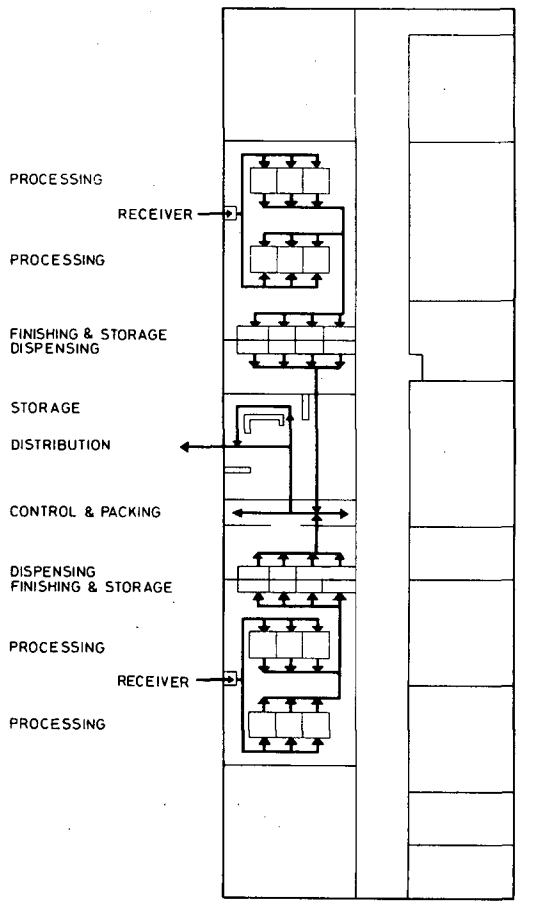

FIG. 13. Diagram illustrating the way in which movement of radioactive materials is limited to defined areas

when the outer door is opened. The system with the extra slide door reduces the possibility of direct outward flow during a transfer operation but will be of value mainly for transfer ports with relatively large dimensions.

The simplest and most practical solution is to use a single sealing door when the transfer ports must be kept relatively small. In most cases an ordinary standard glove port, diameter 15 cm, is suitable for the purpose. If the process enclosures are operated at the usual reduced pressure of a few centimetres of water, the air-flow velocity inwards through an open port of this kind will not drop below 0.5 m/s, the minimum air-flow velocity recommended for hoods. A system like this will give no more risk of laboratory contamination than a double-sealed air-lock provided not more than one port is open simultaneously in the same box. The standard 15 cm glove port is closed by means of a plastic plug with a rubber sealing ring. During a transfer operation such a plug has to be left somewhere; in the case of lead shielded boxes it often has to be placed inside the box. The opening and closing of a port of this kind thus requires a hand inside the shielding wall. In such a case the plugs must be considered active, and never touched by bare hands. It is possible to operate such a system without having radiation dose problems, provided the personnel have the necessary training and discipline. However, a better method is to use a closure which is pressed against the port by a spring, and which can be operated with a handle outside the lead wall. The lead wall should have a hole corresponding with the box port which is closed by a thick steel plug when the port is not in use. Lead plugs have certain disadvantages because of their lack of mechanical strength.

Ventilation system

All working areas in which unsealed radioactive sources are handled need careful ventilation. A well-planned ventilation system in fact forms the basis of contamination control. It should be realized, however, that proper room ventilation alone will not be sufficient protection for the laboratory personnel. The air-flow balance may be altered by opening and closing doors and hoods, and the laboratory equipment and furniture will affect the flow of air to a considerable extent. To overcome irregularities of this kind a quite unreasonable amount of air has to be supplied to the laboratories. The best way to secure safe working conditions in processing rooms is by using sealed boxes with a separate exhaust system. Then it is only necessary to provide sufficient room ventilation to give comfortable working conditions, a reasonable figure being six to eight air changes per hour.

The main principle to be followed in the planning of the laboratory ventilation system is that the direction of air flow should always be towards the zones with the highest levels of radioactivity. In practice, this is arranged by supplying fresh air to the corridors. This air is drawn through the laboratories into the boxes and hoods, and finally filtered before being exhausted to the atmosphere. With a proper air-flow arrangement the relative pressures should be as follows:

Corridor, inactive rooms, etc.: Pressure of the surrounding atmosphere or slightly less

Laboratory rooms: ~10 mm of water-reduced pressure
Production and dispensing boxes: 20–30 mm of water-reduced pressure (10–20 mm relative to laboratory rooms).

In rooms where open fume hoods are to be used the number of air changes has to be increased, otherwise the rooms have to be very large to supply adequate air. It is useful to equip a few research and development rooms, of limited size, with open hoods and to give them more air changes, for example, about 20 changes per hour. The use of fume hoods in the laboratory should then be restricted to these areas.

The inlet air to the laboratory must be cooled or heated according to climatic conditions. In most countries atomic energy centres are not placed close to big cities. Therefore the air is usually clean enough to be fed into the laboratory through cheap, low-grade filters. The exhaust air from the laboratories will not require filtering, but the air exhausted through hoods may contain contamination and should pass through absolute filters before being released to the atmosphere.

The sealed production and dispensing enclosures should be provided with a separate ventilation system. This system should have two exhaust fans, both of them being capable of providing the necessary reduced pressure. Polyvinyl chloride or other suitable plastic material should be used for the pipe work. The diameters of the extract ducts should be diminished stepwise from 18 to 20 cm near the fans to 4 or 5 cm at the box connections. The exhaust air should be filtered through absolute filters and, if the production programme includes work with volatile nuclides like iodine-131, a charcoal filter should be fitted also.

If the boxes are kept well sealed they will consume a negligible amount of air. In many cases, however, both corrosive and contaminated vapours may be present in the box atmosphere and to remove these a minimum rate of air flow should be provided. This is easily arranged with an adjustable air inlet valve with which the required reduced pressure can be obtained. Small absolute filters may be mounted on the inlets but in most cases this will not be necessary.

Vacuum pumps used with active process equipment should be regarded as part of the box ventilation. Air from such pumps may contain contamination and should be exhausted into the box ventilation system.

There is no need for an elaborate automatic control system for the ventilation. The reduced pressure level in production boxes is simply measured by U-tube manometers, and the ventilation balance between working rooms and corridor is sufficiently controlled by observing the position of the swing doors, which under normal conditions should point towards the more active rooms. It is a good practice to have control switches for the fans situated on a central panel, preferably with a control lamp showing that the fan motor is running. If a single room has more than one fume hood, only one switch should be used for all of them, as one hood in operation may draw contamination into the laboratory from another which is shut down. The fans used for supply and exhaust of air to the open working areas should be adjustable, as ventilation balance conditions may be changed during laboratory operation.

A failure in the box ventilation system will cause the reduced pressure in all process enclosures to drop to zero, and under such conditions activity may be released into the rooms. For such emergencies a warning system should be fitted. It can be arranged very simply by means of a pressure indicator placed in the main ventilation duct, which actuates alarm bells in the production rooms if the pressure falls below a predetermined value. Consideration should be given to the provision of an emergency electric generator for the ventilation system, to be used in the event of a main power failure.

Waste management

The key to waste management for a radioisotope plant is to reduce, as far as possible, the amount of waste material that requires special treatment. For all practical purposes waste can be divided into the following categories:

1. Inactive waste
2. Low-activity liquid waste
3. Liquid process waste
4. Solid process waste
5. Solid laboratory waste.

Effluents from the inactive part of the laboratory building can be connected to ordinary sewage. This also applies to cooling water lines to some equipment in the active section, for example, water distillation sets. Particularly in laboratories for research and development work it is practical to provide a few drains leading directly to sewage. The reduced volume of active waste is an advantage, but special care must be taken to avoid the inactive drains being used for discharge of active or potentially active effluents.

All washings and dilute solutions of radioactive materials should be considered as a low-activity liquid waste. In many cases this low-activity waste can be released to the sewage system, but it has to be monitored and, in some cases, stored for decay of the activity. A large delay tank, or two tanks connected in parallel, should be used for collecting the low-activity waste. The tanks should be of at least 5000–10 000 litres capacity and should be surrounded by trays of a sufficient size to collect the tank contents in case of leakage. Suitable materials for such tanks are epoxy-painted mild steel, stainless steel and plastic materials. The price is a conclusive argument against stainless steel, and painted mild steel may cause trouble from corrosion, particularly near pipe connections. Reinforced glass fibre or plastic material seems to be the best solution, and the price will in most cases be only slightly higher than for painted steel. A so-called compound steel (mild steel with a stainless-steel coating) may also be used. It combines the corrosion resistance of a thin sheet of stainless steel with the mechanical strength of an ordinary steel plate. The tanks should be provided with taps for sampling and should be vented through a filter, and some sort of liquid level indicating system will be necessary.

The amount of liquid released into such tanks should be kept to a minimum, allowing storage for decay without exceeding the total delay tank capacity. For this reason, the use of water ejector pumps for providing vacuum should be avoided in active laboratories. Fundamentally, storage for decay is a better approach to the waste problem than dilution, provided personnel are adequately protected against radiation from the storage tanks; dilution does not reduce the amount of radioactivity released to the environment. The nuclides referred to in the introduction all have relatively short half-lives and therefore will decay sufficiently in a period of a few weeks. The treatment of the low activity waste will not give rise to any problems provided its volume is kept to a minimum and a separate waste system is available for highly radioactive solutions.

The liquid process waste from the production and dispensing boxes should be taken out of the boxes through a bottom outlet leading directly down to a plastic container placed either under the box or preferably in the basement, if one exists. Polyethylene is a suitable material for such containers, which should not be larger than 50 to 60 litres. As for all radioactive solutions the principle of double containers should be followed, providing trays with sufficient dimensions to collect the entire contents of a full polyethylene bottle.

Pipe work for process waste should be corrosion resistant. Stainless steel, glass and polyvinyl chloride are suitable. Full containers should be disconnected and replaced by empty ones. With a reasonable number of extra containers available, full containers may be left for decay in a suitable store-room until the waste can be treated as ordinary sewage. It is helpful for the process waste containers to be fitted with some sort of level indicator. This is conveniently arranged with electrodes in the bottom and top of the container, the liquid itself completing the circuit which in turn operates an alarm when the container is filled to the limit.

Active operations will also produce solid radioactive waste consisting mainly of irradiation containers and used target material. A similar system with polyethylene containers placed under the boxes or in the basement is also suitable here. If no basement is provided, it may become difficult to find sufficient space under the boxes. With boxes placed together in a row a single liquid waste bottle may be used to serve three or four boxes, thus freeing space for solid waste containers. In a system for solid waste the tubes should be as straight as possible with no sharp angles where cans and similar objects may get jammed. The need for shielding of the waste containers has to be considered in each case.

All working rooms should be equipped with containers for ordinary laboratory solid waste, like disposable gloves, paper, etc. The type of container widely used in hospitals, with a pedal-operated lid, is suitable.

A view of a waste-treatment facility placed in the basement of a production plant is shown in Fig. 14. Two delay tanks for low-activity waste, each of 10 m^3 volume, are seen to the left. The steel drums in the centre of the picture are lined inside with 7 cm of concrete, and serve simultaneously as shielding and trays for the process waste polyethylene containers. The same type of container and drum is used for both the dry and liquid process waste systems. Full containers are simply carried away together with the

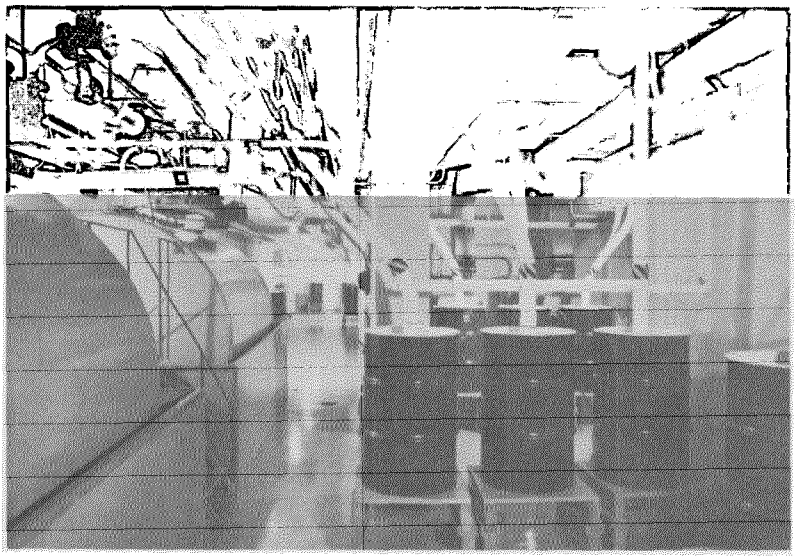

FIG.14. General view of basement for storage and treatment of solid and liquid waste (Kjeller, Norway)

shielding drum and replaced by another by means of a small carriage with a lifting-jack. Tubes carrying radioactive liquid are provided with drip-trays underneath, and the presence of liquid in these, or in the waste container trays, actuates a leakage alarm system by means of simple moisture detectors. Top shields for the waste bottles are usually not necessary, but have to be provided in special cases.

Personnel protection

The most essential aspect of personnel protection in radiochemical laboratories is training and instruction. New personnel should always receive a thorough training in radioactivity before being allowed to operate any of the installations single-handed. Special care should be taken to issue clear instructions for the work, both general instructions for work with radioisotopes and more special regulations concerning the actual laboratory installations. A detailed emergency plan should be made known to all members of the staff.

As previously noted, a well-established system for area monitoring is essential for the safety of a laboratory of this kind. However, there is no need for elaborate fixed automatic monitoring systems; usually simple routine checks using portable equipment are just as effective. A certain degree of control in connection with the waste and ventilation system will be necessary, especially control of fan operation and reduced-pressure measurement in process enclosures. Before starting radioactive work in box units the reduced-pressure conditions must be checked always. Most nuclear energy centres operate a central radiological protection service, which provides services such as personnel film dosimeter monitoring, air filter tests for

airborne contamination, smear tests for surface contamination in the laboratories and also medical supervision of personnel.

Contamination control instruments and dose-rate measuring instruments should always be at hand in the laboratory. Such instruments should preferably be of a battery-operated, light and handy type.

Gas masks with charcoal filters should be provided in the laboratory in a sufficient number (one for each person) and a few sets of plastic overall suits and compressed air respirators should also be available. This equipment may be needed in an emergency and it will be necessary when a box unit has to be opened for some sort of maintenance work. A material that always proves useful in the handling of radioactive materials and contaminated objects is polyvinyl chloride sheet. It may be obtained in various thicknesses and qualities and should always be at hand in sufficient quantities.

A laboratory like this is not very likely to catch fire, but fire-extinguishers should be provided in a sufficient number. The powder-type extinguisher is the most effective in a serious case. For fire inside an enclosure small carbon dioxide units are preferred. If the laboratory should catch fire, the general principle to be followed in such an installation is that the fire is more dangerous than the radioactivity; therefore general rules for the handling of radioactive materials have to be disregarded to some extent if necessary during the fire fighting. Detailed plans on dealing with a fire should always be established with a view to minimizing the risk from the spread of contamination.

The need for sufficient space in changing rooms in the laboratory has already been mentioned. This area should be divided into three parts, an "inactive" cloakroom where the regular staff can leave clothes and things that do not need to be brought into the active area, an "active" wardrobe for laboratory coats and special shoes or shoe covers, and between these a control and decontamination section, equipped with the necessary instruments, sinks for washing and preferably a shower. Decontamination materials and a reserve of spare clothing should also be available. After a contamination accident, the monitoring of people involved can take place in this room.

Conclusions

The handling and processing facilities necessary for maintaining a national isotope production and distribution service have been described in the preceding pages. The general recommendations can be summarized as follows:

A modest production programme, combined with the dispensing of imported isotopes, can be carried out in a small laboratory (~75 m^2) equipped with a few shielded boxes. In such a situation the production group should be closely associated with a nuclear chemistry group which could provide auxiliary space and equipment for analytical control, counting and other services. Such an organization should be considered as temporary.

A programme comprising the production of those isotopes most widely used in medicine will require a special laboratory facility, preferably a separate building or wing specially constructed for the purpose. The laboratory floor area requirement will be at least 400 m^2. The design of such laboratories should not be undertaken without the aid of experts.

A large proportion of the problems encountered during the planning of an isotope production facility will depend on local conditions (climate, terrain, legislation) and cannot be discussed further here. However, a few general principles should be pointed out:

The use of shielding, manipulators and other special equipment should never be carried to extremes. Very often the result of extra investment in shielding and tongs is that operations become more difficult and time-consuming, to such an extent that the dose received is not reduced. If handling methods are made too complicated and inconvenient personnel will not use the equipment properly unless supervised. Much working time can be lost. All handling methods and operations should therefore be carefully examined before deciding upon the amount of remote-handling equipment and shielding to install.

Most of the equipment needed for radioisotope production is now available commercially and in most cases the best results, both technical and economic, will be achieved by the use of such standard equipment. An important point in the planning of a production laboratory is to decide to what degree one should make use of commercial equipment. There are firms today offering for sale complete laboratory facilities of this kind and also standard shielding box units complete with chemical processing equipment, dispensing facilities, etc., ready for installation in suitable laboratories.

Those planning an isotope laboratory are recommended to examine carefully quotations from firms having special experience in the field of small- and medium-sized radioisotope plants before starting to make everything themselves from the beginning. Instead of 5 yr for the gradual development of a full programme, the period may be reduced significantly by utilizing the experience gained by others, and much money will be saved.

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[2] INTERNATIONAL ATOMIC ENERGY AGENCY, Safe Handling of Radioisotopes: First Edition with Revised Appendix I, Safety Series No. 1, IAEA, Vienna (1962) 100 pp.

[3] HEYDRON, K., Production of Radioisotopes in Denmark, Ingeniøren 4 (Sept. 1960) 78.

[4] BEEN, U., "Experience in Radioisotope Production in Norway", Programming and Utilization of Research Reactors, Proc. IAEA Symp., Vienna (Oct. 1961) 3, Academic Press, London (1962) 387.

[5] MAHMOUD, H., EL-GUEBEILY, HALLABA, E., AXELSEN, R., HIDLE, N., "A Radioisotope Production Facility Utilizing the Inchas 2 MW Research Reactor", Programming and Utilization of Research Reactors, Proc. IAEA Symp., Vienna (Oct. 1961) 3 Academic Press, London (1962) 395.

4. DISPENSING OF RADIOISOTOPE SOLUTIONS

When a radioactive isotope has been prepared from an irradiated target the stock solution is generally transferred to a labelled container. Samples are removed for the determination of radioisotopic and chemical purity and

the radioactivity is measured. The solution is not necessarily ready for use, particularly if it is required for medical purposes. The solution will have to be sub-divided, it may have to be diluted, neutralized, buffered and possibly sterilized.

Although it is a relatively simple matter to place dispensing pipettes in with the production equipment, it is usually difficult to find sufficient space for a sealing machine, an autoclave and measuring equipment for checking the content of the filled bottles. It could also lead to unnecessary duplication of equipment if more than one radioisotope solution is regularly handled. The arrangement which is generally preferred is to construct a separate dispensing enclosure at another place in the isotope laboratory. All of the necessary apparatus can then be laid out in the most effective way for routine dispensing operations. The design of the enclosure will, of course, vary according to the radioisotopes and activity being handled. For large amounts of gamma emitters, such as iodine-131, gold-198 and sodium-24, a fully shielded remotely operated enclosure will be required. For small quantities of pure beta emitters, such as phosphorus-32, sulphur-35 and chlorine-36, a glove box or good fume hood will suffice. The design aspects of laboratories and equipment for this purpose have already been discussed in some detail in the preceding section.

The process of dispensing a radioisotope solution can be reduced to about five operations which are discussed in more detail in what follows. Several photographs (Figs. 13-24) illustrating typical dispensing operations have been collected together at the end of this section. Systems and equipment are described in Refs. [1-3].

The storage of solutions

To facilitate subsequent work, and to avoid possible confusion, it is essential that stock solutions of radioisotopes should be properly stored and labelled systematically with sufficient information to identify each solution clearly. Labelling is best kept to a minimum, the symbol for the isotope and production batch number usually being sufficient to identify the stock unambiguously. All necessary further information should be recorded on the "operation sheet", an example of which is shown in Table I.

Operation sheets are usefully prepared in duplicate, one copy being sent to the dispenser and the other used for control laboratory purposes, such as for biological control when this is required for medical isotopes.

Storage of solutions is preferably in glass or in plastic. A good quality neutral glass, such as is used in pharmaceutical preparations, is ideal. Polythene or polystyrene are acceptable. There is an advantage in having a transparent container since any slight turbidity, precipitation or other deterioration of the solutions can be readily observed.

The size and design of the storage area will obviously vary according to local needs. It can be located either within the dispensing area if space permits or, preferably, in a separate enclosure. In either case sufficient space should be allowed for additional stock solutions prepared by dilution from the original since it is often convenient to have solutions of several concentrations available, for example, 1 mCi/ml, 10 mCi/ml and 25 mCi/ml. Shielding must take account of the highest activity likely to be stored.

TABLE I

PREPARATION OF IODINE-131

..... Service

..... Group

Operation No. 58

Catalogue reference: I-S-5

Nature of target:	TeO_2
Weight:	100 g
Container Nos:	101 - 102
Reactor:	W Z 2
Duration of irradiation:	15 d
Flux:	3×10^{12}
Unloading date:	10 March 1964
Carrier:	None
Buffer solution:	Na carbonate + thiosulphate
Volume:	5 ml
Specific activity:	No carrier
Radioactive concentration:	36 mCi/ml
Volume of solution:	50 ml
Total activity:	1800 mCi at ..... hours
Date:	12 March 1964
Spectrographic purity:	Good
pH:	9.5
Observations:	None

Operator .....

Countersignature: .....

A common form of storage area consists of a concrete or lead block containing a series of numbered and plugged cavities into which bottles of stock solution can be placed by means of tongs, or with a simple overhead crane. Small storage units have been made which consist of trays capable of being rotated and raised (Fig. 1) or, more simply still, an isolated area of the laboratory protected by lead bricks (Fig. 2).

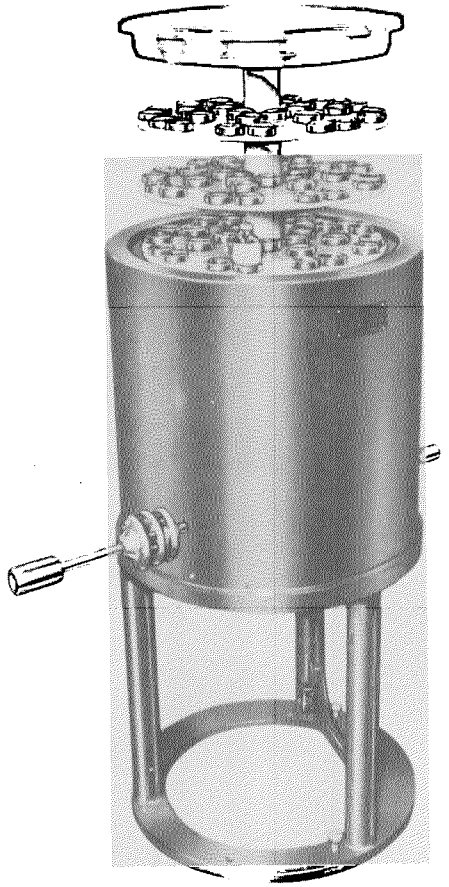

FIG.1. Small storage unit with mobile tray

Sub-division (pipetting)

The most important step in the whole of the dispensing operations is the actual sub-division of the stock solution into the aliquots required by the users. This must be done as accurately as possible and without cross-contamination from other radioisotopes which may be handled in the same enclosure. It is useful to establish a dispensing routine in which certain isotopes are dispensed only on certain days, though such a system must not be too rigid and the dispenser should be in a position to meet urgent orders at short notice. In this way the users become accustomed to the pattern of supply and commonly adjust their orders accordingly. Further, most isotope production laboratories will be tied to regular reactor unload dates which will, to a large extent, determine the times at which radioisotope solutions are available for dispensing and distribution. In this way the risk of cross-contamination and confusion of solutions is also minimized.

TABLE II

PHOSPHORUS-32

of: Friday, 10 January 1964. Date of measurement: 13 January 1964

No.*	Users	Activity requested (mCi)	For use on (Date and time)	Catalogue or other reference No.	Observations and comments	Solution* No.	Volume* (ml)	Volume* activity (mCi/ml)	Specific* activity	No. of* bottles 10 ml	No. of* bottles 30 ml	Remarks
64	DUVAL	5		S-2		13	2.5	2	carrier-free	1		
65	PEETER	10		S-2		13	5	2	"	1		
66	ALFRED	20		S-2		13	10	2	"	1		
67	JOHN	1		S-2		13	0.5	2	"	1		

* To be filled in by dispenser

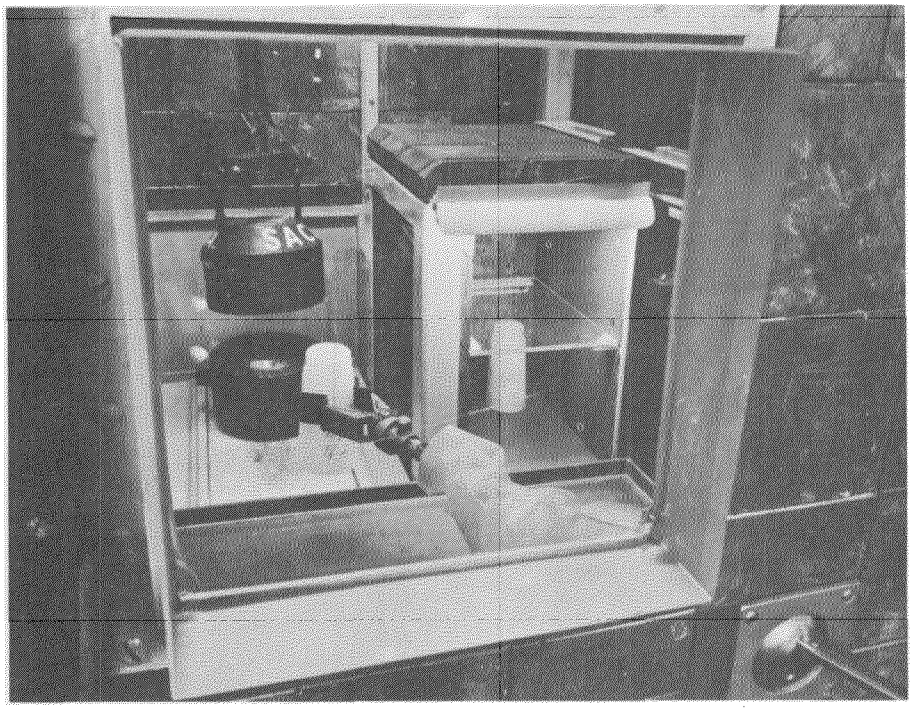

FIG. 2. Isolated area for storage protected by lead bricks

It is convenient to group orders for the same isotope, or orders that are of the same nature, together. For example, orders for radioisotopes for medical use have to go through the same procedure and are therefore conveniently done at the same time. Instructions from users are not always in the same form and sometimes are not very clear. Conversion of orders into standard systematic terms leads to less likelihood of error. These points can be taken care of by using either separate forms for each order or, more usually, by preparing a "Dispensing Sheet" for each group of orders for a given isotope. A typical example of a dispensing sheet is shown in Table II.

The necessary calculations for each order are completed before dispensing operations start. Duplicates of such dispensing sheets can also serve for the preparation of delivery notes and for planning delivery arrangements. All calculations and entries on the dispensing sheet should be checked by a second operator.

Bottles

The choice of bottle for containing radioisotope solutions, and their preparation, requires some care. Screw-capped bottles are convenient for non-medical preparations but multi-dose rubber closed vials, of the the penicillin type, or sealed glass ampoules are essential for injectable radioisotopes which have to be sterilized. The present trend amongst many

established isotope producers is to use only one type of bottle - usually the multi-dose vial.

Bottles should preferably be made of good-quality neutral glass of the type used in the pharmaceuticals industry. Specifications for such glass can be found in several of the national pharmacopoeias. Soft soda glass should be avoided since its soluble alkali content is liable to cause variations of the pH of solutions and loose particulate matter from such glasses can have a marked adsorption for carrier-free radioisotopes.

Bottles should be washed in acid detergent solution and thoroughly rinsed with distilled water, dried and stored in clean dust-free conditions. It is convenient to label the bottles with the details corresponding to each dispensing before filling them. The label need carry only sufficient information to identify the isotope and the amount of activity present. Detailed information is not easily read on a small bottle containing a significant amount of radioactivity, for obvious reasons, and if much information is to be presented it is best put on accompanying package labels or on separate documents. It is obviously necessary also to choose labels which will withstand steam sterilization.

The filling area

Many different systems have been devised for the actual filling operations. It is not possible to describe them all but only to give general guidance and to rely on local invention to design the equipment which best suits local needs. Much can be learned from photographs of existing installations.

The dispensing area has to provide the apparatus for several operations. The stock bottle coming from storage will have to be opened. All bottles have to be moved and handled without the risk of overturning them and for such operations as opening, a jig or vice to hold the bottle is advisable. If the stock solution does not come from the production plant ready for dispensing, it will be necessary to provide, in the dispensing area, means for dilution and pH adjustment. Dilution as, for example, in preparing subsidiary stocks of lower concentration, is carried out by preparing the diluent outside and then introducing it into the installation. The required amount of radioisotope solution is then added and the whole thoroughly mixed, if necessary by the use of a magnetic stirrer, though thorough shaking is usually sufficient.

The adjustment of pH is usefully done with a standard laboratory pH meter outside the installation connected, by means of shielded cable, to electrodes within the cell. If the meter is mobile it can be used to serve several sets of electrodes in different cells or boxes. Standard buffer and a means of rinsing the electrodes should be permanently available within the cell.

The essential step in dispensing radioisotope solutions is of course the actual volumetric sub-division of the stock solution into the aliquots required for each user's order. The problem of devising ways of doing this are not difficult for beta emitters contained in a fume cupboard or simple glove box. If the dose-rates are sufficiently low to allow the use of hands, then all that is needed is a series of graduated glass pipettes (one for each isotope) and a series of hand-operated rubber bulbs for filling the pipettes and discharging a measured volume. When the activity handled requires lead shielding and

remote control the system at once becomes more complex. In its simplest form remote control dispensing can be done with a pipette (one of several taken from a storage rack) held in remote handling tongs and connected by means of a plastic tube to a hypodermic syringe outside the cell. In more highly engineered systems the pipette may be mounted in a fixed location and moved vertically by remote mechanical means. Because of the need to read pipette graduations from a distance "Photophor"-type pipettes will be found useful.

For more advanced mechanical remote control of pipetting operations there is a choice between two alternatives. In the first alternative a fixed pipette, or burette, is used together with a moving platform or revolving tray which carries the stock solution and the bottles into which the radioisotope is to be dispensed; it is an advantage if the platform can both revolve and be raised and lowered. The second commonly used alternative is to mount the pipette on a mobile support similar to a bridge crane and to locate the bottles on the working surface of the enclosure (Fig. 3).

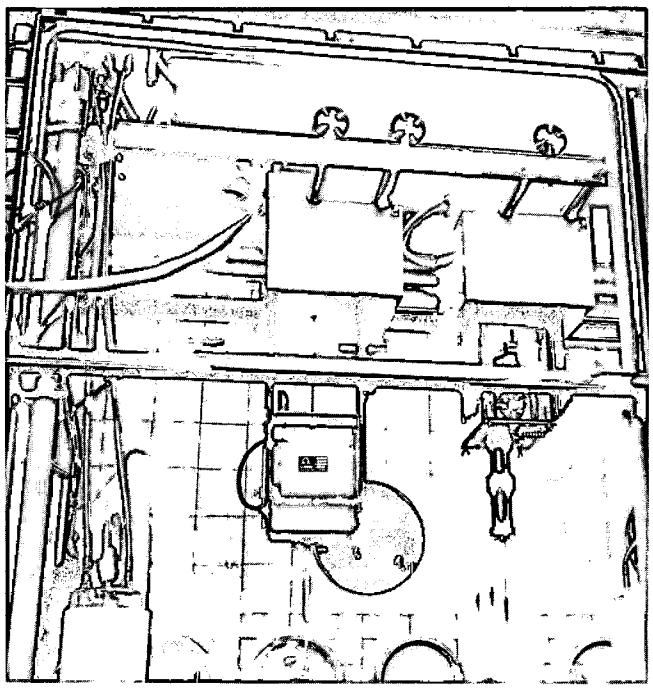

FIG. 3. Pipettes on a mobile support

Two other pieces of equipment are of interest in this context. The Metrohm burette (Fig. 4) and the burette specially designed for this purpose, the CEA burette [4], in which the volume is read on a dial located outside the enclosure. In both of these instruments the draining and refilling operations are effected by means of a motor-driven Teflon piston (Fig. 5).

Where only one pipetting system is installed it must be possible to replace the pipette each time the radioisotope is changed in order to avoid

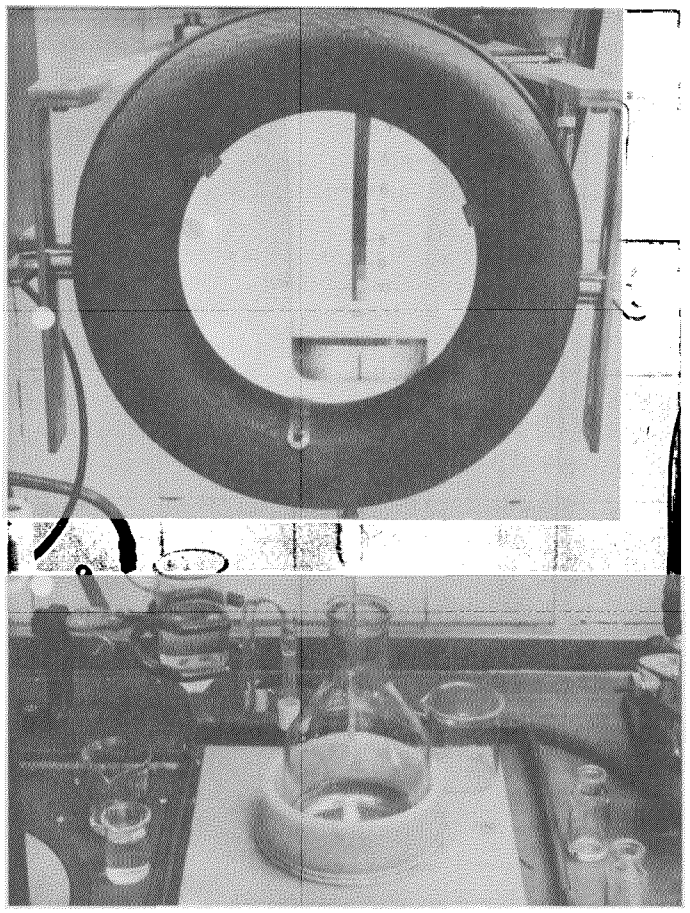

FIG. 4. Metrohm burette

cross-contamination (Fig. 6). Standard pipettes may be used. A standard ground-joint is fused to the upper end of the pipette and attached to the piston assembly which has a similar standard joint. Whatever the system employed, pipettes must be thoroughly rinsed after use. For this purpose, a vessel containing distilled water can be introduced into the cell but it is preferable to have a fixed washing point placed in the pipette's line of movement. Draining of the wash container can be effected by means of a syphon. Pipettes not in use can be stored in a rack and should be clearly marked with the name of the isotope for which they are used. After filling the bottles are then moved to the sealing machine.

Sealing

Bottles should not be moved about the cell without being sealed and this should be done as soon after filling as possible. When screw caps are used the bottle may be locked into a plastic block or vice and the cap applied by

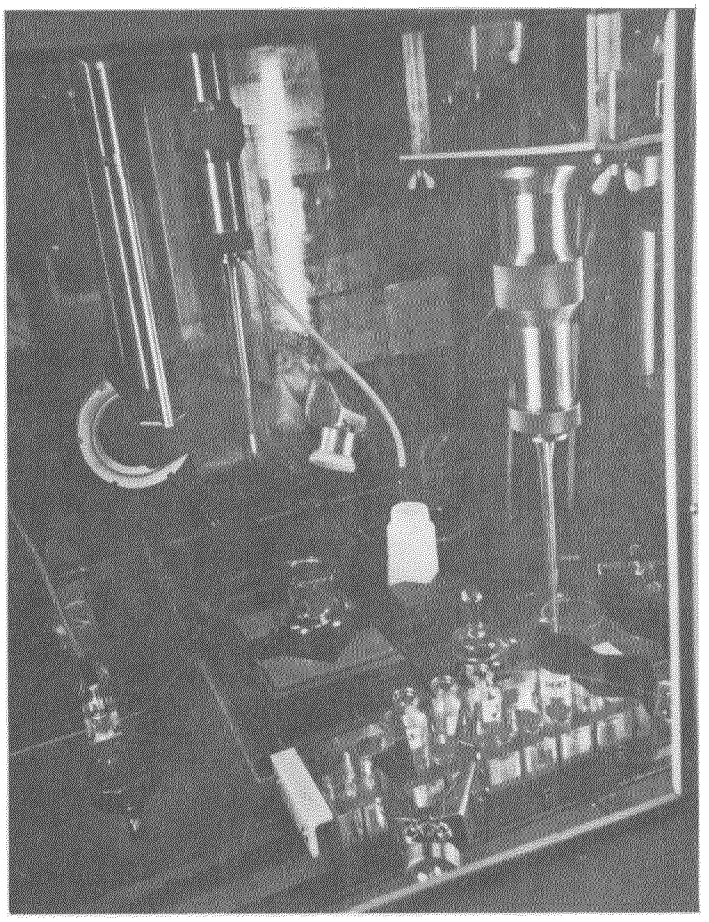

FIG. 5. Pipetting zone

means of screw action tongs. When the "penicillin" type is used the stopper is placed in position with tongs and the cap crimped on with a special sealing machine. The rubber stoppers are made either of latex or of other elastomers. They should be tested before use to ensure that they absorb no activity and that no undesirable impurities are released from them into solution. They should be carefully washed in dilute hydrochloric acid, rinsed thoroughly in distilled water, air-dried and placed for storage in dust-free boxes.

Various types of commercial sealing machines are available which are easily modified for remote control. Figure 7 illustrates one such type. Care must be taken in adjusting these machines since a slight maladjustment in centring can result in bottle breakages. The sealed bottle is now ready for sterilization.

Sterilization [5, 6, 7]

Isotopes for injection should be sterilized as soon as possible after dispensing to avoid bacterial growth and the development of pyrogens. Of the

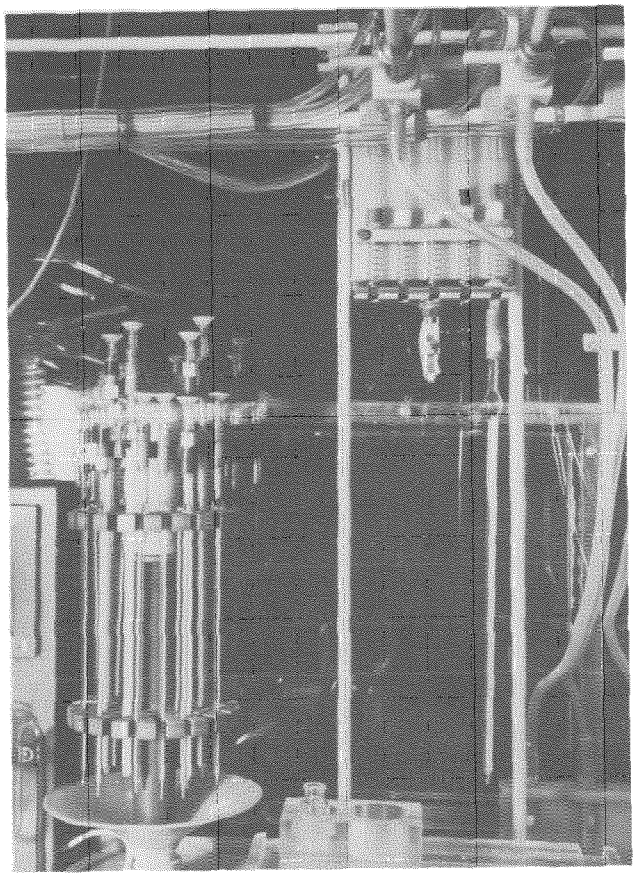

FIG. 6. Interchangeable pipettes

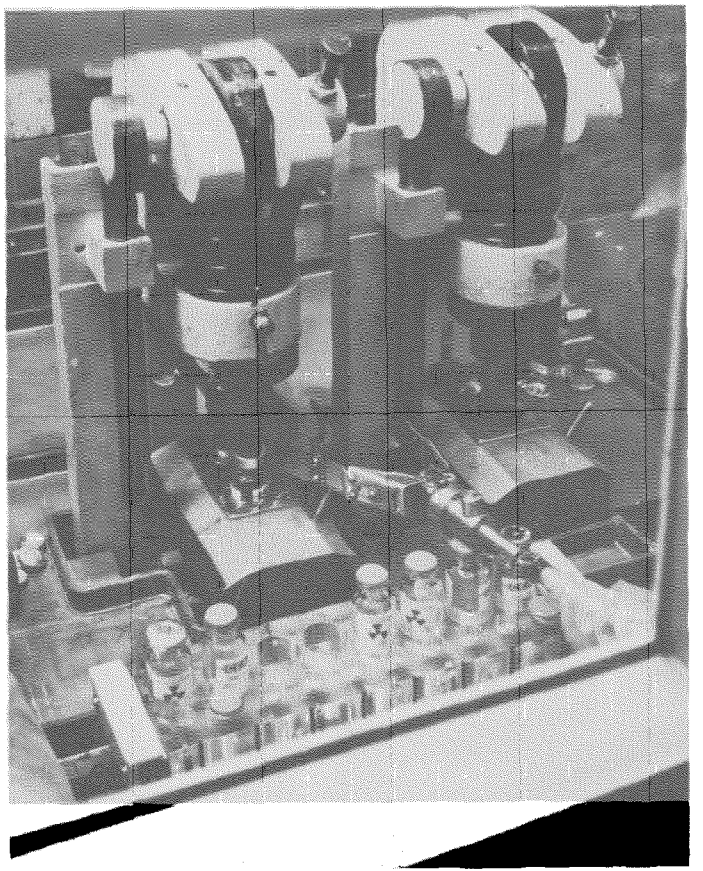

FIG. 7. One type of commercially available sealing machines

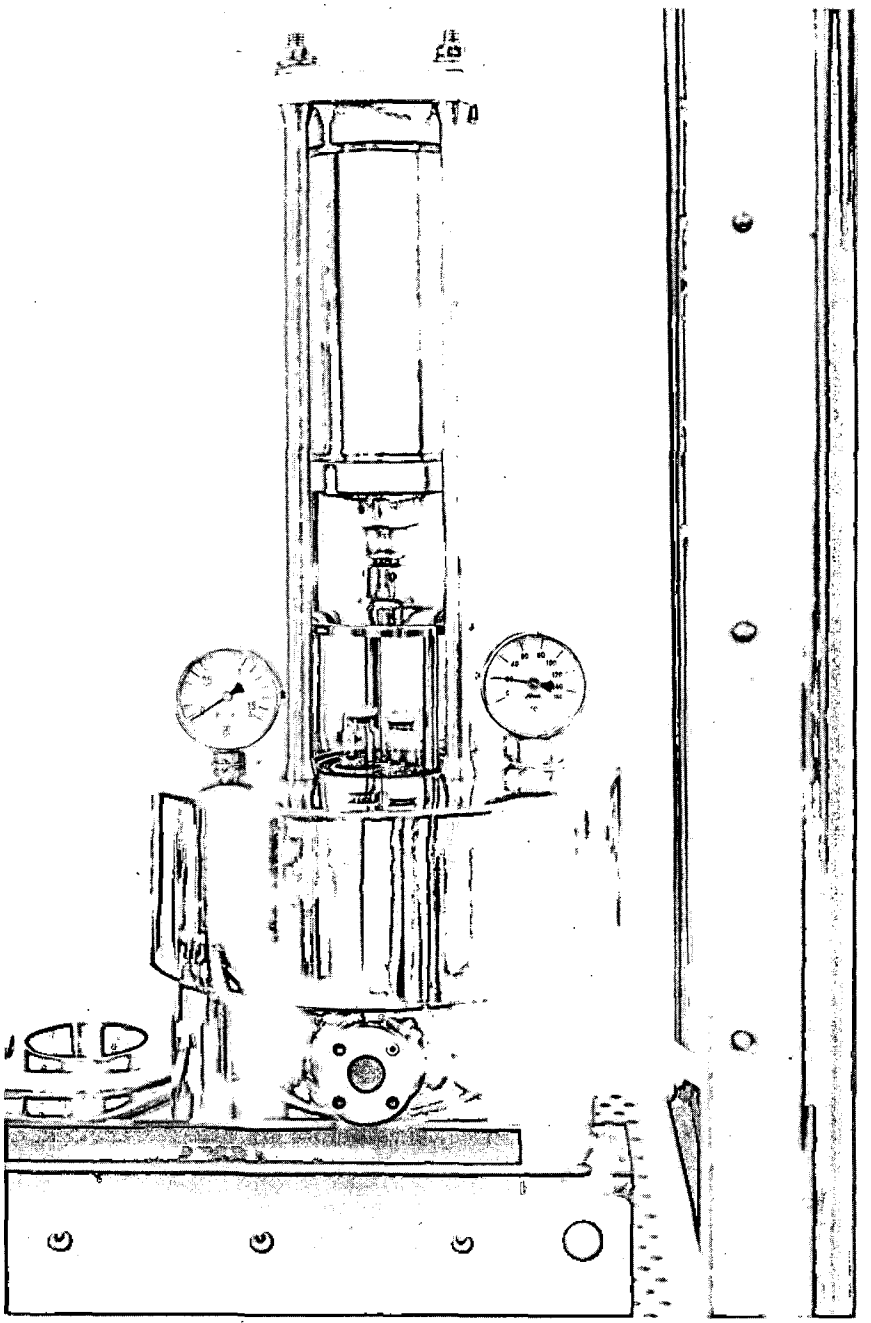

FIG. 8. Commercially available standard autoclave with pneumatic jack

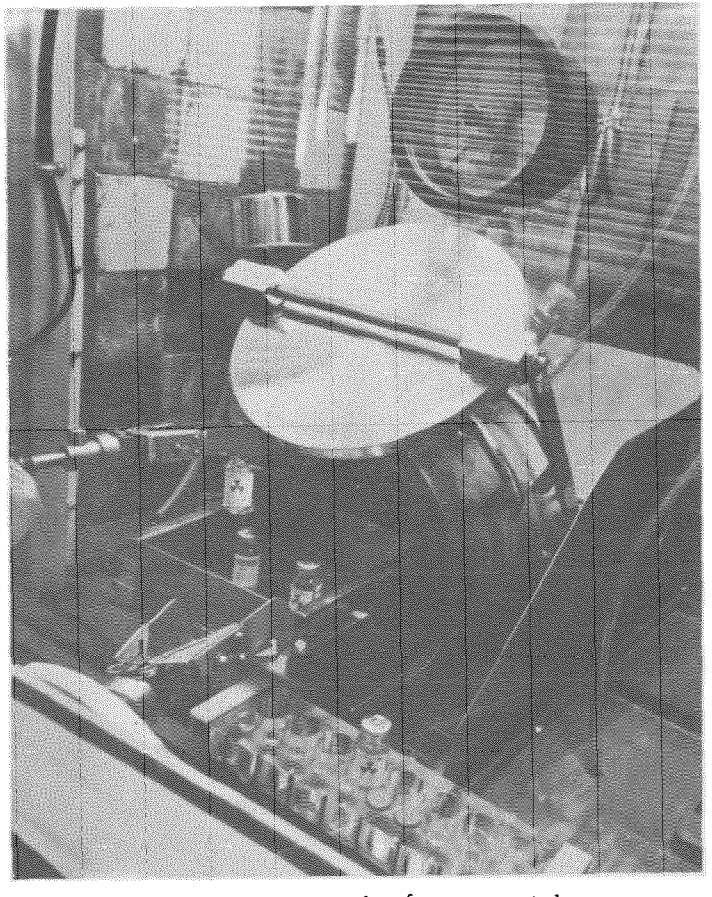

FIG. 9. Horizontal autoclave for remote control

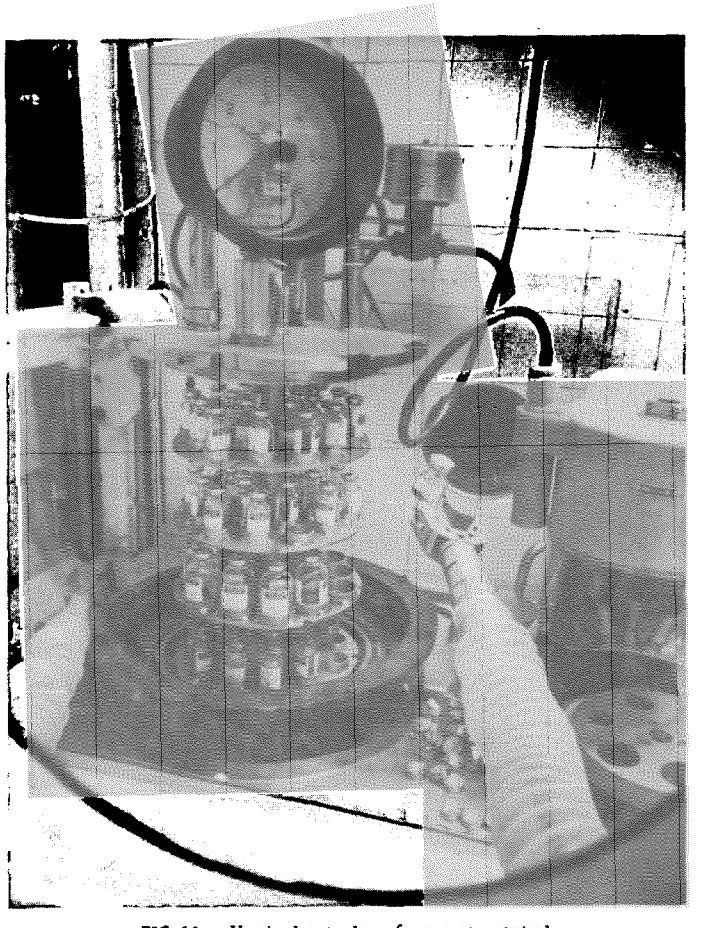

FIG. 10. Vertical autoclave for remote control

various methods used in pharmacy for sterilization, only two are useful for radioactive solutions. The most commonly used is heating in an autoclave (steam sterilization). Occasionally, for heat labile materials, sterilization by filtration is necessary.

Alternative recommended methods are well described in the various pharmacopoeias. For all practical purposes, particularly where short-lived isotopes are being dispensed, heating in an autoclave is the only method which needs to be considered by the small isotope production unit. In this method the sealed bottles are heated at 115°C - 120°C in saturated steam for thirty minutes. This is regarded as an absolute method of sterilization and, provided the time and temperature conditions have been correct, there is no need for routine checks for bacterial contamination, though of course the occasional check is advisable.

Sterilization by heating in an autoclave can be achieved either by means of a suitably modified household pressure-cooker, heated electrically and fitted with an additional pressure gauge, or with one of the commercially available standard autoclaves such as illustrated in Fig. 8. Autoclaves are available, specially modified for the sterilization of radioisotopes and adapted for remote control [8]. Such types are shown in Figs. 9 and 10.

It may be necessary occasionally to resort to sterilization by filtration. This is especially necessary for heat labile organic molecules and is normally carried out at room temperature through special bacteriological filters. The technique is, however, a highly specialized one requiring knowledge of aseptic manipulations and it is recommended that this method is not undertaken without seeking the advice of a skilled bacteriologist or pharmacist.

The same comments apply to the use of added chemical agents such as bactericides and bacteriostatics. The use of these materials in pharmaceutical preparations is usually closely regulated by national legislation [9] and the isotope producer interested in the possible use of such materials in radioactive preparations is strongly recommended to take expert advice.

Packaging

Before despatching the bottle it is a wise precaution to ensure that no errors have crept into the dispensing or into the calculations associated with the particular consignment. Measurements of great accuracy are not required; all that is needed is to make sure, by means of an ionization chamber, whether the activity on the label matches the actual content of the bottle. It is easy to make a mistake in dispensing, for example, by a factor of 10 in the calculations, especially when a large number of bottles is being filled in one operation. The final check enables any irregularity of this sort to be detected before the consignment is shipped. Check measurements need be accurate only to within 10% or so.

Any detector built into a dispensing unit will have to be shielded carefully to avoid measurements being disturbed by the radiation background from the stock solutions awaiting dispensing. If the detector is carefully calibrated in advance for various radioisotopes and long-lived standards kept to hand for occasional checking throughout the day, there is little likelihood of error arising. Beta emitters can be checked in this way if the detector is sensitive to bremsstrahlung.

Lastly, bottles should not be removed from the dispensing enclosure without some form of protection against spillage. It is convenient, for this purpose, to use the inner packaging material (e. g. the tin can) in which the consignment will eventually be shipped.

Finally, the consignment will have to be packed, together with appropriate documents, taking due account of the need for safe transport [10-13].

The entire set-up for the dispensing of gamma emitters is shown in Figs. 11 and 12.

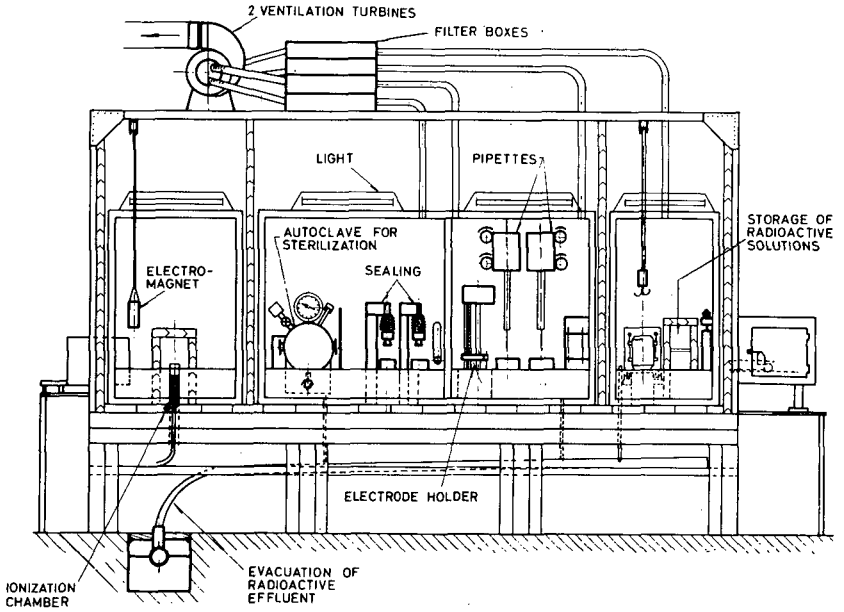

FIG. 11. Dispensing unit for gamma emitters

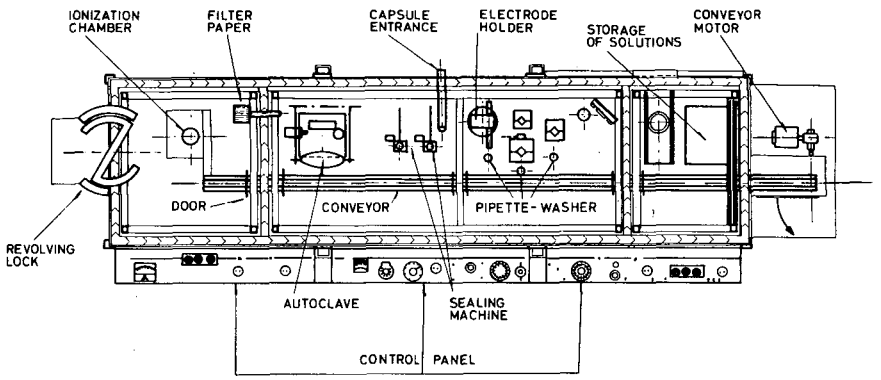

FIG. 12. Dispensing unit for gamma emitters

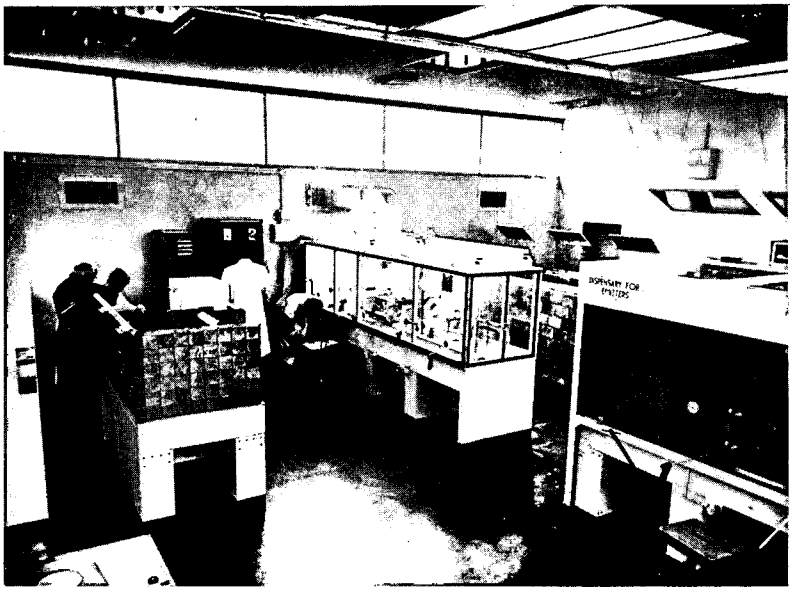

FIG.13. View of a radioisotope laboratory showing a Perspex-shielded dispensary for beta emitters and gamma dispensing shielded with 10 cm lead. In the background is a concrete storage unit for stock solutions
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

FIG.14. A general view of a dispensary for beta emitters. In the background is a direct reading measurement equipment connected to a bremsstrahlung chamber within the dispensing enclosure
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

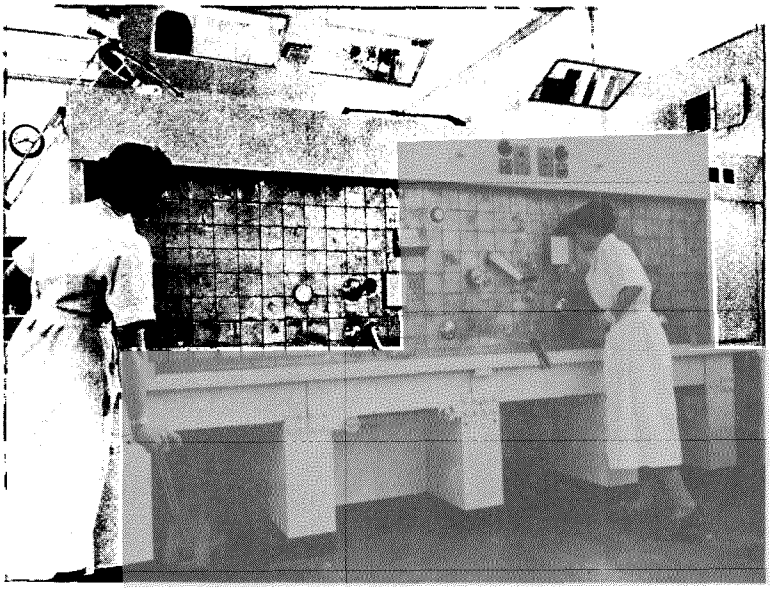

FIG.15. View of a dispensary for gamma emitters. The operations are similar to those illustrated for beta dispensing. Shielding is 10 cm of lead and viewing is through lead glass windows
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

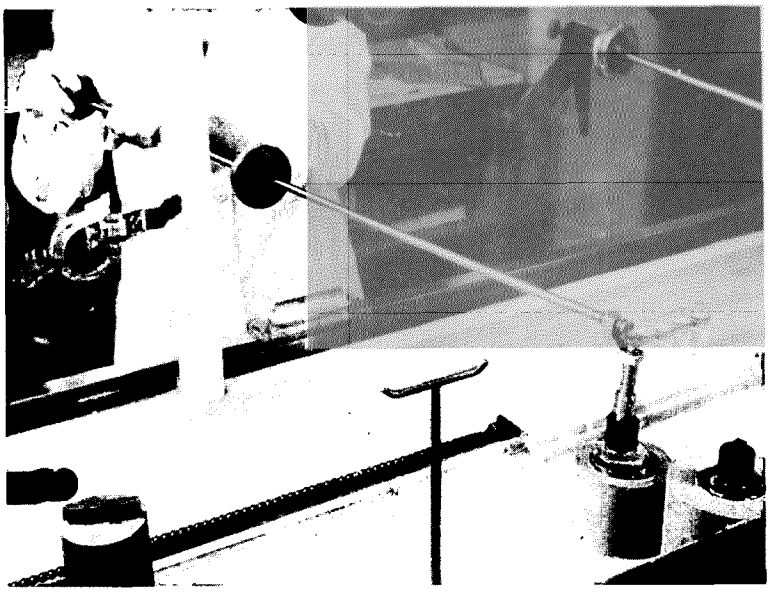

FIG.16. Dispensary for beta emitters. Opening a stock solution of several curies of phosphorus-32
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

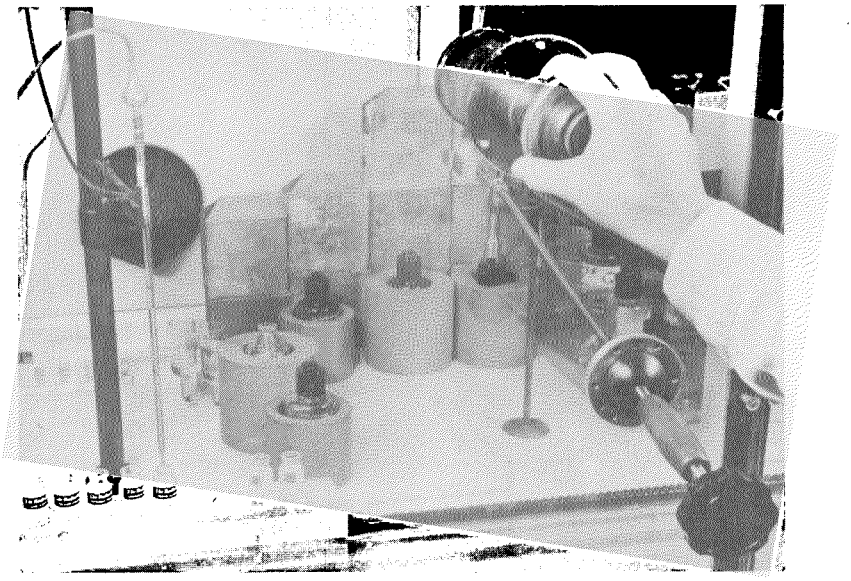

FIG.17. Dispensary for beta emitters showing local shielding of stock solutions and a remotely-controlled pipette operated by means of stainless-steel bellows
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

FIG.18. A close-up of dispensing showing the stock bottle and multi-dose vials ready labelled. The trolley is moved on its track by means of the control on which the operator's left hand is resting
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

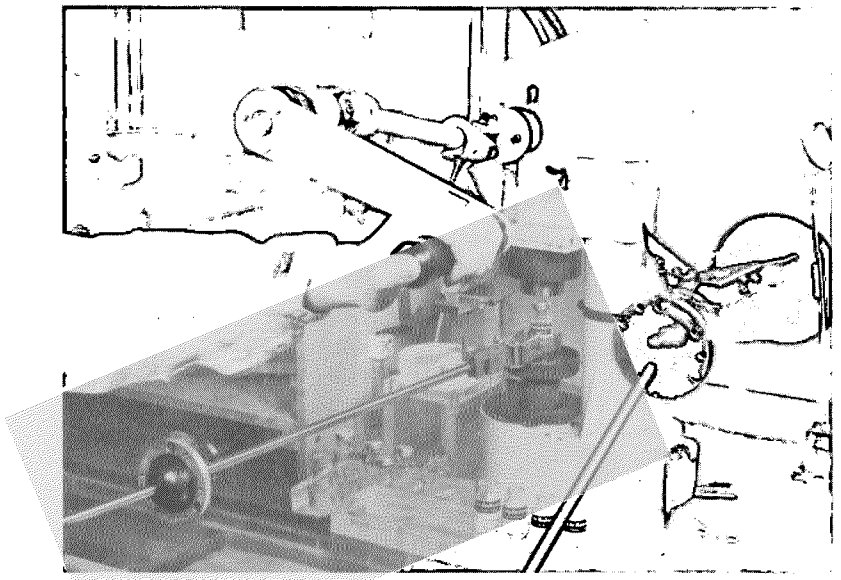

FIG. 19. Dispensary for beta emitters. Sealing the caps on multi-dose vials
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

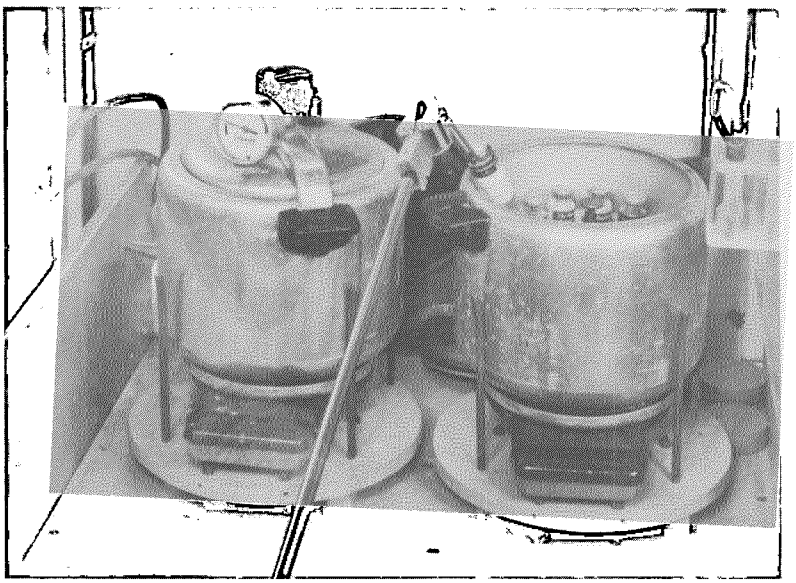

FIG. 20. Dispensary for beta emitters. Two domestic pressure cookers adapted for sterilizing solutions. The lid is closed by hand using the glove at the back of the cell. The temperature and time of the sterilizing cycle are recorded outside the box
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

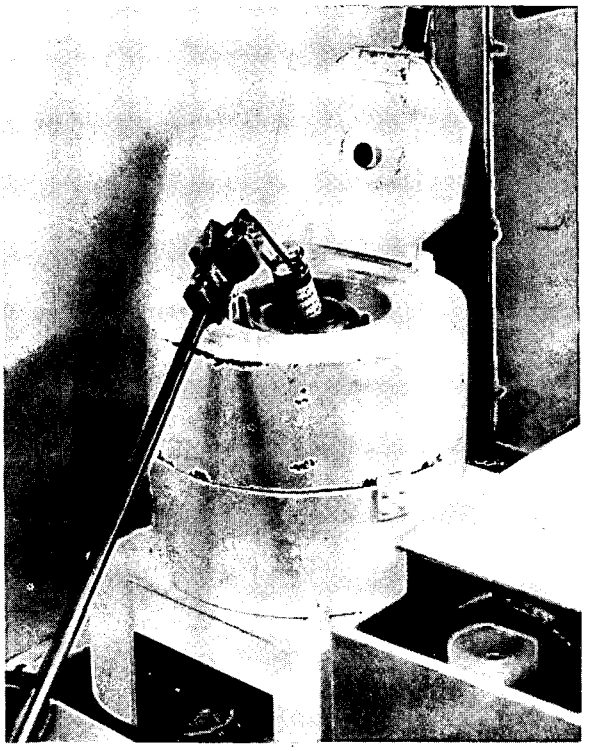

FIG. 21. Dispensary for beta emitters. Checking the activity of a dispensed solution by means of a bremsstrahlung counter
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

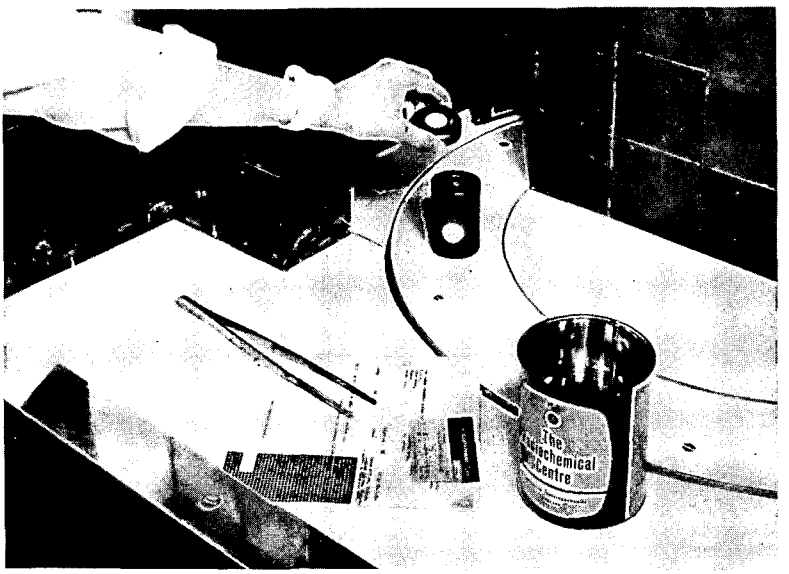

FIG. 22. Dispensing of gamma emitters. Removing a consignment of a gamma-emitting isotope, iodine-131, from the dispensary
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

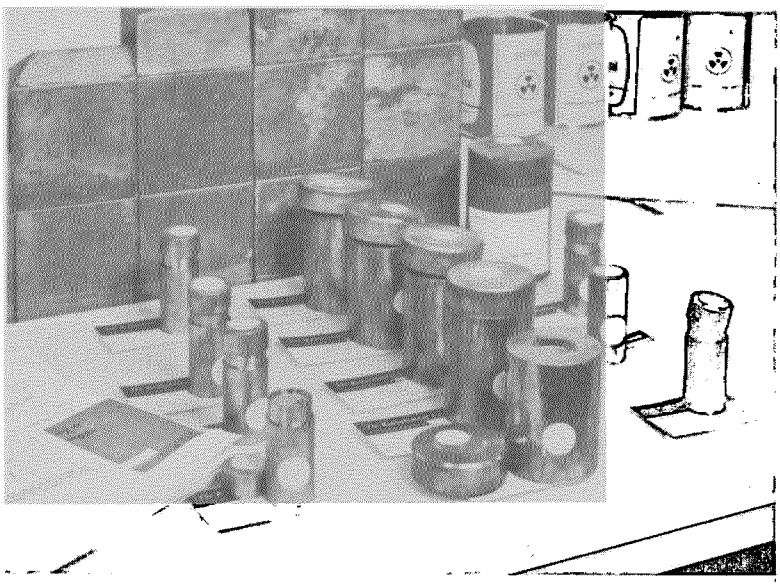

FIG. 23. Dispensing gamma emitters. Lead transport containers, labels and documents ready for packing as consignments are dispensed
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

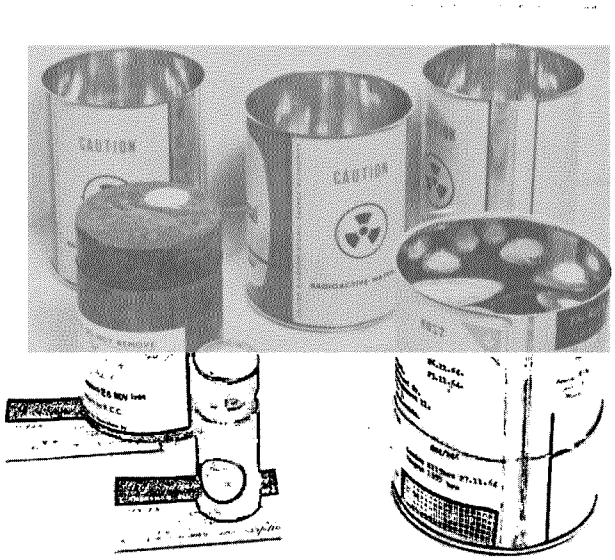

FIG. 24. Dispensing gamma emitters. Inner containers awaiting sealing and packaging for despatch
(By courtesy of the UKAEA Radiochemical Centre, Amersham, United Kingdom)

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5. REQUIREMENTS FOR PRODUCT QUALITY CONTROL

Methods of quality control are discussed here in general terms and are intended only as a guide to good practice. The reader should, however, acquaint himself with other statutory requirements for quality which may exist in his own country, particularly for isotopes used in medical applications.

First, it will be useful to define the main purity concepts before examining them in detail.

The radioisotopic purity (sometimes referred to as radioactive purity or radionuclidic purity) of a radioactive preparation consisting primarily of one radioisotope is the proportion of the total radioactivity which arises from that radioisotope. Radioisotopic impurities are usually the result of inactive impurities in the target material which give rise to isotopes other than the one desired by concurrent nuclear reactions on the target material (for example, a np or $n\alpha$ reaction occurring at the same time as a $n\gamma$ reaction) or of incomplete separation of a radioisotope from its target during chemical processing (e.g. the presence of sulphur-35 in phosphorus-32 separated from irradiated sulphur).

The radiochemical purity of a radioactive preparation in a given chemical form is the proportion of the radioisotope which is in that chemical form. The presence of iodate-I^{131} in a solution intended to be entirely iodide-I^{131} is an example of radiochemical impurity in a solution which is radioisotopically pure.

The chemical purity of a radioactive material concerns the presence of non-radioactive impurities in a preparation. They may arise from the target, the solvent, or from reagents used in processing the radioisotope.

The following list of forms in which radioisotopes might be used in medicine indicates the kind of quality control required:

(a) Irradiated materials used directly, e.g. gold grains, yttrium oxide pellets, cobalt needles, etc. Here quality control is concerned only with dosimetry, namely, with the activity of the source and the radiation dose-rate it produces under certain defined conditions.

(b) Irradiated targets brought into solution, e.g. solutions of sodium-24 chloride or potassium-42 chloride prepared by simple dissolution of the irradiated carbonate in hydrochloric acid. Here radioassay and radioisotopic purity are important. Chemical impurity is unlikely to arise, though pH and isotonicity may be important.

(c) Radioisotopes which are prepared by chemical separation from an irradiated target, e.g. solutions of phosphorus-32 as phosphate and iodine-131 as iodide. Here possibilities of radiochemical impurity are also present.

(d) Radioisotopically labelled compounds used, for example, in diagnosis, such as iodine-131-labelled human serum albumin or iodine-131-labelled insulin. Additional quality control tests here may include verification of the metabolic behaviour of the product since labelling may modify its properties.

(e) Radioisotopes in colloidal form, e.g. colloidal gold-198, yttrium-90 colloid or chromic phosphate-P^{32}, are special cases of radioactive products which may need special additional controls, such as particle size determinations.

Any of the above types of product may need to be tested for sterility and freedom from pyrogens if they are intended for injection into human patients.

The eventual purity of a product is often a compromise between the ideal requirements of the user and what is readily possible from the manufacturing point of view. Extensive purification will often reduce the yield; the choice of test may depend on what is practical by remote control means or what is sufficiently speedy. These factors become especially important when dealing with short-lived radioisotopes.

Control of radioactive properties

Radioactive concentration

Methods of determining the radioactivity, and hence the radioactive concentration, have been dealt with fully in Section 6 and need be mentioned here only as one of the factors in quality control.

Radioactive (radioisotopic) purity

Radioactive impurities arise during the irradiation of the target material by nuclear reactions other than that responsible for the main product, by nuclear reactions on chemical impurities in the target material and, possibly,

by contamination with other radioisotopes during the production processing. The impurities arising by the first two means can be estimated from known nuclear constants [1], the irradiation conditions and the known chemical purity of the target. The extent to which they are present in the product may depend also on the efficiency of the separation process, if one is used. The production of other radioisotopes of the same atomic number as the one required can be reduced by using isotopically enriched targets.

Gamma-emitting impurities can be identified and determined by gamma spectrometry [2, 3]. This method, which is commonly used, has some limitations, since the gamma impurity can be detected only if its gamma energies are sufficiently different from the gamma energies of the main product. In some circumstances, however, it is very sensitive, particularly if at least one of the gamma energies of the impurity is higher than the maximum gamma energy of the main product, e. g. in the determination of sodium-24 in potassium-42. By contrast, the method is not suitable for the determination of radioactive tellurium in iodine-131 [4]; in this case radioactive tellurium can be detected only in amounts greater than 5-8%. Gamma spectrometry is also limited when it is used to determine the presence of gamma-emitters in pure beta-emitters because of the continuous spectrum of bremsstrahlung which may obscure small gamma peaks [5].

The determination of impurities by the method of beta-ray absorption in aluminium absorbers is limited to cases where the maximum beta energy is higher for the impurity than for the main radioisotope [6]. This method is also insufficiently sensitive for the determination of beta-emitting impurities in beta-gamma-emitters: such mixtures may be analysed by means of a variable voltage plastic scintillation counter which will resolve differing beta-energies [7].

The presence of long-lived impurities in short-lived radioisotopes can be estimated, when time allows, by following the radioactive decay over 10-20 half-life periods. This has been used, for example, for the determination of phosphorus-33 in phosphorus-32 [8, 9], for the determination of iodine-129 in iodine-131 [10] and for the presence of iodine-131 in iodine-132 [11]. Clearly this cannot be the method for routine use since it necessitates the almost complete decay of the product before the result is known.

One of the most reliable methods for the determination of radioisotopic impurities is that of chemical separation, using the appropriate carriers, followed by measurement of the activity of the separated fractions. A chemical separation of this sort has been used for the determination of sulphur-35 in phosphorus-32 [12], for the determination of tellurium in iodine-131 [4] and for the presence of sodium-24 in potassium-42 [5]. Separation of constituent impurities by means of paper electrophoresis is another method which has been used, for example, for the determination of phosphorus-32, sulphur-35 and chlorine-36 [13, 14], for the determination of strontium-90 in yttrium-90 [14], and for radioactive tellurium in iodine-131. A review of this method has been published [15]. Ion-exchange separation followed by radioactive measurement of the separated fractions is another variant of the same basic method and has been used for the presence of sodium-24 in potassium-42 [16-18], and for cobalt-60 in iron-59 [19]. Finally, thin-

layer chromatography has been used in a similar manner for the determination of tellurium in iodine-131, sulphur-35 in phosphorus-32 and strontium-90 in yttrium-90 [20]. Some of these methods may be used in combination as, for example, the use of gamma-ray spectrometry in conjunction with chemical separations for the determination of iron-59, zinc-65, antimony-124 and phosphorus-32 [5].

The requirements for purity obviously vary according to the application for which the isotope is intended. In biochemical transport studies an impurity of 0.2% of sodium-24 in potassium-42 is unacceptable. In short-lived isotopes used medically long-lived impurities must not be present because of the possibility of their biological deposition. By contrast in the therapeutic use of gold-198 the presence of 20% of gold-199 is considered as acceptable because of the similar properties of these two radioisotopes.

Radiochemical purity

Radiochemical impurities may arise during the production process or during storage of the product from radiation self-decomposition. For the determination of radiochemical impurities any method may be used which enables the different chemical forms of the radioisotope to be separated. Because radiochemical impurities are usually present only to a small extent the separation methods chosen have to be sensitive. Paper chromatography, paper electrophoresis, ion-exchange and thin-layer chromatography are techniques in common use for this purpose. Some examples will serve to illustrate the kinds of radiochemical impurity which may arise in some commonly used radioactive preparations.

In the preparation of phosphorus-32 solutions as an orthophosphate a small proportion of the phosphorus-32 may be present as pyrophosphate or as higher-condensed polyphophosphate. Such impurities can arise during the evaporation of carrier-free phosphorus-32 solutions, especially if the temperature of the evaporator is high and the solution is not sufficiently acid. In solutions of chromium-51 prepared as chromate, part of the activity may be present as chromic ion, soluble or insoluble [21], if insufficiently oxidized during processing or as a consequence of radiation decomposition of the solution [22]. Lower valency ions may occur in solutions of iron-59 as ferric chloride and in arsenic-76 solutions as arsenate. Arsenic-74 solutions may also contain traces of cacodylic acid if this material has been used as the target and incompletely separated during the production process. Solutions of iodine-131 as iodide may also contain traces of iodate since iodides are oxidized by atmospheric oxygen, especially if in alkaline solution (pH > 8), or in the absence of reducing agents such as sulphite or thiosulphate. Soluble ionic gold may be present in preparations of colloidal gold-198.

Some methods used for the determination of radiochemical impurities are listed in Table I.

Control of chemical factors

Carrier content

If the true specific activity of a separated radioisotope is to be known with any accuracy it is necessary to determine the total element present,

i.e. the radioisotope plus any carrier. This inevitably requires the measurement of very small chemical quantities. The methods available are numerous but the ones selected will in general be those which are adaptable to active solutions and which do not require too large a sample. Colorimetry has been commonly used for the determination of phosphorus as the phosphomolybdate complex [36], for chromium as the chromate [32, 37, 38], or as the diphenylcarbazide [31], for the determination of iron with o-phenanthroline [31], for arsenic as the molybdate complex [31] and for iodine as free iodine in carbon tetrachloride [39].

The total content of sodium chloride in a radioisotope solution, which has been added for purposes of isotonicity, is conveniently measured by determining the conductivity of the solution: pH by means of a small glass electrode [40].

Chemical impurities

Chemical impurities may arise from the target material or from reagents and apparatus used in processing. Impurities may be of the sort that would constitute a risk if administered medically; for example, the commonly recognized toxic or objectionable elements like arsenic, tellurium or selenium (which are likely contaminants of iodine-131 prepared from irradiated tellurium), or they may be entirely non-toxic but be present in sufficient amount to interfere with the normal behaviour of the isotope. The presence of aluminium (arising from the irradiation cans) in phosphorus-32 is an example of the latter.

Impurity limits have been suggested [24, 39, 41]. The selection of methods used to determine small chemical impurities depends to some extent on what equipment is available locally. Spectroscopic analysis is popular [24, 42-44] for the reason that many elements can be measured simultaneously and it requires only a very small volume of active solution. The classical sulphide tests for heavy elements and modifications of the well-established "spot tests" can often be adapted to use with very small volumes of active solution.

The particle size of colloids

The biological behaviour of colloidal radioactive preparations may be influenced by the particle size of the colloid [45]. In general, the particle sizes of a particular colloid should be as uniform as possible. Electron microscopy appears to be one of the best methods for particle size determination [24, 45, 46]. Centrifugal sedimentation has also been used [47] and where the two methods have been used comparatively the particle size distributions are in agreement, within the experimental error, for particles whose shape does not deviate significantly from sphericity [48, 49]. For the particular case of colloidal gold, absorption spectra can also provide information on particle size [50]. The tendency for some colloids, such as colloidal chromic phosphate, to aggregate creates some difficulties in determining particle size by electron microscopy.

TABLE I

METHODS FOR THE DETERMINATION OF RADIOCHEMICAL IMPURITIES

Basic chemical form	Method[x]	Conditions	Separation time (h)	R_F values or mobilities	Reference
$^{32}PO_4^{3-}$	PC-ascending	Isopropanol, water, trichloro-acetic acid, ammonium hydroxide 75:25:5:0.3	16	Phosphates: ortho 0.75 pyro 0.45, poly < 0.35	[23-25]
	PC-ascending	Water, trichloroacetic acid, ammonium hydroxide, acetone 170:25:1.7:325	1-2	phosphates: ortho > pyro > poly	[26]
	PC-descending	t-butylalcohol, water, formic acid 40:20:5	4	Phosphates: ortho > pyro > poly	[27]
	TLC	Ethanol, water, trichloro-acetic acid, ammonium hydroxide 80:10:5:0.3; *cellulose*	0.5	Phosphates: ortho 0.9 pyro 0.6; poly < 0.5	[28]
	PE	0.1 M lactic acid		Phosphates: ortho pyro and poly	[29,30]
$^{51}CrO_4^{2-}$	PC-ascending	Water, ethanol, ammonium hydroxide 125:50:25	2.5	CrO_4^{2-} 0.9; Cr^{3+} 0	[31]

TABLE I (contd.)

	IE	Strongly basic anion exchange resin, dilute nitric acid as eluent		Cr^{3+} in first 25 ml of eluate	[32]
$^{59}Fe^{3+}$	PC-ascending	Butanol, water, acetic acid, ethylacetoacetate 50:30:10:5	6	Fe^{3+} 0.7; Fe^{2+} 0.25	[31]
$^{76}AsO_4^{3-}$	PC-ascending	Ethanol, pyridine, water, ammonium hydroxide 60:20:16:4	2	AsO_4^{3-} 0.04; AsO_3^{3-} 0.18; cacodylic acid 0.35	[31]
	PE	0.01 N sodium hydroxide		AsO_4^{3-} AsO_3^{3-}	[33]
$^{131}I^-$	PC-ascending	Methanol, water 3:1	2.5-4	I^- 0.9; IO_3^- 0.4	[34, 35, 24]
	TLC	Acetone, 6 N ammoniac 1:1; silicagel	0.75	I^- 0.9; IO_3^- 0.4	[20]
	PE	0.01 N sodium hydroxide		I^- IO_3^-	[33]
^{198}Au colloid	PC-ascending	Acetone, water, hydrochloric acid 70:20:10	1	Au soluble 1; colloidal 0	[24]
	TLC	Acetone, water, hydrochloric acid 70:14:16; silicagel	1	Au soluble 0.9; colloidal 0	[20]

[x] PC paper chromatography (ascending or descending)
TLC- thin layer chromatography.
PE- paper electrophoresis.
IE- ion-exchange resin.

Biological control

Radioactive preparations used in medical applications must fulfil the general requirements for other medicines. The quantity of the active ingredient must be accurately known, the purity must be adequately high and, in particular, those preparations intended for injection must be sterile and free from pyrogens. Reference has already been made to sterilization and the need for sterility testing in Section 4. If testing for sterility and freedom from pyrogens is undertaken it is recommended that skilled advice be sought: this is particularly necessary for pyrogen testing since consistent results are difficult to obtain and indeed the presence of radioactivity may confuse results since radiation can itself cause pyrogenic reactions in test animals. However, much can be done in isotope processing to minimize the formation of pyrogens, such as using freshly made reagents, using apparatus washed with pyrogen-free water and not keeping stock solutions of radioisotopes too long before sterilizing them.

It is clear from what has been said in this section that no single set of quality control tests will apply equally to all radioactive products. Quality control has to be matched to the use to which the products are being put. Medical isotopes are in a class which requires the most thorough control, though it is recognized that this may become difficult, especially with short-lived isotopes.

As a summary of what has been said already, and as a guide to suitable accuracies for the control of medical isotopes,

(a) Radioactive concentration should be determined with a 5% reliability.
(b) Radioactive impurity should in general be less than 0.1%.
(c) Radiochemical purity should be greater than 95%.
(d) The specific activity should be known.
(e) Solutions for injection should be neutral and isotonic, sterilized and apyrogenic, and non-toxic.
(f) Biological behaviour of a product should be established.

6. RADIOASSAY

The radioactive products to be measured are, in most cases, in the form of aqueous solutions. Their concentration may vary between some microcuries and several hundreds of millicuries per gram of solution. This range only is discussed here.

A laboratory producing radioisotopes will routinely assay its products by some "relative" procedures, i.e. methods where use is made of apparatus previously calibrated for the radionuclide in question by means of standard sources. These sources can be prepared and calibrated absolutely by the laboratory itself or in many cases more conveniently procured from elsewhere [1].

This section of the Manual is divided into four main sub-sections, as follows: the first gives a short general review of the methods recommended for the routine assay of the radioactive concentration of solutions, preference

being given to techniques for which no special source preparation is necessary; the second contains a description of some "absolute" methods which can be used for the preparation of standard sources; the third contains some practical details on sample preparations; and the last sub-section gives recommendations for the assay and calibration of a number of special nuclides.

General methods of radioassay

As the range of γ-rays in matter is much larger than that of the other radiations emitted from radioactive nuclei (α, β, e- and X-rays), γ-detection will be used whenever sufficiently intense γ-rays are emitted by the sample. Fortunately, most of the important radionuclides are γ-emitters; therefore, the γ-assay is by far the most important tool for routine assay.

Assay of γ-emitting nuclides

To avoid more complicated preparation procedures, whenever possible, the samples to be measured should be in a solution of a volume not less than 1 ml and should be in a closed container. For volumes of less than 1 ml pipetting accuracy may not be sufficient for an accurate standardization.

Since γ-self-absorption may not always be negligible the containers to be used for the determinations should all be of the same dimensions and should all contain the same amount of liquid. When the activity of thick solid sources has to be assayed, self-absorption corrections must be made. In general, this involves more elaborate techniques; however, the simplest way to determine the self-absorption correction for a specific type of source is to measure one source in its original form, then dissolve it and measure all or part of the solution in a calibrated detection arrangement. This calibration factor may then be used for all solid sources of the same form and nuclide.

Ionization chambers. Ionization chambers are the first choice for the routine assay because of their well-known stability. While a standard direct current amplifier (voltage sensitive, high impedance) is sufficient for most purposes, for high precision applications the more expensive vibrating reed electrometers must be used. The so-called 4π-gamma-ionization chambers are widely used because their response is relatively insensitive to changes of position and dimensions of the source [2-4]. Such chambers filled with pressurized argon give larger currents (and backgrounds) but open chambers containing air at atmospheric pressure fulfil most purposes [3].

Since the response of open chambers varies with the air pressure for most accurate measurements, it is recommended to determine the ratio of the ion current from the unknown source to that of a long-lived standard γ-source. Any changes in the sensitivity are, therefore, compensated, since such changes will affect the response to the standard and the unknown source to about the same extent; ^{226}Ra or ^{137}Cs are suitable for this purpose, and one should have a set of these sources to cover the whole range of ion currents generally encountered. Figure 1 shows a 4π gamma-chamber for routine calibrations of various kinds of γ-sources. Table I gives an example of the ionization current per millicurie for a special 4π-gamma-chamber

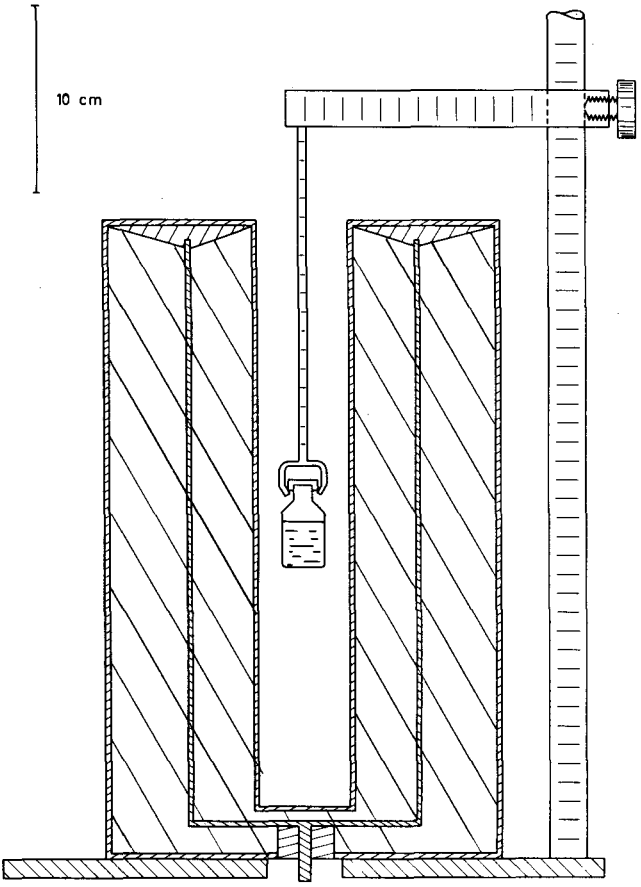

FIG. 1. 4 π gamma ionization chamber [5]

(Fig. 1) and also the activity of each radionuclide equivalent to a special radium source (nominal activity 25 μCi) [5].

When measuring larger activities, outside the range of the amplifier, it may be necessary to reduce the sensitivity. This may be done by connecting condensors in parallel in order to increase the effective input capacity. The wall of the inner tube must be thick enough to stop all β-rays (e.g. 2 mm of brass).

Combined 4π-gamma-beta ionization chambers are also often used (see Fig. 4); for γ-sources they have nearly as good characteristics as the $4\pi\gamma$ chambers meant exclusively for γ-detection. For very large sources ionization chambers of lower geometric efficiency (i.e. lower sensitivity) are useful. The sensitivity may be very simply changed by varying the distance between the chamber and an external source by means of an optical bench [6, 7]. Because the maximum sensitivity is considerably lower than that of 4π chambers, and shielding of the whole assembly is difficult, this technique is rarely used.

TABLE I

RESPONSE OF A TYPICAL 4π-γ-IONIZATION CHAMBER
(height, 34 cm; external diam., 20.5 cm; filling, 1000 mm argon; no shield; background 2×10^{-14} A; 4 ml of solution in a sealed glass ampoule) [5]

Nuclide	Equivalent activity of a Ra standard source (25.0 μg) (μCi)	Current sensitivity (A/mCi)
^{22}Na	16.66	2.54×10^{-10}
^{54}Mn	44.8	0.943
^{51}Cr	788.5	0.0536
^{59}Fe	35.5	1.190
^{60}Co	17.17	2.46
^{65}Zn	71.2	0.593
^{82}Br	14.55	2.90
^{131}I	77.3	0.547
^{137}Cs	60.8	0.695
^{144}Ce	433.4	0.0975
^{198}Au	71.2	0.593
^{203}Hg	90.6	0.466
^{226}Ra	25	1.69

For the assay of radionuclides for which no standard sources are available, a curve of the response of the chamber as a function of the γ-energy may be used. Such a curve may be established by measuring the chamber response for calibrated sources of different γ-energies (e.g. from Table I). To use such a curve the decay schemes have to be known precisely. However, it is preferred, whenever possible, to determine the chamber response (or the current equivalent of the long-lived standard source) for each radionuclide separately by means of a calibrated source of the same nuclide.

NaI scintillation counting. Scintillation counting, using NaI (Tl) crystals is the most important method for the assay of low-activity γ-sources. Convenient counting rates may be obtained for sources up to several millicuries by increasing the distance between source and crystal.

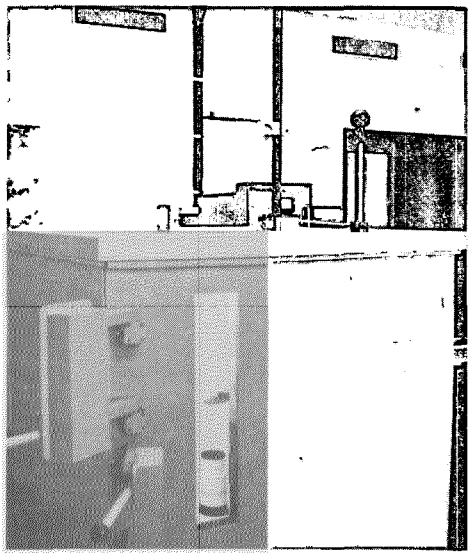

FIG. 2. NaI gamma-spectrometer apparatus [5]

Figure 2 shows an assembly used in the IAEA laboratory, which is connected to a simple counter and also to a multichannel analyser. The sample is in the form of either a dried deposit on a thin polythene disc or 1-2 ml of solution in a standard plastic tube. Figure 3 gives the measured photopeak-efficiency (see Heath [8]) as a function of the γ-energy for a distance of 30 mm between source and detector surface. This efficiency is roughly inversely proportional to the square of the distance. Too small distances should be avoided because the reproducibility of the source position is then the precision limiting factor. A detailed description of all problems concerning accurate γ-measurements, using NaI crystals is given by Heath [8].

Relatively large dimensions of the lead shield are often chosen in order to reduce the backscatter peak in the pulse height spectrum. If the assembly is used only for assay, a small lead castle will be sufficient. For a maximum distance between source and detector (NaI 3 in $\times$ 3 in) of 40 cm, γ-sources from 0.1 to several tens of μCi may be measured. These are easily obtained from the mother solution by aliquoting, if necessary, after dilution.

Since the pulse height spectra of a NaI counter are rather extended, in the case of the most simple counting apparatus the stability of the pulse height discrimination threshold may become a problem if the discriminator level is set so that a substantial part of the pulses is rejected. The discrimination threshold may be safely set anywhere in the spectrum only if a pulse height stabilizing system* is used.

Stability problems may be avoided if amplification and high tension are chosen so that most of the pulses saturate the amplifier, and the threshold is set much lower, e.g. 5% of the saturation pulse height. Then the counting

* Commercially available from many manufacturers of nuclear electronics.

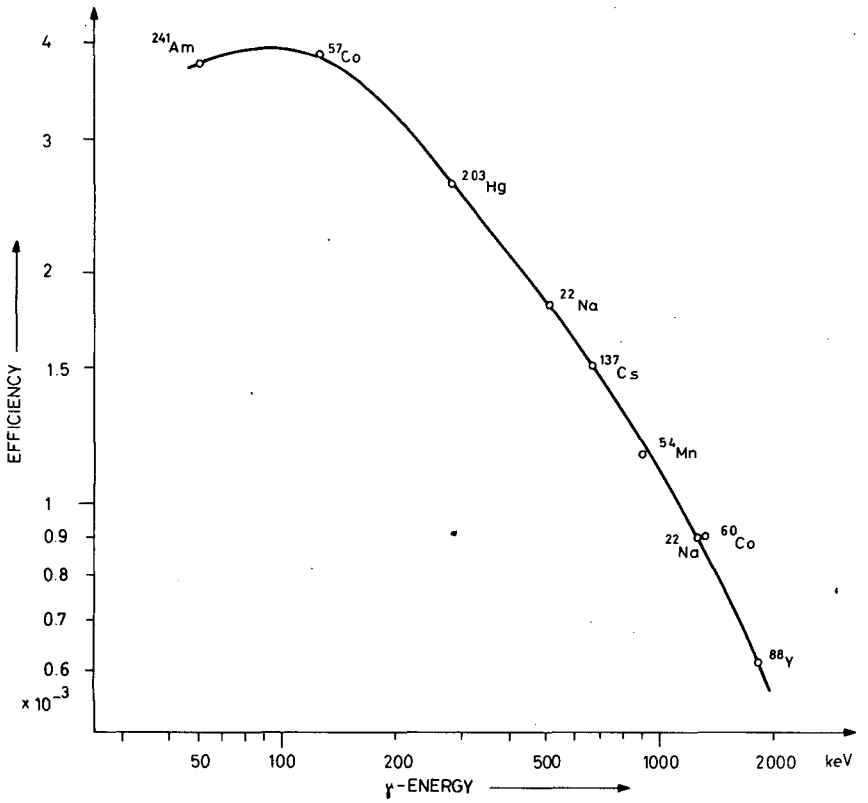

FIG.3. Photopeak efficiency for NaI (3 in × 3 in; distance 30 cm) [5]

rate becomes nearly independent of changes in amplification, high tension and threshold. But in this case, the amplifier must be anti-overload, and for high counting rates large dead-time corrections must be applied. Under these conditions the NaI counter may be used in the same manner as the ionization chamber.

The advantage of the NaI counting techniques over the ionization chamber techniques is that the former offers the greater sensitivity and the possibility of radioactive purity controls. However, there are also disadvantages. Some pulses due to electronic and/or true coincidences have to be corrected for. Further, dead-time corrections must be applied to the NaI counting rate and the measurement of activities higher than several hundred microcuries becomes inconvenient. Should a secondary long-lived standard for the calibration of a given short-lived radionuclide, R, be desired it may be prepared by the following procedure. A calibrated source of R is measured in various positions. The secondary standard, which should emit γ-rays in about the same energy range as R (e.g. ^{133}Ba, ^{137}Cs, and ^{60}Co respectively, for low-, medium- and high-energy γ-rays) is measured in a similar manner. Its equivalent activity, A_E, which gives the same counting rate as A_R millicuries of the radionuclide R, is determined for the different

positions. A_E is then largely independent of possible changes in the experimental conditions and may be used for future assays of R-sources.

A NaI well-crystal arrangement is also often used for the assays of γ-emitters [9]. The reproducibility is very satisfactory and the high efficiency, which may approach 100%, is desirable for low-activity sources. However, this high efficiency is sometimes a drawback for determining larger activities.

Pure β-emitters

Since β-emitters are all subject to strong self-absorption which, in practice, cannot be avoided, it is even more advantageous to assay them in the liquid form than it is for γ-emitters. Thus it is much easier to obtain reproducible conditions with respect to self-absorption from liquid samples than from solid ones.

Except for low-level measurements, the use of solid sources and end-window Geiger counters should be discontinued. Combined β-γ ionization chambers [3, 10], special β-chambers, or proportional counters are much more reliable.

Ionization chambers. The diagram of a combined β-γ ionization chamber [3] is given in Fig. 4. In such a chamber 1 ml of the solution to be assayed

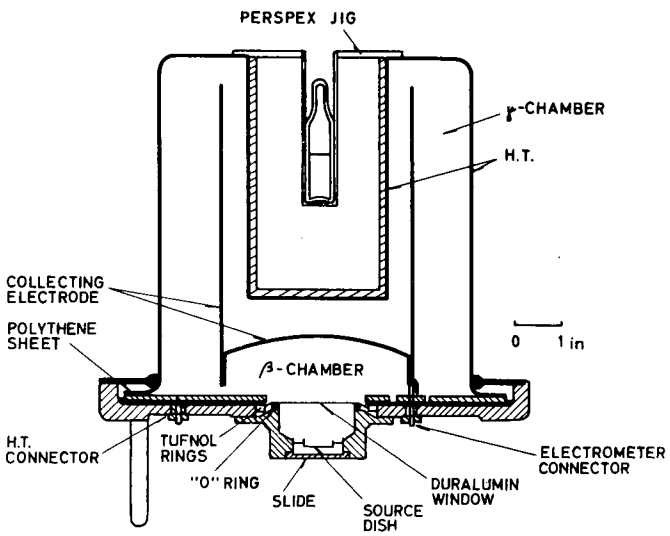

FIG. 4. Combined beta-gamma ionization chamber [3]

is placed in a Polythene planchet. The sensitivities for a number of nuclides are given in Table II. For β-maximum energies lower than ~ 400 keV the sensitivity becomes very small because of the β-absorption by the window and the air; for example, for sulphur-35 it is approximately 3×10^{-12} A/mCi ml.

It should be noted that, for routine assay, counting methods should be avoided which have a low sensitivity for the nuclide to be determined and a

TABLE II

RESPONSE OF A COMBINED $4\pi\gamma$-β-IONIZATION CHAMBER* FOR SOME β-SPECTRA [3]

Radionuclide	Sensitivity (A/mCi ml)
^{32}P	2.68×10^{-10}
^{42}K	4.33
^{82}Br	1.03
^{131}I	0.73
^{198}Au	1.37

* Fig. 4.

large sensitivity for a possible impurity. For example, an impurity of only 0.2% ^{32}P in a ^{35}S solution would, in a chamber of the type shown in Fig. 4, give a ^{35}S activity value 20% too high. To be assured that such false results are not obtained, it is best to use detection techniques in which the counting efficiency of the nuclide to be assayed is at least of the same order of magnitude as that for possible contaminations.

Special ionization chambers for β-emitters may be preferred because of their lower background current [4]. A grid may be used in place of the thin-foil window [Fig. 5] if the chamber works under normal air pressure. To avoid evaporation during lengthy measurements, the cup may be protected by a thin foil cover, such as aluminized Mylar which is commercially available in thicknesses of ~ 1 mg/cm^2, or other plastic films which one can make in the laboratory with less than 30 μg/cm^2. Since the chamber response varies with the air pressure, solid standard sources may be used to determine correction factors.

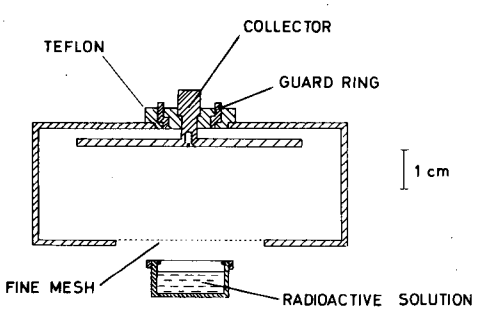

FIG. 5. Beta ionization chamber [5]

Geiger counting of liquid samples. Solutions with specific activities of up to ~ 20 nCi/cm^3 may be conveniently counted in an all-glass Veall-type liquid counter in which the solution counted is contained in an annular space surrounding the Geiger tube [16]. Unfortunately, these counters operate in the Geiger region and rarely keep for longer than one year.

Precise determination of the efficiency of many radionuclides is, therefore, only worthwhile if such counters are used frequently. Table III gives typical values of the efficiencies for some radionuclides.

TABLE III

β-EFFICIENCY OF A CYLINDRICAL GLASS-WALLED GM LIQUID COUNTER

Radionuclide	β maximum energies (MeV)	Liquid counter efficiency (%)
^{42}K	3.84	16.0
	1.92	
^{90}Sr (+ ^{90}Y)	2.18	13.8
	0.53	
^{32}P	1.70	10.1
^{86}Rb	1.80	7.9
	0.72	
^{24}Na	1.39	7.8
^{210}Bi	1.17	2.8
^{198}Au	0.96	2.8
^{204}Tl	0.765	1.46
^{131}I	0.608	0.77

Another type of Geiger counter, useful when large solution volumes are available, is a thin-glass-walled variety which may be dipped directly into the solution to be assayed. This type is easier to clean and may have somewhat higher efficiency.

Proportional counting of liquid samples. When using a windowless 2π proportional flow counter with aqueous solutions, the counting characteristics may be impaired by water vapour. This difficulty can be avoided by diluting the radioactive solution 1 : 9 or less with formamide [2].

In another proportional counter the β-emitting solutions are placed in a tube whose bottom consists of a thin plastic film such as the 1 mg/cm^2

aluminized Mylar. This Mylar foil is at the same time the cover of a hemispherical counter. For such an arrangement the reproducibility is better than ± 0.5% [12]. The efficiencies of such a counter for some β-emitters are given in Table IV.

TABLE IV

β-EFFICIENCIES OF A PROPORTIONAL COUNTER FOR PRECISE RELATIVE CALIBRATION OF β-EMITTING SOLUTIONS [12]

Nuclide	Volume of solution (ml)	Specific activity giving 100 cps (nCi/ml)*	Efficiency (%)
^{35}S	2.0**	670.0	0.2
^{204}Tl	2.0	43.0	3.2
^{32}P	3.5	9.8	7.9
^{90}Sr (+ ^{90}Y)	5.0	6.2	8.7

* Background 1.5 cps.

** Minimum quantity necessary for safely covering the window.

Liquid scintillation counting. While liquid scintillation counting may be the simplest method of assay for very low-energy β-emitters, such as ^{3}H and ^{63}Ni, it also has the great advantage of being able to count samples of relatively large masses with high efficiency [13].

Some details on this technique are given in Section 2. For the routine assay solutions with a lower carrier content other methods are more convenient.

Assay of α-emitters

The range of α-particles is shorter than that of most β-particles. However, the absorption corrections are not as large as one may expect for solid sources if the sources are prepared from solutions of low carrier concentration.

As pure α-emitters play only a minor role in the production of radionuclides, only the most popular methods of assay are mentioned, namely:

2π-ionization chamber

2π-proportional counting [2]

ZnS scintillation counting [3]

Liquid scintillation counting [14].

Assay of pure electron-capture nuclides

When a nucleus decays by K-capture, the K X-rays are emitted with the probability given by the fluorescence yield, ω_K. Otherwise, only the low-energy Auger electron is emitted. Since it is very difficult to count these electrons reproducibly, generally only the K X-rays are used for the assay. In addition to the fluorescence yield, the L-capture/K-capture ratio must be taken into account if the activity is to be calculated from the K X-ray yield [15].

Solid angle techniques are widely used for the assay of these nuclides. The most convenient detector is a thin NaI crystal (thickness 1-2 mm) with a Be-window (thickness about 0.2 mm). If the nuclide has $Z \gtrsim 40$, a NaI crystal in a normal aluminium can (thickness about 0.2 mm) may also be used. As the self-absorption of solid sources may be appreciable, it is recommended to assay the nuclide in solution form.

End-window Geiger counters, filled with krypton or xenon to enhance the absorption of the X-rays in the counting gas, are no longer in much use for this purpose.

Methods for the determination of the absolute disintegration rate

In this paper, a calibration method is considered to be "absolute" if no other standard radioactive source, whose activity was determined elsewhere or by some other method, is needed.

Earlier methods were based mainly on the measurement of the radiation emitted from a point source into a well-defined but small, solid angle. Increasing this angle to 2π or 4π for α and β-emitters has now eliminated numerous sources of error. Small solid angles should be used only in exceptional cases.

Surveys of calibration methods have been published by Gandy [16] and Allen [17]. The latter covers publications till 1963.

The 4π proportional counter

The 4π-counter is now the most important detector for the calibration of β-emitting radionuclides [18-20]. The common type is the "pillbox" counter. For such counters the source consists of an aliquot of the radioactive solution deposited on a very thin film which is then dried. The film is placed over an annular source holder, which represents part of the wall between two "pillboxes" forming the two 2π counters with parallel wire anodes. The counting gas, preferably methane, streams through both counters. The counters are connected in parallel and operate in the proportional region. Also used are the "loop-type", where the anode wires have the form of a loop [19]. These counters may have a somewhat better characteristic than the "pillbox" type, but because of their relatively large height, for $4\pi\beta$-γ-coincidence counting the flat "pillboxes" are preferred.

A low-noise amplifier (about 200 μV rms at the input) with very good overload characteristics is essential. Good statistical accuracy is achieved in reasonable time by using high counting rates (up to 10^4 cps). However,

it is necessary to use a special electronic device which generates a well-defined dead-time. A counter of this type should be able to register every ionizing particle emerging from the source. To reduce self-absorption the sources must be exceedingly thin. Generally several drops, each about 12 mg, of the source solution, which must have a low carrier concentration only, are placed on a plastic film ($\sim 10\ \mu g/cm^2$) which is covered with a layer of evaporated gold (thickness $\sim 12\ \mu g/cm^2$). The gold layer ensures that static charges do not build up on the source. Nevertheless, even for such thin sources, the self-absorption losses are of the order of 0.2% for ^{32}P, 2% for $^{90}Sr + ^{90}Y$, 4% for ^{204}Tl and 6% for ^{35}S. Therefore, the 4π-counter alone can only be used for the calibration of β-emitters with maximum energies above 1 MeV, if accuracies of $\pm$ 1% or better are desired, and even then elaborate techniques have to be used for the film and source preparations [21, 22].

$4\pi\beta$-γ coincidence counting

If two counters, each sensitive for one kind of radiation only (usually one counter for β, α or X-rays, the other for γ-rays) are used, and the single counting rates, as well as the coincidences, are registered, then the absolute disintegration rate of the source can be determined directly for many nuclides; from these data the counter efficiencies may also be calculated. Generally, it is preferable to have the efficiency of one counter as nearly to 100% as possible; for α and β-emitters, the 4π proportional counter is, therefore, most suitable. The γ-rays are detected by one or two NaI crystals [23].

β-γ or α-γ cascades. If the nuclide emits only one β and one γ in cascade, the straightforward coincidence method may be used. If there are several cascades, small correction factors may be necessary [23]. The γ-efficiency of the 4π-counter may also have to be taken into account [24].

Extrapolation method for complicated decay schemes. For complex decay schemes, especially if there is a β-emission leading directly to the ground state, a more complicated method is needed. The self-absorption of the source is varied by adding carrier or sandwiching the source between absorbing films [25], and the β-counting rate is then plotted as a function of the ratio of the coincidences to the γ-counts, i.e. the "mean" efficiency of the 4π-counter for the β-spectra associated with the counted γ-rays. Linear extrapolation of the β-efficiency to 100% then gives the counting rate for zero self-absorption, i.e. the disintegration rate [25-27].

Pure β-emitters. For these nuclides the "efficiency tracing techniques" [26] can be applied. The β-emitter, B, is mixed with a convenient β-γ emitter as tracer whose activity is known from an earlier calibration (e.g. ^{60}Co) or can be determined by the disintegration curve (e.g. ^{82}Br). The self-absorption is varied by additional carrier or foils. If the self-absorption of the β-spectra of tracer and B can be assumed to be proportional, the β-efficiency of the tracer (ratio of coincidences to γ-counts) can be used as

a parameter to extrapolate the β-counting rate of B linearly to 100% β-efficiency [25, 26, 28].

The two foregoing methods, extrapolation and efficiency tracing, are cumbersome, but at present they are the only ones which make it possible to evaluate reliably the self-absorption of solid sources.

γ-γ coincidence counting. This method is, in principle, the most convenient if there are two γ-rays which are emitted in cascade. In contrast to the β-γ coincidence method the efficiencies of one counter for both γ-rays is of the same order of magnitude, which causes considerable complications; sum peaks must be avoided also. If the efficiencies are made very small, and about equal, these difficulties can be overcome [29-32]. Unfortunately, complicated fast-slow coincidence electronics are necessary, and the coincidence counting rate is very low. Consequently, this method is mainly useful for occasionally checking the results obtained by β-γ or X-γ coincidences.

Absolute γ-counting by NaI-crystals. For a number of different crystal sizes and geometries, absolute values for the total and photopeak efficiencies have been calculated [8, 33-35]. A cylindrical NaI crystal, 3 in. diam. and 3 in. height, is the standard detector for this type of measurements [8]; the source-to-detector distances most commonly chosen are between 10 and 30 cm. In the Compton region of the spectrum, the contribution of γ-rays scattered from the source holder, walls of the lead shield, etc. may be significant. Very light source mounts and large shields (up to 100 cm side length of a cube) are, therefore, often used. When the fraction of γ-rays per disintegration is known and the published values for the efficiency used, the activity of the source can be determined very easily; the accuracy is between $\pm$ 3 and $\pm$ 5%.

However, if a better accuracy is desired, the set-up should be calibrated by means of standard sources.

Absolute liquid scintillation counting of β-emitters. In liquid scintillation counting there is no self-absorption in the normal sense of the word, and this method may be used for the calibration of β- and α-emitters.

The aliquot of the aqueous solution to be calibrated is at first diluted with alcohol and then added to the scintillating solution. Small aliquots may also be diluted directly in the scintillator [36].

It is also possible to place a filter paper soaked with the scintillator in a translucent box or directly on the photocathode [37]. The effects of relatively large amounts of carrier may be reduced, if some 10 mg of the radioactive solution are put on the filter paper, which is dried, and then wetted with the scintillator [5].

The detection threshold, which cannot be set lower than several keV, is considerably higher than in $4\pi\beta$ proportional counting. Since a fraction of the low-energy part of the β-spectrum is, therefore, not counted, extrapolation techniques must be used to correct for this [38]. For β-emitters with maximum energies above 150 keV, an accuracy of better than $\pm$ 0.5% has been claimed [39].

The liquid scintillator can also serve as the β-detector in β-γ coincidence counting [40]. As the γ-efficiency is higher than for the 4π proportional counter, and the corresponding corrections difficult to apply, in general, the latter is preferred for coincidence calibrations.

Calibration of α-emitters

For solutions with very little carrier 4π proportional counting gives more than a 99% α-counting efficiency. This has been verified by α-γ coincidence counting. The latter method can be used if some γ or X-rays are emitted in cascade with the α-rays. A precision of $\pm$ 0.5% can be expected [41].

Small-solid-angle techniques have also been claimed to give an accuracy of 0.2% [42]. Apparently, the self-absorption perpendicular to the source is smaller than for 4π-geometry.

Calibration of electron-capture nuclides

E.C. and γ-ray in cascade. Coincidence techniques are the most convenient counting methods when an appreciable fraction of the electron-capture processes are followed by γ-emission. In this case, one detector should be sensitive for X-rays, preferably both for X-rays and the Auger electrons, while the other detector is sensitive only to the γ-rays. An argon- or xenon-filled proportional counter without a window can be used for the X-ray and Auger electron determination, while a Be-window NaI crystal detects only X-rays. The γ-effect in the X-ray detector must usually be corrected for [44]. In general, the calibration of these nuclides is not more difficult than that of β-γ emitters.

E.C. to ground state only. The self-absorption of Auger electrons is so large that it cannot be determined accurately. Therefore, the source is normally sandwiched between foils or films of low Z material which absorbs the Auger electrons completely but attenuates the X-rays only slightly. Complete or nearly complete absorption of the X-rays within the counter is necessary [43, 45]; 4π geometry is preferred but 2π geometry will also do since scattering can be considered negligible if the photo effect in the detector predominates.

Figure 6 shows a hemispherical 2π proportional counter for the calibration of medium Z electron capture nuclides; for X-ray γ-coincidence counting the NaI crystal can be much nearer to the source than in the case of 4π geometry [46]. Small solid angle geometry is not recommended for use with gas proportional counters. A thin NaI crystal as X-ray detector does not need a vacuum system, but should, because of the difficulty of defining the solid angle, only be used for higher Z nuclides where the absorption in the counting gas is too small.

For nuclides with $Z \lesssim 30$ the self-absorption of the X-rays within the small crystals constituting the source may necessitate intricate techniques. It is necessary to extrapolate to zero self-absorption and the ratio of the detected X-rays to the sum of the detected X-rays and Auger electrons for

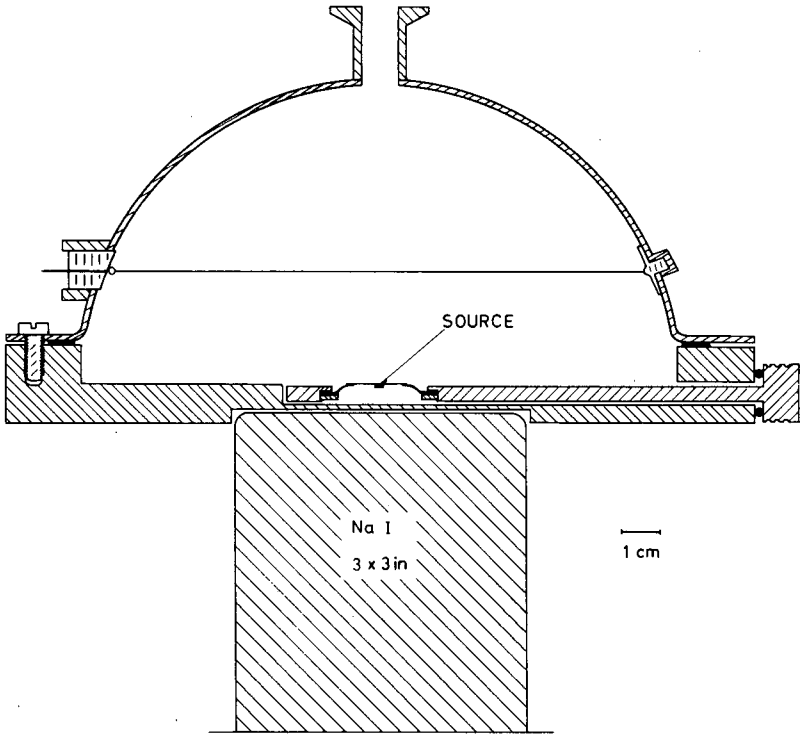

FIG. 6. Proportional gas counter for the calibration of electron capture radionuclides [5]

the bare source may serve as parameter [45]. Support film absorption and incomplete X-ray absorption in the counter have also to be corrected for. Accuracies of ± 2% have been claimed [5, 45]. When only the K X-rays are detected, the fluorescence yield and the K/L capture ratio have to be known accurately.

Some details on sample preparations

Carrier solution

If aliquoting is used for the preparation of liquid samples, the chemical composition of the solution must be appropriate to avoid any separation effects, e.g. adsorption on the walls or precipitation. The minimum carrier content is generally of the order of 10 μg per ml of solution. For cations, in general, less carrier is needed if the acid concentration is made higher. It has been shown that 2 μg/ml Cs or Co are sufficient if the solution is 0.1 N HCl [5]. Nearly neutral solutions seem to be unreliable.

Details on reliable carrier solutions have been given in the literature [17, 47].

Precise diluting

Dilutions by volume are rarely more precise than 1 or 2%; however, if the mass is taken as the criterion, accuracies of better than 0.1% can

be obtained. The specific activity of a solution is, therefore, generally given in units of Ci/g. This also eliminates differences caused by variations of the density. Large dilution factors are possible if the mass taken from the stock solution is determined separately by weighing. A simple pipette may be fabricated from a glass tube by drawing one end to a capillary. Some of the solution to be assayed can be sucked into the capillary by means of a rubber bulb (Fig. 7).

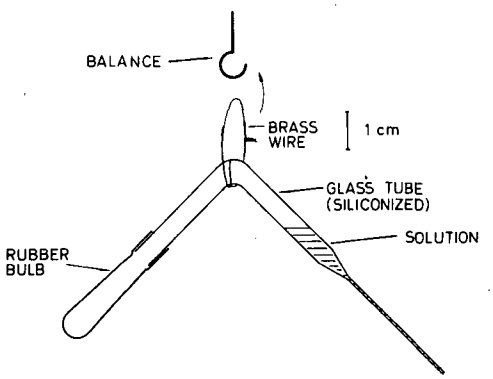

FIG. 7. Pipette for accurate dispensing of solutions [5]

Treating the capillary with silicone prevents drops from clinging to the outside. This pipette is weighed on a semi-micro or micro-balance before and after dropping some liquid into the diluent. If the weight of the latter is large, it can be determined easily on a simple balance [5]. For accurate results one must prevent appreciable evaporation of the solvent.

Preparation of sources

Polythene tubes with a lid, or screw-top bottles, are very practical and inexpensive containers for liquid samples to be assayed by γ-ray detection, although there is some evaporation through the walls.

For $4\pi\beta$ counting the weighed mass of liquid must be deposited on a very thin film. Since sufficiently thin films are not commercially available, the required films ($\sim 25\ \mu g/cm^2$) must be prepared in the laboratory [22]. The following procedure for source preparation gives good results for most nuclides:

Several drops (each ~ 12 mg) are deposited on the film from a pipette. The exact amount of material deposited is determined by the difference in the weight of the pipette before and after. The drops are dried on the film. The crystalline residue is then re-dissolved with two drops of a solution consisting of LUDOX [22] diluted $1:10^4$ and TEEPOL diluted $1:10^5$ with water. The source is then given a final drying.

For some nuclides special treatment is necessary, for example,

Iodine-131: Addition of $AgNO_3$ solution to the deposit (prevents evaporation of the iodine)

Cobalt-60: Precipitation with NH_3 by exposing to NH_3 gas or by the addition of NH_4OH (reduces self-absorption)

Mercury-203: Precipitation as HgS; H_2S as gas or aqueous solution (prevents evaporation of Hg).

The errors of different weighing techniques in preparing these sources have been thoroughly investigated [48].

TABLE V

METHODS RECOMMENDED FOR THE CALIBRATION OF SOME RADIONUCLIDES

Radionuclide	Relative calibration	Absolute calibration		$4\pi\beta$-efficiency (%)
		Method	Precision (%)	
^{18}F	γ, (β)	$4\pi\beta$-γ γ-γ	± 3	95.0
^{24}Na	γ, β	$4\pi\beta$, $4\pi\beta$-γ γ-γ	± 1	99.5
^{28}Mg	γ, (β)	$4\pi\beta$-γ [b]	± 3	
^{32}P	β	$4\pi\beta$	± 1	99.8
^{35}S	β [a]	$4\pi\beta$-γ (tracer) [b]	± 2	94.0
^{42}K	γ, β	$4\pi\beta$, $4\pi\beta$-γ [b]	± 1	99.0
^{51}Cr	γ	X-γ	± 2	-
^{58}Co	γ, (β)	γ-comp.	± 3	
^{59}Fe	γ, (β)	$4\pi\beta$-γ [b]	± 1	95.0
^{65}Zn	γ	X-γ	± 2	-
^{82}Br	γ, (β)	$4\pi\beta$-γ	± 1	96.0
^{90}Y	β	$4\pi\beta$	± 1	99.5
^{131}I	γ, (β)	$4\pi\beta$-γ	± 1	96.0
^{198}Au	γ, (β)	$4\pi\beta$-γ	± 1	98.0

[a] See first main sub-section of the text.
[b] See second main sub-section of the text.

Methods for the calibration of special radionuclides

Table V gives recommendations for the methods most appropriate for the calibration of some radionuclides.

Relative calibration

As emphasized in Chapter 1, γ-assay is to be used whenever possible. If a "β" is also given in column 2 of Table V, β-counting gives good results. If (β) is given, γ-detection should be preferred.

Absolute calibration

In column 3 of Table V the following abbreviations are used:

$4\pi\beta$ = $4\pi\beta$ proportional counter

$4\pi\beta$-γ = β-γ coincidence method using a $4\pi\beta$-counter and a NaI crystal

X-γ = coincidence method, detecting the K X-rays and the γ-rays separately

Cobalt-58 can be calibrated using an interpolated value for the γ-efficiency (805 keV) of a NaI-spectrometer [49].

The "precision" in column 4 of Table V means the agreement which is to be expected between the results measured by different specialized laboratories (standard deviation).

The last column gives the efficiencies of the $4\pi\beta$-counter (average values) for carefully prepared sources.

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7. RADIOLOGICAL PROTECTION

Harmful effects may follow the exposure of the human body to ionizing radiation. These harmful effects may be either of a somatic type and become manifest at an early or late stage in the exposed individual, or of a genetic type and become manifest only in his descendants. It is therefore necessary

to take stringent precautions to prevent undue exposure to radiation of those persons who are engaged in work with radioactive substances. More detailed information on the precautions which are outlined in this section is available in the Agency publications listed in the References.

Types of exposure

The organs and tissues of the body differ both in their sensitivity to ionizing radiation and in their importance for the maintenance of bodily health. Those organs which are most sensitive in particular circumstances of irradiation and which are also most necessary for the maintenance of well-being are referred to as the critical organs for that mode of irradiation.

Two clearly distinguished types of exposure can occur. First, exposure of the whole body, or limited parts of it, to the radiation emitted by sources which remain outside the body; this type is referred to as exposure to external radiation. Second, exposure of organs and tissues to the radiation emitted by radioactive substances which enter the body by inhalation, by ingestion, or by absorption through broken or intact skin; this type is referred to as "exposure to internal radiation". When a radionuclide has entered the body it takes part in the metabolic processes and the extent of any accumulation in the critical organs depends on its chemical identity and form, its solubility and the route by which it entered the body.

Maximum permissible doses

Careful experimental work on animals and the study of accumulated experience on the effects of radiation on the human body have made it possible to formulate a set of permissible dose-equivalents, expressed in rems, which are applicable to all types of ionizing radiation. The permissible values are related to exposure of the whole body or limited parts of it, or to exposure of the various critical organs within the body.

The International Commission on Radiological Protection (ICRP) has issued recommendations on maximum permissible dose-equivalents which are now widely accepted throughout the world [1]. The Commission has been careful to point out that the recommended values are maximum values and has also recommended that all radiation doses should be kept at as low a value as practicable and that all unnecessary exposure to radiation should be avoided.

The maximum permissible dose-equivalents listed in the Agency's Basic Safety Standards for Radiation Protection [9] are based on the recommendations of the ICRP.

On the basis of plausible assumptions regarding the intake of air and water during the period of exposure it is feasible to derive maximum permissible concentrations of specific radionuclides in air inhaled and water consumed which correspond to the maximum permissible dose-equivalents to the whole body and to the critical organs [2]. Such maximum permissible concentrations are listed in Part II for the selected radionuclides.

Methods of controlling exposure to radiation from sealed and unsealed sources

(a) Sealed and unsealed sources

Radioactive substances may be handled in the form of sealed or unsealed sources. In a sealed source the substance is enclosed in a hermetically-sealed container or is bonded in a material in such a way that it will not be dispersed in normal use. All other forms of radioactive substance constitute unsealed sources. A sealed source, as long as it remains sealed, can act as a source of external radiation only; an unsealed source can act as a source of both external and internal radiation.

(b) The handling of sealed sources [3 - 6]

Exposure to external radiation can be minimized by:

(i) Limiting the time spent near the source to the minimum necessary for efficient performance of the work;
(ii) Keeping the body, including the hands, as far from the source as is compatible with rapid and safe work;
(iii) Interposing between the source and the body shielding material of sufficient thickness to reduce the level of the transmitted radiation to an acceptable value.

These three methods are generally used in combination.

Distance provides an inexpensive means of reducing the radiation level, but its use is limited. For a gamma-ray source of small dimensions the exposure rate decreases with distance approximately according to the inverse square law. Increasing the distance between the hands and the source by a factor of ten, for example from one centimetre to ten centimetres, reduces the exposure rate at the hands by a factor of one hundred. For a beta-ray source the level of the radiation also decreases rapidly with distance, though the relationship between the two is complicated by the scattering and absorption of the radiation in the air. The radiation level in the immediate neighbourhood of a beta- or gamma-ray-emitting source of comparatively low activity may be sufficiently high to deliver a large dose in a very short time. Radioactive substances should therefore never be manipulated with the bare hands; some form of protection is always necessary. Forceps which keep the fingers at a distance of ten to fifteen centimetres should be used for the small sources. Tongs which keep the hands at a distance of about one metre may be used for the larger sources.

When remote handling alone is not sufficient to reduce the radiation level to an acceptable value, shielding must be provided.

Beta particles lose their energy within a short distance and have a finite range, even in materials of low density. A layer of transparent plastic 6 mm thick will absorb effectively all beta particles of initial energy less than 1 MeV, and a layer 2.5 cm thick will absorb all those of initial energy less than 4 MeV. Such plastic materials, usually in the form of transparent sheets, are used to provide close shielding around high-activity beta-ray sources, or in the form of barriers behind which the handling procedures are performed. Materials of high atomic number should not be used as

primary shielding for beta radiation as a considerable fraction of the absorbed beta ray energy may then be converted into continuous X-radiation, referred to as bremsstrahlung.

Gamma radiation is much more penetrating. The most commonly used shielding materials are lead, steel and concrete. The thickness of any of these materials which will provide the required attenuation for gamma radiation of specified energy may be obtained from published Tables [6]. For shielding purposes the thicknesses used should be those applicable to attenuation under broad beam conditions. Convenient calculators for estimating the thickness of shielding necessary to reduce the radiation levels to the desired values are obtainable commercially[1].

Gamma-ray shields should be placed as close to the source as circumstances permit. The thickness of the shield is not less when it is in that position, but its surface area and hence its weight and cost are less than if it were placed at a greater distance.

Radiation emerges from a source in all directions and sufficient shielding must therefore always be provided below as well as at the sides of the source. When the direct radiation strikes neighbouring objects a fraction of it is scattered in all directions. If the activity of the source is high, the level of the radiation scattered from overhanging structures and from the air may be unacceptable and it will then be necessary to provide top shielding.

When shielding is required it may also be necessary to provide remote handling devices which can be operated through the shield and provision must be made for viewing the work performed without impairing the shielding.

(c) The handling of unsealed sources [4 - 6]

In the handling of unsealed sources the methods previously outlined for controlling the exposure to external radiation are combined with those necessary for controlling exposure to internal radiation.

Exposure to internal radiation can be minimized by providing adequate containment for the source and any necessary protective devices for preventing the intake or transfer to the skin of dispersed contamination. Containment refers to the measures taken to prevent the spread of contamination to the air, to materials with which it may be ingested, and to the skin or to surfaces from where it may be transferred to the skin.

Radionuclides have been graded in order of their relative radiotoxicity and classified in four categories corresponding to very high, high, moderate and slight relative radiotoxicity [5, 13]. The design of the working place and the nature of containment and protective measures required depend on the radiotoxicity classification and on the activities of the radionuclides which are to be handled [5].

All manipulations of active liquids should be performed within a double container or over a drip-tray lined with absorbent paper in order to confine any spills. Rubber gloves and appropriate protective clothing, such as laboratory coats, overalls, aprons, etc., should always be worn when working with unsealed sources. Overshoes should be worn if it is likely

[1] Isotope Handling Calculator (Mk III), Radiochemical Centre, Amersham, United Kingdom.

that the floor may become contaminated. Great care should be taken to prevent the transfer of contamination to the mouth, and mouth-operated pipettes should never be used in work with radioactive materials. Eating, drinking, smoking and the application of cosmetics should also be prohibited and self-adhesive labels only should be used in areas in which such materials are handled. Before it is cleaned, and if necessary decontaminated, all equipment and glassware used with unsealed sources should be laid in trays lined with absorbent material. Such equipment should be kept in the active working area and should not be used for other work.

If it is reasonable to suppose that the operations could lead to a spread of contamination to the atmosphere they should be performed within a fume hood or within an enclosed box and a ventilation system should be provided which will ensure in all circumstances a movement of air from the inactive towards the more active areas prior to discharge from the building, if necessary through filters. Detailed information on these topics is provided in Section 2 of this manual.

Clearly labelled receptacles for the collection of radioactive wastes should be kept in all working areas where such wastes may originate. Arrangements must be made for the periodic removal of active wastes from the working areas and for their storage and eventual disposal in conformity with the applicable regulations [10].

For work in areas in which it is impossible to keep the level of contamination of the air below the acceptable values, for example for maintenance and repairs within the enclosures, individual protective equipment, including respirators fitted with filters, or enclosed breathing sets supplied with clean air, should be provided and used.

If the level of external radiation is sufficiently high, it is necessary to provide shielding and remote handling devices in addition to the appropriate containment and for very active sources a fully-shielded enclosure may be necessary. Access to such an enclosure for maintenance and repairs is permitted only for persons wearing full protective clothing.

If the level of external radiation is not sufficiently high to warrant the use of a fully shielded enclosure, the unsealed sources may be handled within a fume hood or dry box provided with the appropriate shielding.

Physical and medical surveillance

(a) Physical surveillance

Area monitoring and personnel monitoring techniques are used for checking the effectiveness of the measures adopted for controlling the exposure to external and internal radiation.

Area monitoring comprises the systematic measurement of radiation levels and, if appropriate, of air and surface contamination levels in the working areas and in neighbouring areas. The results of such measurements provide a check on the effectiveness of the shielding and containment of the sources.

Personnel monitoring comprises the measurement of the total radiation reaching the surface of the body in a known time and the assessment of body

burden, that is to say, the quantity of radioactive material actually present within the body [8, 12].

Appropriate instruments should be available for monitoring external radiation and contamination under normal working and emergency conditions. Such instruments may include fixed types, providing a continuous indication of radiation or contamination levels, installed at selected points within the laboratory, and portable types suitable for the detailed surveying of external radiation fields and possibly contaminated areas. Areas in which radiation sources are stored or used, and neighbouring areas, should be monitored at regular intervals. All working places and equipment which may have been contaminated should be monitored when the work has been completed and, if necessary, during the work. Portable radiation detectors or appropriate smear tests may be used for this type of monitoring.

If significant quantities of radioactive substances are handled as unsealed sources, the hands, clothing and shoes of the worker should be monitored before he leaves the working area and all articles used in the working area should also be monitored before they are removed from that area.

Appropriate personnel monitoring devices for determining the exposure to external radiation, such as film badges or pocket dosimeters, should be worn by all persons while engaged in work with radioactive sources. Exposure to internal radiation can be assessed, where necessary, by estimating the intake or evaluating the body burden of radioactive substances. Such an evaluation may be based on bio-assay measurements or on measurements of the radiation emitted by substances retained in the body. Appropriate counting equipment and sensitive radiation measuring devices, such as scintillation detectors and, if necessary, whole-body monitors, should be available for this purpose.

Careful records should be kept of the results of area and personnel monitoring.

(b) Medical surveillance [7]

Medical supervision is necessary for determining a person's fitness for work with radiation sources and for following trends in a worker's state of health. It should include an initial medical examination to determine a worker's suitability for employment, periodic re-examinations at appropriate intervals and special examinations. It should also include advice on first-aid and personal decontamination and the setting-up of arrangements for the treatment of persons who have received excessive radiation doses.

Working rules [5, 11]

Working rules, in the form of written instructions, setting out clearly the procedures to be followed in all routine work which may involve exposure to radiation, should be drawn up and brought to the attention of all workers. These rules should also cover such topics as the entrance of personnel and visitors into classified areas, monitoring and medical supervision procedures.

Procedures should also be established for obtaining approval for special operations, such as entry into shielded enclosures, which might involve exposures exceeding prescribed levels.

Accidents may involve exposure to excessive levels of external radiation, for example through loss of shielding, or exposure to internal radiation following failure of containment and dispersal of contamination. As a precaution against the occurrence of accidents all work should be carried out according to pre-arranged plans.

Special rules should be drawn up specifying the action to be taken in emergency situations following foreseeable types of accidents and should be brought to the attention of all persons who may be involved.

Emergency action should, in general, be directed towards protecting the persons involved in the accident and preventing any further spread of contamination.

Administrative organization [5, 11]

The authority in charge of a laboratory should carry ultimate responsibility for ensuring adequate protection against the effects of radiation, and in discharge of this responsibility should provide an administrative organization in which the tasks related to radiological protection are clearly defined.

These tasks include the provision of appropriate working conditions and equipment, the appointment of qualified persons to advise on radiological safety and to prescribe protective measures and verify their application, the provision of appropriate medical supervision, the designation of radiation workers, the classification of working areas, the provision of training and instruction, and the keeping of records.

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PART II

DESCRIPTION OF SUITABLE REACTORS

NUCLEAR DATA
REFERENCES
PROCEDURES

DESCRIPTION OF REACTORS SUITABLE FOR THE PRODUCTION OF RADIOISOTOPES*

Reactor	Type	Thermal output	Maximum neutron flux (n/cm^2 s) (Thermal)	(Fast)	Operating since	Location
CANADA						
NRX	Tank. Natural U heavy-water-moderated, light-water-cooled, graphite reflected	40 MW	6.4×10^{13}		1947	Atomic Energy of Canada Ltd., Chalk River
NRU	Tank. Natural U heavy-water-moderated, cooled and reflected	200 MW	2.5×10^{14}		1957	-ditto-
CHINA (Taiwan)						
THOR	Pool. Enriched (20%) U, light-water-moderated and cooled, light-water or graphite reflected	1 MW[1]	9.9×10^{12}	3.6×10^{13}	1961	Institute of Nuclear Science, National Tsing Hua University, Hsinchu
CZECHOSLOVAK SOCIALIST REPUBLIC						
WWR-C PRAGUE	Tank. Enriched (10%) U, light-water-moderated and cooled	2 MW	2.0×10^{13}		1957	Institute for Nuclear Energy, Czechoslovak Academy of Sciences, Rez-Prague
FRANCE						
EL-2	Tank. Natural U heavy-water-moderated, carbon-dioxide cooled, graphite reflected	2 MW	7.7×10^{12}		1952	Centre d'études nucléaires de Saclay
EL-3	Tank. Enriched (1.35%) U, heavy-water-cooled and moderated, graphite and heavy-water reflected	15 MW	1.0×10^{14}		1957	-ditto-

* Further information on these reactors may be found in the International Directory of Reactors, Vols. I, II and III, published by the International Atomic Energy Agency, Vienna.

[1] Could be raised to 1.5 MW.

Reactor	Type	Thermal output	Maximum neutron flux (n/cm^2 s) (Thermal)	(Fast)	Operating since	Location
MELUSINE	Pool. Enriched (20%) U, light-water-moderated and cooled	12 MW	1.0×10^{13}		1958	Centre d'études nucléaires de Grenoble
SILOE	Pool. Fully enriched (90%) U, light-water-moderated and cooled, light-water and beryllium reflected	10 MW (design) 15 MW (actual)	9.5×10^{13}		1963	Centre d'études nucléaires de Grenoble
TRITON	Pool. Enriched (20%) U, light-water-moderated and cooled (similar to MELUSINE in Grenoble)	12 MW			1959	Centre d'études nucléaires de Fontenay-aux-Roses
HUNGARY						
WWR-C BUDAPEST	Tank. Enriched (10%) U, light-water-moderated and cooled	2 MW	2.0×10^{13}		1959	Central Institute for Physics, Hungarian Academy of Sciences, Budapest
INDIA						
APSARA	Swimming pool. Enriched (80%) U, light-water-moderated and cooled	1 MW (300 kW operating power)	3×10^{12}		1956	Atomic Energy Establishment Trombay, Bombay
CIR (CANADA-INDIA)	Tank. Natural U, heavy-water-moderated, light-water cooled, graphite reflected	40 MW	6.12×10^{13}		1960	-ditto-
ISRAEL						
IRR-1	Pool. Enriched (20%) U light-water-cooled, moderated and reflected	1 MW	1.4×10^{13}		1959	Soreq Research Establishment, Israel Atomic Energy Commission, Yavne

JAPAN					
JRR-1	Aqueous homogeneous water boiler type, enriched (20%) uranyl sulphate solution, light-water-moderated and cooled, graphite reflected	50 kW	1.2×10^{12}	1957	Tokai Research Establishment, Japan Atomic Energy Research Institute, Tokai, Ibaraki
JRR-2	CP-5. Enriched U (20%), heavy-water-moderated, cooled and reflected	10 MW	1.2×10^{14}	1960	-ditto-
JRR-3	Tank. Natural U, heavy-water-moderated and cooled	10 MW	2.1×10^{13}	1962	-ditto-
NORWAY					
JEEP	Tank. Natural U, heavy-water-moderated and cooled, graphite reflector	450 kW	2.7×10^{12}	1951	Institute for Atomic Energy, Kjeller
JEEP II	Tank. Slightly enriched (3.5%) UO_2, heavy-water-moderated, reflected and cooled	2 MW	2.7×10^{13}	1965	-ditto-
POLAND					
WWR-C-WARSAW	Tank. Enriched (10%) U, light-water-moderated and cooled	4 MW	4.8×10^{13}	1958	Institute of Nuclear Research, Swierk Centre, near Otwock
ROMANIA					
WWR-C-BUCHAREST	Tank. Enriched (10%) UO_2, light-water-moderated and cooled	2 MW		1957	Institute of Atomic Physics, Romanian Academy of Science, Magurele near Bucharest
SPAIN					
JEN-1	Pool. Enriched (20%) U, light-water-moderated and cooled, graphite reflected	3 MW	3.5×10^{13}	1958	Junta de Energía Nuclear, Madrid

Reactor	Type	Thermal output	Maximum neutron flux (n/cm² s) (Thermal)	(Fast)	Operating since	Location
UNITED KINGDOM						
BEPO	Natural U, graphite-moderated and reflected, air-cooled	6.5 MW	1.5×10^{12}		1948	Atomic Energy Research Establishment, Harwell, Bucks.
DIDO	Tank. Fully enriched (93%) U, heavy-water-moderated and cooled, graphite and heavy water reflected	10 MW	1.6×10^{14}		1956	-ditto-
PLUTO	Tank. Fully enriched (93%) fuel, heavy-water-moderated and cooled, graphite and heavy water reflected	10 MW	0.35×10^{14} in heavy water moderator		1957	-ditto-
UNITED STATES OF AMERICA						
LITR	Tank. Highly enriched (30%) U, light-water-moderated and cooled, beryllium reflected	3 MW	3.5×10^{13}		1950	Oak Ridge National Laboratory, Tenn.
ORR	Tank. Fully enriched (90%) U, light-water-moderated and cooled, beryllium reflected	30 MW (design) 20 MW (normal operation)	3×10^{14}		1958	-ditto-
BGRR	Fully enriched (93%) U, graphite-moderated and reflected, air cooled	16 MW (up to 20 MW)	$\sim 2 \times 10^{13}$		1950	Brookhaven National Laboratory, Upton, L.I., N.Y.
YUGOSLAVIA						
R-A	Tank. Enriched (2%) U, heavy-water-moderated and cooled	6.5 MW	6.0×10^{13}		1959	Boris Kidrič Institute of Nuclear Sciences, Vinča

NUCLEAR DATA, REFERENCES AND PROCEDURES

BROMINE-82

NUCLEAR DATA

1. NUCLEAR PROPERTIES

1.1. Half-life

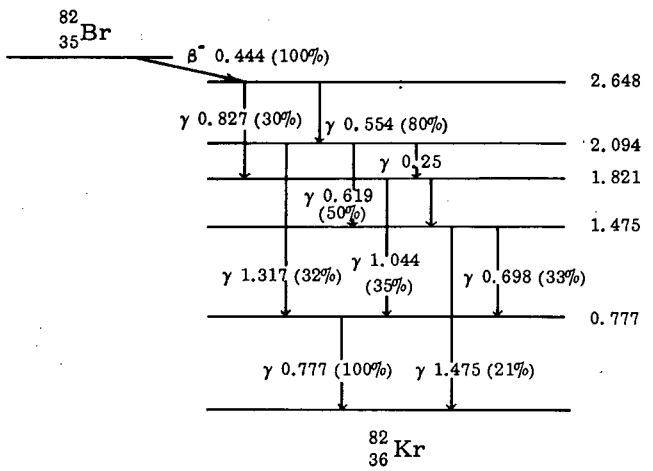
36 h

1.2. Type of decay and energy (MeV)

beta (β^-) 0.444 (100%)

gamma 0.5541 (80%)
0.6187 (50%)
0.6984 (33%)
0.7769 (100%)
0.8276 (30%)
1.0440 (35%)
1.3171 (32%)
1.4753 (21%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Abundance of target nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm^2 s (mCi/g)			Secondary reactions and half-life of nuclide formed
			1 h	24 h	sat.	
$^{81}Br(n,\gamma)^{82}Br$	49.48	3.1	7	113	307	$^{79}Br(n,\gamma)^{88m}Br$ and ^{80}Br ($T_{\frac{1}{2}}$ = 4.4 h and 18 min) isot. abundance: 50.52 σ = 10.4 barns

For nuclear data see Refs. [1-4].

3. APPLICATIONS

Bromine-82 is the most long-lived and consequently the most convenient practical radioisotope of bromine. A brief summary of important published applications is given below.

3.1. Chemistry

Radiometric analysis	[5]
Chemical structure research	[6]
Study of reaction mechanism and kinetics	[7, 8]
Study of ion adsorption	[9]
Hot-atom chemistry studies	[10-25]

3.2. Biology and biochemistry

Haematological studies	[26, 27]
Gastroenterology	[28]
Study of the role of bromine in the animal organism	[29]
Study of desoxyribonucleic acid	[30]

3.3. Medicine

Experiments on thyroid function	[31]
Diagnosis and therapy	[32]

3.4. Industry

Oil refining industry	[34]
Measurement of flow in pipes	[35]
Leak detection in pipe-lines	[36]
Food industry	[37]
Study of sewage-treatment processes	[38, 39]

3.5. *Preparation of labelled compounds*

Labelled compounds commercially available	[40]
Method of labelling triolein	[41]

4. RADIOLOGICAL PROTECTION

4.1. *External exposure*

^{82}Br is a β^- and γ emitter. The dose-rate of 1 mCi activity at 1 cm is 15.48 R/h [42]. Activities up to 50 mCi at 16 mR per 6-h working day can be safely handled, using a 60-mm-thick lead shield.

4.2. *Internal irradiation*

Bromine-82 is classified [43] as a Class 3 (moderate toxicity) isotope and has an effective half-life of 1.3 d [44].

The maximum permissible concentration is [45]:

	(μCi/cm^3)	
	In water	In air
Soluble	8×10^{-3}	10^{-6}
Insoluble	10^{-3}	2×10^{-7}

4.3. *Decontamination*

Contamination from ^{82}Br activity can be adequately removed by washing in plenty of water; the efficiency of decontamination improves with the addition of carrier.

5. SUMMARY OF PRODUCTION METHODS

The production process is based on the reaction $^{81}Br(n, \gamma)^{82}Br$, accompanied by the reaction $^{79}Br(n, \gamma)^{80}Br$. Cooling the irradiated target for about one day is sufficient for ^{80}Br to decay. ^{82}Br may be produced without enrichment if the neutron flux is high enough to obtain a satisfactory specific activity, or by Szilard-Chalmers enrichment.

5.1. *Chemical processes without enrichment*

For the production of ^{82}Br an ammonium bromide target is usually chosen since, of the radioactive nuclides, no other than the bromine isotopes are produced during its short-term irradiation. NH_4^+ can be replaced by other ions (e.g. Na^+, K^+, etc.) with the addition of a suitable alkali solution and subsequent boiling off of the ammonia [46].

Irradiation at high dose-rates results in the radiolysis of ammonium bromide causing considerable gas evolution [47]. The latter can be avoided by the use of barium bromide targets. Ba ions can be replaced to about 100% efficiency by other ions using ion exchange resins [48, 49].

5.2. Chemical processes with Szilard-Chalmers enrichment

The use of bromate targets has been investigated by a number of authors [10–14] and [50–54]. The radioactive recoil atoms are separated, on the dissolution of $KBrO_3$ or $Ca(BrO_3)_2$, in the form of Br^- as the silver salt. An alternative method is the extraction, from the aqueous solution, of irradiated bromate with carbon tetrachloride when all the radiobromine in a lower stable valence than bromate can be separated.

After irradiation of organic compounds of bromine, e.g. alkyl or arylbromides in a reactor, radioactive bromine can be concentrated by extraction in a suitable water solution. p-Dibrombenzene is used frequently as the target material. After irradiation the compound is dissolved in benzene and the radiobromine is extracted from the solution with dilute ammonia. The enrichment factor is about 100 [55]. There is copious literature on the Szilard-Chalmers reactions of the organic compounds of bromine (e.g. [15–25] and [55–58]).

A further method for the concentration of radiobromine is the irradiation of elementary bromine adsorbed on active carbon. The radioactive bromine can be washed out with distilled water by a very simple technique. Enrichment of ^{82}Br reaches 50 – 500 times [59].

6. RADIOASSAY

Radiochemical purity is checked by γ-spectrometry. Activity is measured by one of the usual methods (Section 6 of Part I).

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CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

Bromine-82 is prepared by direct irradiation of ammonium bromide without enrichment by the Szilard-Chalmers effect. The nuclear reactions are as follows:

$$^{79}Br(n,\gamma)^{80}Br \xrightarrow{4.4\ h} {}^{80}Br\ (18\ m)$$

$$^{81}Br(n,\gamma)^{82}Br$$

The neutron fluxes are large enough to obtain satisfactory specific activities for medical purposes.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	500 mg of ammonium bromide.
Irradiation conditions:	1 week at a flux of 2.4×10^{12} n/cm^2 s in EL 2.
	72 h at 10^{13} n/cm^2 s in EL 3.
Yield:	Between 200 and 600 mCi per operation.

The material is not processed until the day after unloading from the reactor to eliminate ^{80}Br.

Chemical treatment

Preparation

The 500 mg of irradiated NH_4Br are poured into 24 ml of N/4 soda and heated to boiling point for five minutes to eliminate the NH_4^+ ions. The solution is neutralized by 1 N hydrochloric acid to pH 6 - 7, and made up to 40 ml with water.

An isotonic solution of sodium bromide is thus obtained.

Apparatus

The above operations are carried out in an ordinary beaker. A combined electrode is used for neutralization.

3. ASSAY AND QUALITY CONTROL

The activity of two 1-ml samples is measured. Purity is periodically checked by gamma-ray spectrometry. The sterility and non-toxicity of the product are proved by biological tests.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{82}Br S-2 - injectable

A neutral, isotonic, sterile and pyrogen-free solution of sodium bromide, meeting the following specifications:
Radioactive concentration, measured to within 5%: up to 10 mCi/ml.
Radioactive purity: ^{80}Br content < 1%.
Specific activity: 100 - 500 mCi/g.
Sterile.
Pyrogen-free.

CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production is based on the thermal neutron induced (n, γ) reaction of the target barium bromide. After irradiation barium ions are removed by cation exchange resin.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Barium bromide, Merck (analytical grade) – amount depending on the request.
Flux:	10^{13} n/cm^2 s.
Time of irradiation:	100 h.
Container:	Quartz ampoule with ground stopper.

Chemical treatment

After irradiation the target is cooled for 48 h in order to eliminate ^{80m}Br activity. Then it is dissolved in distilled water, mixed with Dowex 50 resin in sodium form, and shaken for 30 min; the exchange between Ba^{2+} and Na^{+} ions is quantitative.

3. ASSAY AND QUALITY CONTROL

The purity of the inactive target is previously checked by activation analysis.

The purity of Na^{82}Br is controlled by adding sulphuric acid to prove the absence of Ba^{2+} ions. Radiochemical purity is checked with the aid of a multichannel pulse height analyser.

The pH is measured in the usual way by measuring aliquot samples.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Radioactive purity:	> 90%.	
Specific activity:	1000 mCi/g.	
Chemical form:	Aqueous solution.	
Sodium bromide:	"	" pH 6 - 7.
Potassium bromide:	"	" pH 6 - 7.
Ammonium bromide:	"	" pH 6 - 7.
Barium bromide:	"	" , ^{131}Ba content < 0.1%.

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Bromine-32 is produced by the irradiation of a stable bromide in a nuclear reactor. The target used is potassium bromide. When KBr target is irradiated ^{42}K is also produced by neutron capture in the potassium. Hence, an initial cation-exchange separation is done to separate all the potassium present. Bromine-82 is supplied as sodium bromide in aqueous solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	50 - 100 mg potassium bromide G. R.
Container:	Can type "C" (cold-welded 2 S aluminium can, 44 mm high and 22 mm diam.).
Flux:	1×10^{13} n/cm^2 s.
Irradiation period:	1 week.

Chemical treatment

After opening the can, the irradiated KBr is dissolved in water and is passed down a cation exchange column (Dowex-50, H^+ form) to remove the potassium. The effluent is passed down a second cation exchange column (Dowex-50, sodium form) to obtain the ^{82}Br in the form of Na^{82}Br, which is adjusted for isotonicity and is sterilized.

3. ASSAY AND QUALITY CONTROL

The activity is assayed by measuring a known volume of stock solution in a calibrated ion chamber.

The bromide is estimated by Volhard's method.

Radioactive purity is determined by taking a gamma-ray spectrum of the test sample.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	NaBr in aqueous solution.
Specific activity:	> 1 Ci/g.
Radioactive concentration:	> 1 mCi/ml.
Radioactive purity (exclusive of ^{80m}Br):	> 99%.

MINISTRY OF DEFENCE, ATOMIC ENERGY COMMISSION,
SOREQ RESEARCH ESTABLISHMENT, YAVNE, ISRAEL

A. PRODUCTION OF ^{82}Br as NH_4Br AQUEOUS SOLUTION

1. GENERAL

Irradiation of NH_4Br produces ^{82}Br by the (n, γ) reaction. The irradiated sample is "cooled" for two days, and dissolved in water.

2. EXPERIMENTAL PROCEDURE

Irradiation

The target material is ammonium bromide (AR). For long irradiations calcium bromide (AR) is used.

Irradiations are made in the Israel Research Reactor (IRR-1) at a thermal neutron flux of 10^{13} n/cm^2 s (rabbit) or 3×10^{13} (pool).

Samples are usually "cooled" for 48 h after irradiation to allow the 4.5-h ^{80}Br activity to decay.

Typical conditions

Irradiate 100 mg of NH_4Br for 10 min in the "rabbit" system to obtain 0.34 mCi of ^{82}Br after 48 h decay time. The ^{80m}Br activity will then be less than 1.7%.

Irradiate 40 mg $CaBr_2 \cdot 2H_2O$ for 1 h in the pool to obtain 5 mCi of ^{82}Br after 48 h decay time. The ^{80m}Br activity will then be less than 1.7%.

For pool irradiation the target is sealed into a 15-ml capacity silica ampoule, which is in turn put into an aluminium irradiation container. For "rabbit" irradiation the sample is sealed into a polyethylene vial.

Chemical treatment

Limited, in this case, to sample dissolution in water.

B. PRODUCTION OF ^{82}Br AS ELEMENTARY BROMINE

1. GENERAL

The irradiated NH_4Br is dissolved in a sodium bromate solution. Perchloric acid is added. The evolved bromine is condensed in a refrigerator flask.

2. EXPERIMENTAL PROCEDURE

Irradiation: see (A) above.

Chemical treatment

Transfer irradiated ampoule into lead cell.
Wash ampoule with acetone.
Break ampoule. Dissolve irradiated bromide in water.

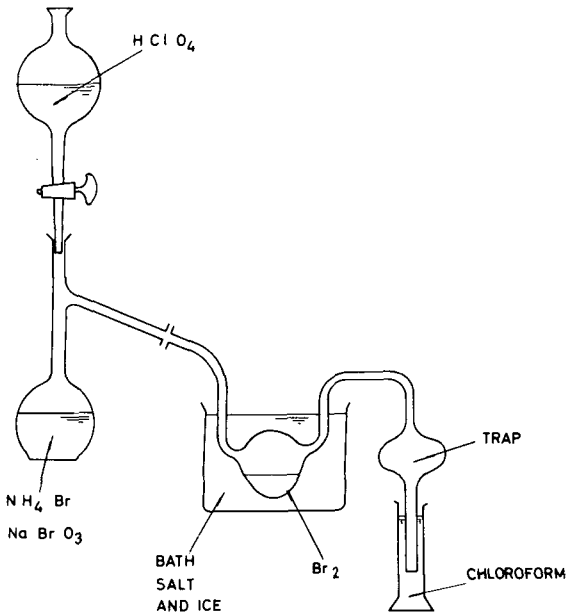

FIG. 1. Production of ^{82}Br elementary bromine

Add stoichiometric amount of $NaBrO_3$ according to the reaction:

$$NaBrO_3 + 5\,NH_4Br + 6\,HClO_4 = 3\,Br_2 + NaClO_4 + 5\,NH_4ClO_4 + 3\,H_2O$$

Transfer solution to distillation flask (see Fig. 1)
Heat distillation flask gently.
Add the perchloric acid slowly, drop by drop.
Receive and condense bromine by means of ice-salt bath.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process is based on irradiation of the ammonium bromide target and dissolution in distilled water.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	5.0 g NH_4Br (JISGR[1]) for JRR-1; 1.0 for JRR-2.
Container:	Sealed in the polyethylene sheet, then placed in the polyethylene capsule (JRR-1).
	Placed in the polyethylene bottle, then in the polyethylene capsule (JRR-2).
Flux:	$\sim 3 \times 10^{11}$ n/cm^2 s (JRR-1).
	$\sim 2 \times 10^{13}$ n/cm^2 s (JRR-2).
Irradiation time:	15 h (5 h × 3 d) for JRR-1; 20 min for JRR-2.
Side reactions:	Formation of ^{80}Br, ^{80m}Br, which are eliminated by cooling.

Chemical treatment

The apparatus is shown in Fig. 1.

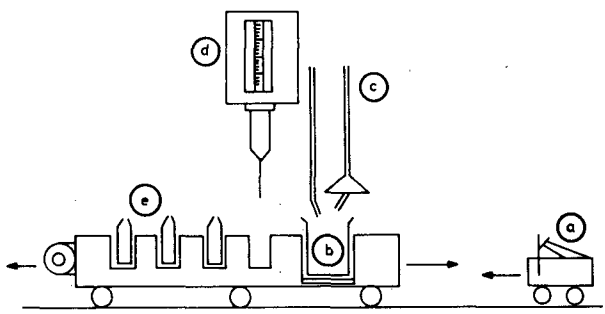

FIG. 1. Arrangement of apparatus for ^{82}Br production

a. Polyethylene capsule cutter
b. Dissolving vessel
c. Reagent feed pipes
d. Remote pipetter for dispensing
e. Bottles of product

Cut the polyethylene inner capsule by the cutter (a).
Place the target in the dissolving vessel (b), then add 5 - 8 ml/g of NH_4Br distilled water from the reagent feed pipe (c) to dissolve the target.
Warm up the solution for about one minute to remove free bromine.
The product solution is dispensed in the sample bottles.

[1] Japan Industrial Standard Grade Reagent.

3. ASSAY AND QUALITY CONTROL

The routine assay is made by the well-type ionization chamber. The calibration is made by a $4\pi\beta$-γ coincidence counter. The free bromine content is determined by the colorimetric method.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	NH_4Br in aqueous solution.
Radiochemical purity:	> 99%.
Specific activity:	~ 4.5 mCi/g of Br (JRR-1 product).
	~ 10 mCi/g of Br (JRR-2 product).
Concentration:	~ 0.7 mCi/ml (JRR-1 product).
	~ 1.0 mCi/ml (JRR-2 product).

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

^{82}Br is produced by irradiating ammonium bromide: $^{81}Br(n,\gamma)^{82}Br$. The target material is dissolved and converted to sodium bromide.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	200 mg NH_4Br, Merck, p.a.
Time of irradiation:	2 d.
Container:	Aluminium can with a sealed polyethylene inner container.
Flux:	Approximately 2×10^{12} n/cm^2 s.
Side reactions:	$^{79}Br(n,\gamma)^{80m}Br/^{80}Br$ (4.4 h/18 min). After irradiation the target material is stored for one day to reduce activity due to ^{80m}Br and ^{80}Br.

Chemical treatment

The irradiated ammonium bromide is dissolved in water, sodium hydroxide is added, and the solution is evaporated to dryness. After dissolution of the residue in water a small quantity of dilute hydrochloric acid is added for neutralization, and sodium thiosulphate solution is added as a preservative.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative ionization chamber measurements.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control, emission spectrography.
Radiochemical purity control, radiochromatography.
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

BRIS - sodium bromide in neutral isotonic solution, sterilized.

Radioactive concentration:	1 - 1.5 mCi/ml.
Isotopic purity:	^{80m}Br less than 5%.
Radiochemical purity:	99% as bromide.
Specific activity:	100 mCi/g Br.
pH:	7
Chemical purity:	Metals, spectrographically determined, less than 10 μg/ml.

INSTITUTE OF NUCLEAR RESEARCH, SWIERK NEAR OTWOCK, POLAND

1. GENERAL

Bromine-82 is obtained by the irradiation of ammonium bromide in the neutron flux

$$^{81}Br(n, \gamma)^{82}Br$$

Irradiated ammonium bromide is dissolved and then transformed into sodium bromide.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Approximately 500 mg of ammonium bromide, analytical reagent.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	24 h.

Container: Quartz ampoule, hermetically closed, wrapped in aluminium foil and closed in an aluminium capsule by welding.

Chemical treatment

Target material is stored for 24 h after irradiation in order to allow decay of short-lived ^{80}Br.

Irradiated and "cooled" ammonium bromide is dissolved in 0.25 N NaOH and boiled for 5 min in order to remove ammonia. The solution obtained after cooling is brought with 1 N HCl to pH 6 - 7 and then isotonic solution of sodium bromide is obtained by the addition of an appropriate volume of water.

The product is packed in penicillin-type vials which are stoppered with rubber stoppers and closed with aluminium tops. The vials are sterilized at 2.5 atm for 25 min.

3. ASSAY AND QUALITY CONTROL

The activity of the product is measured in the ionization chamber calibrated with a standard.

Bromides are determined by silver nitrate titration.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Sodium bromide in aqueous solution, isotonic, sterile.

Specific activity:	100 - 150 mCi/g Br.
Radiochemical activity:	Bromine-80m less than 2%.
pH:	6 - 7.

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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Ammonium bromide is irradiated in a thermal neutron flux $^{81}Br(n,\gamma)^{82}Br$. The final product is made available in two chemical forms, ammonium and sodium bromide.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Ammonium bromide A. R.
Amount:	Up to 0. 5 g.
Irradiation time:	6 d.
Container:	Primary and secondary screw-top aluminium containers.
Flux:	10^{12} n/cm^2 s.
Side reactions:	$^{79}Br(n, \gamma)^{80m}Br/^{80}Br$. The half-lives of these isotopes are sufficiently short to make the level insignificant after one day's storage.

Chemical treatment

The target material is dissolved in water, free bromine being removed by the passage of an air stream. The remaining solution is adjusted for isotonicity. To convert into the sodium salt, the ammonium bromide solution is passed down a cation exchanger in the sodium form.

3. ASSAY AND QUALITY CONTROL

Identity is by γ-spectrometry. Assay is by ion chamber against ^{226}Ra. pH by Capillator and bromide ion by titration against silver nitrate.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Bromine-82 is produced by a (n, γ) reaction in a KBr target $^{81}Br(n,\gamma)^{82}Br$. The isotope is separated by ion exchange in columns conditioned with HCl and KOH in succession. Potassium remains on the first column, and bromine elutes from the second as KBr.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	150 mg KBr.
Neutron flux:	2×10^{14} n/cm^2 s.
Irradiation time:	40 h.
Reactor yield:	4 Ci.

Chemical treatment

Apparatus

Two ion exchange columns (Fig. 1) and a hot off-gas scrubber unit (Fig.2) are required for processing.

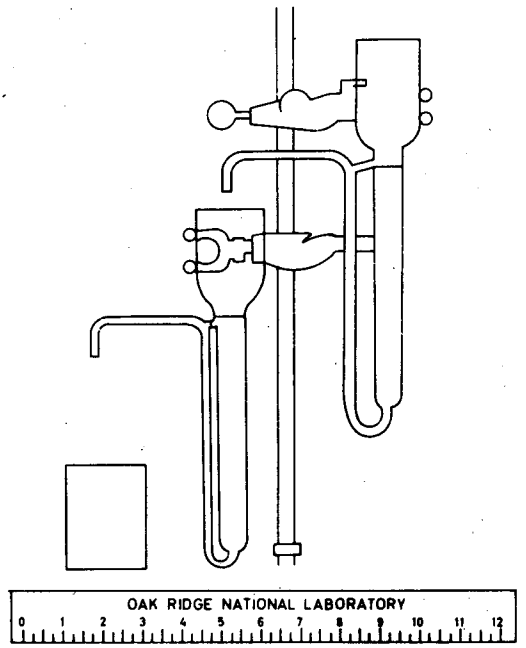


FIG. 1. Double ion exchange column for ^{82}Br purification

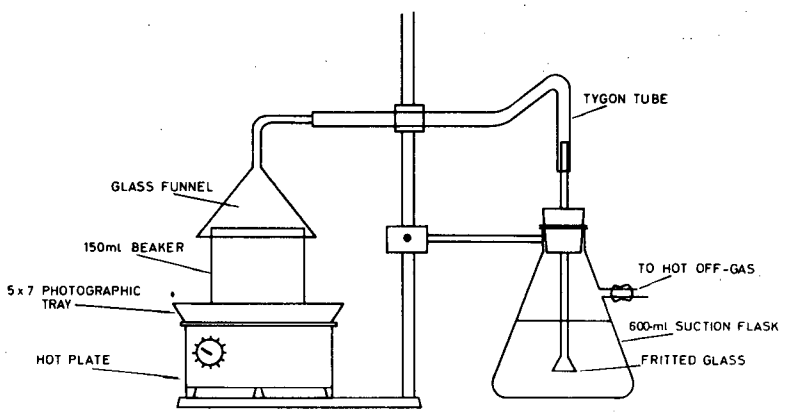


FIG. 2. Hot off-gas scrubber unit

Processing

Yield: > 90%.

The irradiation can is opened, and the target is dissolved in water in a beaker placed under the hot off-gas assembly.

Two 50-ml ion exchange columns are prepared with Amberlite IR-120 cation resin. One column is conditioned with 6 M HCl and washed with distilled H_2O until the effluent is neutral. A second column is conditioned to potassium form with 1 M KOH solution and washed with distilled H_2O until neutral.

The dissolved target solution is placed in the head tank of the first column. Effluent from this column is transferred directly to the head tank of the second column. When the solution has passed through both columns, they receive three 25-ml washes of distilled H_2O. Potassium remains on the first column, and ^{82}Br elutes from the second column as KBr. Effluents are combined into a clean beaker and evaporated to 50 ml.

3. ASSAY AND QUALITY CONTROL

A sample is analysed for ^{82}Br concentration, radiochemical purity, and total solids according to the ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733131.

The precision and accuracy of the ^{82}Br are: Calibration by $4\pi\beta$-γ coincidence counter. Routine assay by ionization chamber and well-type scintillation counter. Estimated limit of error in disintegration – rate concentration of routine shipment, 5%. Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity ^{82}Br is delivered in the form of KBr in water. Other specifications of interest are:

Concentration:	> 1 mCi/ml.
Specific activity:	≅ 1000 mCi/g Br.
Radiochemical purity:	> 98%.

CHROMIUM-51

NUCLEAR DATA

1. NUCLEAR PROPERTIES

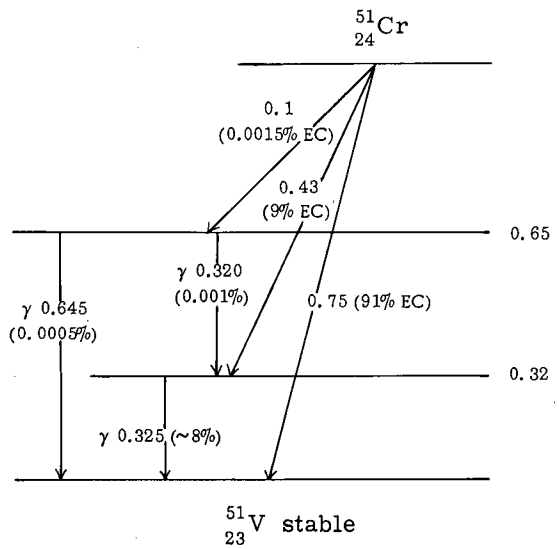
1.1. Half-life

27.8 d

1.2. Type of decay and energy (MeV)

EC (100%) gamma 0.005 (characteristic X-ray from vanadium)
0.325 (~8%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barns)	Activity of element at 10^{12} n/cm^2 s			Secondary reactions and half-life of nuclide formed
			1 week	4 weeks	saturation	
$^{50}_{24}Cr(n,\gamma)^{51}_{24}Cr$	4.31	15.900 (th)	15.5 mCi/g	31 mCi/g	222 mCi/g	
$^{52}_{24}Cr(n,2n)^{51}_{24}Cr$	83.76					
$^{54}_{26}Fe(n,\alpha)^{51}_{24}Cr$	5.82	0.00074 (f)	5.5 μCi/g	31 μCi/g	222 μCi/g	$^{54}_{26}Fe(n,\gamma)^{55}_{26}Fe$ (T = 2.6 yr) σ = 2.8 barns $^{54}_{26}Fe(n,p)^{54}_{25}Mn$ (T = 278 d) σ = 56 mbarns $^{56}_{26}Fe(n,p)^{56}_{25}Mn$ (T = 2.58 h) isot. abund.: 91.6% σ = 0.8 ? 0.4 mbarns $^{58}_{26}Fe(n,\gamma)^{59}_{26}Fe$ (T = 45 d) isot. abund.: 0.33% σ = 1.01 barns

(th): for thermal neutrons.
(f): for fast neutrons.

For nuclear data see Refs. [1-6].

For the production of ^{51}Cr use is made of the (n, γ) reaction on ^{50}Cr. There are two ways of proceeding:

- starting with enriched ^{50}Cr (in the form of CrO_3 or Cr_2O_3)
- starting with potassium chromate and using the Szilard-Chalmers effect.

3. APPLICATIONS

3.1. Industrial

Chromium-51 has been used for:
Self-diffusion measurements
Corrosion research [7, 8]
Studies on wear [9, 10]
Studies on arc-welding [11]
It is also used as a tracer in sedimentology [12].
For general works referring to the uses of ^{51}Cr see [13].

3.2. Medical and biological

Chromium-51 is used solely for diagnostic work, in the form of sodium chromate and chromic chloride.

3.2.1. Applications of sodium chromate [14-18]

The main application of sodium chromate is for labelling red blood cells. It permits determination of the blood volume (doses of the order of 5-10 μCi) [19], the lifetime of the red blood cells and their renewal rate (doses of the order of 50 μCi).

Sodium chromate is also used for:

labelling various cells:	leukocytes
	thrombocytes
	ascitic cells
labelling various molecules:	haemoglobin
	endotoxin of Escherichia coli
	dextran
	casein

3.2.2. Applications of chromic chloride [14-18, 20]

It is used for labelling various proteins:
human serum albumin to an activity level of 50 μCi (this is the most important application) and bovine serum albumin
human and rabbit plasma protein
human haemoglobin
endotoxin of Escherichia coli.

The medical applications of ^{51}Cr are dealt with in other works [25].

4. RADIOLOGICAL PROTECTION

4.1. External exposure

4.1.1. Irradiation doses

The dose delivered by 1 Ci of ^{51}Cr at a distance of 50 cm is 0.0628 rem/h [22].

4.1.2. Safety measures

In Table I are shown tenth-thicknesses[1] for lead and ordinary concrete which give some idea of the amount of protection needed in handling ^{51}Cr.

In practice, the following thicknesses of lead are required to reduce the dose to 1 mR/h at 50 cm:

0.15 cm for handling 10 mCi of ^{51}Cr
0.5 cm " " 100 mCi " "
1.2 cm " " 1 Ci " "

[1] The tenth-thickness is the thickness of shielding required to reduce the intensity of a γ-radiation of given energy by a factor of ten.

TABLE I

PROTECTION IN HANDLING ^{51}Cr [22]

	1/10 thickness (cm)	
	Pb	ordinary concrete d = 2.3
For a γ of 0.325 MeV	0.65	9.5

4.2. Internal irradiation

Chromium-51 is classified as a weakly toxic (category 4) isotope [23]. Its effective half-life, allowing for both radioactive decay and excretory processes, is 26.6 d [24].

In the case of internal irradiation (ingestion or inhalation), the maximum permissible concentrations in air and water respectively, for a 40-h exposure, are:

10^{-5} μCi/cm^3 and 0.05 μCi/cm^3 (soluble form)
2×10^{-6} μCi/cm^3 and 0.05 μCi/cm^3 (insoluble form) [25]

4.3. Decontamination

Except in one or two particular cases, there is no special decontamination method for any given radioisotope. General texts on this subject [26-30] indicate that the following measures are adequate.

4.3.1. Skin

Rapid and repeated washing with good-quality soap, warm water and a soft brush. If this is not sufficient, use can be made of detergents or 5 - 10% solutions of complexing agents of the EDTA (ethylenediamine tetra-acetic acid) type. It is also possible to apply saturated permanganate solutions followed by rinsing with a 5% bisulphite solution to neutralize and remove stain. Abrasive powders should not be used and the addition of entraining agents has proved disappointing.

If any wounds are contaminated, they must be treated rapidly by bleeding, washing with water, decontamination as for the skin and sometimes by additional surgical cleaning.

4.3.2. Hair

If the hair is contaminated, it is important not to take a shower, but merely to wash the head. A normal, good-quality shampoo is usually sufficient. If contamination is persistent, the following solutions can be used:

paraisopropylorthocresol
lavandin oil

AC compounded terpene-free lemon
glycerin diacetin
benzoic acid

Contamination is much easier to remove if the hair is not greasy.

4.3.3. Laboratory equipment

Glasswear is usually cleaned by steeping and this is mainly a radiochemical problem. The use of a specific entraining agent or solutions of complexing agents gives good results and so do solutions of chromic acid, concentrated nitric acid, ammonium citrate, pentasodium triphosphate or ammonium bifluoride.

5. SUMMARY OF PRODUCTION METHODS

Two main methods of preparing ^{51}Cr can be found in the literature.

5.1. By the (n, γ) reaction

5.1.1. On metallic chromium, either natural [31] or enriched in chromium-50 [31, 32]

The target is dissolved in the minimum quantity of 12 M hydrochloric acid. This is followed by filtering, and finishing in 1 M hydrochloric acid.

5.1.2. On the oxide of chromium enriched in ^{50}Cr

Hudswell et al. [33] propose the following method: The irradiated oxide is dissolved in potassium acid sulphate solution. To cool the solid, it is dissolved in water (with a little sulphuric acid if necessary) and the chromium hydroxide is precipitated with a slight excess of dilute ammonia in the presence of ammonium chloride. The precipitate is separated from the hot solution on 541 Whatman paper. The paper is washed several times with 1% ammonium nitrate and the precipitate is then extracted with a current of pyrogen-free hot water. After treating the suspension with caustic soda, the chromium is then all oxidized to chromate with sodium peroxide and the pH adjusted to 8 with hydrochloric acid.

5.2. By the (n, γ) reaction followed by enrichment by Szilard-Chalmers effect

5.2.1. On potassium chromate (this is the target normally used)

There are different processes for separating the "hot atoms".

Separation by precipitation without the addition of entraining agents [34]

This is the simplest method. It consists of dissolving the irradiated potassium chromate in double-deionized water of pH between 6 and 7, and

separating the Cr^{3+} by filtration on a No. 4 fritted disc without the addition of entraining agent. This facilitates washing of the chromium hydroxide precipitate remaining absorbed on the fritted disc and subsequent oxidation of the Cr^{3+} to Cr^{6+}. This oxidation is performed at 100°C by alkaline hydrogen peroxide. When oxidation is finished, the solution is filtered and its pH adjusted to 6.5 - 7 with 1 N hydrochloric acid. The enrichment factor is between 1000 and 3000.

Separation by precipitation using as entraining agents

Chromium [35, 36]
Iron [37-39]
Aluminium [40-42]
Lanthanum [43]

Separation by chromatography

- on an alumina column [44]. The irradiated potassium chromate is dissolved in a dilute solution of ammonia. This solution is passed through an alumina column treated several times in advance with dilute acid and dilute ammonia. The chromate is eluted by washing with dilute ammonia and water. The Cr^{III} retained on the alumina is eluted with 0.1 N hydrochloric acid.

- by ion exchange [45]. There are two stages. First, the irradiated potassium chromate is dissolved in dilute hydrochloric acid and the Cr^{3+} ions formed during irradiation of the $Cr_2O_7^{--}$ ions are separated by passing through an anion resin (Dowex 1X8). The $Cr_2O_7^{--}$ ions are adsorbed whilst the Cr^{3+} ions pass through. These Cr^{3+} ions are then oxidized to CrO_4^{-}; one then has a solution of K_2CrO_4—KCl.

The second part of the method consists of eliminating the potassium ions. To do this, the K_2CrO_4—KCl solution obtained as above is passed through another anion-resin column. The CrO_4^{-} ions are adsorbed on the resin whilst the K^+ ions pass through. Finally, the chromium is eluted from the column using a reducing mixture of ascorbic acid, ethyl alcohol and hydrochloric acid.

5.2.2. On chromium oxide with separation by ion exchange [46]

5.2.3. On ammonium bichromate and chromium acetylacetonate [47]

5.2.4. On chromium hexacarbonyl with separation by extraction [48]

5.2.5. On different organic compounds [39, 49-51]

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PROCEDURES

ATOMIC ENERGY OF CANADA LIMITED, CHALK RIVER, CANADA

1. GENERAL

Chromium-51 is a beta gamma emitter with a half-life of 27.8 d. It is produced in the reactor by the irradiation of enriched chromium-50

$$^{50}Cr(n, \gamma)^{51}Cr$$

After irradiation the target is processed to the chloride form. A portion of this is further processed to the chromate form. Both forms are shipped to the pharmaceutical industry for further processing and distribution to the medical profession.

2. EXPERIMENTAL PROCEDURE

Irradiation

The irradiation target at Chalk River consists of 5 - 10 mg of chromium metal enriched to 90% in ^{50}Cr. This is sealed into a small inner aluminium vial because of the small quantity and then in a standard reactor capsule. The usual yield is from 250 to 800 Ci/g depending on flux and duration of the irradiation. An appropriate number of capsules are held under irradiation to provide normal requirements.

Chemical treatment

The chemical process consists of dissolving the irradiated target in HCl. This produces $CrCl_3$ solution which is one form of our standard product. A portion of this solution is converted with NaOH to Na_2CrO_4 which is another form of our standard product.

The irradiated capsule is transferred with extension tongs from a transfer container to the processing equipment. The capsule is opened mechanically and the contents transferred to a tared weighing vessel on a balance by means of which the weight of Cr metal is determined to the nearest 0.05 mg. A small quantity of 1 N HCl is added. Dissolution is brought about by heating the mixture with an infra-red lamp. The solution is filtered and passed into a volumetric flask. The flask is made up to volume with additional 1 N HCl. The product is now in the form of $CrCl_3$. A small sample is withdrawn at this stage for chemical and radiochemical analysis.

To prepare sodium chromate, an appropriate aliquot of the chloride form is withdrawn. It is converted by the rapid addition of a freshly prepared alkaline peroxide solution. The excess peroxide is destroyed by heating the solution with an infra-red lamp. The final solution is filtered and passed into a volumetric flask and made up to volume with distilled water.

Equipment

The processing equipment consists of a weighing beaker and balance, glass funnel and filter paper, small beakers, volumetric flasks, reagent bottles and an infra-red lamp. These are placed in a glove box having 4 in. (10 cm) of lead shielding on all sides. Fitted through the walls are ball joint manipulators and a lead glass window to permit remote viewing and operation. The box is exhausted through absolute filters.

3. ASSAY AND QUALITY CONTROL

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical

When the preparation is in the chloride form, a small sample is withdrawn for a total solids determination and spectrographic analysis. Another

small sample of the chromate form is withdrawn for analysis and pH adjustment.

Radiochemical

Specific activity. This is calculated from the weight of the chromium processed and the measured total ^{51}Cr activity obtained.

Activity concentration

The principal radiation measured is the 0.323-MeV gamma ray. The output from a suitable dilution of the active solution is analysed on a 512-channel analyser. The count-rate in the peaks indicates the activity concentration and the spectrum is used to check the radiochemical purity.

INSTITUTE OF NUCLEAR SCIENCE,
NATIONAL TSING HUA UNIVERSITY,
HSINCHU, TAIWAN, REPUBLIC OF CHINA

(1)

1. GENERAL

Chromium-51 is prepared by nuclear reaction $^{50}Cr(n, \gamma)^{51}Cr$ using potassium chromate as a target material. The ruptured chromium (III) is separated from the target by precipitating as hydroxide, which is then oxidized to chromate form.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	50 g potassium chromate (Baker's analysed reagent).
Irradiation container:	Aluminium can 4.7 cm diam., 9 cm high.
Irradiation condition:	Neutron flux 2×10^{12} n/cm^2 s.
Irradiation time:	60 h.

Chemical treatment

Fifty grams of irradiated potassium chromate is dissolved in 120 ml of re-distilled water. After the pH of the solution is adjusted to 8 ~ 9, the solution is warmed in a water bath for about 10 min. The precipitate is then filtered with Toyo Filter paper No. 5C. The precipitate on the filter paper is then washed thoroughly until the filtrate is free from chromate ion, and dissolved with a small amount of hydrochloric acid. The chromium (III) is then oxidized with sodium peroxide in an alkaline solution.

3. ASSAY AND QUALITY CONTROL

The chemical analysis of the product is carried out according to Oak Ridge National Laboratory Master Analytical Manual, 900712110 and 907332111-3. Pharmaceutical control is carried out according to "Minimum Requirements of Radioactive Drugs", Ministry of Health and Welfare, Japan (1962).

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	Na_2CrO_4 in NaCl solution.
Concentration:	2 mCi/ml.
Specific activity:	20 mCi/mg Cr.
Acidity:	pH 7 ~ 8
Radiochemical purity:	> 99%.

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

(2)

1. GENERAL

Chromium-51 is prepared by the Szilard-Chalmers effect using a K_2CrO_4 target, $^{50}Cr(n, \gamma)\,^{51}Cr$. The method at present utilized [1] consists of separating the "Szilard" Cr by filtering on a fritted glass. The method has been improved by dissolving the K_2CrO_4 target not in water, but in a 10% KCl solution to flocculate the chromium hydroxide.

The chromium hydroxide precipitate remains absorbed on the fritted glass and the Cr^{3+} is oxidized to Cr^{6+}.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Potassium chromate (Prolabo RP).
Irradiation conditions:	13 ~ 40 g per capsule at a mean flux of 10^{12} n/cm^2 s for five weeks, or to 5 ~ 40 g per capsule at a flux of 1.5×10^{13} n/cm^2 s for 10 d.
Yield:	0.8 Ci with a specific activity of 100 to 200 mCi/mg for one week's irradiation, 2.4 Ci with a specific activity of 30 - 50 mCi/mg for 10 days' irradiation.

Chemical treatment

Preparation

Four hundred grams of irradiated potassium chromate are dissolved in 100 ml of a 10% solution of potassium chloride. The solution is then passed

into a filtration apparatus fitted with a No. 4 fritted plate. Filtration is performed at ordinary pressure. Washing is then carried out with doubly distilled water until a colourless filtrate is obtained.

The chromium hydroxide on the plate is then redissolved cold with 75 ml of 6 per mille NaOH plus 50 ml H_2O_2 in a 110-mm vacuum. The solution is collected in a neutralization vessel and heated to boiling point for 30 min. It is left to cool and then neutralized with 0.5 N HCl to pH 7 - 8. It is made up to 70 ml.

A solution of isotonic sodium chromate in sodium chloride is thus obtained.

The solution is filtered on a small No. 4 fritted plate to eliminate any foreign hydroxides that may be present.

Apparatus

The K_2CrO_4 is dissolved in a 1500-ml bottle surmounted by a ground glass joint. Mixing is ensured by a magnetic agitator.

The chromate solution is filtered on a No. 4 fritted glass plate.

Oxidation of the Cr^{III} to Cr^{VI} is carried out in the neutralization apparatus heated by an infra-red heater and fitted with a condenser.

The final solution is passed through a second apparatus of the same design as the first, but smaller.

3. ASSAY AND QUALITY CONTROL

After each operation the following tests are carried out:
A radiochemical purity test by gamma-ray spectrometry on the 325 keV line.
Measurement of the activity of two samples in an ionization chamber.
Determination of carrier content.
Paper chromatography to determine the quantity of Cr^{3+} in the solution.
Biological tests to determine the yield of labelled erythrocytes and the sterility of the product.

4. CHARACTERISTICS OF THE FINAL SOLUTIONS

Reference: ^{51}Cr S-1 - injectable

A neutral, isotonic, sterile and pyrogen-free solution of sodium chromate, meeting the following specifications:

Radioactive concentration, measured to within 5%:	1 - 20 mCi/ml.
Radioactive purity:	^{51}Cr content > 99.9% (gamma-ray spectrum characteristic of ^{51}Cr).
Radiochemical purity:	Chromium content > 95%.
Specific activity:	20 - 200 mCi/mg.
Affinity for erythrocytes:	In vitro labelling yield of rabbit erythrocytes > 75%.
Sterile	
Pyrogen-free	

Reference: ^{51}Cr S-2 - non-injectable

An isotonic solution of chromium chloride, pH 2 - 3, meeting the following specifications:

Radioactive concentration, measured to within 5%: 1 - 20 mCi/ml.
Radioactive purity: ^{51}Cr content > 99.9% (gamma-ray spectrum characteristic of ^{51}Cr).
Radiochemical purity: Trivalent chromium content > 95%.
Specific activity: 20 - 200 mCi/mg.
Affinity for plasma proteins.

Reference: ^{51}Cr S-3

A chromium chloride solution in an HCl medium free from sodium ions: 10 - 20 mCi/mg.

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CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production is based on the nuclear reaction $^{50}Cr(n, \gamma)^{51}Cr$.

For products for industrial use, processing consists of the dissolution of the irradiated metal in hydrochloric acid and the conversion of the chromic chloride solution into the required chemical form.

For the preparation of sodium chromate for medical use, the Szilard-Chalmers process is used in order to obtain high specific activity.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Chromium metal, Johnson-Matthey (spec pure) for industrial uses. Potassium chromate, Merck (analytical grade) for medical uses. Weight of target variable.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	600 h for ^{51}Cr for industrial uses. 10 h for ^{51}Cr for medical uses.
Container:	Quartz ampoule with ground stopper for ^{51}Cr for industrial uses. Aluminium capsule with threaded stopper for ^{51}Cr for medical uses.

Chemical treatment

Chromium-51 for industrial use: The irradiated metal is dissolved in hydrochloric acid and thereafter converted to the required compound in conventional chemical ways.

Chromium-51 for medical uses: In preparing sodium chromate for medical use the irradiated potassium chromate is dissolved in sulphuric acid, ferric chloride is added, and "hot" chromic ions are co-precipitated with ammonium hydroxide. After filtration and washing, the precipitate is dissolved in hydrochloric acid and the precipitation is repeated several times. Finally hot sodium hydroxide and hydrogen peroxide are added to the precipitate, and the filtrate, containing the ^{51}Cr in the form of sodium chromate, is diluted with sodium chloride solution to adjust isotonicity. The solution is sterilized in an autoclave at 120°C for 40 min.

3. ASSAY AND QUALITY CONTROL

The chromium content of the solution is determined colorimetrically by comparing the absorption with calibrated standard solutions.

pH and sterility are measured and controlled in the usual manner.

Radiochemical purity is checked by γ-spectrometry with the aid of a multichannel pulse height analyser.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Isotonic solution of sodium chromate diluted with sodium chloride solution.
Radioactive purity: 99.9%
Specific activity: $10^4 - 2 \times 10^4$ mCi/g
Sterile

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

(4)

When crystalline potassium chromate is irradiated with thermal neutrons in a reactor the ^{51}Cr formed by radiative capture is enriched in the trivalent state in accordance with the Szilard-Chalmers recoil process. The enriched ^{51}Cr (III) can be separated from the irradiated K_2CrO_4 by selective precipitation on a column of chromatographic grade alumina.

A dilute ammoniacal solution of the irradiated potassium chromate is passed down an alumina column when the enriched trivalent chromium activity is retained on the column, whereas the chromate passes down. After washing the column free of chromate, the ^{51}Cr (III) activity is leached out

with dilute acid and the eluate is evaporated to dryness. The residue is leached out with alkaline peroxide to give ^{51}Cr in the form of sodium chromate.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 60 g of reagent grade potassium chromate crystals.

In APSARA: Container type "A" (screw-capped 1S aluminium can 73 mm high and 26.5 mm in diam.). 20 g × 3 cans.
Flux: 3×10^{12} n/cm^2 s.
Irradiation period: 1 week.

In CIR: Container type "C" (cold-welded 2S aluminium can, 44 mm high and 22 mm in diam.). 10 g × 6 cans.
Flux: 1 - 1.5×10^{13} n/cm^2 s.
Irradiation period: 1 week.

Chemical treatment

After cutting open the cans the irradiated chromate crystals are tapped on to the top of an alumina column (1 cm^2 × 6 cm long, alkali washed). 250 ml of 1 M ammonia solution is added in 50-ml portions on to the column till all the chromate is dissolved. Then the column is washed with 100 ml of doubly distilled water and the washings are rejected.

The adsorbed ^{51}Cr is then eluted from the column by adding 150 ml of 1 M HCl in 50-ml portions. The combined eluate is then evaporated to dryness in a distillation flask. The activity is leached out with 20 ml of 0.1 M HCl and again concentrated to about 1 ml.

A known amount of standard sodium hydroxide is added to the contents of the flask and the pH is adjusted to 9. A few drops of 30% H_2O_2 are added and the solution is boiled to remove excess peroxide. After cooling the pH is again adjusted to 7 and the chromate solution is adjusted for isotonicity and then the solution is centrifuged to separate traces of aluminium hydroxide. The clean supernatant solution is dispensed into different vials, sealed and autoclaved at 15 lb/in^2 for 45 min.

3. ASSAY AND QUALITY CONTROL

The radioactive concentration is determined by measuring a known volume of the stock solution in a calibrated ionization chamber.

The pH of the stock solution is determined. This should be 7 - 8.

The total solid content is determined by evaporating a known volume and weighing the residue.

The radiochemical purity is determined by separating Cr^{3+} and CrO_4^{--} on an alumina column and measuring the activities individually.

The radioactive purity is confirmed by gamma spectrometry.

The chromium content is estimated by reading the absorption of the stock solution in a 1-cm cell at 370 mμ and reading off the concentration from the calibration curve.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity: > 50 Ci/g.
Chemical composition: Sodium chromate in isotonic saline solutions, pH 7.
Radiochemical purity: > 95%.
Concentration: > 1 mCi/ml.

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

(5)

Chromium-51 is produced by irradiating potassium chromate, $^{50}Cr(n, \gamma)^{51}Cr$. A Szilard-Chalmers reaction in the target material crystals K_2CrO_4, causes (depending on the conditions during irradiation, temperature, neutron flux, etc.) 25% of the radioactivity produced to be present as trivalent chromium. This part of the total activity is separated from the hexavalent target compound by means of anion exchange. Anion exchange is also used to remove unwanted elements, mainly potassium ions, from the product solution. The process has been patented (see Norwegian Patents Nos. 102 733 and 102 958, and relevant references [1 - 2]).

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 30 g K_2CrO_4, dried, Merck, p.a.
Time of irradiation: 20 d.
Container: Aluminium can.
Flux: 10^{12} n/cm^2 s.
Temperature: The temperature of the target material during irradiation should not exceed 60°C.
Side reactions: $^{41}K(n, \gamma)^{42}K$. The target material is stored for a few days before separation to reduce the radioactivity due to ^{42}K.

Chemical treatment

The irradiated potassium chromate is dissolved in dilute hydrochloric acid, and the solution is transferred to an anion exchange column. The hexavalent part of the chromium is adsorbed on to the column resin, while the

trivalent chromium passes through together with unwanted cations from the target material solution. After oxidation with hydrogen peroxide the radioactive chromium, now in the hexavalent state, is adsorbed to the resin of a second anion exchange column. The potassium, together with cationic impurities, is washed directly to the waste system and by reduction with a mixture of ascorbic acid, ethyl alcohol and hydrochloric acid the radioactive chromium is regenerated from the column resin. Finally the solution is oxidized by means of hydrogen peroxide and neutralized to give the desired product.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative ionization chamber measurements.
Isotopic purity control, β-absorption analysis;
γ-spectrography.
pH
Chemical purity control, emission spectrography;
dry matter content (evaporation);
peroxide content (spot test, $KMnO_4$);
potassium content (Na-tetraphenylborate).
Specific activity control, chromium content (spectrophotometry).
Radiochemical purity control, radiochromatography.
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

CRIS - sodium chromate in neutral isotonic solution, sterilized.

Radioactive concentration:	1 - 2 mCi/ml.
Isotopic purity:	Greater than 99%.
Radiochemical purity:	At least 95% as Cr^{6+}.
Specific activity:	Greater than 10 mCi/mg Cr.
pH:	7.
Chemical purity:	Metals, spectrographically determined (except Cr), less than 10 μg/ml.

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[2] BIRKELUND, O.R., DAHL, J.B., Tagging of Human Red Cells with Chromium-51, Kjeller Report KR 63 (1964).

INSTITUTE OF NUCLEAR RESEARCH,
SWIERK NEAR OTWOCK, POLAND

1. GENERAL

Chromium-51 is obtained in the form of sodium chromate by irradiation in the reactor of enriched 85 - 90% chromium oxide, subsequent oxidation of the target with perchloric acid and dissolution of CrO_3 in sodium hydroxide solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	15 mg of enriched 85 - 90% chromium oxide.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	4 - 6 weeks (reactor working 86 h per week at full power).
Container:	Aluminium capsule closed by welding.
Activity obtained:	400 - 700 mCi.

Chemical treatment

Fifteen mg of the irradiated chromium oxide is dissolved in 30 ml of perchloric acid. The dissolution is carried out at 180 - 185°C. After dissolution of Cr_2O_3 the temperature is maintained at 180 - 185°C for 15 min in order to produce complete oxidation of Cr^{3+} to Cr^{6+} (CrO_3). During oxidation the colour of the solution turns from light green to pale yellow. After oxidation the solution is cooled for 30 - 45 min. After cooling CrO_3 in the form of small red crystals is filtered onto a G-3 sintered glass filter. For transformation of obtained CrO_3 into sodium chromate the crystals obtained are dissolved in a small volume of 1 N NaOH on the filter and then the filter is washed with a few millilitres of pyrogen-free water. Activity of the solution obtained in this way is adjusted to the required pH by neutralization of the excess NaOH with 0.1 HCl to a pH of 6.5 to 7.5. Isotonicity of the solutions is produced by the addition of an appropriate volume of water. The operations are carried out in an enclosure shielded with 5-cm lead plates.

3. ASSAY AND QUALITY CONTROL

Determination of the activity of the final product: the principal radiation measured is the 0.323-MeV gamma ray.
The chemical purity is determined spectrally.
The radiochemical purity is determined by quantitative determination of Cr^{3+} in chromate or Cr^{6+} in chloride (impurities).
Radiation purity is checked by gamma spectrometry.
Sodium chloride concentration is determined by silver nitrate titration.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Sodium chromate in isotonic saline.
Radioactive concentration 0.5 - 2 mCi/ml.
Radiochemical purity not less than 99%.
Specific activity 10 - 70 mCi/mg.
Sterile, pyrogen-free, pH 6 - 8.

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JUNTA DE ENERGIA NUCLEAR, MADRID, SPAIN

1. GENERAL

The production process is based on the irradiation of K_2CrO_4 and the method originally developed by Douis and Valade [1], which employs the adsorption of ^{51}Cr on the porous glass plate.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 40 g, potassium chromate of analytical grade quality.
Container: Leak-tight, aluminium container, 24×26 mm diam.
Flux: 5×10^{11} n/cm^2 s (JEN-1).
Irradiation time: 3 weeks, equivalent to 136 h of continuous reactor operation at 1 MW.
Approximate yield is 70 mCi with the specific activity of 20 - 30 mCi/g.

Chemical treatment

Separation method

The $Cr(OH)_3$ precipitate is adsorbed on a porous glass plate. The entire process comprises the following steps [2]:

Dissolve the irradiated K_2CrO_4 in water at the ratio of 25 ml/10 g of chromate. Leave the solution for at least 4 h.

The $Cr(OH)_3$ precipitate is filtered by a No. 4 porous glass plate; a slight suction is applied at the beginning. Wash the precipitate with approximately 250 ml of water.

Dissolve the washed precipitate with 5 ml of 10% HCl, and heat gently. The $Cr(OH)_3$ is re-precipitated, and the solution is neutralized with 10% NH_4OH against the phenolphthalein indicator.

The $Cr(OH)_3$ is oxidized to $CrO_4^{=}$ with 1 ml of 30% H_2O_2 (Perhydrol Merck) and 5 ml of 0.1 M NaOH. Excess oxidant is removed by boiling.

The chromate solution is made isotonic by the addition of 1 ml of H_3PO_4 (1 : 5) and adjustment of the pH to 7 with 1 M NaOH. The volume of the solution is made to 10 ml.

A possible method to improve the specific activity is currently being investigated [3]. It is established that favourable results can be obtained if:

The flux density is increased, and the irradiation period is decreased.

About 6 d are allowed to pass between the time the irradiated material is removed from the reactor and the time it is placed in solution.

Apparatus

The operation is carried out on a laboratory bench with a shield made of lead bricks.

3. ASSAY AND QUALITY CONTROL

The determination of chemical purity is made by emission spectrography as for ^{32}P preparations.

The precise chromium content needed for the determination of specific activity is determined as follows [4]:

Take 0.5 ml of the chromate solution, then dilute to 10 ml with distilled water.

Place 2 ml of the resulting solution in a 25-ml flask. Add 4 drops of concentrated H_2SO_4 and 5 ml of water.

Heat the solution to the fuming of $SO_3^{=}$, then allow to cool.

Add 1 ml of 10% ammonium persulphate and 1 ml of 1% $AgNO_3$ solutions. Heat gently until the persulphate is removed. Boil further for 10 min.

The solution is allowed to cool, then transferred to a 25-ml measuring flask. The remainder of the treated sample is entrained with water.

Add 0.5 ml of 1% diphenylcarbazide solution, and bring the solution to 25 ml. Stir. After 5 min measurement is made with a 1 cm optical cell and at 540 mμ in a Beckman Model B spectrophotometer.

Radioactive purity is determined by gamma spectrometry. The apparatus is described in the procedures for ^{32}P.

Radiochemical purity is determined by measuring the quantity of chromium in the form of chromate present in radioactive solution of this radioelement. This is done by precipitating lead chromate with lead acetate and measuring the activity of the precipitate with a scintillation counter [5].

The Cr^{3+} present in the solution of radioactive sodium chromate is determined by ascending chromatography on No. 2 Whatman paper. The solvent used is the mixture of water, 95% alcohol and ammonium hydroxide (d: 0.925), at the ratio of 5 : 2 : 1. The R_f values are: Cr^{3+} = 0.0, $CrO_4^{=}$ = 0.9. The activity measurement is made with an ionization chamber (see ^{32}P). An error of less than 10% is allowed.

Biological tests indicate over 75% labelling of red blood cells in vitro with radioactive sodium chromate [5].

4. CHARACTERISTICS OF THE FINAL SOLUTION

Sodium chromate - ^{51}Cr injectable

Neutral (pH 5 - 7), isotonic, sterile and pyrogen-free solution of sodium chromate meeting the following specifications:

Chemical purity:	Results of a typical analysis are: Elements not detected: Cd, La, Mn, Ni, Pb, Si, Sn, As, and Te. Elements with concentration of less than 3 μg/ml: Al, B, Mg. Ditto at less than 10 μg/ml: Ca, Fe.
Radioactive purity:	^{51}Cr content > 99.5%.
Radiochemical purity:	Chromate content > 95%.
Radioactive concentration:	1 - 20 mCi/ml.
Specific activity:	Above 20 mCi/mg.
Sterility:	Sterilization is carried out in an autoclave at 120°C for about 1 h.
Analysis of pyrogens[1]:	
Isotonicity:	Tested by means of conductimetric measurements.

^{51}Cr - chromium chloride, non injectable

Isotonic solution of chromium chloride, pH 3 - 4, meeting the following specifications:

Chemical purity:	As for sodium chromate - ^{51}Cr injectable
Radioactive purity:	^{51}Cr content > 99.5%.
Radiochemical purity:	$^{51}Cr^{3+}$ content > 95%.
Radioactive concentration:	1 - 20 mCi/ml
Specific activity:	over 20 mCi/mg.

[1] See the section on ^{32}P provided by the Junta de Energía Nuclear, Madrid, Spain.

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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Chromium, as chromic oxide, electromagnetically enriched to 85-90% in ^{50}Cr, is irradiated in a high thermal neutron flux, $^{50}Cr(n, \gamma)^{51}Cr$.

The processing is aimed to convert the oxide to the chloride.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Chromic oxide EM enriched in ^{50}Cr to 85 - 90%.
Amount:	20 mg.
Irradiation time:	21 d.
Container:	Sealed silica ampoule - primary; aluminium tube secondary.
Flux:	10^{14} n/cm^2 s.
Side reactions:	None.

Chemical treatment

The chromic oxide is dissolved in perchloric acid, the excess of which is reduced with SO_2. The hydroxide is precipitated at pH 2-4 with hexammine, and then centrifuged and washed. It is treated with excess sodium hydroxide and hydrogen peroxide. The excess NaOH is neutralized and the solution of sodium chromate made isotonic. Chromic chloride is obtained by reducing the chromate solution with SO_2.

3. ASSAY AND QUALITY CONTROL

Identity by gamma spectrometry; assay by scintillation counting against a ^{137}Cs reference. pH by Capillator; Cr element by polarography; cationic impurities by ion exchange; NaCl by silver nitrate titration.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Preparation:	Sodium chromate in isotonic saline.
Concentration of radioelement:	0.5 - 1 mCi/ml.
Concentration total element:	10 - 15 μg/ml.
Specific activity:	30 - 100 mCi/mg Cr.
Radioisotopic purity:	Not less than 99%.
Total solids:	< 10 mg/ml.
Appearance:	Clear, slightly yellow solution.
Acidity, alkalinity or pH:	pH 6 - 8
Organic matter:	Nil
Total alpha:	Nil
Metallic impurities:	As and Pb < 5 ppm.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Chromium-51 is produced by the $^{50}Cr(n,\gamma)^{51}Cr$ reaction in an enriched (to 98% ^{50}Cr) chromium metal target. **The metal is converted to chloride form** in HCl solution and filtered for the final product.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	15 mg chromium metal enriched to 98% ^{50}Cr.
Neutron flux:	2×10^{14} n/cm^2 s.
Irradiation time:	26 weeks.
Reactor yield:	11 Ci.

Chemical treatment

Apparatus

A hot off-gas scrubber unit for target dissolution (see Fig. 2 of section on ^{82}Br) and a 3-in fine, sintered-glass filter are used.

Processing

Yield: > 90%.

The target material is dissolved in a minimum amount of 12 M HCl under low heat. Solids are filtered out and the volume adjusted to 50 ml of 1 M HCl. A clear green solution results.

3. ASSAY AND QUALITY CONTROL

A sample is analysed for total solids, molarity of HCl, ^{51}Cr concentration, and radiochemical purity according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733211.

Precision and accuracy of the ^{51}Cr assay are:
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 5%.
Estimated precision, 3%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chromium-51 is supplied as $CrCl_3$ in HCl in processed enriched form as a stock item. Other specifications of interest are:

Acidity:	1 N ± 50%.
Concentration:	> 10 mCi/ml.
Specific activity:	≅ 100 000 mCi/g of Cr.
Radiochemical purity:	> 99%.

BORIS KIDRIČ INSTITUTE OF NUCLEAR SCIENCES, VINČA, YUGOSLAVIA

1. GENERAL

Irradiation of a K_2CrO_4 target gives rise to ^{51}Cr by the $^{50}Cr(n, \gamma)^{51}Cr$ reaction. For the production of ^{51}Cr the method of Douis and Valade [1] is used. This method has been improved by omitting the addition of NaOH during the oxidation of Cr^{3+} to Cr^{6+}. The degradation of the glass is thus avoided.

(7)

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 15 g of reagent grade K_2CrO_4.

The cross-section of the reaction $^{50}Cr(n, \gamma)^{51}Cr$ is $\sigma_{n,\gamma}$: 11.5 barns. Owing to the ^{50}Cr content in the natural element (4.4%), the value of 0.58 barns should be taken into account in calculating the activity. The formation of isotope ^{42}K by the reaction: $^{41}K(n, \gamma)^{42}K$, $\sigma_{n,\gamma}$: 1.1 barns (i.e. 0.076 barns with respect to the ^{41}K content in natural mixture) should be noted.

Thermal flux: $2-3\times10^{13}$ n/cm^2 · s (RA reactor at Vinča).
Irradiation time: 23 h. After irradiation the target is left to cool for 7 d for radioactive ^{42}K decay.
Irradiation containers: Cylindrical, aluminium cans with screwed covers: internal length: → 70 mm; internal diameter: → 25 mm.

Chemical treatment

Separation method

Irradiated K_2CrO_4 is dissolved in distilled water in vessel A. The pH of the distilled water is made up to pH 7 with NaOH so as to obtain optimal conditions for $^{51}Cr(OH)_3$ precipitation. After dissolving the chromate the solution is transferred to vessel B and then to a vessel for waste solutions F when $^{51}Cr(OH)_3$ remains on the sintered glass of vessel A. The sintered glass is then rinsed with water to remove the remaining chromate. After rinsing, oxidation is performed by adding 30% H_2O_2. Oxidation proceeds with heating and $^{51}Cr^{3+}$ oxidizes to red perchromic acid (H_3CrO_8) which, on heating, quantitatively decomposes into H_2CrO_4. After transferring the acid to vessel B the acid is evaporated to dryness by slow heating to remove the excess of H_2O_2. The dissolving of chromic acid in a 0.9% NaCl solution produces $Na_2{}^{51}CrO_4$ in an isotonic NaCl solution.

Apparatus

The process is carried out in an apparatus of Pyrex glass. A diagram of the apparatus is shown in Fig. 1.

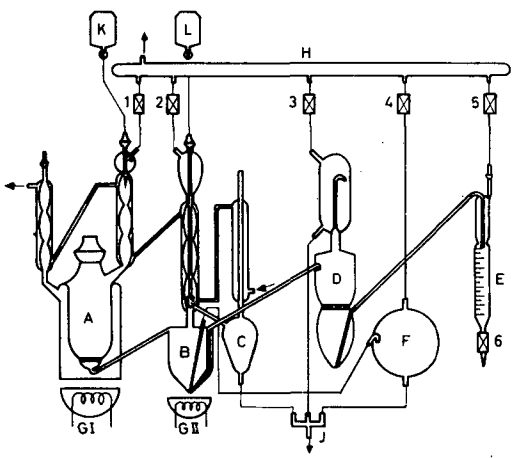

FIG. 1. Apparatus for the production of ^{51}Cr
Vessel for dissolution and oxidation (A)
Vessel for evaporation (B)
Vessels for waste solutions (C) (F)
Vessel for filtration of the final product (D)
Burette (E)
Heaters (G I and G II)
Distribution tube for transportable vacuum (H)
Vessels for adding chemicals (K and L)
Plastic stopcocks (1-6)

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.
Radioactive control.
Chemical purity control. Determination of Cr^{3+} content [4-6].

Quantitative determination of Cr content [2, 3].
Sterility control [7].

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVCr 51/2, $Na_2{}^{51}CrO_4$ in sterile isotonic NaCl solution

A sterile solution of $Na_2{}^{51}CrO_4$ in isotonic NaCl solution, meeting the following specifications:
Radioactive concentration, measured to within 10%: 0.5 mCi/ml.
Radioactive purity: ^{51}Cr content more than 99.9%.
Radiochemical purity: Na_2CrO_4 content more than 90%.
Specific activity: 20 mCi/mg.
Sterile

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COBALT-58

NUCLEAR DATA

1. NUCLEAR PROPERTIES

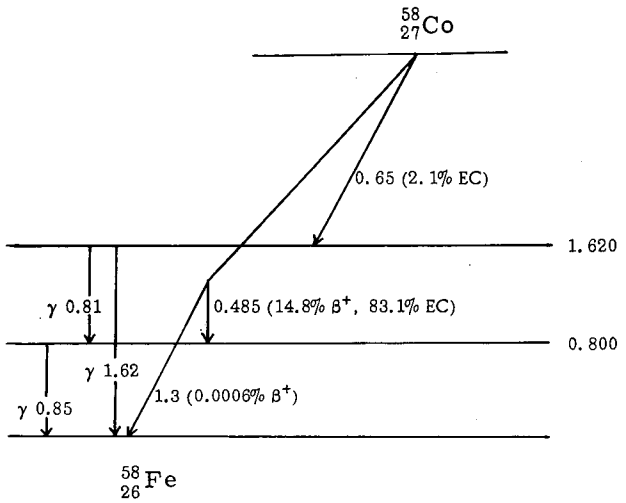
1.1. Half-life

72 d

1.2. Type of decay and energy (MeV)

EC	(85%)	gamma	2 γ-rays of annihilation energy 0.51
beta (β^+)	0.485 (14.8%)		0.805 (34%)
	1.3 (6.3×10^{-4}%)		0.810 (77%)
			1.62 (0.5%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm^2 s (mCi/g)			Secondary reactions and half-life of nuclide formed
			1 d	1 week	saturation	
$^{58}_{28}Ni(n,p)^{58}_{27}Co$	67.88	0.09 (f)	0.017	1	17	$^{58}_{28}Ni(n,\gamma)^{59}_{28}Ni$ (T = 7.5×10^4 yr) σ = 4.4 barn $^{58}_{28}Ni(n,\alpha)^{55}_{26}Fe$ (T = 2.6 yr) σ = 0.17 mbarn $^{60}_{28}Ni(n,p)^{60}_{27}Co$ (T = 5.27 yr) isot. abund.: 26.23% σ = ~ 5 mbarn $^{61}_{28}Ni(n,p)^{61}_{27}Co$ (T = 1.65 h) isot. abund.: 1.19% $^{62}_{28}Ni(n,\gamma)^{63}_{28}Ni$ (T = 120 yr) isot. abund.: 3.66% σ = 15 barn $^{62}_{28}Ni(n,\alpha)^{59}_{26}Fe$ (T = 45 d) σ = 0.002 mbarn $^{64}_{28}Ni(n,\gamma)^{65}_{28}Ni$ (T = 2.56 h) isot. abund.: 1.08% σ = 1.52 barn
$^{59}_{27}Co(n,2n)^{58}_{27}Co$	100%					

(f): for fast neutrons.
For nuclear data see Refs. [1,2].

The target normally used for the preparation of cobalt-58 is nickel oxide (NiO).

3. APPLICATIONS

3.1. Industrial

Absolute measurement of the activity of the ^{58}Co formed by the nuclear reaction $^{58}Ni(n,p)^{58}Co$ is used for determining fast neutron flux [4].

Cobalt-58 can be used as an internal standard in liquid scintillation or as a tracer in cobalt studies, for example to label the $[Co(Cn_6)]^{3-}$ used in hydrology [5].

General references on applications may be found in [6].

3.2. Medical and biological

Cobalt-58 is used for labelling vitamin B_{12} [7-12] utilized in studies of metabolism, especially for the diagnosis of pernicious anaemia. The dose administered is generally of the order of 0.5 μCi [7]. Other references on this subject are in [13].

4. RADIOLOGICAL PROTECTION

4.1. External exposure

4.1.1. Irradiation doses

The dose delivered by 1 Ci of ^{58}Co at a distance of 50 cm is 2.2 rem/h. [14, 15].

4.1.2. Safety measures

In Table I are shown tenth-thicknesses[1] for lead and ordinary concrete which give some idea of the amount of protection needed in handling ^{58}Co.

TABLE I

PROTECTION IN HANDLING ^{58}Co

	1/10 thickness (cm)	
	Pb	Ordinary concrete d = 2.3
For a γ of 0.81 MeV	2.4	15.0
For a γ of 1.6 MeV	4.1	22.5

In practice, the following thicknesses of lead are required to reduce the dose to 1 mR/h at 50 cm:

3.2 cm for handling 10 mCi of ^{58}Co
5.6 cm " " 100 mCi " "
8 cm " " 1 Ci " "

[1] The tenth-thickness is the thickness of shielding required to reduce the intensity of a γ-radiation of given energy by a factor of ten.

4.2. Internal irradiation

Cobalt-58 is classified as a moderately toxic (Category 3) isotope [17]. Its effective half-life, allowing for both radioactive decay and excretory processes, is 8.4 d [18].

In the case of internal irradiation (ingestion or inhalation), the maximum permissible concentrations in air and water, respectively, for a 40-h exposure, are:

8×10^{-7} μCi/cm^3 and 4×10^{-3} μCi/cm^3 (soluble form)
5×10^{-8} μCi/cm^3 and 3×10^{-3} μCi/cm^3 (insoluble form) [19]

4.3. Decontamination

Except in one or two particular cases, there is no special decontamination method for any given radioisotope. General texts on this subject [20-24] indicate that the following measures are adequate:

4.3.1. Skin

Rapid and repeated washing with good-quality soap, warm water and a soft brush. If this is not sufficient, use can be made of detergents or 5 - 10% solutions of complexing agents of the EDTA (ethylenediamine tetra-acetic acid) type. It is also possible to apply saturated permanganate solutions followed by rinsing with a 5% bisulphite solution to neutralize and remove stain. Abrasive powders should not be used and the addition of entraining agents has proved disappointing.

If any wounds are contaminated they must be treated rapidly by bleeding, washing with water, decontamination as for the skin and sometimes by additional surgical cleaning.

4.3.2. Hair

If the hair is contaminated, it is important not to take a shower, but merely to wash the head. A normal, good-quality shampoo is usually sufficient. If contamination is persistent, the following solutions can be used:

paraisopropylorthocresol
lavandin oil
AC compounded terpene-free lemon
glycerine diacetin
benzoic acid

Contamination is much easier to remove if the hair is not greasy.

4.3.3. Laboratory equipment

Glassware is usually cleaned by steeping and this is mainly a radiochemical problem. The use of a specific entraining agent or solutions of complexing agents gives good results and so do solutions of chromic acid, concentrated nitric acid, ammonium citrate, pentasodium triphosphate or ammonium bifluoride.

5. SUMMARY OF PRODUCTION METHODS

Cobalt-58 is generally prepared by the (n, p) reaction on nickel-58. The nickel target must be perfectly pure in order to avoid secondary nuclear reactions such as $^{59}Co(n, \gamma)^{60}Co$. (It can be purified before irradiation by passing it through anion resin to separate any cobalt-59 which may be present.)

The cobalt-58 formed can be separated from the target in two ways:

By ion-exchange on anion resin [25-29]. The irradiated NiO target is dissolved in 12 N hydrochloric acid or in aqua regia; in the latter case, the nitric acid is eliminated and one finishes in 12 N hydrochloric acid. This solution is passed through a Dowex 1X8 anion resin (previously treated with 12 N hydrochloric acid). The cobalt-58 is fixed, but not the nickel. The cobalt-58 is eluted with 4 N hydrochloric acid.

By solvent extraction [30, 31]. Extraction is performed using tributylphosphate starting with a solution of chlorides. To prepare carrier-free cobalt-58, however, it is necessary to purify quantities of nickel several times greater than the quantity of cobalt. In view of this, a single extraction under static conditions is not enough. To increase the separation efficiency, the semi-countercurrent method must be used. Levin, Golutvina, and Tikhominova, [31] show the layout of the extraction apparatus employed.

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PROCEDURES

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

Cobalt-58 is obtained by the reaction $^{58}Ni(n, p)^{58}Co$. At the same time radioactive nickel is formed by the reaction $^{62}Ni(n, \gamma)^{63}Ni$.

Carrier-free ^{58}Co is separated from a nickel target by passing chlorides in a hydrochloric solution over an anion resin which retains the cobalt in the form of a complex [1].

The equivalent nickel complex does not form under these conditions. Nickel-63 is recovered free of ^{58}Co.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 25 g of the nickel oxide is purified by passage over an anion resin; this eliminates the cobalt and iron which, under irradiation, would yield unwanted radioisotopes.
Irradiation: In a fast neutron flux of about 2×10^{12} n/cm^2 s for six months.
Yield: 100 mCi.

Chemical treatment

Preparation

The flowsheet for the preparation of ^{58}Co is shown in Fig. 1 and the apparatus used is shown in Fig. 2. The 25 g of irradiated nickel oxide are dissolved in 250 ml of aqua regia, which is introduced in stages.

The preparation is heated until complete dissolution.

The nitric acid is evaporated off, concentrated hydrochloric acid (50 ml) being added from time to time.

Fifty millilitres of concentrated hydrochloric acid are added at the end of the operation.

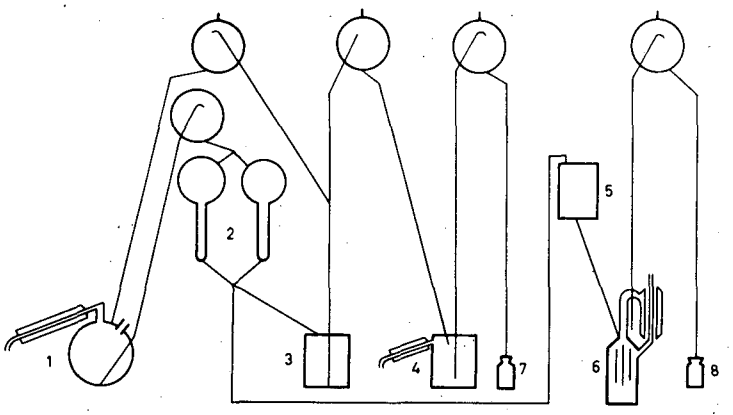


FIG. 1. ^{58}Co flowsheet
1. Dissolution flask
2. Resin columns
3. Measuring bottle
4. Ni evaporator
5. Co intermediate vessel
6. Co evaporator
7. Ni final vessel
8. Co final vessel

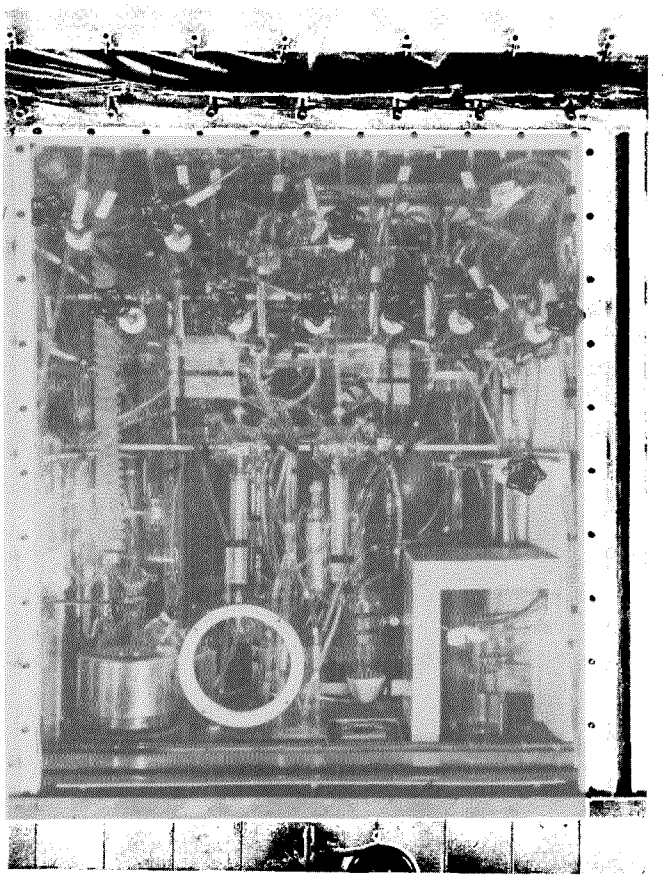


FIG. 2. Apparatus for the production of ^{58}Co

The solution is then passed over Dowex 1 X8 anion resin.

This fixes the ^{58}Co and any iron which may have been introduced as an impurity in the reagents (hydrochloric acid, nitric acid).

The nickel is not fixed.

One passage over the resin column is usually not enough to retain all the ^{58}Co.

By collecting the products passing out of the resin columns in an intermediate vessel and placing it over an ionization chamber, the γ activity present can be measured and the amount of ^{58}Co remaining in the nickel solution thus determined.

From the intermediate vessel, the solutions can either be returned to the dissolution apparatus to concentrate the nickel solutions contaminated with ^{58}Co, or placed in an evaporator to concentrate the pure ^{63}Ni solutions.

The ^{58}Co is diluted by 4 N hydrochloric acid (200 ml per column). This solution is passed into a ^{58}Co concentrator.

The resin columns are washed with doubly distilled water.

Apparatus

The nickel oxide is dissolved in a 1-litre flask placed in an electric heating jacket. The flask is surmounted by two male ground-glass ball-joints, one of which is capped with a condenser, and the other with a lead-lined plug for introducing the irradiated substances.

The resin columns are fitted with a siphon to prevent drying out of the resin. They are surmounted by a flask which acts as a reservoir.

The solutions are evaporated in a cylindrical receptacle filled with a condenser.

Lastly, there is an intermediate vessel to recover the nickel solutions after they have passed over the resins. It is placed over an ionization chamber to measure the residual γ-activity of the solution and is protected by a shield of lead bricks.

3. ASSAY AND QUALITY CONTROL

The ^{58}Co activity of two 1-ml samples is measured with an ionization chamber.

The percentage of ^{60}Co is measured by counting the 1.7 - 1.33 MeV lines in a gamma-spectrometer.

Finally the quantity of carrier cobalt in the solution is determined.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{58}Co - S

A carrier-free cobalt chloride hydrochloric solution containing less than 5% ^{60}Co.

Specific activity: > 10 000 Ci/g.

REFERENCE

[1] MELLISH, C.E., PAYNE, J.A., Production of carrier-free cobalt-58 by pile irradiation of nickel, Nature, London 178 4527 (1956) 275, 276.

CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production is based on the fast neutron-induced reaction on a nickel target; $^{58}Ni(n,p)^{58}Co$. To enhance the (n, p) process and decrease the effect of (n, γ) reactions, the target is covered with cadmium shielding. After irradiation separation is carried out with the aid of ion exchange.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Nickel oxide, Merck (analytical grade). Amount, depending on the request.
Flux:	2×10^{13} n/cm^2 s (th).
Time of irradiation:	80 h.
Container:	Quartz ampoule with ground stopper, wrapped in cadmium foil.

Chemical treatment

After irradiation the target is dissolved in concentrated hydrochloric acid and the solution is fed onto a column, filled with Dowex resin. The primary eluate contains the nickel activity. The elution of ^{58}Co from the resin is made by hydrochloric acid as eluting agent.

3. ASSAY AND QUALITY CONTROL

Radiochemical purity is controlled with the aid of a multichannel pulse height analyser. The pH is determined in the usual manner.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Radioactive purity: concentration of ^{60}Co <0.5%.
Specific activity: 2.2 mCi/g.

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Carrier-free cobalt-58 is produced by the irradiation of nickel. The activities produced are: $^{58}Ni(n, \gamma)^{59}Ni$, $^{58}Ni(n, p)^{58}Co$, $^{62}Ni(n, \gamma)^{63}Ni$ and $^{64}Ni(n, \gamma)^{65}Ni$. Nickel-59 is formed in very small amounts, while the short-lived ^{65}Ni decays rapidly.

The irradiated nickel is first converted to chloride and this chloride solution in 9 M HCl is passed down an anion exchange column. Cobalt-58 activity is retained while nickel passes down. The ^{58}Co is eluted out with 5 M HCl.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 10 g of spec-pure nickel metal (cobalt content less than 1 ppm).

Irradiation period: 6 months to 1 yr.

Chemical treatment

The irradiated nickel is dissolved in nitric and hydrochloric acids and the chloride is taken up in 9 M HCl. The solution is passed down a 50 cm $\times 1$ cm^2 column of Dowex-1 (chloride form, washed with 9 M HCl), where the ^{59}Co activity is retained and the nickel passes down. The column is washed free of all nickel with 9 M HCl and the ^{58}Co is eluted out with 5 M HCl. The eluate is concentrated and is further purified by passing down a second 30 cm $\times 1$ cm^2 anion exchange column. Finally the ^{58}Co in hydrochloric acid solution is concentrated, the organic impurities are destroyed by nitric acid and the ^{58}Co activity is taken up in 0.1 M HCl.

3. ASSAY AND QUALITY CONTROL

The radioactive concentration is determined either by ion current measurement in an ionization chamber or by gamma scintillation counting using a well-type sodium iodide crystal.

The acidity of the stock solution is determined by titration against 0.1 N NaOH solution.

The total solid content is determined by evaporating a known volume and weighing the residue.

The radionuclide is identified by the 0.81 MeV photo-peak.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity:	Carrier-free.
Chemical form:	Cobalt chloride in dilute hydrochloric acid.
Acidity:	0.1 M HCl.
Concentration:	1 - 5 mCi/ml.
Radiochemical and Radioactive purity:	Greater than 99%.
Percentage of ^{60}Co:	< 1%.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process of ^{58}Co is based on the irradiation of nickel oxide target, and the adsorption of ^{58}Co on the anion exchange resin in the form of chloride complex [1]. The elution of cobalt is carried out with 4 N HCl.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	20 g nickel oxide (NiO) purified from nickel chloride (JISGR) by anion exchange resin; practically free of cobalt.
Container:	Target is wrapped with aluminium foil and placed in the aluminium capsule.
Flux in JRR-I Fast:	1.5×10^{12} n/cm^2 s.
Flux in JRR-I Thermal:	1.3×10^{12} n/cm^2 s.

Chemical treatment

Dissolve the irradiated target in hydrochloric acid at the concentration of 9 N.
Pass through the anion exchange resin.
Wash the column with 9 N HCl.
Elute ^{58}Co with 4 N HCl.

3. ASSAY AND QUALITY CONTROL

The radiochemical analysis and assay are carried out by gamma spectrometry.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form: $CoCl_2$ in HCl solution; acidity is ~ 1 N.
Radiochemical purity: > 99%.
Specific activity: Carrier-free.

REFERENCE

[1] SHIKATA, C., SHIKATA, E., SHIBATA, N., Research of radioisotope production with fast neutrons; preparation of carrier-free Co^{58}, J. Atomic Energy Soc., Japan 4 (1962) 105.

JUNTA DE ENERGIA NUCLEAR, MADRID, SPAIN

1. GENERAL

The production process is based on the irradiation of nickel oxide target and the adsorption of cobalt chloride complex on an anion exchange resin. The elution of ^{58}Co from the resin is made with water [1].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 10 g nickel oxide (Ni_2O_3) of analytical grade quality.
Container: Aluminium container, 8×10 mm diam.
Flux: 4×10^{12} n/cm^2 s, next to the surface of the adjoining fuel elements (JEN-1).
Irradiation time: Five weeks, equivalent to 236 h of continuous operation at 1 MW.
Approximate yield is 12 mCi ^{58}Co with the specific activity of 1 Ci/mg Co.

Chemical treatment

Separation method

One week after it has been removed from the reactor, the target is put into solution with concentrated HCl. Evaporate the solution almost to dryness, and redissolve the residue in 50 ml of 7 N HCl.

Pass the solution through a Dowex-2-X8 100-200 mesh anion exchange resin column in chloride form equilibrated with 7 N HCl (125 g dry resin). Percolate the solution through the column at a rate of 0.5 ml/min.

Pass 250 ml of 7 N HCl and collect the effluent. Nickel is recovered from the effluent, re-oxidized, and again used for the irradiation.

Continue the elution with water. A total of 150 ml of the effluent is collected, then evaporated down to a few millilitres.

Apparatus

Cobalt-58 production is not performed regularly. Therefore no special apparatus has been provided.

3. ASSAY AND QUALITY CONTROL[1]

Determination of chemical purity is made by emission spectrometry.
Radioactive purity is determined by gamma spectrometry.
Activity measurements are made by ionization chamber.

4. CHARACTERISTICS OF THE FINAL SOLUTION

^{58}Co, cobalt chloride solution, non injectable

A carrier-free cobalt chloride solution in HCl.

Chemical purity:	Magnesium and iron in concentrations of less than 1 ppm are the only impurities which are occasionally detected. The cobalt content lies outside the sensitivity range of the method (0.5 ppm).
Radioactive purity:	^{58}Co content > 99.5%; no ^{60}Co is detected (^{60}Co < 1%).
Specific activity:	> 1 Ci/mg Co.

REFERENCE

[1] ANGOSO, M., Preparación de cobalto-58, Report JEN-DQ-Qr 0404/I-4.

THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Nickel metal is irradiated in a fast neutron flux, ^{58}Ni(n, p)^{58}Co. The processing is intended to separate carrier-free cobalt-58 as cobalt chloride.

[1] For details, see the Section on phosphorus-32 provided by the Junta de Energía Nuclear, Madrid, Spain.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Johnson Matthey spec-pure nickel rods.
Amount:	3 g.
Irradiation time:	2 - 3 months.
Container:	Aluminium tube.
Flux:	10^{13} n/cm^2 s.
Side reactions:	^{62}Ni(n, γ)^{63}Ni
	^{59}Co (impurity) n, γ ^{60}Co.

Chemical treatment

The nickel rod is dissolved in 9 N hydrochloric acid. The solution is passed down a column of anion exchange resin in the chloride form and saturated with 9 N HCl. The column is washed repeatedly with 9 N HCl until free of nickel. Carrier-free cobalt is eluted with 4 N HCl. The latter solution may still contain some nickel in which case the separation in 9 N HCl is repeated.

3. ASSAY AND QUALITY CONTROL

Identification by γ-spectrometry; assay by scintillation counting against a ^{137}Cs reference.
Cobalt element by emission spectrometry.
Cobalt-60 by coincidence counting (0.1% at the start of shelf life of new stock).

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Cobalt-58 is produced by (n, p) transmutation in a nickel target, ^{58}Ni(n, p)^{58}Co. About 5% ^{60}Co is also made by an (n, γ) reaction. In processing, the target is converted to chloride form and purified from Ni by ion exchange. After organic residues are removed with HNO_3, $^{58}CoCl_2$ is prepared as product.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	1 g nickel metal.
Neutron flux:	2×10^{14} n/cm^2 s.

Irradiation time: 1 yr.
Reactor yield: 400 mCi.

Chemical treatment

Apparatus

A hot off-gas scrubber unit[1] and 70-ml ion exchange column (Fig. 1) are used in the chemical processing of ^{58}Co.

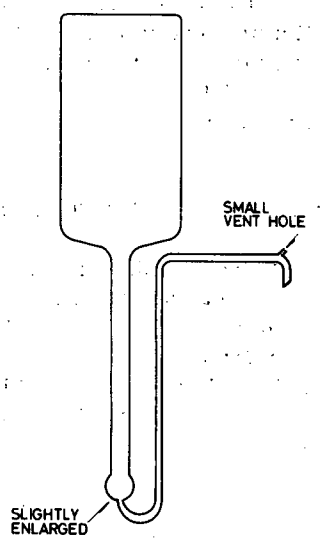


FIG. 1. Ion exchange column with head vessel

Processing

Yield: > 95%.

The irradiated target is washed into an evaporation dish with 12 M HCl, and heated under the hot off-gas scrubber assembly to dissolve NiO. The resulting $NiCl_2 \cdot 6\,H_2O$ crystals are dissolved in 12 M HCl. (Approximately 100 ml of 12 M HCl are used per gram of nickel; heat is used if necessary to produce a clear solution.) The $NiCl_2$ solution is evaporated to dryness and fumed with 12 M HCl. Care is taken to avoid converting chloride to oxide. A Dowex-1 resin column is prepared for ^{58}Co separation with 100-mesh resin, conditioned with 12 M HCl. Resin volume is ~70 ml/g nickel in solution. The solution is passed through the resin column, and the column rinsed with three column volumes to elute the nickel completely. Cobalt-58 remains on the column. The ion exchange column is then eluted with distilled H_2O and the effluent checked for ^{58}Co activity to determine the efficiency of removal from the column. The effluent is collected in a beaker and evaporated to near dryness under the hot off-gas scrubber assembly. The residue is formed with 16 M HNO_3 to destroy the organic compound and then with 12 M

[1] See Fig. 2 in the section on ^{82}Br provided by the Oak Ridge National Laboratory, Tenn., United States of America.

HCl to remove nitric acid. The resulting compound is dissolved in 50 ml of 1 M HCl.

3. ASSAY AND QUALITY CONTROL

A sample is analysed for molarity of HCl, ^{58}Co concentration, radiochemical purity, and total solids according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733601.

The precision and accuracy of the ^{58}Co assay are:
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 10%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, carrier-free ^{58}Co is delivered in the form of $CoCl_2$ in HCl solution as a stock item. Other specifications of interest are:

Acidity:	1 N ± 50%.
Concentration:	> 1 mCi/ml.
Total solids:	< 10 mg/mCi.
Radiochemical purity:	> 98%, exclusive of ^{60}Co.
^{60}Co:	< 5%.

COPPER-64

NUCLEAR DATA

1. NUCLEAR PROPERTIES

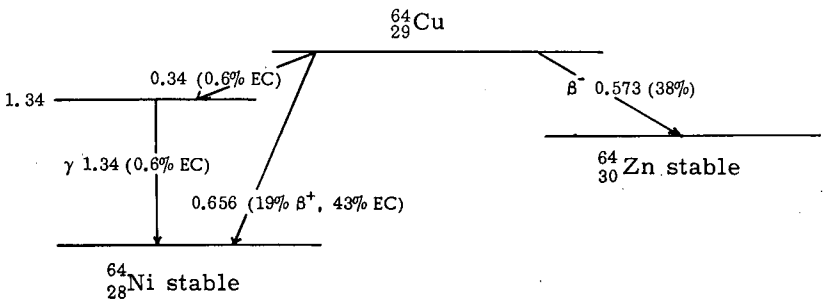
1.1. Half-life

12.8 h

1.2. Type of decay and energy (MeV)

beta (β^-)	0.573 (38%)	gamma from β^+	0.51 (annihilation)
beta (β^+)	0.656 (19%)	gamma from EC	1.34 (0.6%)
EC	(43%)		

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm^2 s (mCi/g)			Secondary reactions and half-life of nuclide formed
			1 h	24 h	sat.	
$^{63}Cu(n,\gamma)^{64}Cu$	69.09	4.3 (th)	40.5	555	764	$^{65}Cu(n,\gamma)^{66}Cu$ (T = 5.1 min) isot. abund.: 30.9% σ = 2.2 barn
$^{64}Zn(n,p)^{64}Cu$	48.89	0.035 (f)	2.3	31.2	43	$^{64}Zn(n,\gamma)^{65}Zn$ (T = 245 d) isot. abund.: 48.9% σ = 0.44 barn $^{68}Zn(n,\gamma)^{69m}Zn$, ^{69}Zn (T = 13.9 h, 55 min) σ = 97 millibarn, 1.0 barn

For nuclear data see Refs. [1-5].
(th) = thermal neutrons.
(f) = fission spectrum neutrons.

3. APPLICATIONS

Copper-64 is the most extensively used and is the only practical radioisotope of copper. Its relatively short half-life presents some limitations. The longer-lived ^{67}Cu ($T_{\frac{1}{2}}$ = 58 h) is difficult to produce, requiring a cyclotron for the $^{67}Zn(d, 2p)^{67}Cu$ reaction.

3.1. Chemistry

Determination of diffusion coefficients	[6]
Hot atom chemistry studies	[7-12]

3.2. Biochemistry and biology

Enzymological studies	[13]
Haematological studies	[14]
Microdetermination of proteins	[15]
Study of blood serum proteins	[16, 17]

3.3. Medicine

Study of the Wilson's disease	[18]
Diagnosis and therapy	[19-21]
Experimental tropical medicine	[22]

3.4. Hydro-metallurgy

Study of minerals	[23, 24]
Investigation of flotation processes	[25]

3.5. Food industry [26]

4. RADIOLOGICAL PROTECTION

4.1. External irradiation

Copper-64 is an emitter of mixed radiation. The dose-rate of 1 mCi activity at 1 cm is 1.19 R/h [27]. Activities up to 50 mCi (maximum permissible dose: 16 mR/6-h working day) can be safely handled, using a 20-mm-thick lead shield.

4.2. Internal radiation

Copper-64 is classified [28] as a class 3 (moderate toxicity) isotope and has an effective half-life of 0.53 d [29]. Critical organs: spleen, gastro-intestines. Maximum permissible amount in whole body, 10 μCi.

Maximum permissible concentration, $\mu Ci/cm^3$ [30]:

	In water	In air
Soluble	0.01	2×10^{-6}
Insoluble	6×10^{-3}	10^{-6}

4.3. Decontamination

Contamination from ^{64}Cu (II) compounds can be satisfactorily removed by ammonia-water solution in which the copper ions combine to form complexes which are easier to remove from surfaces.

5. SUMMARY OF PRODUCTION METHODS

The production process is generally based on the reaction $^{63}Cu(n, \gamma)^{64}Cu$. After irradiation, Szilard-Chalmers enrichment of ^{64}Cu may be employed. If a carrier-free preparation is desired, the $^{64}Zn(n, p)^{64}Cu$ reaction must be used. The production processes can be classified according to the nuclear reaction employed.

5.1. Chemical processes using the (n, γ) reaction

5.1.1. Targets for production without enrichment

The target material is usually Cu metal or CuO, and the product is prepared by dissolution of the irradiated target, e.g. in nitric acid.

5.1.2. Concentration of ^{64}Cu by the Szilard-Chalmers method

Processes reported to date differ, depending on the chemical form of the target used.

From a solution of irradiated copper-8-hydroxy-quinoline in an organic solvent only about 10% of the ^{64}Cu can be recovered by aqueous solvent extraction [31].

After irradiating a solution of copper salicyl-aldehyde o-phenylendicinin in pyridine, 80% of the ^{64}Cu can be separated in the form of copper sulphide with an enrichment factor of about 10^4 [7].

From irradiated dissolved copper phthalocyanine dissolved in concentrated sulphuric acid, phthalocyanine precipitates upon dilution, while ^{64}Cu is retained by the solution [8]. After irradiating Cu-phthalocyanine powder, the ^{64}Cu can be extracted in boiling dilute H_2SO_4 [9-11]. The method, combined with ion exchange separation, yields specific activities up to 50 mCi/mg [12]. An electrolytic purification procedure for the concentration of ^{64}Cu with an enrichment factor of 500-1000 and with elimination of organic radiolytic decomposition products has also been proposed [32].

5.2. Chemical processes using the $^{64}Zn(n, p)^{64}Cu$ reaction

The most commonly used method is to irradiate Zn metal (less frequently $ZnCl_2$) and to dissolve the metal in mineral acid. Copper-64 is then separated from the solution by precipitation, electrochemical, ion exchange or extraction techniques.

5.2.1. Co-precipitation

By the dissolution of irradiated Zn powder, e.g., in hydrochloric acid, and the addition of a small amount of carrier, copper can be precipitated in the form of CuS [33].

Copper-64 can be also co-precipitated from the aqueous solution of $ZnSO_4$ with freshly prepared Bi_2S_3. The precipitate is then dissolved in HNO_3 and the bismuth carrier can be separated in $NH_4(OH)$ [34].

If the irradiated Zn is not dissolved wholly in concentrated hydrochloric acid solution, the copper isotope is retained almost to 100% and the undissolved filtered residue yields a solution with higher Cu concentration [35].

5.2.2. Electrochemical separation

Cu is deposited on metallic surfaces of zinc or lead plates [33, 36] or hydrogen-saturated Pt foils [35] immersed in the solution containing the copper isotope. The copper isotope can be separated from the dissolved target material by electrolytic deposition on cathodes made of various metals (e.g. Cu, Mo, Pt, W, etc.) [35-38].

The lengthy procedure of the electrolytic separation can be shortened, its efficiency improved and a single step separation of the copper isotope from concentrated zinc salt solution is made possible by the use of a special electrolyser [39]. The essential feature of the device is the large surface

cathode consisting of small Pt wire rings introduced into a glass tube similar in design to a chromatographic column. The solution flowing downwards in the column and gradually decreasing in Cu concentration continuously encounters fresh electrode surfaces.

5.2.3. Solvent extraction and ion-exchange

Copper isotope can be extracted from aqueous zinc chloride-hydrochloric acid solution with a carbon tetrachloride solution of dithizone [40]. Copper can be separated from zinc by adsorption on a cation exchange resin from a solution containing chloride ions (e.g. in the form of hydrochloric acid or lithium chloride) [41, 42].

6. RADIOASSAY

The activity of the prepared samples is usually measured in an ionization chamber and radiochemical purity can be checked by γ-spectrometry (Part I, Section 6).

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PROCEDURES

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

Copper-64 is prepared from a copper phthalocyanine target, $^{63}Cu(n,\gamma)^{64}Cu$. The ^{64}Cu, enriched by the Szilard-Chalmers effect, is separated by dissolving the phthalocyanine in concentrated sulphuric acid, reprecipitating with water and then filtering [1, 2].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Copper phthalocyanine, purified by dissolution in sulphuric acid, reprecipitation with water and then washing with distilled water to eliminate free copper.
Irradiation conditions:	5 g at a flux of 2×10^{12} n/cm^2 s for 1 week in El2, or 1 g for 72 h at a flux of 10^{13} n/cm^2 s in EL3. In this way, 50 mCi of ^{64}Cu are obtained 30 h after unloading with a specific activity of about 50 mCi/mg.

Chemical treatment

Preparation

The irradiated copper phthalocyanine is poured onto the fritted plate of a filter apparatus. To bring the phthalocyanine into solution 12 ml of concentrated sulphuric acid are then added, pressure being raised slightly above atmospheric by the application of compressed air below the fritted plate. The phthalocyanine is then reprecipitated by the addition of water. The solution is filtered and passed into a dilution vessel, where it is diluted with 1 litre of water before being passed over a Dowex 50 (X8 120 mesh) resin column. The Cu^{++} is fixed on the resin and the sulphuric acid solution is discharged.

The Cu is washed with 100 ml of water and then eluted with a 4 N solution of hydrochloric acid which is collected in an evaporator. It is evaporated down to about 1 ml and made up with 20 ml of water.

Apparatus

Solution, precipitation and filtration of the phthalocyanine are carried out in the same filtration apparatus. The flowsheet is shown in Fig. 1.

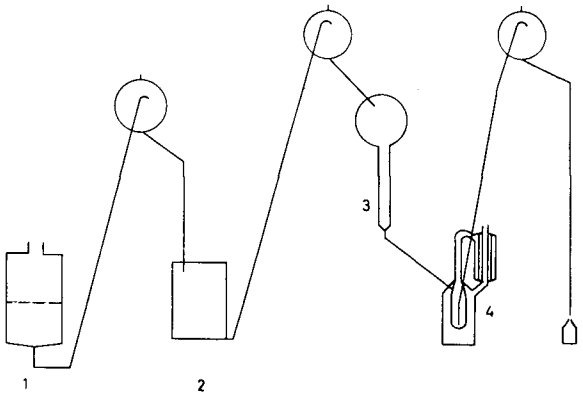

FIG. 1. ^{64}Cu flowsheet
1. Precipitation and filtration bottle
2. Dilution bottle
3. Resin column
4. Evaporator
5. Distribution bottle

This is a cylindrical apparatus closed at the top by a male joint capped by a female joint, weighted with lead.

At each side are two inlets for reagents.

About half way along a fritted glass is welded in. Above the fritted glass, in the sides of the vessel, are two lateral ports for pressurizing or evacuating, i. e. enabling either bubbling or filtration to be carried out.

Dilution is carried out in a cylindrical vessel of 1500 ml capacity placed in a magnetic agitator. The solution is then passed over a column 16 mm in diameter, terminated by a capillary tube siphon to prevent the desiccation of the resin and surmounted by a 500-ml capacity reservoir.

The solution is collected in an evaporator with a heating jacket containing cyclohexanol.

3. ASSAY AND QUALITY CONTROL

Two 1-ml samples are counted in an ionization chamber, and subjected to a gamma spectrometry test for radiochemical purity and to a test for determination of the carrier copper.

Finally, biological tests are applied to establish the non-toxicity and sterility of the product.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{64}Cu S - Injectable

An aqueous, isotonic, pyrogen-free solution of copper chloride, pH 5, meeting the following specifications:
Radioactive concentration, measured to within 5%: 0.5 - 5 mCi/ml
Radioactive purity: ^{64}Cu content > 99.9%

Specific activity: Above 20 mCi/mg
Sterile
Pyrogen-free
Isotonic

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HUNGARIAN INSTITUTE OF ISOTOPES,
NATIONAL ATOMIC ENERGY COMMISSION,
BUDAPEST, HUNGARY

1. GENERAL

Production of ^{64}Cu is based on fast neutron-induced reaction on a zinc target. To decrease the thermal neutron flux which causes the (n, γ) reaction of the zinc target, the target is wrapped with a cadmium foil. The separation of carrier-free ^{64}Cu, which is present in relatively large amounts, is carried out by an electrolytic process.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Zinc oxide, Merck (analytical grade), amount of target depending on the request.
Flux:	2×10^{13} n/cm^2 s (th).
Time of irradiation:	24 h.
Container:	Quartz ampoule with ground stopper wrapped in a cadmium foil.

Chemical treatment

The irradiated zinc oxide is dissolved in sulphuric acid, the pH of the solution being strictly adjusted afterwards. The device for carrying out electrolytic separation of carrier-free ^{64}Cu from irradiated zinc consists of a column filled with platinum (Fig. 1). Before electrolysis, hydrochloric acid is fed into the column and polarized for a period of 5 min.

After washing through the column with nitric acid and zinc sulphate solution, the active zinc sulphate is continuously fed, and the electrolytic se-

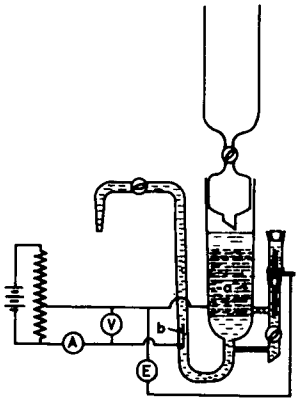

FIG.1. Apparatus for electrolytical deposition of carrier-free samples
a. Pt-packing coupled as cathode
b. Pt-anode

paration is begun by adjustment of potential. After having fed the active solution, hydrochloric acid is added, the flow of inlet and outlet is shut down, the poles are interchanged and the current is adjusted to the value needed. Five minutes later the stopcock at the bottom is opened and the solution is allowed to flow out. The solution collected in such a manner contains about 90% of the ^{64}Cu produced, practically without contamination. The solution is evaporated to dryness, then the desired solution is prepared by adding the corresponding acid.

3. ASSAY AND QUALITY CONTROL

The pH is determined from aliquot samples; radiochemical purity is checked by a multichannel pulse height analyser. In the case of products for medical use pharmaceutical control is carried out regarding sterility.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Radioactive concentration: Copper chloride, 0.1 mCi/ml.
Radioactive purity: > 99.5%.
Specific activity: Carrier free.

^{64}Cu produced by $^{63}Cu(n, \gamma)^{64}Cu$ reaction

Radiochemical purity: > 99%.
Specific activity: ~ 390 mCi/g for $CuSO_4$, ~470 mCi/g for $CuCl_2$, ~ 1000 mCi/g for Cu.
Chemical form: Copper metal.
Copper chloride: Greenish-blue transparent 0.1 N solution.
Copper sulphate: Greenish-blue transparent 0.1 N solution.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

Production is based on the irradiation of copper metal shavings. The irradiated target is dissolved in hydrochloric acid with subsequent treatment for the adjustment of acidity.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 1.0 g copper shaving metal (99.9% purity) for JRR-1.
0.2 g for JRR-2.

Container: Placed in a polyethylene bottle, then in a polyethylene capsule.

Flux: $\sim 4\times10^{11}$ n/cm^2 s (JRR-1 pneumatic tube).
$\sim 2\times10^{13}$ n/cm^2 s (JRR-2 pneumatic tube).

Irradiation time: 2 h for JRR-1.
20 min for JRR-2.

Chemical treatment

The irradiated target is dissolved in the concentrated hydrochloric acid and hydrogen peroxide, evaporated to dryness, then redissolved in 1 N HCl. The apparatus is shown in Fig. 1.

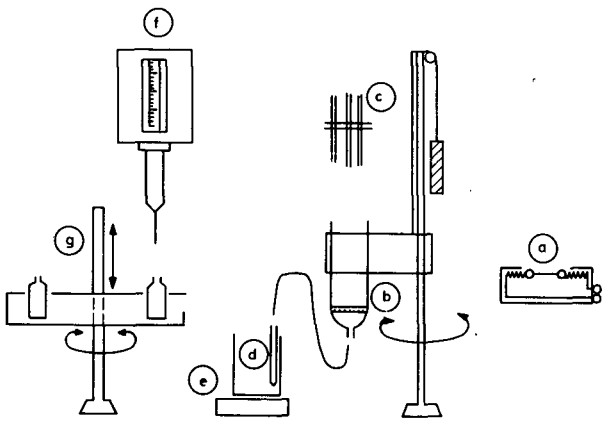

FIG.1. Apparatus for ^{64}Cu production

a. Electric polyethylene capsule cutter
b. Dissolving vessel
c. Reagent feed pipes
d. Receiver
e. Electric heater
f. Remote pipetter for dispensing
g. Turret of bottles

Cut the polyethylene inner capsule with electric cutter (a).

Place the target in the dissolving vessel (b) with the glass filter bottom, then add 2 - 3 ml concentrated HCl and about 3 drops of 30% H_2O_2 from the reagent feed pipe (c) to dissolve the target.

Transfer the dissolved solution to the receiver (d).

Repeat the procedures (b) and (c) until the target is completely dissolved.

Evaporate the solution to dryness by the heater (e).

Dissolve the residue by the following reagent:

~ 8 ml ~ 1 N HCl/g of target (in production with JRR-1).

~ 300 ml ~ 1 N HCl/g of target (in production with JRR-2).

Distribute the product solution into the sample bottles by the remote control burette.

3. ASSAY AND QUALITY CONTROL

Routine assay of the product is made by the well-type ionization chamber. The amount of carrier is calculated from the weight of the target. Acidity is determined by titration or by potentiometric titration.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	$CuCl_2$ in HCl solution, acidity ~ 1 N.
Radiochemical purity:	> 99%.
Specific activity:	~ 8 mCi/g of Cu (JRR-1 product).
	~ 130 mCi/g of Cu (JRR-2 product).
Concentration:	~ 1.0 mCi/ml (JRR-1 product).
	~ 1.0 mCi/ml (JRR-2 product).

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Copper is irradiated in the form of cupric oxide, CuO, in a thermal neutron flux, $^{63}Cu(n, \gamma)^{64}Cu$. After irradiation the oxide is dissolved in hydrochloric acid to give a cupric chloride solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	100 mg CuO, spec-pure, Johnson, Matthey & Co.
Time of irradiation:	1 d.
Container:	Aluminium can with a sealed polyethylene inner container.
Flux:	Ab. 10^{12} n/cm^2 s.
Side reactions:	Effects of side reactions are considered negligible.

Chemical treatment

The irradiated target material is treated with concentrated hydrochloric acid. The resulting chloride solution is evaporated to dryness and the residue dissolved in water.

3. ASSAY AND QUALITY CONTROL

Radioactivity, ionization chamber measurements.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control, emission spectrography.

4. CHARACTERISTICS OF THE FINAL SOLUTION

CU-copper chloride in weak HCl solution.

Radioactive concentration:	1.5 - 2 mCi/ml.
Isotopic purity:	99%.
Specific activity:	200 mCi/g Cu.
pH:	3 - 4.
Chemical purity:	Metals, spectrographically determined (except Cu), less than 10 μg/ml.

THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Copper in the form of copper oxide is irradiated in a thermal neutron flux. The reaction is $^{63}Cu(n, \gamma)^{64}Cu$. The copper oxide is converted into chloride or other chemical forms as required.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Johnson Matthey spec-pure CuO.
Amount:	Up to 0.5 g.
Irradiation time:	2 - 3 d.
Container:	Screw-top aluminium container
Flux:	10^{12} n/cm^2 s.
Side reactions:	Do not interfere.

Chemical treatment

The target is dissolved in 6 N HCl, the solution evaporated to dryness and dissolved in water.

3. ASSAY AND QUALITY CONTROL

Scintillation count against ^{137}Cs reference. Identity by γ-spectrometry. pH by Capillator.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Copper-64 is produced by the (n, γ) reaction in a copper metal target, $^{63}Cu(n, \gamma)^{64}Cu$, and is prepared as $Cu(NO_3)_2$ in HNO_3 solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	10 mg copper metal.
Neutron flux:	2×10^{14} n/cm^2 s.
Irradiation time:	40 h.
Reactor yield:	850 mCi.

Chemical treatment

Apparatus

A hot off-gas scrubber unit[1] is used in processing.

Processing

Yield: > 95%.

The irradiated copper target is dissolved in about 3.5 ml of 16 M HNO_3 under a hot off-gas scrubber unit. The volume of the product is adjusted to 50 ml of 1 M HNO_3 to form a clear blue solution.

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[1] See Fig. 2 in the section on ^{82}Br provided by the Oak Ridge National Laboratory, Tenn., United States of America.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for molarity of HNO_3, total solids, ^{64}Cu concentration, and radiochemical purity according to ORNL Master Analytical Manual (TID-7012), procedure No. 9 0733231.

The precision and accuracy of the ^{64}Cu assay are:
Calibration by windowless 2π proportional counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 5%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity ^{64}Cu is delivered in the form of $Cu(NO_3)_2$ in HNO_3 solution as a stock item. Other specifications of interest are:

Acidity:	1 N ± 50%.
Concentration:	> 10 mCi/ml.
Specific activity:	≅ 25 000 mCi/g of Cu.
Radiochemical purity:	> 98%.

FLUORINE-18

NUCLEAR DATA

1. NUCLEAR PROPERTIES

All nuclear data are taken from Nuclear Data Sheets, except where later values were published, in which case the reference is given.

1.1. Half-life [1, 2, 45]

109.7 min

1.2. Type of decay and particle energy [3-6]

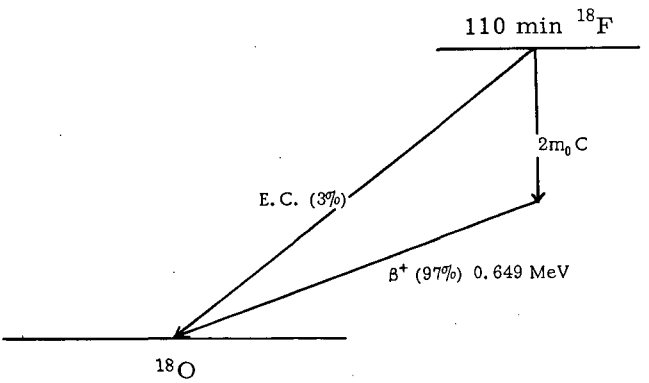
Fluorine-18 decays by positron emission (97%)

$E_{max}(\beta^+)$ = 0.635 ± 0.015 MeV
0.649 ± 0.009

and by electron capture (3%)

E.C./β^+ = 0.030 ± 0.002

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTIONS

Reaction	Abundance of target nuclide (%)	Cross-section	Specific activity produced in target mg/g Li_2CO_3 at thermal flux of 10^{13} n/cm² s 1 h 6 h sat.	Side reactions	Ref.
$^{6}Li(n,\alpha)t$ followed by $^{16}O(t,p)^{18}F$	7.42 99.76	950 barn 100 mb (2.7 MeV triton)	1.1 3.3 3.7	$^{23}N(n,\gamma)^{24}Na$ $T_{\frac{1}{2}}$ = 15 h	[7,8]
$^{18}O(p,n)^{18}F$	0.20	250 mb			[9,10]
$^{19}F(n,2n)^{18}F$	100				[11]

3. APPLICATIONS

Fluorine-18 is the only convenient radioisotope of fluorine for tracer studies, because of its comparatively long half-life, ~ 110 min. Compounds labelled with ^{18}F are useful in biological and chemical systems. A survey of applications published in the literature is given below.

3.1. Biochemistry and biology

Chemical exchange reactions of organic fluoroderivatives [12-14]
Distribution of ^{18}F in various biological systems [15, 16]

3.2. Medicine

^{18}F for brain tumour localization [17-19]
^{18}F in thyroid physiology studies [20, 21]
Use of ^{18}F in bone survey [19, 21, 22]
Fluorine in dental studies [23-25]

3.3. Analytical and physical chemistry

Determination of oxygen in various systems [26, 27]
Quantitative kinetic studies of fluorine exchange reactions [28-30]
Model for UO_2 diffusion process [31]

3.4. Plant metabolism

Metabolic properties of various materials [32, 33]

4. RADIOLOGICAL PROTECTION

The brief summary given below should be read in conjunction with Safe Handling of Radioisotopes, Safety Series No. 1, published by the International Atomic Energy Agency.

4. 1. External irradiation

Fluorine-18 is practically a pure positron emitter. The maximum range of its 0. 65-MeV positron is 300 mg/cm^2. On annihilation of the positron two gamma rays of 0. 511 MeV are emitted in opposite directions.

One and a half inches of lead for shielding are required as a protection from annihilation radiation and hard gamma rays of ^{24}Na impurities present at the production stage.

4. 2. Internal radiation

Fluorine-18 is classified as a class 4 (slightly toxic) isotope. The maximum permissible concentration (MPC) of ^{18}F in air and in water for occupational exposure is summarized in Table I.

TABLE I

MAXIMUM PERMISSIBLE CONCENTRATION

Critical body organ	Soluble or Insoluble	Maximum permissible concentration			
		40-h week		168-h week	
		$(MPC)_w$ $\mu Ci/cm^3$	$(MPC)_a$ $\mu Ci/cm^3$	$(MPC)_w$ $\mu Ci/cm^3$	$(MPC)_a$ $\mu Ci/cm^3$
Gastrointestinal tract Small intestine	Soluble	0. 02	5×10^{-6}	8×10^{-3}	2×10^{-6}
Gastrointestinal tract Upper large intestine	Insoluble	0. 01	3×10^{-6}	5×10^{-3}	9×10^{-7}

Precautions should be taken also against tritium contamination accompanying ^{18}F when produced in Li containing compounds.

5. SURVEY OF PRODUCTION METHODS

Fluorine-18 may be produced by several nuclear reactions. The common method of production is the sequence of reactions Li(n, t)^{4}He and ^{16}O(t, p)^{18}F,

which may yield carrier-free ^{18}F. The $^{19}F(n, 2n)^{18}F$ and $^{19}F(\gamma, n)^{18}F$ reactions can be utilized for ^{18}F production only when copious fluxes of energetic neutrons are available.

The production processes reported to date can be classified according to the chemical form of the targets and the nature of the processing procedures.

5.1. Targets

5.1.1. Fluorine-containing targets undergo the $^{19}F(\gamma, n)$ and $^{19}F(n, 2n)$ reactions

Targets include:

HF, KHF_2 or any other inorganic fluorine compound	[28, 35]
Fluoroorganic compounds, such as Teflon [43]	[34, 42]

5.1.2. Lithium- and oxygen-containing substances which undergo successively $Li(n, t)^4He$ and $^{16}O(t, n)^{18}F$ reactions

Due to the short range of the tritons, it is a prerequisite to have the lithium and oxygen intimately mixed as fine powder or in a solution or preferably to have both in one chemical species. The presence of atoms other than ^6Li and ^{16}O should be kept as low as possible to avoid attenuation of the effective flux of tritons. Targets include:

Inorganic lithium salts, such as $LiNO_3$, Li_2CO_3, $LiAlO_2$, $LiF + Al_2O_3$, Li_2O, or LiOH. Lithium carbonate is advantageous as a target because of its high thermal stability, high chemical purity and its good yields [35, 36, 41, 44].

Organic materials containing both lithium and oxygen, such as lithium salts of oxygen-containing acids. Organic compounds may be labelled with ^{18}F by recoil even if they do not include lithium or oxygen in the molecule by dissolving them in hydrogen-free lithium salt, such as LiCNO [34, 39].

The lithium target is either natural (7.5% ^6Li) or enriched (> 90% ^6Li) [41, 44]. The reaction $^{16}O(t, n)^{18}F$ being a secondary reaction is more susceptible to contamination. The main contaminants are isotopes of Cl, Br and Na, which are present as impurities in the lithium compound. Target purification may be achieved by melting and recrystallization of solids or distillation of liquids, or alternatively, by chromatographic columns, [35, 38, 41]. Tritium activity is also present due to triton formation in the primary reaction.

5.2. Chemical processes

The following is a brief description of the separation and purification processes reported in the literature.

5.2.1. Dissolution of target

Lithium nitrate or organo-lithium compounds may be dissolved in water [34, 36, 39]. Lithium carbonate targets are dissolved in nitric [36, 38] acid, or in concentrated hydrochloric acid [37, 38, 40, 41].

5.2.2. Separation of fluorine

The separation of fluorine may be classified according to the chemical process involved. These are coprecipitation, chromatographic adsorption, or distillation.

Fluorine is precipitated by the following methods:

5.2.2.1. Precipitation

A precipitate of PbClF is obtained from a solution of KF and lead acetate on the addition of concentrated HCl [36].

Fluorine may be carried as $Ca(OH)_2 . CaF_2$ coprecipitate, formed by the addition of calcium hydroxide to the dissolved target material [36, 38].

A $Ca_3(PO_4)_2 . CaF_2$ coprecipitate may be formed by the addition of H_3PO_4 and calcium carbonate followed by neutralization [18, 37].

5.2.2.2. Chromatographic adsorption

Carrier-free ^{18}F in acidic solution may be adsorbed on a Woelm alumina column conditioned by washing with 0.1 N NaOH and water. Sodium-24 and chloride or bromide impurities are removed in this high selectivity separation. Adsorption is followed by washing with 30 ml H_2O containing one drop of concentrated hydrochloric acid [41, 40] or by washing with a small volume of NaCl followed by another washing with water.

The fluorine activity is eluted either with a NaF solution, or with NaOH if a carrier-free solution is desired. Elution yields are 80-90% [39-41].

Fluorine-18 may also be adsorbed on a magnesium oxide adsorption column; the ^{18}F is totally retained in the column by the formation of magnesium fluoride. The major drawback of this procedure is the difficulty in re-obtaining the fluorine in solution [39].

5.2.2.3. Distillation

The lithium carbonate target is dissolved in 1:1 sulphuric acid and carrier-free ^{18}F may be distilled and collected in a slightly alkaline solution. A chemical yield of 70% is reported [44].

5.2.3. Preparation of final product

(a) PbClF precipitate is dissolved in a 25% NaOH solution. Lead is removed as the sulphate by precipitation with 10% sulphuric acid. The supernate after decantation is made alkaline with aqueous KOH to constitute the final product [36].

(b) Fluorine-18, coprecipitated as $Ca(OH)_2CaF_2$, is recovered and purified by two methods.

The calcium hydroxide is dissolved in acetic acid and separated by centrifugation. The calcium fluoride is then dissolved in a strong acid, diluted and passed through a suitable ion exchange column into a potassium hydroxide solution. Overall yields of 80 to 85% are reported [36].

The $Ca(OH)_2CaF_2$ precipitate is washed and dissolved in concentrated sulphuric acid; ^{18}F is carried over a preheated, steam-saturated, nitrogen gas flow, and adsorbed in 0.1 N sodium hydroxide. In this procedure 7 - 8 mCi ^{18}F/g irradiated target are obtained [38].

(c) Fluorine-18, coprecipitated with calcium phosphate, is purified by the following procedures:

The precipitate is washed with water and dissolved in 6 N hydrochloric acid. The solution is diluted, neutralized, and prepared as an isotonic solution, neutralized, to constitute the final product. Radiochemical purity is one part in a hundred thousand [36].

The precipitate is dissolved in 1 : 1 hydrochloric acid. A 25% solution of potassium bicarbonate is added until precipitation begins. The $Ca(OH)_2CaF_2$ precipitate is centrifuged and washed with water. The final product is prepared by redissolving the precipitate in 1 : 1 hydrochloric acid [18].

(d) Carrier-free ^{18}F solutions prepared by alumina adsorption are further purified as follows:

Cations are removed from the solution using a cation exchange column in acid form. In this procedure some ^{18}F is lost on the column. This may be removed completely by adding small amounts of NaF to the alkaline solution before adsorption. This procedure gives carrier solutions [39].

The alkaline solution is distilled from concentrated sulphuric acid and collected in dilute sodium hydroxide. Carrier-free $Na^{18}F$ of 99.99% radiochemical purity is obtained [41].

(e) Fluorine-18 adsorbed on magnesium oxide is recovered by dissolving the oxide in an acid. Magnesium ions are removed by adsorption on a cationic resin [38].

5.2.4. Preparation of labelled compounds

Two general procedures for the production of ^{18}F-labelled compounds are commonly used.

(a) Isotopic exchange between carrier-free ^{18}F and fluorine-containing substances. For example, labelled potassium fluoroborate is prepared by adding KBF_4 into a ^{18}F carrier-free solution at pH 1, heating for two minutes to 100°C, cooling and neutralizing with sodium bicarbonate to pH 5 [18, 34].

(b) Direct production of ^{18}F-labelled organic compounds by the $^{16}O(t, n)^{18}F$ or $^{19}F(n, 2n)^{18}F$ reactions as mentioned above. The hot fluorine-18 atoms produced substitute hydrogen on carbon. This method may also be used for

labelling fluoro derivatives. The labelling yield of these reactions is proportioned to the number of hydrogens or substituted fluorine available for the appropriate reactions [34].

6. RADIOASSAY

Fluorine-18 emits a 0.65-MeV positron which is detected by the associated pair of annihilation gamma rays of 0.511 MeV. Counting is performed by any standard method of positron detection. Geiger-Müller tubes or NaI(Tl) 3 in. × 3 in. crystal scintillation counter, connected with a multichannel pulse analyser, may be used [28, 35, 41]. Counting efficiencies of 5 - 10% were obtained by two 2 in. × 2 in. sodium iodide scintillation crystals 6 mm apart, in coincidence with two single-channel analysers [34].

Fluorine-18 may be radioassayed as solid PbClF or NaF, as a liquid HF or as a gas - HF, F_2ClF_3, BrF_5, IF_7 [28, 35].

Radiochemical purity is tested by gamma-ray spectroscopy and half-life measurements. Tritium contamination is measured, using a liquid scintillation counter [44].

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MINISTRY OF DEFENCE, ATOMIC ENERGY COMMISSION,
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A. PRODUCTION AND SEPARATION OF ^{18}F AS CaF^+ ION

1. GENERAL

Nuclear reaction: $^{6}Li(n, \alpha)t$ followed by $^{16}O(t, n)^{18}F$.
Separation of ^{18}F: by dissolving the irradiated Li_2CO_3 target and precipitating $Ca_2(Po_4)_3$. Precipitate carries $Ca^{18}F_2$.

2. EXPERIMENTAL PROCEDURE

Irradiation

Ten grams of Li_2CO_3 (AR) are sealed into four silica vials, 9 cm long by 1 cm diam. (2.5 g per vial). The vials, conditioned into a polyethylene container, are irradiated for 1 h at a thermal neutron flux of 3×10^{13} n/cm^2 s. After irradiation the samples are quickly transferred for processing by means of a lead transfer-container (2 in. internal diam., 2 in. thick).

Other activities = ^{24}Na from impurities in Li_2CO_3.

Chemical treatment

This is carried out in an open lead box which has a wall 2 in. thick.

(a) Transfer irradiated ampoules to lead box.
(b) Wash ampoules with acetone.
(c) Crush ampoules. Pour Li_2CO_3 and silica fragments into dissolution flask.
(d) Dissolve with 40 ml of 1 : 1 hydrochloric acid.
(e) Filter. Rinse with water. Receive filtrate and washings into beaker containing 1 ml of 15% phosphoric acid.
(f) Add 100 mg of calcium carbonate.
(g) Add 25% potassium bicarbonate solution, dropwise, until precipitation begins. Add 2 more drops.
(h) Transfer solution and precipitate to centrifuge tubes. Centrifugate for 3 min. (Solution to waste.)
(i) Dissolve with a few millilitres of 1 : 1 hydrochloric acid.
(j) Add 25% potassium bicarbonate solution to the centrifuge tubes as in step (g) above.
(k) Centrifuge, discard solution.
(l) Wash with a few millilitres of water. Centrifuge, discard solution.
(m) Re-dissolve precipitate with 1 : 1 HCl (total volume 5 to 10 ml).
(n) Transfer to delivery bottle.

The absence of ^{24}Na is checked by γ-ray spectrography.

B. *PREPARATION OF ^{18}F-LABELLED KBF_4*

1. GENERAL

Fluorine-18 is obtained as in A above. Exchange with KBF_4 proceeds quickly under the appropriate conditions.

2. EXPERIMENTAL PROCEDURE[1]

Irradiation: as in A above

Chemical treatment

Prepare ^{18}F as above, steps (a) to (m).
Adjust to pH 1; add 100 mg KBF_4. Heat to 100°C. After 1-2 min, cool quickly.
Neutralize with sodium bicarbonate to pH 5.5.
Pass through a column of chromatographic alumina for quantitative removal of fluoride ions.

3. ASSAY AND QUALITY CONTROL

Radioactive purity is tested by γ-ray spectrography and by following the decay curve.
The fluoride ion content is tested as follows: Take an aliquot of final solution; take to 1 ml volume; add 0.5 ml of 0.1 N NaF and 0.5 ml of 0.4 N NaCl. Add $Rb(NO_3)_2$ solution. Filter. Wash the PbClF precipitate with 90% ethanol. Count.

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1. GENERAL

The production process is based on the method developed by Stang [1, 2]. The irradiated lithium carbonate target is dissolved in hydrochloric acid, and the separation of ^{18}F is made by adsorption on alumina.

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[1] This procedure is based on current literature, especially: ASKENASY, H.M., ANBAR, M., LAOR, Y., LEWITUS, Z., KOSARY, I.Z., GUTTMANN, S., Radium therapy and nuclear medicine, Am. J. Roentgenology LXXXVIII 2 (Aug. 1962).

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 5 g of lithium carbonate (Li_2CO_3) (JISRG[2]).
Container: Sealed in the polyethylene sheet, and placed in the acetyl cellulose capsule for the pneumatic tube.
Flux: 6×10^{11} n/cm^2 s (JRR-1 pneumatic tube).
Irradiation time: 1 or 2 h.
Side reactions: Formation of tritium.

Chemical treatment

Production is based on the adsorption of ^{18}F on alumina with the subsequent elution by dilute sodium hydroxide.
The irradiated lithium carbonate target is dissolved in concentrated hydrochloric acid.
Neutralize the dissolved solution with sodium hydroxide.
The neutralized solution is passed through the acid alumina column, 0.8 cm diam. and 2.0 cm long.
Wash the column with 30 ml water.
Elute ^{18}F adsorbed on the column with 0.1 N NaOH.
Chemical forms are determined by paper chromatography.
Filter paper: Toyo filter paper No. 51A.
Reagent: Butanol - methanol - water (1 : 3 : 1).
Method: Ascending method.
Time: 2 h.
R_f value: F^- ---- 0.58.

The percentage of chemical forms other than F^- is determined to be approximately 16% (probably Al - F complexes).

3. ASSAY AND QUALITY CONTROL

The following chemical analysis is carried out:
Inactive fluorine: colorimetric method by Erichromecyanine R;
Lithium: flame photometry;
Aluminium: colorimetric method by 8-hydroxyquinoline.

Radiochemical impurities are determined by gamma-ray spectrometry and half-life measurement.

Assay is made by gamma spectrometry.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form: $Na^{18}F$ in NaOH solution.
Radiochemical purity: > 99%.
Specific activity: Carrier-free; approximately 0.1 mCi ^{18}F/g of Li_2CO_3.

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[2] Japan Industrial Standard Reagent Grade.

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BROOKHAVEN NATIONAL LABORATORY,
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1. GENERAL

The production of ^{18}F is based on the irradiation of lithium carbonate; $^{6}Li(n, t)^{4}He$, $^{16}O(t, n)^{18}F$. Fluorine-18 produced is separated by the adsorption on alumina column with the subsequent elution with sodium hydroxide.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	10 g of lithium carbonate (unenriched).
Irradiation conditions:	Irradiation for six hours at a flux of 1.2×10^{13} n/cm^2 s. Reactor yield approximately 40 mCi; chemical yield 70 - 80%.

Chemical treatment

Target preparation

Insert an aluminium tube coaxially inside a standard aluminium isotope can and pack the annular space with ~10 g Li_2CO_3.

The annular space should be ~1/8 in. thick. Because of the high σ of ^{6}Li, if the annular layer were appreciably thicker than this, the internal neutron flux would be so depressed that the material inside would contribute little or no additional product and would only add undesirable bulk to the process.

Crimp the top of the can.

The top should have a small hole covered with Scotch tape to prevent pressure build-up.

Post-irradiation processing

The following facilities are needed: a glove box or fume hood suitable for handling ^{3}H contamination; isotope can opening tools and crimping press for closing; 1.5 in. shielding locally.

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* Extracted from BNL-864 (T-347).

Remove the top from the isotope can and transfer Li_2CO_3 powder to the Erlenmeyer flask containing ~ 20 ml H_2O and magnetic stirring bar. Use a wide neck funnel and rinse with H_2O.

Add concentrated HCl slowly with stirring to dissolve Li_2CO_3. Avoid rapid CO_2 evolution.

Adjust the pH to the acid side of the Brom Tymol Blue indicator with NaOH solution.

Pass the solution through the alumina column, using vacuum to attain 1 - 2 ml/min.

Column preparation: Slurry 10 g Woelm alumina (neutral grade) with 50 ml 0.5 M HCl, decanting and discarding fines. Wash with two 50-ml portions of H_2O, discarding fines. To a 1-cm diam. glass tube to which is sealed a coarse frit, transfer enough alumina to stand 3 cm above the frit. Wash a few times with H_2O. A pad of glass wool on top of the alumina will prevent it from plugging.

Wash the column with 30 ml H_2O containing 1 drop concentrated HCl. Use vacuum if necessary.

Elute ^{18}F with 40 ml 0.1 N NaOH containing Brom Thymol Blue indicator. Collect in 3 portions:

(a) until the blue colour starts to come through the frit, 10-12 ml;

(b) the next 15 ml contains most of the ^{18}F;

(c) remainder of the effluent.

Collect portions in large test tubes inside the side-arm flask on which a slight vacuum is pulled.

Assay portion (b) and transfer to shipping bottle. Count annihilation gammas in calibrated well-type scintillation counter.

Note: The product is an aluminium fluoride complex, which may be converted to NaF by distillation from concentrated H_2SO_4, collecting distillate in dilute NaOH.

3. ASSAY AND QUALITY CONTROL

Assay by well-type scintillation counter standardized against 4π counter.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Product composition:	$Na^{18}F$ trace of $NaAlO_2$ in 0.1 M NaOH. The chemical form is an aluminium fluoride complex, which may be converted to NaF by distillation from concentrated H_2SO_4, collecting distillate in dilute NaOH.
Radiochemical purity:	Over 99.99%; trace of ^3H.
Specific activity:	Carrier-free.

GOLD-198

NUCLEAR DATA

1. NUCLEAR PROPERTIES

1.1. Half-life [1-3]

2.7 d

1.2. Type of decay and energy (MeV) [4-8, 90]

Gold-198 decays by the emission of beta particles followed by gamma rays. The per cent abundance of each radiation is given.

Energies and abundances

(a)

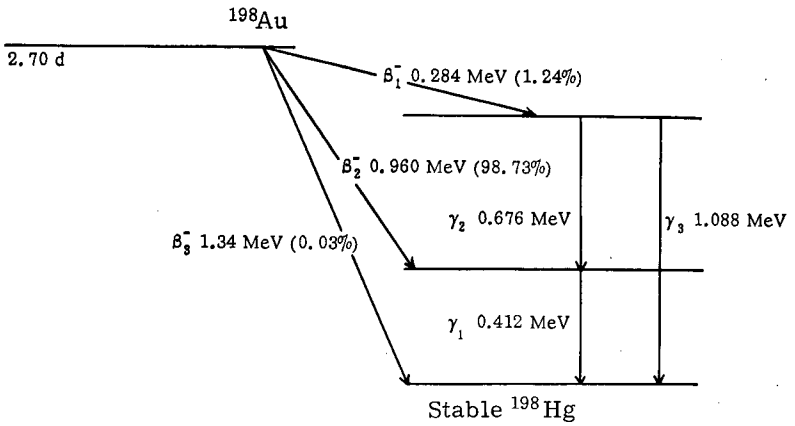
	E_{max}	Abundance (%)
β_1	0.290	1.0
	0.290	1.1
	0.284	1.24
β_2	0.966	99.0
	0.962	98.9
	0.960	98.73
β_3	1.378	0.01
	1.374	0.03
	1.372	0.03

$\bar{E}(\beta^-) = 0.317$

(b) γ (^{198}Hg)

γ_1	0.41177	99.8
	0.411772	
γ_2	0.6765	0.82
	0.6765	0.93
γ_3	1.088	
	1.089	0.16
	1.088	

1.3. Decay scheme [6]



2. NUCLEAR REACTIONS AND PRODUCTION

The reaction used for the production of ^{198}Au is: ^{197}Au(n, γ)^{198}Au. The abundance of the target nuclide is 100% and the cross-section for the reaction with thermal neutrons is 99b. The specific activities obtained as a function of irradiation time for various neutron fluxes are given in Table I.

TABLE I

SPECIFIC ACTIVITIES AS A FUNCTION OF IRRADIATION TIME FOR VARIOUS NEUTRON FLUXES [90]

Thermal neutron flux (n/cm^2 s)	Specific activity (Ci/g of target) for irradiation time (half-life units) of				Side reaction
	0.01	0.1	1.00	A_{max}*	
2×10^{13}	1.13	10.9	77.5	139	^{198}Au(n,γ)^{199}Au (3.15 d)
2×10^{14}	11.2	103	505	586	The cross-section for this "burn-up" reaction is 26 000 b. Gold-199 is therefore always present as a contaminant in reactor-produced ^{198}Au. The relative amount of ^{199}Au increases with the neutron flux.
2×10^{15}	106	637	847	866	

Gold-198 may also be produced with an accelerator using the reaction: ^{197}Au(d, p)^{198}Au [9].

Carrier-free ^{198}Au may be produced using the reaction: ^{198}Hg(n,p)^{198}Au [80].

3. APPLICATIONS

Gold-198 is a moderate-energy beta and gamma emitter. It has found applications in many fields, especially in medicine. A brief classified survey of published applications is given below.

3.1. Biology

Radiation induced tumours in animals	[10, 11]
Distribution of radioactive gold in animals	[81]

3.2. Medicine

Determination of liver blood flow	[12-14, 84, 86]
Liver scanning and localization of hydatic liver cyst	[15-21]
Bone-marrow scanning	[22, 23]
Treatment of prostatic cancer	[24-26]
Treatment of ovarian cancer	[27, 28, 85]
Tumours of the urinary bladder	[29-31]
Treatment of bronchial carcinoma	[32, 79, 82]
Leukaemia treatment	[33, 34]
Carcinoma of the pleura and peritoneum	[35-40]
Treatment of pericardial effusions	[41, 42]
Hypophysectomy and pallation of metastatic carcinoma	[43, 44]
Pituitary ablation	[45-47]
Treatment of carcinoma of the cervix	[48-50]
Techniques for interstitial implantations	[51-53]
Knee effusion treatment	[54]

3.3. Metallurgy

Radioactive tracers in aluminium manufacturing	[55, 56]
Thickness measurements of thin metal films	[57, 58]
Radiography in solid-liquid metal interface research	[59, 60]
Molten metal flow in a copper refractory furnace	[61, 87]
Movement of steel in solidifying ingots	[66]

3.4. Hydrology and hydrodynamics *[62-65]*

Flow measurements
Sand movement tracing

4. RADIOLOGICAL PROTECTION[1]

4.1. External irradiation

The maximum range in aluminium of the 960-keV beta particles of ^{198}Au is 450 mg/cm^2. The half thickness in lead for the 412-keV gamma radiation is 0.28 cm. The gamma exposure rate at a distance of 1 cm from a 1-mCi

[1] This brief summary should be read in conjunction with Safe Handling of Radioisotopes, Safety Series No. 1, IAEA, Vienna (1962) 100.

point-source (K factor) is 2.36 R/h. Table II gives exposure rates as a function of distance and shielding for a 1-Ci ^{198}Au source.

Radioactive gold administered to a patient gives an appreciable exposure rate to the surroundings. Table III lists the maximum permissible times which hospital personnel are allowed at various distances from a patient as a function of the dose [68].

TABLE II

EXPOSURE RATES FROM A 1-Ci ^{198}Au SOURCE AS A FUNCTION OF DISTANCE AND SHIELDING

Lead thickness (cm)	Exposure rates (mR/h) at	
	30 cm distance	100 cm distance
2.0	0.38	3.5
2.5	0.17	1.5
4.0	2.2	0.2
4.5	1.1	0.1

Body liquids, removed for tests, from patients treated with radioactive gold, are handled in stainless-steel beakers as protection from the radiation [67].

For radiological protection procedures of hospital personnel see references [67-69].

4.2. Internal irradiation

Gold-198 is classified as a moderately toxic isotope. The minimum significant activity is 10 μCi. The maximum permissible concentrations of radionuclides in air and in water are listed in Table IV.

4.3. Decontamination

Care should be taken to avoid direct contact between the radioactive colloid and the skin since this may result in severe burns due to beta rays. In case of spillage the colloid should be immediately washed off with water, since it becomes adherent when dry.

Colloidal gold does not adhere to polished surfaces and may be removed by brushing. Since ^{198}Au is a relatively short-lived isotope it is worth while in most cases to allow for decay before decontamination is attempted.

TABLE III

MAXIMUM PERMISSIBLE TIME NEAR A PATIENT AS A FUNCTION OF DISTANCE AND DOSE

Distance (m)	Maximum permissible times (h) for doses of				
	25 mCi	50 mCi	100 mCi	150 mCi	200 mCi
0.50	2.0	1.0	0.5	0.3	0.25
1.0	8.0	4.0	2.0	1.5	1.0
1.5	18.0	9.0	4.5	3.25	2.5
2.0	24.0	16.0	8.0	6.0	4.0

TABLE IV

MAXIMUM PERMISSIBLE CONCENTRATIONS OF RADIONUCLIDES

Critical organ	Soluble or insoluble	Maximum permissible concentration			
		For 40-h week		For 168-week	
		$(MPC)_W$ $\mu Ci/cm^3$	$(MPC)_A$ $\mu Ci/cm^3$	$(MPC)_W$ $\mu Ci/cm^3$	$(MPC)_A$ $\mu Ci/cm^3$
Gastrointestinal tract Lower large intestine	soluble	2×10^{-3}	3×10^{-7}	5×10^{-4}	10^{-7}
Gastrointestinal tract Lower large intestine	insoluble	10^{-3}	2×10^{-7}	5×10^{-4}	8×10^{-8}

5. SUMMARY OF PRODUCTION METHODS

Radioactive gold is used in metallic form (e.g. gold grains for implantations), in solution or as a colloidal suspension. A summary of reported production methods is given below.

5.1. Targets

Metallic gold is invariably used as the target. It is available in the form of thin foils with a purity of 99.99%, or spectroscopically pure. For implantation purposes where radioactive gold needles are used, the target is in its final form, without any further processing [53, 70]. Gold grains for

irradiation are available commercially in a platinum sheath which absorbs beta radiation. Targets are sealed in quartz tubes or standard aluminium cans and irradiated in a flux of thermal neutrons for periods of up to one week.

5.2. Chemical processing

All processing methods reported include as first stage the preparation of chlorauric acid solution.

5.2.1. Preparation of chlorauric acid solution

The irradiated gold foil is dissolved in hot (90°C) aqua regia. The dissolved target solution contains the gold as $(AuCl_4)^-$ anions. Pure chlorauric acid is obtained by the following procedures:

(a) Crystallization of chlorauric acid and dissolution in purified water

The excess aqua regia is evaporated in a water bath by heating to 90-100°C at a pressure of 70 - 100 mm Hg. Evaporation should not be prolonged and the solution should not be overheated, in order to avoid decomposition of chlorauric acid. Air should be bubbled through the solution to enhance evaporation. Pure chlorauric acid crystals are needle-like and light yellow. The presence of dark short crystals indicate partial decomposition. Should this happen, a drop of HCl is added and the evaporation repeated. The chlorauric acid crystals are dissolved in distilled water (Pyrogen-free for medical use) [72, 73].

(b) Liquid-liquid extraction

Ethyl acetate is added to the aurochloric acid solution and the mixture is shaken vigorously. The organic phase containing the aurochloric acid is separated and washed with 0.1 N HCl. The ethyl acetate is evaporated by heating in a water bath, and the residue may be taken up in water slightly acidified with HCl [74, 80].

5.2.2. Colloidal preparation

Colloidal suspensions of radioactive gold for medical use must fulfil the following requirements: the colloid should be stable and free of aggregates; there should be uniformity of particle size - the optimum diameter is approximately 250 Å; and radiogold in forms other than colloidal (ionic gold) should not be present.

The chlorauric acid solution can be converted into a colloidal suspension by reduction, or by adsorption on activated carbon. Silver coating and amino-gold salt formation techniques are also in use.

5.2.2.1. Colloid preparation by reduction

Chlorauric acid is always reduced to metallic gold in the presence of gelatine. The gelatine is added as a "protective colloid" for stabilizing the

colloidal gold solution. The reduction of chlorauric acid to metallic gold and the formation of a colloidal suspension involve two simultaneous processes, the formation of new colloidal nuclei and the growth of existing nuclei. If one allows these two competing reactions to take place simultaneously one obtains a multi-dispersed colloid, i.e. a colloid with a broad range of particle sizes. To obtain a colloid with a narrow range of particle sizes and a predetermined mean diameter it is essential that nucleation and growth be successive instead of simultaneous [71].

(a) Formation of colloid without prior seeding

The chlorauric acid solution is neutralized with 1 N sodium hydroxide to form sodium chloraurate. A gelatine solution is added, keeping the temperature at 45-50°C. The reduction to metallic gold is achieved by the dropwise addition of glucose or 0.5% ascorbic acid. Particle sizes obtained by this procedure range from 25 to 200 Å [72, 73].

(b) Growth of colloid on pre-formed seeds

A non-radioactive gold "seed solution" is prepared in the following manner:

Chlorauric acid crystals are dissolved in water and added dropwise into a basic solution of glucose and gelatine preheated to 70°C. A uniform-size inactive gold colloid with mean particle diameter of 50 Å is thus obtained. The seed solution is cooled, sealed in penicillin flasks and sterilized at 120°C for 1 h. The sterilized solution should be kept in a refrigerator and may be used over a period of one month. The radioactive chlorauric acid solution is neutralized with sodium hydroxide as above. Chlorauric crystals may also be dissolved in 0.01% NaCl solution instead of water, to enhance aurate ion formation on the addition of sodium hydroxide. The sodium aurate solution is further purified by filtration on a fritted plate, and added dropwise to a mixture of seed solution, 20% gelatine solution in water, preheated to 70°C. The aurate solution is added slowly for about 20 min, with constant stirring to ensure homogeneity. After the addition of the chloraurate the mixture is heated to 80°C in a water bath for half an hour. Ionic gold reduction is completed by the dropwise addition of 10 ml sodium ascorbate solution [72, 73].

The radioactive gold colloid produced by either method must be sterilized at 120°C for 30 min. Specific activities required for therapeutic purposes are about 25 mCi/ml. For diagnostic uses such a suspension may be diluted by the addition of a gelatine solution.

5.2.2.2. Colloid preparation by adsorption on carbon

The high polarizing effect of activated charcoal enhances the adsorption of gold. This is used for the preparation of colloidal ^{198}Au [76].

5.2.2.3. Silver coating and salt formation techniques

A suspension of silver-coated colloid of ^{198}Au may be used for lung tumour treatment. This may be prepared by the introduction of high-specific-activity colloidal radiogold into a silver nitrate solution. Silver ions are

reduced in the presence of stabilizing protective colloid forming silver-coated gold colloids [31, 79].

Radioactive ^{198}Au for industrial radiotracing is used in the form of stable, oil-soluble gold amino salts [76].

6. QUALITY CONTROL

6.1. Non-radioactive assay

Colloid particle size is determined by electron microscopy [74] or by the Schlesinger Centrifuging method [73]. Quantitative determination of soluble gold in radioactive colloidal gold solution is performed by ascending chromatography. pH determination can be made with any standard meter [73].

6.2. Radioassay

Activity measurement may be made by beta, or gamma, counting methods. Relative activity measurements are made with a gamma scintillation counter [73], a Geiger-Müller counter [69, 74, 80] or a beta proportional counter [74]. The counting apparatus should be periodically checked with absolute standards. The allowed error in the activity measurements is 5 - 10% [73].

The main radioactive contaminant is ^{199}Au, produced by the nuclear reaction $^{198}Au(n, \gamma)^{199}Au$. The ^{198}Au cross-section for thermal neutron capture is 2.6×10^4 barn. Gold-199 decays with a 3.15-d half-life, by the emission of 250-and 300-keV beta particles, followed by 208-and 158-keV gamma rays.

The ^{199}Au to ^{198}Au ratio can be determined by gamma spectrometric technique within an accuracy of 5% [78].

Radioactive purity is determined by gamma spectroscopy and half-life measurements.

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1. GENERAL

A nuclear reaction $^{197}Au(n, \gamma)^{198}Au$ is used to obtain ^{198}Au. The preparation of colloidal ^{198}Au solution consists of three steps, i. e. preparation

of a glucose solution containing gold nucleus, dissolution of the irradiated pure gold target and the reduction of gold ion by glucose solution. Gelatine is used to stabilize the colloidal gold solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 0.3 g pure gold wire.
Irradiation container: Polyethylene capsule.
Irradiation condition: Neutron flux 4×10^{12}.
Irradiation time: 5 h.

Chemical treatment

Solution 1. The nucleus solution is prepared by dissolving 0.3 g of pure gold wire with 3 ml aqua regia. After the gold wire is completely dissolved the excess aqua regia is removed by evaporation. To this residue 30 ml of re-distilled water is added to make a gold solution.
Solution 2. Separately, 16.8 g of glucose is dissolved with 30 ml of re-distilled water to which 12 ml of 20% gelatine solution is added gradually at 90°C. The solution is kept at 55°C and 3 ml of 5 N sodium hydroxide solution is added.

Solution 1 is then added to this mixture drop by drop with constant stirring; this takes about 30 min. The container of Solution 1 is rinsed with 10 ml of re-distilled water which is also added to the resulting solution; the mixture is then placed in the water bath for half an hour for sterilization.

The colloidal ^{198}Au solution is prepared by dissolving 0.3 g of irradiated gold wire with 3 ml of aqua regia. The gold solution is prepared as for Solution 1; the resulting gold ion solution is then reduced by adding the reducing agent solution. This is made of 12 ml 20%-gelatine solution, 0.5 ml nucleus solution and 26 ml re-distilled water, according to the following procedure: add 1 N sodium hydroxide solution to gold ion solution to adjust its pH to ~9. The reducing agent solution is placed in a reduction vessel and kept at 80°C. The gold solution is also kept at 80°C and added to the reducing agent solution drop by drop through a G-4 porosity sintered glass filter with constant stirring. About half an hour is needed to complete the reduction process. The product of about 250 mCi is obtained, which is a stable colloidal ^{198}Au solution of a deep purple colour.

3. ASSAY AND QUALITY CONTROL

The content of free gold ion is determined by paper chromatography and the size of the gold particle with an electron microscope. Radiochemical analysis of the product is performed according to the Oak Ridge National Laboratory Master Analytical Manual No. 90733331-3. Pharmaceutical control is carried out according to the "Minimum Requirements of Radio-

active Drugs" published by the Japanese Ministry of Health and Welfare (1962).

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	Au-colloid.
Concentration:	2.7 mCi/ml.
Specific activity:	0.8 mCi/mg Au.
Acidity:	pH 7 ~ 8.
Free gold ion content:	~ 1%.
Radiochemical purity:	> 99%.

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

The therapeutic use of radioactive gold colloid requires a final product having: high chemical stability; high radioactive concentration; no harmful admixtures; pH not less than 5; and particle size approximately 300 Å.

The method used, which was developed by Henry, Herczeg and Fisher [1], is based on the observations of Turkevitch [2] on the formation of gold sols, in which he distinguished two phases: nucleation, during which 40-50 Å particles are formed; and growth, during which the size of the particles increases.

To obtain a regular colloid it is essential that the two phases should be successive, so as to avoid the beginning of growth by some particles whilst others are only being formed.

In the method described the radioactive colloid is prepared by making use of the reducing properties of gelatine itself (amino groups, guanidines), which is seeded with a small quantity of previously formed colloid whose particles become centres of crystallization.

The seed used is prepared by glucose reduction utilizing a method which results in the formation of small (50 Å) regular particles. Checking of particle size by electron microscopy enables defective preprations to be eliminated and thus guarantees the regularity of colloids formed from these seeds.

The production of ^{198}Au is based on the nuclear reaction $^{197}Au(n, \gamma)^{198}Au$.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	A 500-mg gold leaf of 99.999% purity.
Irradiation conditions:	Irradiation at a flux of 2.4×10^{12} n/cm^2 s for 144 h in the EL 2 reactor which represents an activity of 7.45 Ci on unloading.

Irradiation container: Threaded aluminium irradiation capsule with an internal diameter of 22.5 mm and an internal length of 70 mm.

Activity produced: The activity per gram of element at 10^{12} n/cm^2 s is 6.2 Ci after one week's irradiation, and 7.9 Ci at saturation.

Chemical treatment

Preparation

After irradiation, the gold leaf (500 mg) is washed in chloroform and dried.

The treatment breaks down into two successive phases:

(a) Preparation of the reducing medium for production of the radioactive colloid

A solution containing 20 ml of 20% gelatine previously liquefied and 1.5 ml of seed extracted with a sterilized hypodermic syringe is prepared in a 50-ml beaker. The mixture is placed in the reduction bottle which is filled up with 48 ml of doubly distilled water. The heating system of the reduction chamber is set to maintain the temperature of the solution at 70°C throughout the operation, the solution being stirred to ensure homogeneity.

(b) Dissolution of the gold leaf and formation of the colloid

After placing the leaf in the evaporator, 4 ml of aqua regia are introduced together with two portions of doubly distilled water of 1 ml each. The leaf is dissolved by heating to boiling point.

Excess aqua regia is eliminated by hot evaporation in a vacuum of 110 mmHg. Red–brown crystals are formed on the walls of the evaporator.

These crystals are dissolved in 40 ml of doubly distilled water. The solution is then neutralized with 12.5 ml of 1 N NaOH; finally the vessel is rinsed with 10 ml of doubly distilled water.

The sodium chloraurate thus formed is purified by filtration on a fritted plate. It is then ready to be passed into the reducing mixture.

After the temperature of the reducing mixture has been checked (70°C), the tap admitting the chloraurate solution into the reducer is adjusted to a rate of one drop per second. The whole solution should take about 20 min to pass. The evaporating flask is rinsed with

8 ml of doubly distilled water,

1 ml of 1 N NaOH, and again

7 ml of doubly distilled water.

The rinsing water is passed into the reducing bottle in the same way. Reduction is completed by introducing drop by drop a solution of 10 ml of 10% sodium ascorbate to reduce the last traces of free gold.

Reagents required

Aqua regia as solvent: 20 ml HCl RP (d: 1.19) + 10 ml HNO_3 RP (d: 1.33). It should be prepared 15 min before use in a 125-ml stoppered bottle.

20% gelatine solution: 40 g of solid gelatine are dissolved in 200 ml of doubly distilled water, heated to 65°C in a water bath, and then hot-filtered on a No. 3 fritted glass in a vacuum; the gelatine solution is divided out in the proportion of 20 ml per 30-ml penicillin bottle; the bottles are sterilized for 30 min at 2 mg/cm^2.

1 N NaOH solution.

10% ascorbate solution: 10 g of ascorbic acid are dissolved in about 50 ml of doubly distilled water; after being brought to pH 6 the solution is made up to 100 ml in a calibrated phial.

Gold seed:

- Preparation of the reducing fluid: 16.8 g of glucose are dissolved in 30 ml of doubly distilled water and the luke-warm solution filtered on a No. 3 fritted glass; it is then introduced into the reduction bottle of the apparatus with 12 ml of 20% gelatine; the bottle is heated to 70°C and 3 ml of 5 N soda are introduced.
- Dissolution of the gold and formation of the seed: a 300-mg gold leaf, which has been previously cleaned, is hot dissolved in 3 ml of aqua regia together with two portions of doubly distilled water of 1 ml each; after hot evaporation in a vacuum and re-dissolution with 30 ml of doubly distilled water by the same procedure, the solution is passed drop by drop into the reducing fluid, taking about 20 min; the evaporator is rinsed with 10 ml of doubly distilled water which are passed drop by drop into the reducing fluid.

The seed is allowed to cool to 40°C and then the 85 ml of seed are distributed amongst the five 30-ml penicillin bottles. The bottles are sterilized for 30 min at 2 kg/cm^2.

Apparatus

The apparatus for preparing colloidal gold-198 (Fig.1) consists essentially of: an irradiation tube unloading area; a colloid preparation area; and a colloid distribution area.

Irradiation tube unloading area

This area is fitted with a door, through which the lead castle containing the irradiation tube can be passed. The tube is unscrewed with special tongs. A mechanical extractor is also provided in case a cold soldered tube is used.

A belt conveyor carries materials from one area to another.

Colloid preparation area

The area is shown on the flowsheet for the colloidal gold-198 production process (Fig. 2). It consists mainly of: an evaporating vessel for dissolving the gold leaf; two siphon bulbs, one of which is fitted with a fritted glass filtering plate; and a reducing bottle in which the colloid is prepared.

The evaporator is heated by an infra-red heater. It is also connected to a turbine pump producing a 110-mm vacuum for evaporation.

The reducing bottle is also infra-red heated and the temperature of 70°C is obtained by regulation with a contact thermometer. The colloidal solution is stirred by imparting a to-and-fro movement to the liquid.

The vessels are interconnected by welded glass tubes.

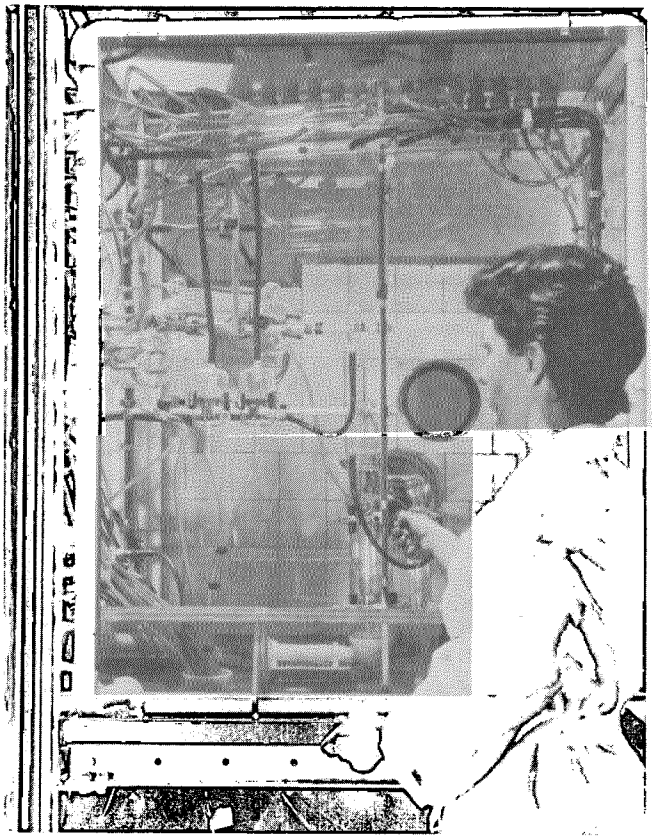

FIG. 1. Apparatus for the production of colloidal ^{198}Au (back guard raised). Dissolving and evaporation area

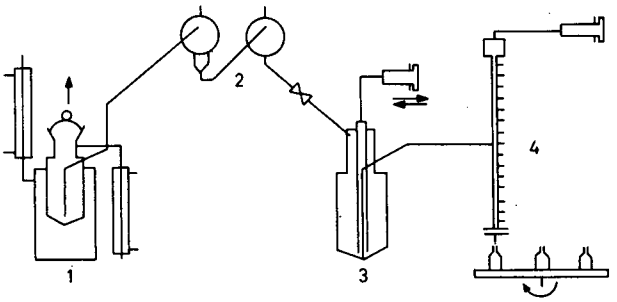

FIG. 2. Colloidal ^{198}Au flowsheet
1. Evaporator
2. Siphon bulbs
3. Reducing bottle
4. Distributing burette

Colloid distribution area

This area contains the distributor burette into which the colloid is fed through a glass tube immersed in the reducing bottle. It is filled by suction by means of a high-capacity syringe.

A pH meter has also been installed for systematic checking of the pH of each solution prepared.

Before each operation the apparatus is carefully washed with dilute aqua regia (600 ml HCl + 300 ml conc. HNO_3 + 300 ml H_2O) and again with boiling water.

Afterwards, the whole apparatus is rinsed with doubly distilled water until pH 7 is obtained in the glassware.

It is recommended that after each operation the reducing bottle and the burette is filled with doubly distilled water to avoid the tubes being blocked by coagulation of the gelatine.

Determination of chemical forms

The colloidal solution is chemically tested to check its freedom from soluble radioactive substances [3]. The test consists of paper chromatography. A drop of the gold colloid is placed on a paper strip which is allowed to dip into a tank containing a chromatographic mixture which causes migration of the soluble phase. The soluble derivatives of gold are colourless. A G-M counter connected to a recorder permits determination of the radioactivity of the soluble phase, i.e. the content.

3. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{198}Au S-2 - Injectable

A sterile and pyrogen-free solution of colloidal gold ^{198}Au, pH 5 - 7, particle size 20 - 40 mμ, meeting the following specifications:

Radioactive concentration, measured to within 5%: 30 mCi/ml average, with maximum up to 50 mCi/ml.

Radioactive purity: ^{198}Au content > 99.9% (gamma-ray spectrum characteristic of ^{198}Au).

Radiochemical purity: Soluble gold content < 2%.

Composition of solution: As indicated in the French Pharmacopoeia:

Colloidal gold	3.5	mg
Glucose	2	mg
Ascorbic acid	7	mg
NaCl	5	mg
Medicinal gelatine	30	mg
Distilled water	1	ml

Reference: ^{198}Au S-3 (for diagnosis)

A solution of colloidal gold ^{198}Au S-2 diluted in the following solution:

Gelatine	30 mg
Distilled water	1 ml
Radioactive concentration	1 mCi/ml

Reference: ^{198}Au S-6 (small particles)

A sterile and pyrogen-free solution of colloidal gold ^{198}Au, pH 5 - 7, particle size 3 - 5 mμ, meeting the following specifications:

Radioactive concentration:	20 mCi/ml average.		
Radioactive purity:	$^{198}Au > 99.9\%$.		
Radiochemical purity:	Soluble gold content $< 2\%$.		
Composition of solution:	Colloidal gold	3.5	mg
	Glucose	200	mg
	NaCl	5	mg
	Medicinal gelatine	30	mg
	Distilled water	1	ml

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CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production is based on the irradiation of gold metal. When producing ^{198}Au metal or $^{198}AuCl_3$ no special problems arise. In the case of colloidal gold for medical use special care is taken regarding sterility and radiochemical purity.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Gold metal, Johnson Matthey. The amount of target depends on the request.
Flux:	10^{13} n/cm^2 s.
Time:	200 h.
Container:	Quartz ampoule with ground stopper.

Chemical treatment

In the production of ^{198}Au metal, no processing is necessary. To obtain $^{198}AuCl_3$ the irradiated metal is dissolved in hot aqua regia, the nitrate ions being removed by addition of hydrochloric acid.

When colloidal gold is to be produced the $^{198}AuCl_3$ solution obtained as described above is neutralized with sodium carbonate and gelatine is added at a temperature of 40 - 50°C; finally the solution is reduced with a calculated amount of 0.5% ascorbic acid. The colloidal solution is sterilized in an autoclave at 120°C for 40 min.

3. ASSAY AND QUALITY CONTROL

The gold content of the solution is determined as follows: The colloid is decomposed with excess aqua regia. After evaporating to dryness, the solid residue is dissolved in distilled water. Glucose and potassium carbonate are added and the relative absorption is photometrically measured by comparison with the standardized reference solutions. The chloride content is determined titrimetrically with standard silver nitrate solutions, using potassium chromate as indicator. The pH is measured by the usual method. For radiochemical purity the gamma spectrum is determined with the aid of a multichannel pulse height analyser. Sterility is controlled in the usual manner on aliquot samples.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Gold metal

Radiochemical purity: > 90%.
Specific activity: 3 - 30 mCi/mg Au.

Chlorauric acid ($HAuCl_4$)

Radiochemical purity: > 90%.
Specific activity: 12 - 30 mCi/mg Au.
Solution: Pale yellow transparent solution; 1 - 2 mg of Au/ml.

Colloidal solution

pH: 6 - 8
Radiochemical purity: > 90% (possible impurity: ^{199}Au ($T_{\frac{1}{2}}$: 3.15 d))
Specific activity: 12 - 30 mCi/mg Au.
Solution:

Colloidal gold	1 - 2	mg/ml.
Gelatine	0.5	mg/mg Au.
Ascorbic acid	2	mg/mg Au.

Isotonic
Sterile

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Gold-198 is produced by the neutron irradiation of spectroscopically pure gold metal in the form of thin foils.

The method adopted for the processing of colloidal gold-198 consists of two stages:

(a) The initial preparation of a seed, or nucleating agent, which is a colloid prepared by reducing chlorauric acid with a mixture of glucose, gelatine and sodium hydroxide.

(b) The preparation of the final colloid by the growth of the seed colloid. At this stage, sodium aurate is added to a mixture of gelatine and seed colloid; the gelatine acts as a reducing agent as well as a stabilizer.

By this two-stage method it is possible to obtain a colloid of fairly uniform particle size (300 Å) and practically free from toxic products.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Spec-pure thin gold foil, 150 mg in a type "A" (screw-capped 1 S aluminium can, 73 mm high and 26.5 mm diam.) or type "C" can (cold-welded 2 S aluminium can, 44 mm high and 22 mm diam.).
Irradiation period:	One week.
Flux in APSARA:	$(2 \text{ to } 3) \times 10^{12}$ n/cm^2 s.
" " CIR:	$(5 \text{ to } 10) \times 10^{12}$ n/cm^2 s.

Chemical treatment

Preparation of seed colloid

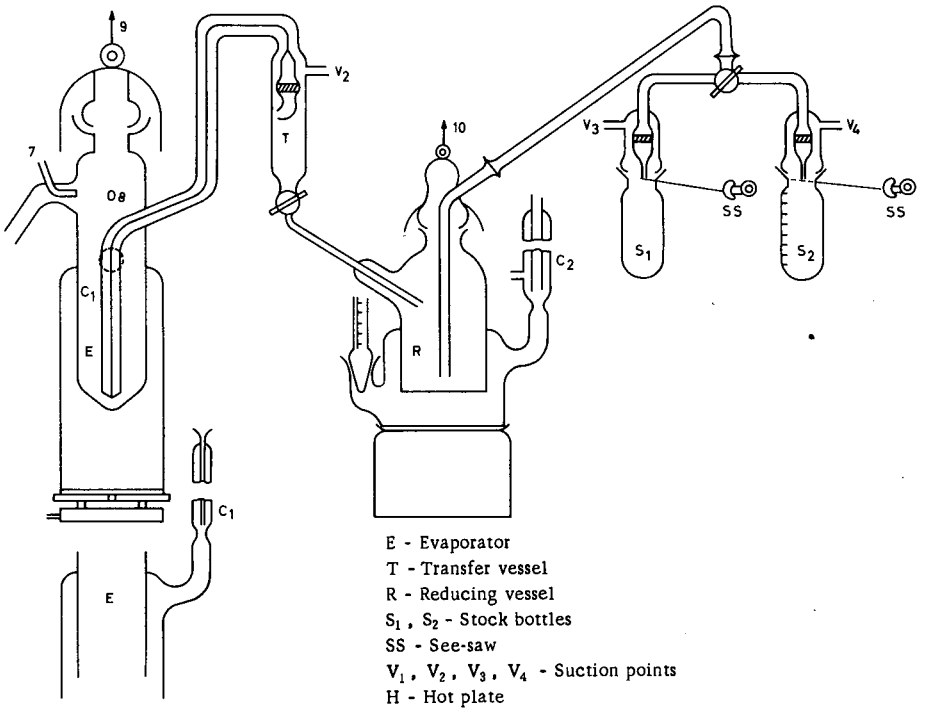
This is a non-radioactive gold colloid and is prepared in the assembly shown in Fig. 1. Before commencing the operation, the whole assembly is washed well, rinsed with distilled water and finally with pyrogen-free water and then dried.

One hundred milligrams of (99.99% pure) gold foil is dropped in the evaporator (E) and 1 ml of aqua regia is added. The evaporator is heated in a bath of isopropanol. The dissolution of the gold foil is completed in about 15 min.

The excess acid is evaporated under controlled conditions of temperature and pressure till orange yellow crystals of chlorauric acid appear. The crystals are dissolved in 10 ml pyrogen-free water and the solution is transferred to vessel T.

In the meantime, 4 ml gelatine solution (20% wt./vol.) and 10 ml of glucose solution (56%) are transferred into reaction vessel (R) and heated to about 80°C with continuous stirring, using a magnetic stirrer. One millilitre of 5 N NaOH is then added, the temperature is brought to 90°C and the chlorauric acid solution is added dropwise. The evaporator vessel is washed with 3 ml of pyrogen-free water and the washings are also added to this mixture. The solution is kept at this temperature with stirring for 15 min more and then allowed to cool. The pH of this seed colloid is measured and is usually between 5 and 7. The colloid is dispensed in small volumes into different vials, sealed and autoclaved at 15 lb/in^2 for 45 min.

A vial once opened for the preparation of colloidal gold-198 is not used again. The seed colloid can be preserved for about a month, after which the colloid particles may aggregate.



E - Evaporator
T - Transfer vessel
R - Reducing vessel
S_1, S_2 - Stock bottles
SS - See-saw
V_1, V_2, V_3, V_4 - Suction points
H - Hot plate
M - Magnetic stirrer-cum-hot plate
C_1 - C_2 - Condensors
7 - Connection to separating funnel 7, in front of lead wall
8 - Connection to separating funnel 8 in front of lead wall
9 and 10 - To pulley

FIG. 1. Plant assembly for gold-198

Preparation of radiogold colloid

The entire glass assembly is washed well and rinsed with pyrogen-free water, and dried; 1.5 ml of aqua regia is added to the evaporator vessel. The reducing mixture, consisting of 3.5 ml of 20% gelatine, 0.25 ml of seed colloid, and 10 ml of pyrogen-free water is placed in the reaction vessel.

The irradiated gold foil (150 mg) is washed with water and then dropped into the evaporator vessel. The dissolution of gold and crystallization of chlorauric acid are carried out by careful heating under suction.

The crystals are dissolved in 6 ml pyrogen-free water and 3.5 ml of 1 N NaOH is added and kept ready for addition.

During the above operation the mixture in the reaction vessel is brought to 70°C. The sodium aurate solution is added dropwise to the solution; 4-ml rinsings of the evaporator vessel are also added into the reaction vessel. The temperature is then raised to 80°C and kept constant for about an hour with continuous stirring. Finally the solution is cooled. The colloid is then transferred to various vials, sealed, autoclaved and stored in lead pots.

3. ASSAY AND QUALITY CONTROL

The activity assay is done by measuring the ion current of a known volume of stock solution in a calibrated ion chamber.

The radioactive purity is determined by gamma-ray spectrometry.

The radiochemical purity is determined by dialyzing the auric ion out or by paper chromatography.

Pyrogen testing is done by injecting an aliquot of a dummy colloidal gold preparation (run carried out prior to active run) into each of three rabbits and observing the temperature rise, if any.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Non-medical form

Specific activity:	> 5 Ci/g.
Chemical form:	$HAuCl_4$ in solution.

Medical form

Specific activity:	1 - 5 Ci/g.
Chemical form:	Colloid, stabilized with gelatine pH 5-7 sterilized.
Radiochemical purity:	> 95%.
Particle size of colloid:	300 Å.
Gold content:	3.5 mg/ml.
Gelatine concentration:	About 3%.

MINISTRY OF DEFENCE, ATOMIC ENERGY COMMISSION, SOREQ RESEARCH ESTABLISHMENT, YAVNE, ISRAEL

1. GENERAL

The irradiation of metallic gold in the reactor produces gold-198 by the (n, γ) reaction. The activated sample is dissolved in aqua regia and the resulting solution is evaporated. Aurochloric acid is neutralized and added to a seed solution, which contains colloidal gold nuclei and reducing and stabilizing agents.

2. EXPERIMENTAL PROCEDURE

Irradiation

The target is 100 mg of metallic gold (spec-pure); 1 mil[1]-thick foil is used. The gold is washed with 1:2 nitric acid, water and ether, and

[1] 1 mil is 0.001 in.

sealed into a silica vial. Irradiation is made at a thermal neutron flux of 3×10^{13} n/cm^2 s.

Chemical treatment

The apparatus is shown in Fig. 1.

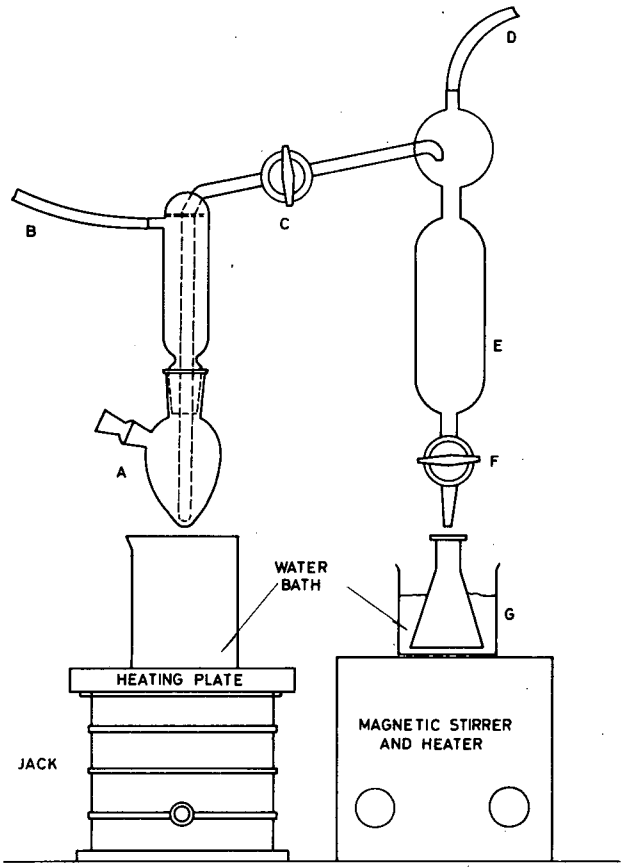


FIG. 1. Apparatus for the production of colloidal gold

Preparation of seed solution[2]

Dissolve 300 mg of gold in aqua regia and evaporate (see above). Dissolve crystals with 30 ml H_2O.

Dissolve 16.8 mg glucose into 30 ml H_2O. Add 12 ml of 20% gelatine solution. Heat to 90°C. Stop heating. Add 3 ml of 5 N NaOH while stirring. Keep stirring for 10 min. Add the previous solution, always stirring.

Rinse the evaporator with 10 ml distilled water and add to colloid.

[2] This procedure is based on current literature. Modifications were made by the Commission's staff and Dr. E. Edguer.

Sterilize for 1 h at 120°C. The solution thus obtained may be used for one month after preparation.

For the colloidal gold production, put into a conical flask 12 ml of water and dissolve 0.8 g of gelatine. Add 0.2 ml of seed solution and 50 mg ascorbic acid.

After preparation of the seed solution the following steps are then taken:

Transfer the irradiated sample into a shielded cell.

Wash the ampoule with acetone and then crush the ampoule.

Put gold into dissolving flask "A" and add 1 ml aqua regia.

Heat the water bath to 90°C. Raise the water bath.

When the gold is dissolved, start heating the solution marked G in Fig.1.

Apply a 100-mm Hg vacuum through B. Open C, so that an air stream bubbles through the solution. When the solution is almost completely evaporated, open C completely and lower the water bath, to obtain pale yellow needle-like aurochloric acid crystals.

Dissolve with 10 ml of 0.01% NaCl solution. Add 2.4 ml of 1 N NaOH solution. Transfer by vacuum to E.

The seed solution should be at 80°C. Add the solution from E slowly, dropwise, with continuous stirring. The addition should take 15 to 20 min; the temperature should be kept at 80°C.

Rinse the apparatus with 3 ml H_2O + 0.3 ml 1 N NaOH. Add to the colloid.

Transfer to the dispensing burette. Deliver sample for calibration.

Deliver the required amounts into penicillin-type bottles and close the bottles.

Sterilize for 1 h at 120°C.

Use pyrogen-free distilled water throughout the whole procedure.

3. ASSAY AND QUALITY CONTROL

The colloidal/ionic ratio is determined by ascending chromatography on Whatman No. 1 paper. The solvent is 30 wt./vol. HCl + 70 wt./vol. acetone.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process of ^{198}Au is based on the irradiation of gold wire and dissolution in aqua regia with the subsequent adjustment of acidity.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 0.2 g of gold wire (99.99% purity) for JRR-1.
0.05 g of gold wire (99.99% purity) for JRR-2.

Container: Polyethylene bottle, then a polyethylene capsule.
Flux: $\sim 3 \times 10^{11}$ n/cm^2 s (JRR-1).
$\sim 2 \times 10^{13}$ n/cm^2 s (JRR-2).
Irradiation time: 15 h (5 h×3 d) for JRR-1.
20 min for JRR-2.
Side reactions: Formation of ^{199}Au; approximately 5% in the final product.

Chemical treatment

The irradiated target is dissolved in aqua regia, evaporated to dryness, then redissolved in 1 N HCl. The apparatus is shown in Fig. 1.

a. Electric polyethylene capsule cutter
b. Dissolving vessel
c. Reagent feed pipe
d. Remote pipetter for dispensing
e. Turret of bottles

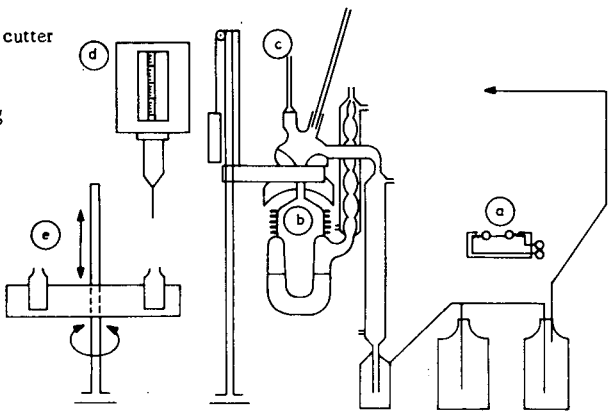


FIG. 1. Arrangement of apparatus for ^{198}Au production

Cut the inner capsule by the cutter (a).

Place the target in the dissolving vessel (b), add aqua regia of 6 ml/0.2 g of target, then evaporate to near dryness under the slight vacuum by indirect heating.

Add the following amount of 1 N HCl from the reagent feed pipe (c):
100 ml/g of target for the irradiation with JRR-1.
400 ml/g of target for the irradiation with JRR-2.
The product solution is dispensed into the sample bottles.

3. ASSAY AND QUALITY CONTROL

The routine assay is carried out with a well-type ionization chamber. The calibration is made with a $4\pi\beta$-coincidence counter. A routine acidity check is also made.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form: $AuCl_3$ in HCl and HNO_3 solution; acidity ~ 1 N.
Radiochemical purity: > 99% (exclusive of ^{199}Au).

Specific activity:	~ 130 mCi/g of Au (JRR-1 product).
	~ 12 Ci/g of Au (JRR-2 product).
Concentration:	~ 1 mCi/ml (JRR-1 product).
	~ 10 mCi/ml (JRR-2 product).

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Gold-198 is prepared as a colloidal suspension of metallic gold, stabilized with gelatine. Gold foils, cut in narrow bands and rolled together, are irradiated in a thermal neutron flux: $^{197}Au(n, \gamma)^{198}Au$. The product particle size is approximately 200 Å.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	200 mg gold foils, spectral pure[1].
Time of irradiation:	7 d.
Container:	Aluminium can.
Flux:	Approximately 2×10^{12} n/cm^2 s.

Chemical treatment

The irradiated gold foils are converted to gold chloride by reaction with aqua regia at 100°C. The excess of aqua regia is evaporated, and the residual gold chloride is dissolved in water.

The colloidal suspension is prepared by adding this solution of radioactive gold chloride dropwise to an alkaline solution of gelatine and water, previously mixed with gold colloid seeding solution and heated to approximately 70°C.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative ionization chamber measurements.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Radiochemical purity control, radiochromatography.
Toxicity and pyrogen control, test on animals.

The colloid particle size is checked occasionally by electron microscopy.

All products are subject to individual inspection and approval by pharmaceutical personnel.

[1] Johnson. Matthey & Co.

4. CHARACTERISTICS OF THE FINAL SOLUTION

GK - colloidal suspension of metallic gold stabilized with gelatine, sterilized.

Radioactive concentration:	Approximately 40 mCi/ml.
Isotopic purity:	At least 99% as ^{198}Au.
Radiochemical purity:	Ionic gold content less than 2%.
Specific activity:	Approximately 10 mCi/mg Au.
pH:	Around 6.
Composition of suspension:	Gold content 3.5 mg/ml;
	Gelatine content 30 mg/ml;
	Glucose content 1 mg/ml.

JUNTA DE ENERGIA NUCLEAR, MADRID, SPAIN

1. GENERAL

The preparation of colloidal gold is based on the method originally developed by Henry et al. [1, 2]. A small volume of non-radioactive colloid (the seed solution) is grown from a solution of radioactive chlorauric acid prepared from neutron irradiated gold strips.

2. EXPERIMENTAL PROCELURE

Irradiation

Target material:	0.4 g gold strips, 0.05 mm thick, purity 99.999%[1].
Container:	Leak-tight aluminium container, 8×10 mm diam.
Flux:	4×10^{12} n/cm^2 s; next to the surface of adjoining fuel elements (JEN-1).
Irradiation period:	1 week, approximate yield is 25 - 30 mCi/ml.

Chemical treatment

Method of preparation

The process involves the following steps:

Preparation of the seed solution: 0.3 g of gold is dissolved in 3 ml of aqua regia (HCl and HNO_3, analytical grade).

Evaporate the solution to dryness in a water bath under a vacuum of 70 mm Hg. Evaporation should not last longer than necessary and care is taken not to make the vacuum excessively high in order to avoid decomposition of the chlorauric acid.

[1] Supplied by Williams Gold Refining Co., United States of America.

In another recipient vessel the following mixture is heated to 90°C: 16.8 g of glucose (Merck product for microscopy and bacteriology) in 30 ml of distilled water, 12 ml of a 20% gelatine solution, (Schuchardt, analytical grade) and 5 ml of 5 N NaOH. Chlorauric acid crystals are dissolved in 30 ml of water; the solution is immediately poured dropwise into the glucose solution at a temperature of 90°C, with continuous stirring. After completion of the addition of chlorauric acid solution, a further 10 ml of water are introduced. The seed solution is allowed to cool and is distributed in penicillin flasks; seal, encapsulate and sterilize at 120°C for 30 min. The flasks are kept in a refrigerator and the seed solution can be used over a period of several months. A syringe fitted with a sterilized hypodermic needle is used to extract necessary volumes.

Growth of colloid: 400 mg of irradiated gold are dissolved in 4 ml of aqua regia, then evaporated to dryness under vacuum (70 - 80 mm Hg); this is done in the water-bath evaporator. The residue is dissolved in 40 ml of distilled water, then 9.3 ml of 1 N NaOH are added. The solution thus obtained is slowly dropped into a reducing mixture consisting of 16 ml of 20% gelatine, 1 ml of the seed colloid and 40 ml of distilled water. The resulting solution is heated to 100°C in a water bath while continuously stirring, Fig. 1 (R).

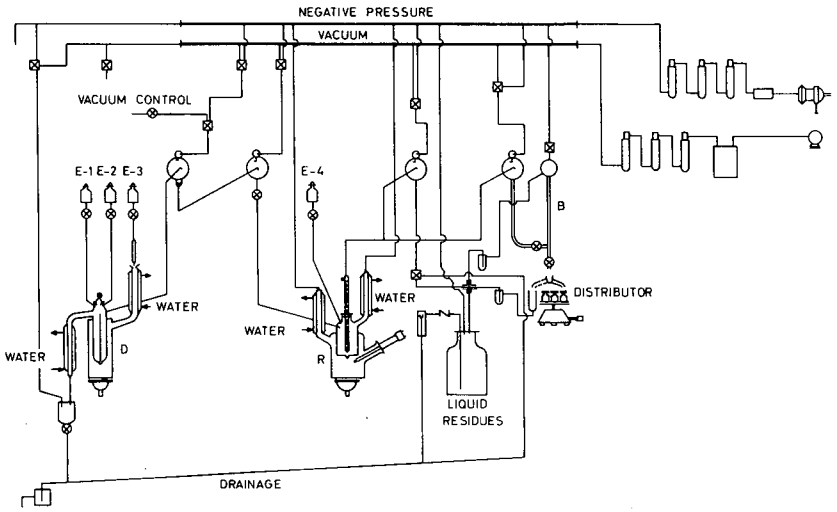


FIG. 1. Production of colloidal gold-198

After the addition of the chlorauric acid solution, heating is continued for 30 min. Then, 0.4 g of ascorbic acid dissolved in 2 ml of water and 1 ml of 1 N NaOH are added. The product is distributed in penicillin bottles and sterilized at 120°C for 1 h.

Apparatus

The production is carried out in an enclosure of the same design and size as those used for the production of ^{32}P and ^{132}I; it is shielded with 5-cm

lead bricks. The preparation assembly embodies the ancillary pieces needed (funnels, syphoning balls, etc.). The parts D, R and B (burette) are linked together by glass tubing.

3. ASSAY AND QUALITY CONTROL

General assay

Radiochemical purity is determined by ascending paper chromatography. No. 1 Whatman paper is used [6]. The eluent is a mixture of acetone, water, hydrochloric acid (d = 1.19) at the ratio of 70 : 20 : 10 [5, 6]. The following Rf are observed: colloidal gold, Rf = 0.0; soluble gold compounds, Rf = 0.9–1.0.

Activity measurements are made with an ionization chamber (see ^{32}P). An error of 5 – 10% is allowed. In special cases the error may be less than 5%. Biological tests include the determination of time duration for the stay of colloidal particles in the injected zone and the activity distributions in blood and urine. Rats are used and the solution is injected into the pleura or peritoneum. Acceptable values are 0.05% activity in blood and 0.5 – 0.7% in urine within a few hours from the administration [5, 6].

Determination of particle size

The determination of particle size is made by the Shlesinger centrifuge method [3, 4], a Wifug X-2 centrifuge is employed.

The following formula gives the particle size:

$$2\rho = \frac{A}{\omega}\sqrt{\frac{h}{T}\log\frac{C_0}{C}}$$

$$A = 6.15\times10^8\sqrt{\frac{\eta}{(\sigma-\sigma')R}}$$

where:

ρ = radius in mμ (1 mμ = 10 Å)
ω = speed of rotation (rpm)
C_0/C = ratio of colloid concentration before the centrifugation to final colloid concentration
h = height of liquid in centrifuging tube (flat-bottomed cylinder)
T = duration of centrifugation
η = viscosity (poises)
σ = density of the gold
σ' = density of the colloid solution
R = distance between the absorbent (filter paper at the bottom of centrifuge tube) and the axis of rotation of the centrifuge.

Variations in the concentration of the colloid are followed by spectrophotometry at the absorption peak of 527 mμ; a Beckman model B apparatus with 10-mm optical cells is employed.

The speed of the centrifuge is of the order of 4500 rpm. Four discs of No. 40 Whatman paper are used as the absorbent. The values for σ and

σ' are 19.2 and 1 respectively. The sizes for the seeds vary between 45 and 70 Å, and for the final colloid between 240 and 340 Å.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Colloidal gold ^{198}Au, injectable

A sterile, pyrogen-free, and isotonic solution of colloidal gold ^{198}Au, pH 6 - 7, particle size 300 Å, meeting the following specifications:

Radioactive purity:	^{198}Au content > 99.5%.
Radiochemical purity:	Soluble gold content < 2%.
Radioactive concentration:	Maximum 30 mCi/ml.
Chemical concentration:	3 - 5 mg Au/ml; gelatine, 3%.
Sterility:	Sterilization is carried out in autoclave at 120°C for about 1 h.
Analysis of pyrogens:	See ^{32}P.
Isotonicity:	Adjusted by means of cryoscopic measurements [7].

Colloidal gold ^{198}Au, injectable

A sterile, pyrogen-free and isotonic solution obtained from the above solution by diluting with 3% gelatine.

Radioactive purity:	As above.
Radiochemical purity:	As above.
Radioactive concentration:	About 1 mCi/ml.
Chemical concentration:	0.25 - 5 mg Au/ml.
Sterility:	As above.
Analysis of pyrogens:	As above.
Isotonicity:	As above.

^{198}Au gold chloride, non-injectable

A solution of gold chloride in hydrochloric acid meeting the following specifications:

Radioactive purity:	^{198}Au content > 99.5%.
Radiochemical purity:	$^{198}Au^{3+}$ content > 99%.
Specific activity:	Up to 3 Ci/g.

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[6] REBOLLO, D.V., Sección de Isótopos, Dirección de Química e Isótopos de la JEN, private communication.
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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Gold-198 is prepared as a sterilized colloidal suspension of metallic gold, stabilized with gelatine. The normal product has a wide spectrum of particle sizes ranging from 25 to 250 Å. A second colloid, produced by a seeding technique, in which the particle size is restricted to the range 200 - 300 Å, is also prepared.

2. EXPERIMENTAL PROCEDURE [1]

Irradiation

Target material: 2.4 g ash cohesive gold foil, dental grade.
Irradiation container: Screw-topped aluminium can.
Irradiation conditions: Flux ~ 10^{12} n/cm^2 s for 7 to 10 d.

Chemical treatment

The irradiated gold foil is converted to chlorauric acid by dissolving in aqua regia and then pumping off the excess acid. The $HAuCl_4$ is dissolved in water and converted to gold in a colloidal form with glucose, gelatine and sodium hydroxide.

3. ASSAY AND QUALITY CONTROL

Colloids are assayed for particle size (by electron microscopy) and ionic gold (by paper chromatography and dialysis).

Irradiation conditions are selected such that <1% ^{199}Au is formed by the burn-up of ^{198}Au.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form: Colloidal suspension of metallic gold stabilized with gelatine.
Radioactive concentration: ~ 100 mCi ^{198}Au/ml.
Concentration total element: 10 mg Au/ml.

Radioisotopic purity: < 1% ^{199}Au.

Radiochemical purity: Prolonged dialysis tests and paper chromatographic examinations have detected no traces of ionic gold (< 0.01%).

Composition: The colloidal solution has the following constituents:

	(%) (wt./vol.)
Gold	1.0
Gelatine	3.5
Glucose (including decomposition products)	~28.0
Sodium chloride	~ 0.7

Particle size: Not routinely determined. Electron microscope measurements of particle size distribution show that the number of particles decreases with increasing particle size. No particles greater than 225 Å. Particles of diameter 100 - 125 Å account for the greatest proportion of the activity.

REFERENCE

[1] AERE Report No. I/R. 1341.

OAK RIDGE NATIONAL LABORATORY,
TENN., UNITED STATES OF AMERICA

1. GENERAL

Gold-198 is produced by the (n, γ) reaction in a gold metal target, $^{197}Au(n, \gamma)^{198}Au$, and is prepared as $AuCl_3$ in mixed HCl and HNO_3 solution. About 5% ^{199}Au is also produced.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 50 mg gold metal.
Neutron flux: 0.7×10^{13} n/cm^2 s.
Irradiation time: 61 h.
Reactor yield: 2.9 Ci.

Chemical treatment

Apparatus

A hot off-gas scrubber unit (Fig. 1) is used in processing.

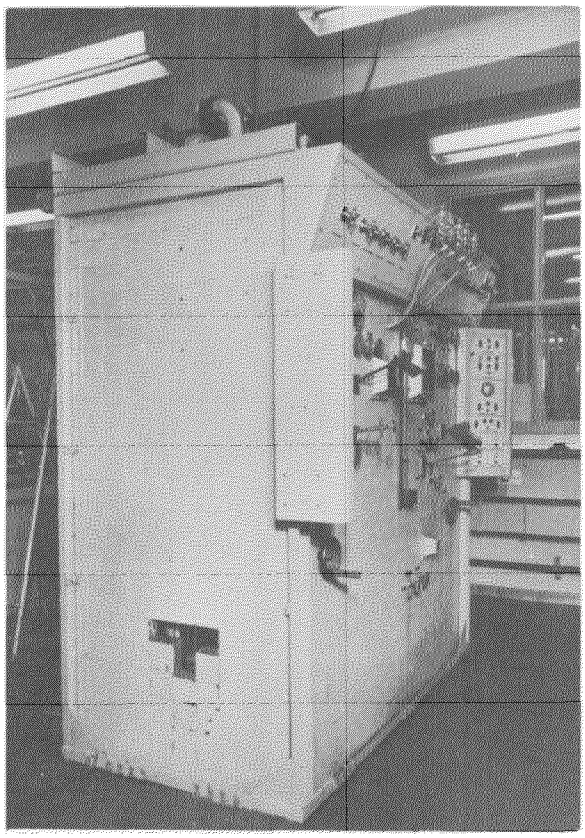

FIG. 1. Unit for the production of colloidal gold-198

Processing

Yield: > 95%.

The irradiated gold target is heated in 3.5 ml of aqua regia under the hot off-gas scrubber unit. After the target is dissolved, the solution is diluted to 50 ml with distilled water.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for molarity of HCl, total solids, ^{198}Au and ^{199}Au concentrations, and radiochemical purity, according to ORNL Master Analytical Manual (TID-7012), procedure No. 9 0733381.

Precision and accuracy of the ^{198}Au assay are:
Calibration by $4\pi\beta-\gamma$ coincidence counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 3%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity ^{198}Au is delivered as $AuCl_3$ in HCl and HNO_3 solution as a stock item. Other specifications of interest are:

Acidity:	1 N total acids ±50%.
Concentration:	> 10 mCi/ml.
Specific activity:	≅ 25 000 mCi/g Au.
Radiochemical purity:	> 98% (exclusive of ^{199}Au).
^{199}Au:	~ 5%.

BORIS KIDRIČ INSTITUTE OF NUCLEAR SCIENCES,
VINČA, YUGOSLAVIA

1. GENERAL

Irradiation of gold foils in a reactor produces the radioactive gold isotope ^{198}Au by the (n, γ) reaction. Chemical treatment of these irradiated foils produces radioactive colloidal ^{198}Au used for medical purposes. Radioactive colloidal gold is produced by the method of Constant and co-workers [1, 2] in a modified French apparatus built in a shielded cell. The method provides radioactive colloidal ^{198}Au of high radiochemical purity, colloid particles of fixed dispersity and a pH-value corresponding to medical requirements.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	2×200 mg of gold foils, 99.999% purity.
Irradiation containers:	Cylindrical Al-cans with screwed covers, 70 mm internal length, 25 mm internal diameter.
Thermal neutron flux:	$2-5\times10^{12}$ n/cm^2 s (RA reactor at Vinča);
Irradiation time:	7 d.

The gold isotope ^{199}Au is produced by the reaction: $^{198}Au(n, \gamma)^{199}Au$.

The cross-section of this reaction is $\sigma_{n,\gamma}$: 26 000 barn. This gold isotope is produced at fluxes considerably higher than 10^{13} n/cm^2 s.

Chemical treatment

Production method

After degreasing in chloroform, radioactive gold foils are put in a flask A where they are dissolved in 3 - 4 ml of aqua regia by heating over a water-bath.

The $HAuCl_4$ solution is evaporated to dryness, in vacuo, by heating, obtaining $AuCl_4 \cdot 4H_2O$.

After cooling, $AuCl_4 \cdot 4H_2O$ is dissolved in $H_2O + 1$ N NaOH. $NaAuCl_4$ is obtained and through a G-5 sintered glass it is filtered into vessel B (filtration vessel).

The filtrate is added dropwise to a reducing solution containing an aqueous solution of the "germ" (inactive gold colloid) of low dispersion in a solution of glucose and sodium hydroxide [3, 4] and 20% of gelatine. $^{198}Au^{3+}$ + $^{197}Au^{3+}$ is reduced to the metal colloidal state by heating, and mixed by pulsation.

Non-reduced $NaAuCl_4$ is reduced by a dropwise addition of sodium ascorbate.

Apparatus

A vessel for dissolving irradiated gold and evaporating $NaAuCl_4$ to dryness, in vacuo, thus producing $AuCl_4 \cdot 4H_2O$ (Fig. 1, A).

Vessel for filtering and the dropwise addition of $NaAuCl_4$ with built-in G-5 sintered glass (Fig. 1, B).

Reducer in which radioactive colloidal gold ^{198}Au is produced by reducing the $Na\,^{198}AuCl_4$ solution (Fig. 1, C).

Burette for distributing radioactive colloidal gold in penicillin bottles (Fig. 1, D).

Distribution system for constant, transportable and high vacuum (Fig. 1, E).

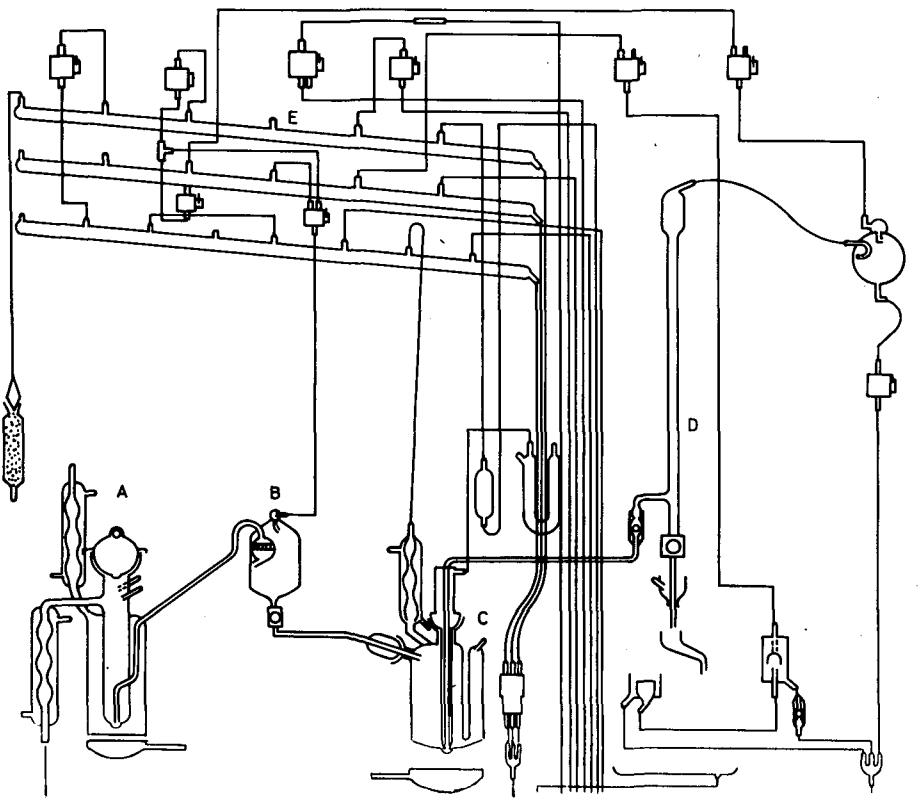

FIG. 1. Apparatus for the preparation of colloidal gold

3. ASSAY AND QUALITY CONTROL

Qualitative and quantitative analysis of gold foils.
Pyrogenic test of the solutions used.
Radioactive measurement of the colloidal solution.
Radioactive control.
Determination of particle size on an electron-microscope.
pH of the colloidal solution.

Radiochemical purity control (% ^{198}Au colloidal + % $^{198}Au^{3+}$). Carried out by ascending paper chromatography [5]. Filter paper: Whatman No. 1. Chromatogram: 25×2 cm; start 2.5 cm from the bottom. Developing agent: ethyl acetate (9 volumes) + conc. HNO_3 (1 volume). Development time: about 3 h.

Sterility test of the colloidal solution [6].

Distribution and fixation of radioactive colloidal gold in organs of experimental animals (white mice).

Elimination of radioactive colloidal gold ^{198}Au from experimental animals by urine excretion.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVAu 198/1, gold-198 sterile colloidal gold solution

Sterile colloidal gold ^{198}Au solution, pH 5 - 7, meeting the following specifications:

Radioactive concentration:	Measured to within 10%; 25-50 mCi/ml.	
Radioactive purity:	^{198}Au content higher than 99%.	
Radiochemical purity:	Colloidal ^{198}Au content higher than 99%.	
Particle size:	250 ± 50 Å.	
Composition of the solution:	Au concentration:	3.5 mg/ml
	Gelatine concentration:	3%
	Glucose concentration:	0.1%
	NaCl concentration:	5 mg/ml

Sterile.
Pyrogen-free.

Reference: YVAu 198/4, gold-198 sterile dilute colloidal gold solution

Sterile colloidal gold solution, diluted with 20% gelatine, for diagnostic purposes.

Radioactive concentration:	Measured to within 10%; one to a few mCi/ml.
Radioactive purity:	^{198}Au content higher than 99%.
Radiochemical purity:	Colloidal ^{198}Au content higher than 99%.
Particle size:	250 ± 50 Å.

Sterile.
Pyrogen-free.

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IODINE-131

NUCLEAR DATA

1. NUCLEAR PROPERTIES

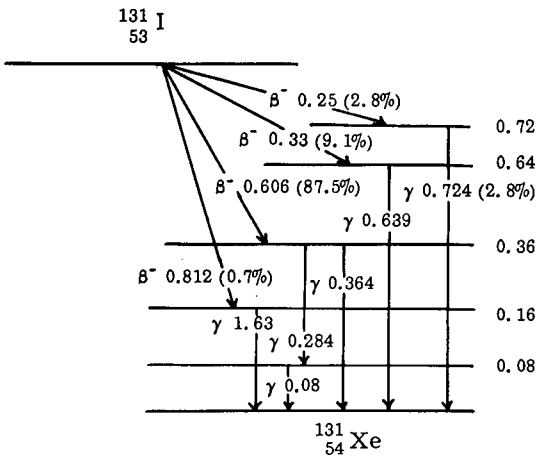
1.1. Half-life

8.06 d

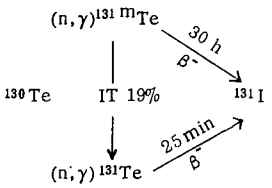
1.2. Type of decay, and energy (MeV)

beta (β^-)	0.250 (2.8%)	gamma 0.080 (2.2%)	IC (4%)
	0.33 (9.1%)	0.284 (5.5%)	(0.3%)
	0.606 (87.5%)	0.364 (81%)	(1%)
	0.812 (0.7%)	0.639 (9.1%)	
		0.724 (2.8%)	
		0.163 (0%)	(0.7%)
		(via 12 d ^{131m}Xe)	

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Abundance of target nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm^2 s (mCi/g) 24 h	7 d	sat.	Side reactions
	34.59	< 0.008 0.22	0.8	4.4	9.6	$^{120}Te(n,\gamma)^{121}Te$ (T = 154 d) isot. abund.: 0.089% $^{122}Te(n,\gamma)^{123m}Te$ (T = 104 d) isot. abund.: 2.46% σ = 2.8 barn $^{124}Te(n,\gamma)^{125m}Te$ (T = 58 d) isot. abund.: 4.61% σ = 6.8 barn $^{126}Te(n,\gamma)^{127}Te$ (T = 9.4 h) isot. abund.: 18.71% σ = 0.8 barn $^{126}Te(n,\gamma)^{127m}Te$ (T = 105 d) σ = 0.09 barn $^{128}Te(n,\gamma)^{129m}Te$ (T = 33 d) isot. abund.: 31.79% σ = 0.015 barn $^{128}Te(n,\gamma)^{129}Te$ (T = 72 min) σ = 0.13 barn

For nuclear data see Ref. [1].

Iodine-131 may also be extracted from fission products: $U(n,f) \longrightarrow {}^{131}I$. $U(n,f) \longrightarrow {}^{131}Te \xrightarrow[24.8\ min]{\beta^-} {}^{131}I$. Fission yield: 2.9%.

3. APPLICATIONS

Iodine-131 is the radionuclide most widely used in medical therapy and diagnosis. Besides this it has found application as a tracer. A brief survey of published applications is given below.

3.1. Medicine

3.1.1. Applications of ^{131}I as primary isotope

Treatment of hyperthyroidism, thyroid cancer and heart diseases	[2-16, 28]
Diagnostic use, thyroid function test	[25-28]
Preparation of labelled compounds	[17]

3.1.2. Applications of organic ^{131}I-labelled molecules

Iodinated human serum albumin	[2, 18-21]
Iodofluorescein	[24]
^{131}I-Rose Bengal	[2, 21, 22]
Sodium ortho-iodohippurate	[23]

3.2. Technical applications

Hydrology	[29-32]
Pulp and paper research	[33]

4. RADIOLOGICAL PROTECTION

4.1. External radiation

The unshielded exposure rate per curie ^{131}I at a distance of 1 m is about 300 mR/h [57]. The necessary lead shielding thickness for reduction of this exposure rate by a factor of 100 is about 3 cm [57]. Thus a practical shield for the handling of amounts of ^{131}I up to around 1 Ci is a lead wall 5 cm thick.

4.2. Internal radiation

Iodine-131 is classified as a class 2, high-toxicity nuclide [34]. The biological half-life of iodine is 138 d [56], giving an effective half-life of 7.6 d, referred to the total body. The excretion of iodine from kidneys, liver and bone is more rapid as is shown in Table I.

TABLE I

EXCRETION OF IODINE

Organ of reference	Biological half-life of iodine (d)	Effective half-life of ^{131}I (d)
Thyroid gland	138	7.6
Kidneys, liver, spleen	7	3.7
Bone	14	5.1

Because of the volatility of iodine this nuclide usually represents the main health physics problem in a laboratory for the production of radioisotopes for medical and scientific applications. Production facilities need careful ventilation with special filtering of exhaust air.

4.3. Decontamination

Decontamination of glassware and equipment is most effectively achieved by means of strong mineral acid solutions, e.g. a mixture of nitric acid (2 - 5%) and hydrofluoric acid (2%). Decontamination processes of this kind should always be performed within a ventilated containment because of the volatility of the iodine in acid media.

Removal of ^{131}I from clothing and skin is facilitated by the presence of iodide - iodate carrier. General instructions for decontamination of personnel, equipment and working surfaces are given in Ref. [34].

5. SURVEY OF PRODUCTION METHODS

5.1. Neutron irradiation of tellurium or tellurium compounds

Metallic tellurium, tellurium dioxide, orthotelluric acid, H_6TeO_6, and metatelluric acid, H_2TeO_4, are the target materials in general use for ^{131}I production. Tellurium is usually processed by dissolving it in a strong mineral acid, preferably H_2SO_4. After the addition of an oxidant (H_2O_2, $KMnO_4$, etc.) the iodine is distilled off and collected in a sodium sulphite or thiosulphate solution [35, 36]. Other methods for separation are ion exchange techniques and precipitation [37]. Telluric acid, H_6TeO_6, is also usually used together with a separation process based on dissolution and distillation [38, 39] or column chromatography [40].

Another method for the separation of ^{131}I from dissolved tellurium targets is by adsorption on specially prepared platinum electrode surfaces, followed by an electrochemical desorption [41, 42].

Gleason [43, 44] proposes metatelluric acid instead of orthotelluric acid, on account of the higher decomposition temperature and also higher tellurium content.

A number of isotope production centres are using tellurium dioxide as target material for ^{131}I production. Two different methods are in use for separation. The wet method, which comprises the suspension of TeO_2 in water and sulphuric acid, oxidation with hydrogen peroxide and distillation [45, 46] or dissolution in 10% sodium hydroxide, oxidation with hydrogen peroxide, acidification and distillation in the presence of Na_2MoO_4 [47]. The dry method makes use of direct distillation of the iodine by heating the irradiated target material to around 700°C [48–50].

5.2. Preparation from fission products

Fission product ^{131}I is formed in uranium in a reactor during irradiation, and the general method for separation is to release the iodine by means of heating or dissolution in nitric acid, trap it in a suitable medium, reduce the volume and finally apply a chemical purification method [52–54].

6. RADIOASSAY

See Part I, Section 6 of this Manual.

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CHALK RIVER, ONT., CANADA

1. GENERAL

Iodine-131 is a beta-gamma emitter with a half-life of eight days. It is produced in the reactor by the irradiation of tellurium, $^{130}Te(n, gamma)^{131}Te$ (beta decay)^{131}I.

After irradiation, the ^{131}I is chemically separated from the tellurium target and shipped as required to the pharmaceutical industry for further processing and distribution to the medical profession.

2. EXPERIMENTAL PROCEDURE

Irradiation

The irradiation target consists of 35-40 g of tellurium metal shot sealed in a standard reactor capsule. The normal irradiation time is one month. The usual yield is from 8 to 15 Ci from each capsule, depending on the flux. An appropriate number of capsules are held under irradiation to provide normal local and standby requirements.

Chemical treatment

The irradiated tellurium is dissolved in an oxidizing medium wherein the elemental iodine is released from the tellurium crystalline lattice and converted to iodic acid (HIO_3). This is reduced with oxalic acid releasing elemental iodine vapour, which is collected in alkaline scrubbers as sodium iodide in sodium sulphate solution - which is the standard product of the Atomic Energy of Canada Ltd. (AECL).

Irradiated capsules are pneumatically entered to the process equipment from a transfer flask. The capsules are mechanically opened and irradiated tellurium poured into a 5-litre glass reaction flask where it is dissolved in chromic and sulphuric acids. The solution is refluxed for about two hours to ensure full oxidation of the tellurium to telluric acid and iodine to iodic acid. Continuous temperature and conductivity control of the solution is necessary to ensure complete oxidation, and a safe reaction rate.

Upon completion of the oxidation, the HIO_3 is reduced by the addition of oxalic acid in a sulphuric acid medium to convert the iodine to the elemental form. The addition is made slowly and at a reduced temperature to permit controlled release of the large quantities of CO_2 formed in the breakdown of the oxalic acid. When the addition is complete, the temperature is raised and the iodine vapour is released. The vapour is passed through a series of scrubbers initially containing 1 molar sodium bisulphite ($NaHSO_3$) in 0.5 N NaOH solution. The resulting product forms as NaI in

Na_2SO_4, the bisulphite being oxidized to the sulphate form. The radiation from each scrubber is monitored to observe build-up of activity. Filters in the equipment exhaust system are also monitored to observe any release of ^{131}I during the process.

Equipment

The processing equipment is a sealed chemical glassware system with valves, stopcocks and reagent entry lines mounted at appropriate points. The system is contained in a chemical fumehood provided with 4 in. (10 cm) of lead shielding. Fitted through the walls are stopcock turners, ball joint manipulators, valve controls and lead glass windows to permit remote viewing and operation. The fumehood exhaust leads into a series of absolute filters and activated charcoal filters which remove all particulate material and iodine vapour. All electronic instrumentation is brought out through the shielding walls to a remote control panel. Solid waste (such as empty irradiation capsules) is dropped through a shielded pipe in the floor of the hood to a shielded waste container. Liquid waste is drawn off and piped to plastic lined and shielded drums stored in a remote location.

3. ASSAY AND QUALITY CONTROL

Chemical

Samples of the final product are assayed for total solids, total non-volatile solids, chromium content, oxidizing materials and pH. Archive samples are retained to check for composition changes in ageing of the product.

Radiochemical

Samples of the product are routinely measured for ^{131}I content using a calibrated quartz fibre gamma electroscope to measure the 0.364 MeV gamma ray. The radiochemical purity is periodically checked using a 512-channel analyser.

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1. GENERAL

Iodine-131 is separated from irradiated telluric acid dissolved in sulphuric acid by adsorbing ^{131}I on to a platinum plate. It is then desorbed into dilute reducing agent solution by electrolysis. This process is simple,

neat and easy to perform. It is particularly suitable for small- and medium-scale production of ^{131}I.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	150 g telluric acid (Extra Pure Grade[1]).
Irradiation container:	Aluminium can 4.7 cm diam. × 9 cm.
Irradiation condition:	Neutron flux 4×10^{12} n/cm^2 s.
Irradiation time:	30 h.

Chemical treatment

One hundred and fifty grams of irradiated telluric acid is dissolved in 400 ml of 1 N sulphuric acid. The platinum plate is immersed in the telluric acid solution to adsorb ^{131}I. After 24 h, the platinum is taken out from the solution and washed very thoroughly with distilled water.

In a small electrolytic cell, 0.1% sodium sulphite solution is placed. The platinum plate on which the ^{131}I is adsorbed is inserted into the cell and is made the cathode. Another small platinum plate is used as anode. By applying 2.6 ~ 2.8 V D.C., ^{131}I is desorbed into the solution of reducing agent within a few minutes. About 250 mCi of ^{131}I is obtained.

3. ASSAY AND QUALITY CONTROL

The chemical analysis of the product is carried out according to Oak Ridge National Laboratory Master Analytical Manual 9073391-1 ~ 4. The radiochemical purity assay is made according to 9073392-1 ~ 6. The chemical form of ^{131}I is determined by ascending paper chromatography. Pharmaceutical control is carried out according to Minimum Requirements of Radioactive Drugs, Ministry of Health and Welfare, Japan (1962).

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	NaI in 0.1% Na_2SO_3 solution.
Concentration:	5 mCi/ml.
Specific activity:	Carrier-free.
Acidity:	pH = 7 ~ 8.
Iodate:	< 1%.
Radiochemical purity:	> 99%.

[1] Product of Kanto Chemical Co. Inc. Japan.

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

The method of preparation, reported by Douis and Rosa [1, 2], consists of wet-treatment of a tellurous anhydride target to bring the iodine produced by irradiation to valencies corresponding to a volatile - and therefore, by distillation, easily recoverable - product. The production is based on the nuclear reaction $^{130}Te(n,\gamma)^{131}Te \xrightarrow{\beta^-} {}^{131}I$.

Tellurous anhydride dissolved in a soda solution gives sodium tellurite which is converted into tellurate by oxidation. The iodine, which is assumed to be mainly at valency I^{5+} and I^-, must, if sufficient H^+ ions are present, transform to valency I^0, which is capable of distillation.

To avoid the conversion of sodium tellurite into TeO_2, which precipitates after direct acidification, prior oxidation with H_2O_2 in the presence of a catalyst was necessary; sodium molybdate was selected for the catalyst because it was not liable to distil with iodine under the working conditions used.

After the addition of a sufficient amount of sulphuric acid to obtain a 6 - 8 N solution, i. e. the optimum concentration for the purpose of iodine distillation, distillation is then carried out. In this way a solution with a specific activity of 50 - 100 mCi/ml is obtained directly.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:

Tellurous anhydride TeO_2 B. D. H., more than 99% purity. Maximum quantity: 160 - 180 g per operation.
Irradiation capsule and conditions (Fig. 1):

EL 2	Aluminium "central channel" capsule - internal length 110 mm; internal diam. 50 mm. Closed by crimping. Maximum capacity: 180 g of target. Use of central hole: flux 7×10^{12} n/cm^2 s.
EL 3 and TRITON	Aluminium tube - internal length 65 mm; internal diam. 22. 5 mm. Closed by crimping. Maximum capacity: 53 g of target. Use of "heavy water" channel at EL-3: flux $1\sim2\times10^{13}$ n/cm^2 s. TRITON: flux $\sim10^{13}$ n/cm^2 s.
SILOE	Aluminium tube - internal length 55 mm; internal diam. 19. 9 mm. Closed by crimping. Maximum capacity: 40 g of target. SILOE: flux $\sim7\times10^{13}$ n/cm^2 s.

Activity produced:

Iodine-131 activity, produced by irradiation at 10^{12} n/cm^2 s, is summarized below:

Activity (mCi/g of target)	8 d	15 d	Saturation
Te metal	4.85	7.25	9.70
TeO_2	4.37	6.65	8.75

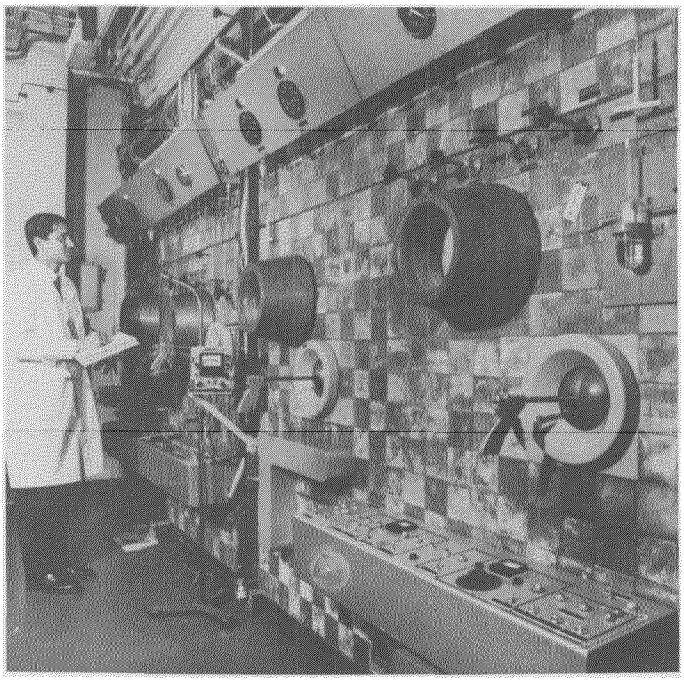

FIG. 1. Apparatus for the production of ^{131}I (front view)

Chemical treatment

Separation method

After uncrimping the irradiation tubes, the powder is poured into the dissolving bottle; 500 ml of 15% NaOH are introduced and the stirring system is set in motion until dissolution is complete. The sodium tellurite solution thus obtained in the dissolving bottle is then passed through a siphon connection. The dissolving bottle is rinsed with 100 ml of 15% NaOH and two portions of doubly-distilled water (5 ml each), which then accompany the tellurite solution. The rinsing is completed with two more portions of doubly-distilled water (20 ml each), which are passed into the distillation flask with the remainder of the solution.

A 5-ml buffer solution of M/40 sodium carbonate and M/5 sodium bicarbonate is placed in the distillation receiver bottle, after which oxidization of the tellurite solution is carried out. For this purpose 40 ml of 15% sodium molybdate, then 70 ml of 110-volume hydrogen peroxide are placed in the distillation bottle. Acidification is then carried out by means of 240 ml of

concentrated sulphuric acid which must be carefully poured in very small portions to avoid excessive bubbling.

Reflux boiling is then carried out in a stream of nitrogen for one hour, followed by distillation; 50 ml of the final solution is collected, after which distillation is stopped. An ^{131}I solution of pH 8 - 10 is thus obtained carrier-free and also free of reducing agent.

Preparation of ^{131}I in isotonic solution

After normal preparation the sulphuric tellurate solution is kept for 24 h to allow a certain quantity of ^{131}I to reform. After placing 3 ml of 0.025 M NaOH + 0.3 ml of M thiosulphate in the receiver and adding 70 ml of hydrogen peroxide the solution is reflux-boiled for one hour. Distillation (Fig. 2) is then carried out in the same manner and 30 ml is recovered. This solution is recuperated in a bottle containing 3 ml of an isotonic phosphate buffer.

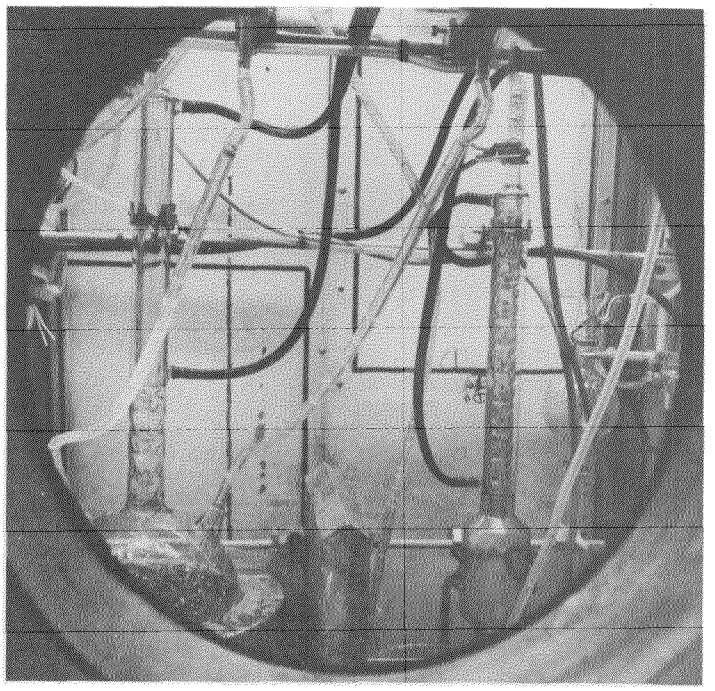

FIG. 2. Apparatus for the production of ^{131}I (distillation area)

Reagents necessary for the preparation:

NaOH at 15%.

Sodium molybdate at 15%.

Carbonate-bircarbonate buffer { Na_2CO_3 M/40 ; $NaHCO_3$ M/5.

Isotonic phosphate buffer at 9000 γ/ml of P NaH_2PO_4 21 g ; NaCl 45 g.

Bring up to 500 ml with doubly-distilled water. Adjust the pH to 6.3 with 4 N NaOH. Filter. Sterilize for half an hour at 1 kg/cm^2.

Equipment

Composed essentially of:
1 dissolving bottle to which is fitted a glass rotary stirrer.
1 glass distillation flask with several plunger tubes surmounted by Vigreux pins and a reflux condenser.
1 receiver flask, with a plunger tube.
Several siphon connections for transferring the solution.

3. ASSAY AND QUALITY CONTROL

After one complete process the following operations are performed:
Radioactivity measurement.

Spark spectrography, to determine the metallic impurity content. This is generally lower than 5 μg/ml.

Chemical control [3], to verify that the ^{131}I is indeed present in the form of NaI and not in an oxidized form. Chromatography is carried out on Whatman No. 1 paper dipped in a chromatographic mixture of three volumes of methanol to one volume of water. The Rf of sodium iodine is 1, of sodium iodate 0.46. The respective positions of the two iodized compounds are shown by the brown colour formed by the iodide-iodate reaction in an acidic medium. If we compare the results with an autoradiogram or record the radioactivity along the chromatogram we can confirm that there is no iodate in the sodium iodide (^{131}I) solution.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{131}I S-1 - Solution of sodium iodide (^{131}I), carrier-free, non-injectable

A sterile, aqueous solution of sodium iodide Na^{131}I, pH 7 - 10, meeting the following specifications:

Radioactive concentration, measured to within 5%: 20 - 30 mCi/ml average; 100 mCi/ml maximum.

Radioactive purity: ^{131}I content > 99.9%.

Radiochemical purity: Iodides content > 95%.

Specific activity: Above 1 Ci/mg.

Composition of the solution: As indicated in the French Pharmacopoeia:

Sodium radioiodide	unweighable quantity
Anhydrous Na_2CO_3	0.26 mg
Anhydrous $NaHCO_3$	1.68 mg
Anhydrous $Na_2S_2O_3$	1.50 mg
Distilled water	1 ml

No undesirable chemical impurities

Reference: ^{131}I S-2 - Solution of sodium iodide (^{131}I) at 2 mCi/ml, injectable

An aqueous, sterile, isotonic and pyrogen-free solution of sodium iodide $Na^{131}I$ in a phosphate buffer, pH 7, meeting the following specifications:

Radioactive concentration, measured to within 5%: 2 mCi/ml.

Radioactive purity: ^{131}I content > 99.9% (gamma spectrum characteristic of ^{131}I).

Radiochemical purity: Iodide content > 95%.

Specific activity: Above 1 Ci/mg.

Composition of the solution:

Sodium radioiodide	unweighable quantity
NaH_2PO_4, H_2O	4.2 mg
NaCl	9 mg
NaOH pH	quantity sufficient to give a pH of 7
$Na_2S_2O_3$, $5H_2O$	2.48 mg
Distilled water	1 ml

Sterile.

Pyrogen-free.

Reference: ^{131}I D - Capsules of sodium radioiodide (^{131}I)

Coloured capsules of assimilable gelatine containing, after evaporation of a carrier-free sodium iodide $Na^{131}I$ solution, a diagnostic dose of ^{131}I and meeting the following specifications:

Radioactivity per capsule, measured to within 5% and indicated by means of a colour code: up to 50 mCi.

Radioactive purity: ^{131}I content > 99.9% (gamma spectrum characteristic of iodine).

Radiochemical purity: Iodides content > 95%.

Specific activity: Above 1 Ci/mg.

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CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production of ^{131}I is based on the nuclear reaction $^{130}Te(n, \gamma)^{131m}Te \xrightarrow{IT} {}^{131}Te \xrightarrow{\beta^-} {}^{131}I$. The irradiated tellurium dioxide target is dissolved in sodium hydroxide solution; sulphuric acid and ferric sulphate are added and

the carrier-free iodine is distilled into a receiver containing dilute sodium hydroxide solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Tellurium dioxide, (BDH/purity 99%).
Flux:	4×10^{13} n/cm^2 s.
Time of irradiation:	200 h.
Container:	Quartz ampoule.

Chemical treatment

The irradiated target is forwarded through an air lock into a box hermetically closed and fitted with special shielding, where it is opened. Tellurium dioxide is poured into the distillation bottle placed into a separate box. Distillation is carried out after adding concentrated sulphuric acid. Iodine is collected in a receiver containing sodium hydroxide. The product is sealed in ampoules and sterilized in an autoclave at 120°C for 40 min.

3. ASSAY AND QUALITY CONTROL

The purity of the target is previously checked with the aid of spectrometric methods and activation analysis. Aliquot samples from the product are taken and the purity is controlled spectrometrically and, with the aid of a multichannel pulse height analyser, by comparing the spectrum with that of a "mock iodine" standard. Samples from each charge are checked for half-life. pH and sterility are controlled in the usual way.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Radiochemical purity: 99%.

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Iodine-131 is produced by the fission of uranium, as well as by the thermal neutron irradiation of tellurium, tellurium dioxide or telluric acid. At Trombay, ^{131}I is produced on a routine basis by the neutron irradiation of tellurium metal.

The ^{131}I is recovered from the irradiated tellurium by dissolving the target in a mixture of chromic and sulphuric acid, followed by reduction of the iodate with oxalic acid. The iodine is distilled into sodium sulphite solution. The product is purified by one more oxidation reduction cycle followed by distillation. The distillate is concentrated after adjusting the pH to ~ 8 to bring ^{131}I into sodium iodide.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Pure tellurium metal powder.

In APSARA: 50 g in 1 capsule, type A (screw-capped 1 S aluminium can, 73 mm high and 26.5 mm diam.)
Flux: 2 to 3×10^{12} n/cm^2 s.
Irradiation period: 4 weeks.

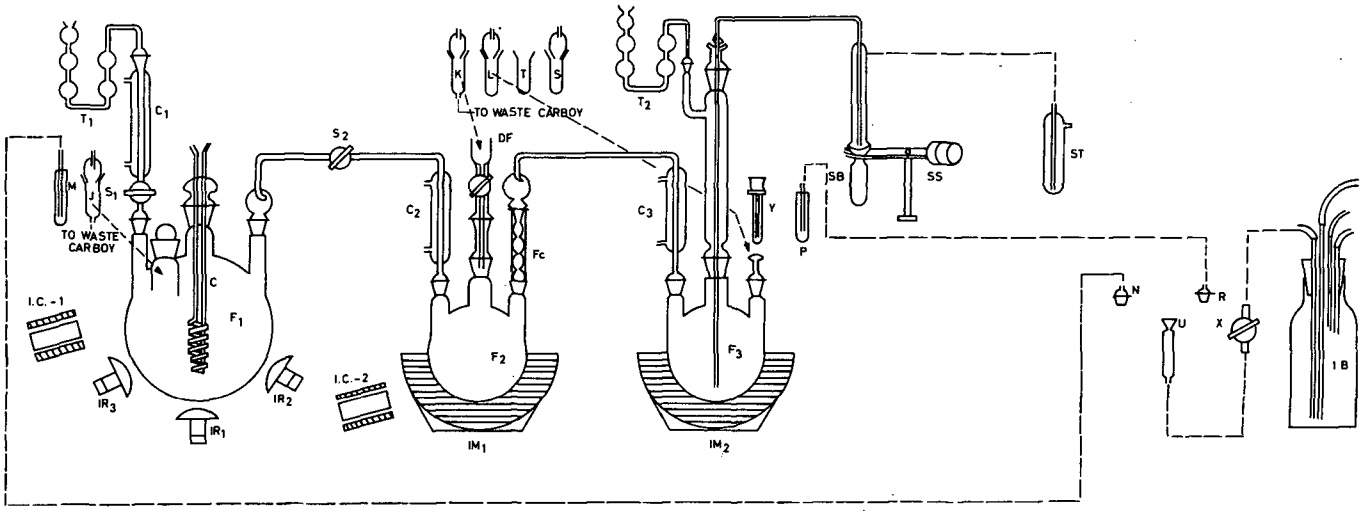
In CIR: 25 g in 1 capsule, type C (cold-welded 2 S aluminium can, 44 mm high and 22 mm diam.)
Flux: 4 to 6×10^{13} n/cm^2 s.
Irradiation period: 4 weeks.

Chemical treatment

The irradiated can containing 50 g Te powder is opened, and the contents are transferred into flask F_1 (see Fig. 1). The oxidation mixture consisting of 300 ml of 15 N chromic acid solution, and 700 ml of 50% H_2SO_4 is loaded into flask F_1. The mixture is then refluxed for two hours using infra-red lamps for heating the flask. The stopper of the reflux condenser (C_1) is kept open while the stopcock S_2 is kept closed. After dissolution, the mixture is cooled for two hours by passing water through the cooling coil. After cooling, 165 g of oxalic acid dihydrate are added to reduce the excess of chromic acid. After about 1 h the water circulation in the cooling coil is stopped and the heating is started by switching on the infra-red lamps. Ten millilitres of 0.1 N NaOH is kept in flask F_2. The stopcock S_2 is opened now and the distillation is carried out till no more iodine distils into flask F_2. (As shown by the reading of the ion-chamber kept near F_1.) More than 90% of iodine distils into flask F_2.

The contents of flask F_2 are then made about 16 N with respect to sulphuric acid and the solution is heated to boiling point. Potassium-permanganate solution is added dropwise until a permanent pink colour is obtained. Boiling is continued for 15 min more. At this stage 5.0 ml of a solution of 1 mg/ml sodium sulphite is kept in flask F_3. Oxalic acid is then added to flask F_2 dropwise till the pink colour disappears. Iodine will start distilling and the distillation will be over in about 30 min.

The pH of the distillate is adjusted to about 8 by adding hydroxide, and the solution is concentrated to a small volume to obtain a radioactive concentration of not less than 10 mCi/ml. Finally the solution is transferred into a storage bottle.



F_1	Dissolution flask	J, K, L	Receptacles for ends of reagents lines
F_2	Purification flask	DF	Dropping funnel
F_3	Concentration flask	FC	Fractionating column
C_1, C_2, C_3	Condensers	Y	Capillary tube (used for adjusting pH)
C	Cooling coil	MN, PR	Waste lines
IR_1 - IR_3	Infra-red lamps	IB	Intermediate waste bottle
IM_1 - IM_2	Isomantles	SB	Storage bottle
IC_1, IC_2	Ion chambers	U	Socket for N and R
S_1, S_2	Stopcocks	X	Stopcock connecting U to IB
T_1, T_2	Traps	SS	See-saw
ST	Safety trap		

FIG.1. Iodine-131 production plant

3. ASSAY AND QUALITY CONTROL

The activity is assayed by taking the ion current measurement of a known volume of stock solution in a calibrated ion chamber.

Radionuclide identification is performed by checking the 0.36 MeV (80%) gamma peak. The gamma-ray spectrum is examined for any other gamma-emitting impurities.

Radiochemical purity

This is determined by running a paper chromatogram, using iodide and iodate carrier, and a solvent mixture of 75% methanol and 25% water adjusted to pH 7 - 8 with potassium carbonate.

Rf value for I^- = 0.75

Rf value for IO_3^- = 0.50

Rf value for IO_4^- = 0.00

The iodide content must be more than 95% in a typical batch.

The total solid content is determined by evaporating a known volume of the stock solution and weighing the residue.

Any heavy metal impurities are estimated colorimetrically.

Total reducing agents

A known amount of stock solution is treated with a known excess of permanganate solution and the excess of permanganate is back-titrated against standard oxalic acid solution. The reducing agent content is expressed in millilitres of $\underline{N}/10$ $KMnO_4$ per ml $Na^{131}I$ solution.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Code IOM-1 (Medical)

Iodine-131 as carrier-free sodium iodide in dilute sodium sulphite solution. pH 8. Solution autoclaved. Radioactive concentration = 10 - 50 mCi/ml.

Code IOM-2 (Medical)

Carrier-free sodium iodide absorbed on anhydrous sodium phosphate in gelatine capsules.

Activity per capsule = 50 μCi.

Code 101

Carrier-free sodium iodide in dilute sodium sulphite solution pH 8. Radioactive concentration 10 - 50 mCi/ml.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

Both wet and dry distillation methods are employed. In the wet distillation method, iodine is released from the irradiated telluric acid target dissolved in concentrated sulphuric acid and ammonium persulphate. The dry method employs tellurium dioxide target, and iodine is distilled from the irradiated target under a stream of nitrogen.

2. EXPERIMENTAL PROCEDURE

A. Wet distillation method (Figs. 1, 2)

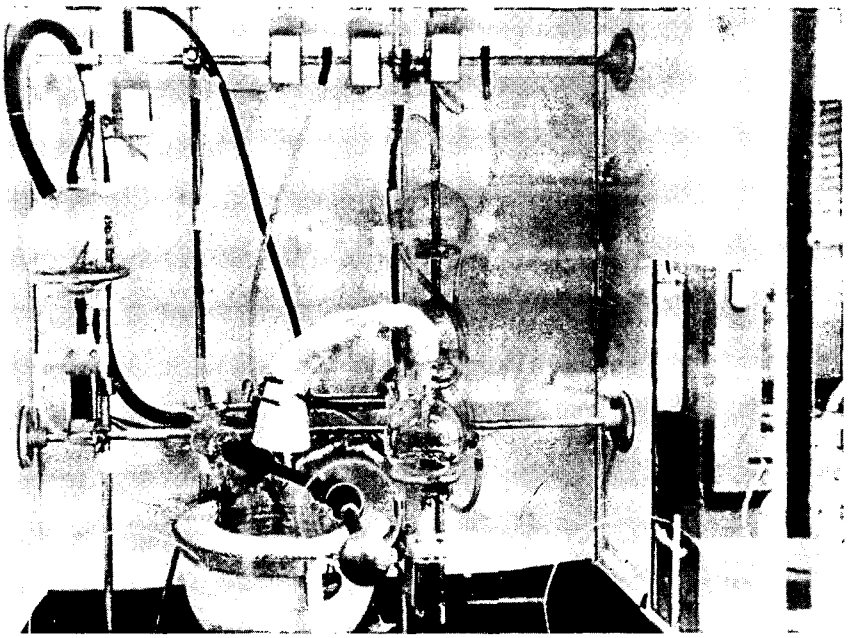


FIG. 1. Apparatus for the wet distillation method

Irradiation

Target material: 10 g of telluric acid (H_2TeO_4); purity > 99%.
Container: Cold weld-type aluminium capsule (Fig. 3).
Flux: $\sim 3 \times 10^{13}$ n/cm^{2}s (JRR-2).
Irradiation time: 130 h.

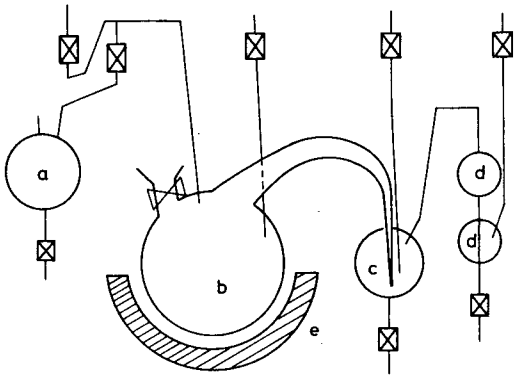


FIG.2. Arrangement of the apparatus for ^{131}I production in the wet distillation method

a. Suction bottle
b. Distillation vessel
c. Collector bottle of product
d. Trap bottle
e. Mantle heater

⊠ Electro-magnetic valve

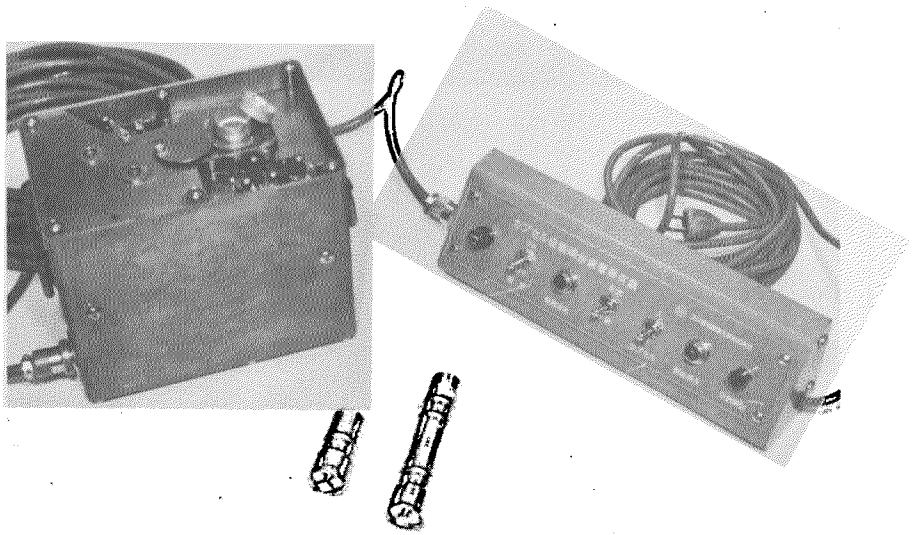


FIG.3. Aluminium capsule cutter

Chemical treatment

The irradiated target is dissolved in 18 $\underline{N}$ H_2SO_4, and the iodine is distilled with the addition of ammonium persulphate. The distilled iodine is collected in 0.1% NaOH and 0.05% sodium hydrogen sulphite.

Ten grams of irradiated target are dissolved in 200 g of 18 $\underline{N}$ H_2SO_4. Add one gram of ammonium persulphate.

Iodine is distilled under the nitrogen stream by heating.

Distilled iodine is collected in the collector solution (10 ml, mixed solution of 0.1% NaOH and 0.05% sodium hydrogen sulphite). Uncollected iodine is then collected in the second collector solution.

Transfer the collector solutions into the flask, then adjust the acidity to pH 7 - 9 by the addition of 0.1% NaOH.

Chemical forms are determined by paper chromatography:

Filter paper: Toyo filter paper No. 51A
Reagent: 75% methanol solution
Time: 3 h (20 cm)
R_f: IO_3^- — 0.4 - 0.5; I^- — 0.7 - 0.8; I_2 — > 0.9

B. Dry distillation method (Fig. 4)

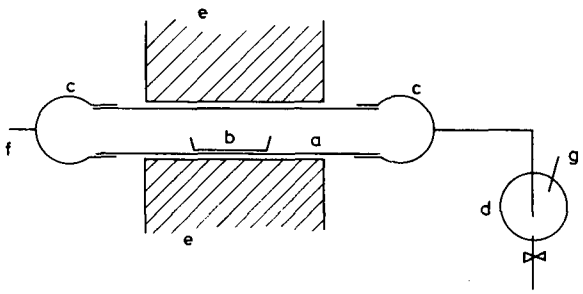


FIG.4. Arrangement of the apparatus for ^{131}I production in the dry distillation method

a. Quartz column
b. Ceramic boat
c. Glass cap
d. Collector bottle of product
e. Electric furnace
f. Carrier gas inlet
g. Carrier gas outlet

Irradiation

Target material: 10 - 50 g of tellurium dioxide (TeO_2) (JISGR[1]), 100 - 200 mesh powder.
Container: Placed in the polyethylene sheet, then in the polyethylene capsule.
Flux: $2 - 3 \times 10^{11}$ n/cm^2 s (JRR-1).
Irradiation time: 15 h (5 h×3 d).

Chemical treatment

By the direct distillation of the irradiated target, iodine is collected in the collector solution (0.05% NaOH and 0.1% $NaHSO_3$).

Place the irradiated target in the porcelain vessel, then in the quartz heating tube (50 mm diam. and 500 mm long).

Heat for 5 h at 750°C under the nitrogen or air stream. The distilled iodine is collected in the collector solution (50 ml of 0.05% NaOH and 0.1% $NaHSO_3$) with bubbling by carrier gas.

[1] Japan Industrial Standard Reagent Grade.

Determination of chemical forms is made by paper chromatography. The form, I^-, was the only one detected by chromatography with 75% methanol solution.

3. ASSAY AND QUALITY CONTROL

The contents of total solids, non-volatile materials, and heavy metals are determined by the following methods:
Total solids: Evaporation and drying at 110°C of one millilitre sample solution.
Non-volatile materials: Evaporation and drying at 600°C of one millilitre sample solution.
Heavy metals: Comparison of colour development with the standard lead solution by the addition of hydrogen sulphide.
The tellurium content is determined by the polarographic method.
The routine assay of the product is made by a well-type ionization chamber; for calibration, a 4π β-γ coincidence counter is employed.
The amount of carrier is determined by the spectrophotometric method, utilizing iodine-starch reaction.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	Iodine in dilute thiosulphate solution.
pH:	7 - 9.
Radiochemical purity:	> 99%.
Specific activity:	Carrier-free.

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

In a thermal neutron flux ^{131}I is produced from tellurium dioxide according to the reaction: $^{130}Te(n, \gamma)^{131}Te \xrightarrow[25\ min]{\beta^-} {}^{131}I$. The iodine produced is separated from the target material by means of dry distillation at 700°C and is absorbed in dilute sodium hydroxide solution, giving a slightly alkaline solution of $Na^{131}I$.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	TeO_2, 99.6% pure, Johnson, Matthey & Co., pretreated by sintering at 650°C and re-ground.

Amount:	300 g.
Time of irradiation:	2 weeks.
Container:	Aluminium can with quartz inner container.
Flux:	About 2×10^{12} n/cm^2 s.
Side reactions:	Effects of side reactions are considered negligible.

Chemical treatment

The irradiated tellurium dioxide is heated to 700°C in a stream of air. The air is circulated through a small absorption column, where the released iodine vapour is absorbed in a dilute sodium hydroxide solution. The processing time is around 3 h. Sodium thiosulphate is added to the solution for protection against oxidation of the ^{131}I ion.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative scintillation counting or Geiger-Müller counting.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control, emission spectrography,
dry matter content (evaporation).
Radiochemical purity control, radiochromatography.
Specific activity control, iodine content (spectrophotometry).
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

IO - sodium iodide in dilute sodium thiosulphate solution.

Radioactive concentration:	20 - 100 mCi/ml.
Isotopic purity:	Greater than 99.9%.
Radiochemical purity:	100% as iodide + iodate, at least 95% as iodide.
Specific activity:	10 000 mCi/mg I.
pH:	8 - 10.
Total solids:	Less than 4 mg/ml.
Chemical purity:	As, Se, Te, Pb less than 5 μg/ml. Other metals spectrographically determined, less than 10 μg/ml.

ISI - sodium iodide in isotonic solution, sterilized.

pH:	7 - 8.
Total solids:	Approx. 15 mg/ml.

Other specifications as for IO.

IOR - sodium iodide in sodium hydroxide solution, without reducing agents.

Radioactive concentration:	150 - 200 mCi/ml.
Total solids:	Less than 2 mg/ml.

Other specifications as for IO.

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INSTITUTE OF NUCLEAR RESEARCH, SWIERK NEAR OTWOCK, POLAND

1. GENERAL

Iodine-131 is obtained by steam distillation of irradiated tellurium dioxide target. Distillate, containing elementary iodine, is absorbed in various solutions depending on the final product required. The yield is 85-95%.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Tellurium dioxide, analytical grade, 160 g.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	4 to 6 weeks (reactor working 86 h per week at full power).
Container:	Aluminium capsule closed by welding.
Activity obtained:	5 Ci of ^{131}I.

Chemical treatment

One hundred and sixty grams of irradiated tellurium dioxide target are dissolved in 20% NaOH in the presence of sodium molybdate at room temperature under pulse stirring. The resulting solution is placed in a distillation flask and 30% H_2O_2 and H_2SO_4 are added to produce 3.0 M concentration of sulphuric acid, then H_2O_2 is added again. The distillation flask is connected with a source of nitrogen which passes through the apparatus at a rate of 2-3 bubbles per second during the whole operation and with a system of condensers. The flask is fitted with a reflux condenser, whose upper end is connected to a yielding condenser. The distillate receiver is filled with an iodine-absorbing solution.

The solution in the distillation flask is refluxed for one hour, then the reflux condenser is turned off and the distillation begins. After collecting an appropriate volume of the distillate the distillation can be interrupted by turning on the reflux condenser. Thus the product can be collected and the receiver can be refilled with the absorbing solution.

The amounts of reagents required for the processing of typical amounts of TeO_2 are:

TeO_2 (g)	NaOH (20%) (ml)	Na_2MoO_4 (50%) (ml)	H_2O_2 (30%) (ml)	H_2SO_4 (98%) (ml)	H_2O_2 (30%) (ml)
105	315	25	46	137	17
160	480	48	70	208	25
210	630	50	92	274	33
265	795	73	116	345	41.5

The distillation is carried out so that the absorbing solution is diluted ten times with the distillate (e.g. volume of absorbing solution, 5 ml; final volume after distillation, 50 ml).

The operations are carried out from behind a lead shield 5-10 cm thick.

3. ASSAY AND QUALITY CONTROL

The activity of the final product is measured with an ionization chamber calibrated with a standard.
The chemical purity is determined spectrally.
The radiochemical purity is determined by paper chromatography.
The radiation purity is determined by gamma spectrometry.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Note: All the final product compositions below show the amount of sodium salts in 1 ml of distilled water.

Sodium iodide	For labelling		Medical (oral and for injection[a])	
Carrier-free			$NaH_2PO_4.H_2O$	4.14 mg
Final product composition	NaOH	2 mg	NaCl	6.43 mg
			$Na_2S_2O_3$	1.58 mg
	Na_2CO_3	0.26 mg	NaOH	pH 7-9
	$NaHCO_3$	1.68 mg		

[a] For injections: sterile, pyrogen-free

CHARACTERISTICS OF THE FINAL SOLUTION (cont.)

Radiation purity:	99.9%
Radiochemical purity:	95%
Specific activity:	10 Ci/mg
Impurities As, Pb, Te:	5 ppm
pH:	7-9
Radioactive concentration:	Technical 30-150 mCi/ml
	Medical (oral) 20-30 mCi/ml [b,c]
	Medical (for injection) 2 mCi/ml [c]

[b] On request up to 100 mCi/ml

[c] Accuracy of determinations ± 7%

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INSTITUTE FOR ATOMIC PHYSICS, BUCHAREST, ROMANIA

1. GENERAL

The nuclear reactions employed are: $^{130}Te(n,\gamma)^{131}Te$, followed by $^{131}Te \xrightarrow{\beta^-} {}^{131}I$. The separation of ^{131}I was made by distillation, after target dissolution, acidification and oxidation.

2. EXPERIMENTAL PROCEDURE [1-3]

Irradiation

Target:	TeO_2 purum, the amount depending on the request.
Flux:	1×10^{13} n/cm^2 s.
Time of irradiation:	160 h.
Container:	Aluminium cans.
Side reactions:	$^{124}Te(n,\gamma)^{125}Te$ and $^{126}Te(n,\gamma)^{127}Te$.

Chemical treatment

This is carried out in a lead box having a wall thickness of 100 mm.
Transfer irradiated target to lead box.
Dissolve with NaOH 10% solution in a beaker.
Filter in the distillation vessel.
Add concentrated H_2SO_4 and 2-3 ml H_2O_2.
Distil under reduced pressure. Receive distillate in NaOH and some milligrams of $Na_2S_2O_3$.
Concentrate the solution to the desired specific activity.
Neutralize the excess NaOH with HCl.
Isotonization (for medical use).
Transfer to delivery bottle.

3. ASSAY AND QUALITY CONTROL

The radiochemical purity is controlled by paper chromatography; the chemical purity, pH, and sterility are controlled in the usual way.

4. CHARACTERISTICS OF THE FINAL SOLUTION

The total activity delivered weekly amounts to 2000 - 3000 mCi. Deliveries of radioiodine are usually made twice a week.

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JUNTA DE ENERGIA NUCLEAR, MADRID, SPAIN

1. GENERAL

The irradiated telluric acid target is dissolved in phosphoric acid in the presence of hydrogen peroxide, and iodine is distilled under a nitrogen stream [1].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	300 g telluric acid of analytical grade quality.
Container:	Leaktight aluminium container, 24×26 mm diam.
Flux:	4×10^{12} n/cm^{2}s (JEN-1).
Irradiation time:	Two weeks, equivalent to 80 h of continuous operation at 1 MW.
	Approximate yield is 1000 mCi.

Chemical treatment

Separation method

The irradiated target is distilled in the presence of phosphoric acid in an oxidizing medium and a stream of nitrogen. The apparatus used is shown in Fig. 1 and the entire process comprises the following steps:

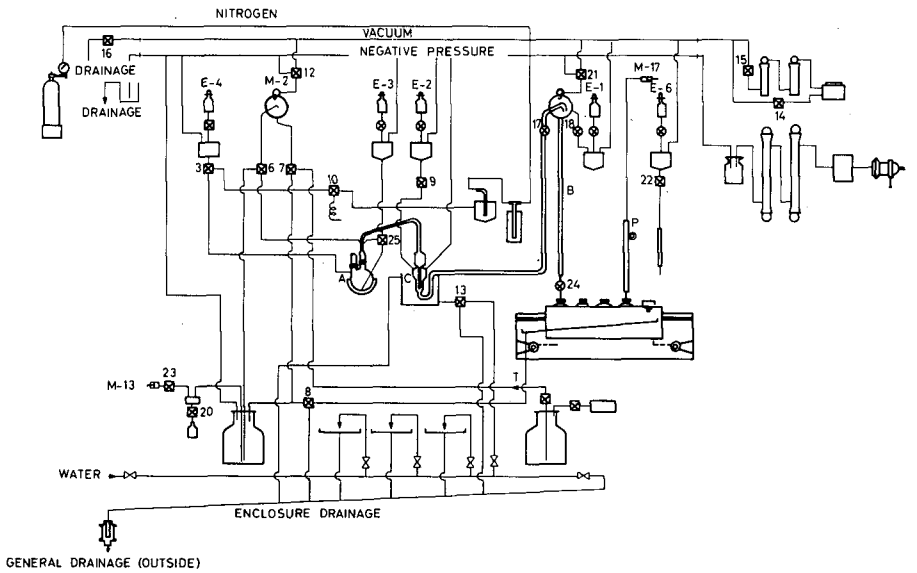

FIG. 1. Iodine-131 production process

The irradiated telluric acid target is placed in the flask (A) which contains 1 litre of concentrated H_3PO_4. Add 100 ml of 30% H_2O_2 (analytical grade), and heat the flask gently to decompose hydrogen peroxide while passing a gentle stream of nitrogen.

Raise the temperature to initiate the distillation of water. The water entrains all the iodine which is collected in the receiver (C). The trapping solution for the iodine is a mixture of 1 ml of 0.1 M NaOH and 2 ml of 0.1 M $Na_2S_2O_3$, introduced in the receiver (C) at the beginning of the operation.

Distillation with less than 18 ml of water will ensure the complete iodine collection.

Transfer the solution containing iodine to a penicillin bottle which contains 2 ml of phosphate buffer solution; phosphate buffer is prepared by the neutralization of saturated NaH_2PO_4 solution with NaOH with subsequent filtration. A conductometric determination is then made to establish what volume of the solution will be necessary, when made up to 20 ml, to yield the same conductivity as a solution of 9 g NaCl/l.

If the iodine is to be collected in an alkaline medium without a reducing agent, 2 ml of 1 M NaOH are introduced into the receiver (C).

Apparatus

The production is carried out in an enclosure having the same dimensions and overall design as that used for ^{32}P production. The differences are the following:

The air-tight box is surrounded by a shield made of lead bricks 5 cm thick (see Fig. 2).

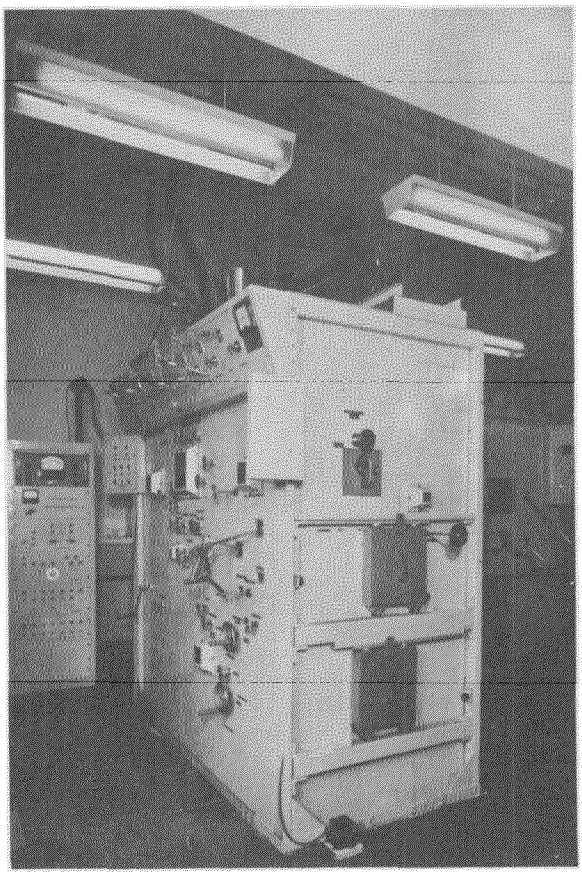

FIG. 2. Unit for the production of iodine-131

The ventilation system necessary to clean the inner atmosphere of the box or to keep it at a negative pressure is connected to a trap loaded with silver-impregnated active carbon to fix the iodine that may escape eventually.

Besides the equipment described above, the apparatus includes some ancillary parts, such as funnels (E-1 to E-6), siphoning vacuum balls (M-1), a burette (B), a sampling pipette P, by-pass stopcocks (8, 13), liquid wastes receivers, etc. (Fig. 1).

3. ASSAY AND QUALITY CONTROL

No chemical purity determination is made, except the periodical check of tellurium by emission spectroscopy.

Radioactive purity is determined by gamma spectrometry[1].

Half-life measurements are made from time to time.

Radiochemical purity controls are carried out in accordance with British Pharmacopoeia [2]. This involves study of the presence of iodate by means of ascending chromatography in methyl alcohol and water (3 : 1).

Autoradiography is used to localize radioactivity on the chromatograms [2, 3]. The Rf values given in reference [3] for iodide and iodate are adopted.

Activity measurements are made with an ionization chamber[1].

The apparatus is periodically checked with solutions of absolute standards measured by $4\pi\beta$-γ coincidence. In general, an error of 5 - 10% is allowed. In special cases the error may be less than 5%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Sodium iodide, ^{131}I, carrier-free, non-injectable[2]

Sodium iodide solution in OHNa, without reducing agents meeting the following specifications:

Radioactive purity:	^{131}I content > 99.5%.
Radiochemical purity:	Iodide content > 95%.
Radioactive concentration:	Maximum 20 mCi/ml.
Specific activity:	> 1 Ci/mg.

Sodium iodide, ^{131}I, carrier-free, injectable[2]

Neutral (pH 6-8), sterile, isotonic and pyrogen-free solution of sodium iodide in phosphate buffer meeting the following specifications:

Radioactive purity:	^{131}I content > 99.5%.
Radiochemical purity:	Iodide content > 95%.
Radioactive concentration:	1-10 mCi/ml.
Specific activity:	> 1 Ci/mg.

[1] See the Section on ^{32}P provided by the Junta de Energía Nuclear, Madrid, Spain.

[2] ORTEGA, J., Technique for the preparation of carrier-free radioiodine (^{131}I) from neutron-irradiated telluric acid, Iodine-131. Spanish patent No. 287.350.

Sterility:	Sterilization is carried out in an autoclave at 120°C for about 1 h.
Analysis of pyrogens:	See footnote [1].
Isotonicity:	Adjusted by means of conductimetric measurements.

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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Iodine-131 is produced by the neutron irradiation of tellurium according to the nuclear reaction $^{130}Te(n, \gamma)^{131}Te \xrightarrow{\beta^-} {}^{131}I$. The iodine is separated from the target material by dry distillation at 800°C and trapped in dilute sodium hydroxide solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	2 kg natural TeO_2, Johnson Matthey Co. Ltd., purified by sintering at 700°C and then re-ground.
Irradiation container:	Cluster of aluminium cans each sealed by argon arc welding.
Irradiation conditions:	Flux 5×10^{12} n/cm^{2}s for 7 to 17 d.

Chemical treatment

The target material is purified by heating to 700°C for 8 h to remove volatile impurities (mainly SeO_2). After irradiation the TeO_2 is heated to 800°C in a stream of nitrogen. Under these conditions the iodine is released from the matrix of the target, as vapour which is then trapped out in sodium hydroxide scrubbers. The product is stabilized against radiolytic oxidation by the addition of sodium thiosulphate.

[1] See the Section on ^{32}P provided by the Junta de Energía Nuclear, Madrid, Spain.

3. ASSAY AND QUALITY CONTROL

Chemical purity, As, Pb, Te and Se content determined.
Radioisotopic purity, determined by γ-spectrometry.
Radiochemical purity, ^{131}I in the form of IODIDE determined by electrophoresis.
Specific activity - determined periodically.[1]

4. CHARACTERISTICS OF THE FINAL SOLUTION

IBS. 1	Iodine-131[2]
Chemical form:	Sodium iodide in dilute sodium hydroxide solution stabilized with sodium thiosulphate.
Specific activity:	Carrier-free; 10-30 Ci/mg iodine.
Radioactive concentration:	Up to 200 mCi/ml.
Radioisotopic purity:	No other radioisotopes detectable by γ-spectrography.
Radiochemical purity:	99% as iodide; not more than 1% as iodate[3].
Chemical purity:	As and Pb < 5 ppm. Te and Se < 10 ppm.
Total solids:	Sodium hydroxide and sodium thiosulphate (10 to 15 mg/ml).
pH:	8 - 11.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Iodine-131 is produced by fission of ^{235}U in an aluminium-clad fuel cylinder (fission yield 2.9%). Fixed process equipment at the ORNL Iodine Facility is used to dissolve the aluminium, and to distil and redistil iodine.

---

[1] Accompanying the main nuclear reaction:

$$^{130}Te(n,\gamma)^{131}Te \xrightarrow{\beta} {}^{131}I$$

are two concurrent reactions

$$^{126}Te(n,\gamma)^{127}Te \xrightarrow{\beta} {}^{127}I \text{ (stable)}$$

$$^{128}Te(n,\gamma)^{129}Te \xrightarrow{\beta} {}^{129}I \text{ (very long-lived)}$$

which tend to lower the specific activity of the ^{131}I. The specific activity of each batch produced is calculated and checked experimentally from time to time.

[2] British Patent No. 763 865.

[3] Carrier free sodium iodide - ^{131}I in aqueous solution is oxidized by its own radiation to form iodine and iodate. Sodium thiosulphate is added to prevent this and to preserve the iodine-131 as iodide. Sodium thiosulphate is itself oxidized at a rate proportional to the radioactive concentration. An amount of sodium thiosulphate is added equal to 5×10^{-4} mM/mCi iodine-131. This concentration ensures that some reducing agent is present in the solution throughout the life of the iodine-131.

In further purification, iodine is oxidized to iodate with $KMnO_4$ and H_2SO_4, then reduced to elemental iodine with concentrated H_3PO_3 and H_2O_2 and distilled. The product solution is neutralized with $NaHCO_3$ and adjusted to pH 8.

2. EXPERIMENTAL PROCEDURE

Irradiation

An Al-clad fuel cylinder composed of 5 g of 93% ^{235}U alloyed with 31 g of aluminium (9 in. long by 1.74 in. outside diam.; weight 109 g) is irradiated. The irradiated fuel cylinder is transferred from the ORR to the Iodine Facility in a shielded transfer container.

Production method: Fission.
Target: 5 g U-Al alloy.
Neutron flux: $\sim 2 \times 10^{14}$ n/cm^{2}s.
Irradiation time: 21 d.
Reactor yield: ~200 Ci.

Chemical treatment

Apparatus

Fixed process equipment (Fig. 1) is used. The shielded cell has remote controls on the process vessels, 6-8 in. lead equivalent. Hot off-gas lines

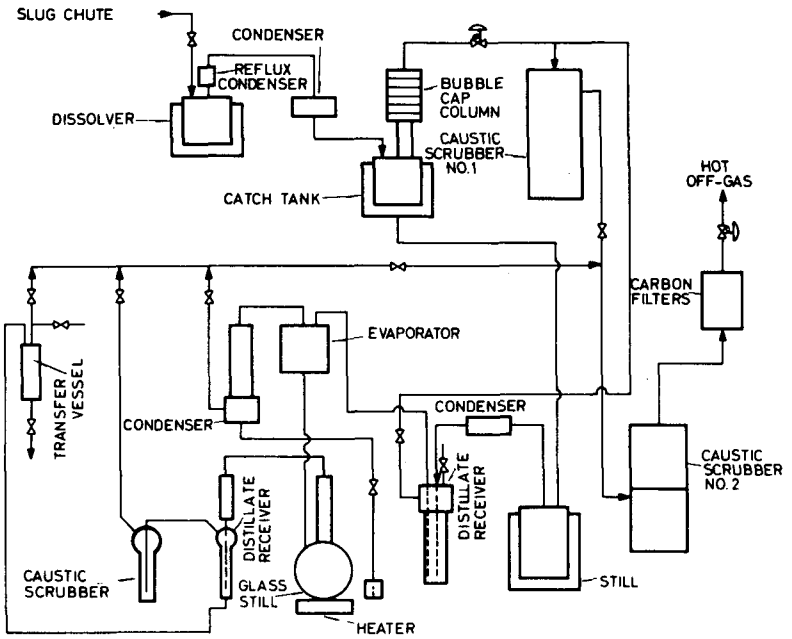


FIG. 1. Flow diagram for ^{131}I purification

and cell ventilation are equipped with caustic scrubber, CWS filters, and charcoal filters.

Processing

Yield: 50-75%.

For clarity, processing is given in steps and explained (Fig. 1).

Procedure	Notes
(1) Prepare equipment.	
(2) Charge scrubbers with ~ 10% NaOH and bubble cap column with ~0. 05% NaOH.	
(3) Check scrubber caustic circulation pump and circulate caustic through off-gas scrubber.	
(4) Introduce irradiated uranium cylinder into dissolver tank.	
(5) Introduce chilled H_2O (10°C) to dissolver reflux condenser, catch-tank cooling coil, catch-tank condenser, and bubble-cap column.	
(6) Add caustic solution (250 g NaOH in 1 litre of H_2O) to dissolver.	
(7) Heat the dissolver to ~ 105°C for ~ 1 h.	This dissolves the aluminium on the cylinder and exposes the uranium.
(8) Stop chilled H_2O flow to dissolver reflux condenser and introduce steam.	This prevents reflux of iodine obtained in the next step.

Procedure	Notes
(9) Add 8 M HNO_3 slowly to dissolver until iodine is liberated, as noted on the ionization chamber at catch tank.	Nitric acid is added to neutralize excess caustic and to acidify the solution from which the elemental iodine is distilled into the catch tank.
(10) Continue distillation until no additional iodine is distilled into the catch tank, as indicated by the ionization chamber at the catch tank.	The addition of H_2O_2 increases the rate of distillation of iodine. The volume is maintained at 2 litres as noted on the liquid-level gauge.
(11) Cool the dissolver and reflux condenser.	
(12) Transfer the condensate containing ^{131}I from the catch tank to the second distillation system.	

(13)	Charge the distillate receiver with 200 ml of H_2O containing 30 g of NaOH.	
(14)	Add 2.5 litres of ~30% H_2O_2 and 130 ml of 70% HNO_3 to the still.	Nitric acid neutralizes caustic and acidifies the solution from which iodine is distilled; H_2O_2 oxidizes the iodide to iodine and provides sweep gas for the removal of iodine.
(15)	With cooling H_2O on the still condenser, distil iodine into the distillate receiver.	Note the completion of ^{131}I removal by ion chamber readings at the distillate receiver.
(16)	Transfer the iodine solution to the evaporator and evaporate to 1 litre.	The iodine remains in the caustic solution in the evaporator.
(17)	Transfer the evaporated solution to the glass still for final purification.	
(18)	Prepare the distillate receiver by adding 6 ml of 6% H_2SO_3.	
(19)	To the distillation flask, add saturated $KMnO_4$ solution until an excess is noted by a pink colour, and then add 140 ml of 21 M H_2SO_4.	Add H_2SO_4 slowly to prevent local heating. The iodide is oxidized to iodate. The $KMnO_4$ colour should persist after the H_2SO_4 addition.
(20)	Distil ~400 ml and discard.	This removes traces of HNO_3.
(21)	Recharge the distillate receiver with 6 ml of 6% H_2SO_3. Slowly add concentrated H_3PO_3 to the flask until the $KMnO_4$ colour is cleared; then add 30% H_2O_2 dropwise during the distillation.	The iodate is reduced to elemental iodine and is distilled into the H_2SO_3 in the distillate receiver. Collect approximately 100 ml of distillate.
(22)	Neutralize solution with $NaHCO_3$ and adjust to a pH of ~8 in the distillate receiver. Transfer to the product bottle.	This neutralizes excess H_2SO_3 and the H_2SO_4 produced by oxidation of H_2SO_3. The purpose of this is to provide a basic solution to protect against later accidental acidification and release of I_2 by air or radiation decomposition (of H_2O) oxidation. Higher pH's shift iodine equilibrium toward IO_3^- formation.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for ^{131}I and ^{133}I concentration, heavy metals, iodide/iodate ratio, total reducing agents, pH and radiochemical purity according to ORNL Master Analytical Manual (TID-7015), procedure Nos. 9 0733391, 9 0733392, 9 0733393 and 9 0733394.

The precision and accuracy of the ^{131}I assay are:
Calibration by $4\pi\ \beta$-γ coincidence counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 3%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, carrier-free ^{131}I is delivered as NaI in basic sodium sulphite solution as a stock item. Other specifications of interest are:

pH:	7 - 8.5.
Concentration:	≧ 50 mCi/ml.
Total solids:	< 0.2 mg/mCi.
Heavy metals (as Pb):	< 2 μg/mCi.
Purity:	> 99.9% (exclusive of ^{133}I).
^{133}I:	< 2%.

Elemental iodine with carrier added is quoted separately.

BORIS KIDRIČ INSTITUTE OF NUCLEAR SCIENCES,
VINČA, YUGOSLAVIA

1. GENERAL

Irradiation of tellurium in the form of a telluric acid target gives rise to ^{131}I by the reaction $^{130}Te(n,\gamma)^{131}Te \xrightarrow{\beta^-} {}^{131}I$. Carrier-free ^{131}I is produced by Constant's method [1] modified as follows:

The dissolution vessel is separated from the distillation vessel [2], the latter thus becoming a closed system not in contact with the atmosphere;

Since there is no possibility of cooling the target, the temperature of the telluric acid rises during irradiation, exceeding 100°C. Since it barely dissolves in this condition, the acid to be irradiated is first dehydrated. After irradiation it then dissolves easily in KOH [3].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Telluric acid (60 g) dried at 160°C for 24 h.
Containers:	Cylindrical aluminium cans with screwed covers, internal length - 70 mm, internal diam. - 25 mm.
Thermal flux:	3.3×10^{13} n/cm^2 s (RA reactor at Vinča).
Irradiation time:	8-10 d.

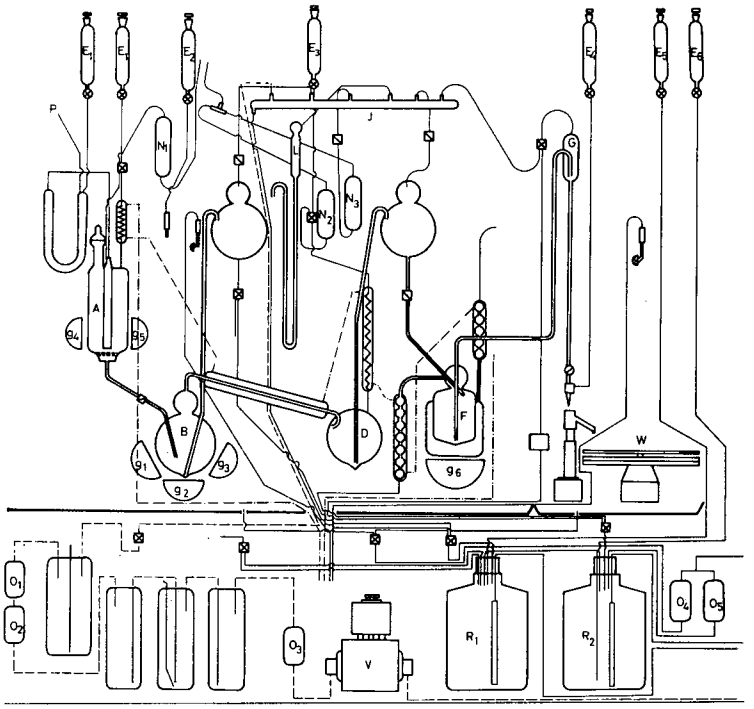
Chemical treatment

Separation method

Sixty grams of dehydrated and irradiated telluric acid are dissolved in 450 ml 10% KOH slightly heated. After transferring it to the vessel for distillation, 334 ml of water and 416 ml of sulphuric acid (1 : 1) are added to this solution and the radioactive iodine distilled into a reducing solution containing $Na_2S_2O_3$ (0.0025 M), Na_2CO_3 (0.005 M) and $NaHCO_3$ (0.005 M).

Apparatus

The apparatus (Fig. 1) is made of Pyrex glass placed in a box of 10-mm plexiglass shielded by a 5-cm-thick lead wall.



A	Dissolution vessel
B	Distillation flask
D	Vessel for receiving distillates
E_1 - E_6	Vessels for adding chemicals
F	Evaporator: double jacket reservoir with xylene as the heat transferer
G	Burette
g_1 - g_6	Heaters
L	Mercury manometer
N_1 - N_3 and O_1 - O_5	Carbon filters
P	Connection to pulsator
R_1 - R_2	Waste water flasks
V	Vacuum pump
W	Disc for distribution of ^{131}I solution

FIG. 1. Apparatus for ^{131}I production

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.
Radioactive purity control.
pH control.
Qualitative and quantitative spectrographic control of the target.
Chemical purity control [4–7] of the solution. Spectrography and ascending paper chromatography are used.
Radiochemical purity control. Ascending paper chromatography is used [7].
Sterility control [8].
Pyrogenity control of the solutions is used.
The fixation of ^{131}I in the thyroid gland of rats.

Routine control of each charge includes the first, third, fifth and seventh measurement and control.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVI131/1x, $Na^{131}I$ in dilute $Na_2S_2O_3$, Na_2CO_3 and $NaHCO_3$

Radioactive concentration:	Measured to within 10%, 10 mCi/ml average, 50 mCi/ml maximum.
Radioactive purity:	^{131}I content 99.9%.
Radiochemical purity:	Iodide content more than 95%.
Specific activity:	10 Ci/mg.

No troublesome chemical impurities.

Reference: YVI131/2x, $Na^{131}I$ in sterile isotonic solution, phosphate buffer

Radioactive concentration:	Measured to within 10%, 0.5 – 2 mCi/ml.
Radioactive purity:	^{131}I content 99.9%.
Radiochemical purity:	Iodide content more than 95%.
Specific activity:	10 Ci/mg.

Sterile.
Pyrogen-free.

Reference: YVI131/3x, $Na^{131}I$ in sterile 0.01 N NaOH solution

Radioactive concentration:	Measured to within 10%, 10 mCi/ml average, 50 mCi/ml maximum.
Radioactive purity:	^{131}I content 99.9%.
Radiochemical purity:	Iodide content more than 95%.
Specific activity:	10 Ci/mg.

Sterile.

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IRON-59

NUCLEAR DATA

1. NUCLEAR PROPERTIES

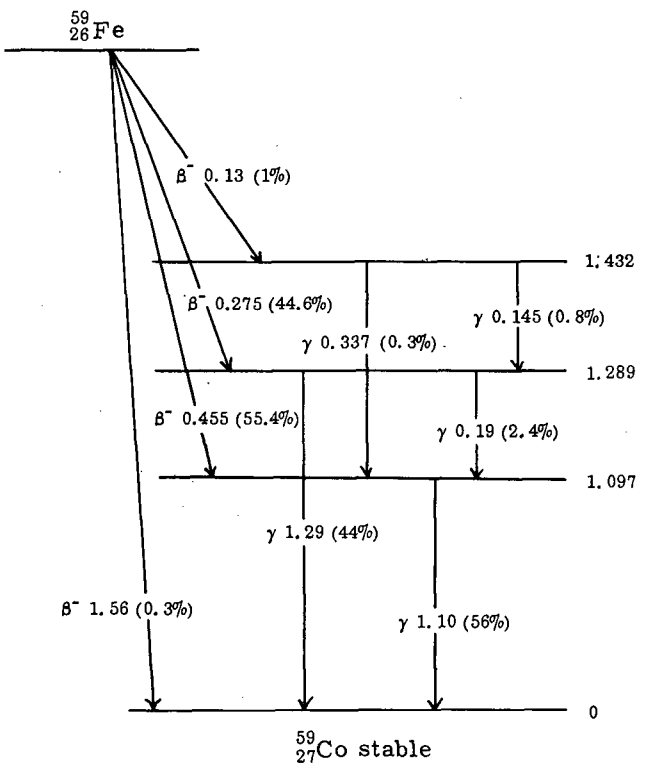
1.1. Half-life

45.6 d

1.2. Type of decay, and energy (MeV)

beta (β^-)	0.13 (1%)	gamma	0.145 (0.8%)
	0.275 (44.6%)		0.19 (2.4%)
	0.455 (55.4%)		0.337 (0.3%)
	1.56 (≈ 0.3%)		1.10 (56%)
			1.29 (44%)

1.3. Decay scheme



Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm² s (μCi/g)			Secondary reactions and half-life of the radionuclide formed
			24 h	1 week	sat.	
$^{58}_{26}Fe(n,\gamma)^{59}_{26}Fe$	0.33	1.01 (th)	14	96	960	$^{54}_{26}Fe(n,\gamma)^{55}_{26}Fe$ (T = 2.6 yr) isot. abund.: 5.82% σ = 2.8 barn $^{54}_{26}Fe(n,p)^{54}_{25}Mn$ (T = 278 d) σ ~ 56 mbarn) $^{54}_{26}Fe(n,\alpha)^{51}_{24}Cr$ (T = 27.8 d) σ = 0.74 mbarn) $^{56}_{26}Fe(n,p)^{56}_{25}Mn$ (T = 2.58 h) σ = 0.8? 0.4 mbarn?
$^{59}_{27}Co(n,p)^{59}_{26}Fe$	100	0.0003? 0.0057 (f)				$^{59}_{27}Co(n,\gamma)^{60}_{27}Co$ (T = 5.27 yr) σ = 36 barn $^{59}_{27}Co(n,\alpha)^{56}_{25}Mn$ (T = 2.58 h)
$^{62}_{28}Ni(n,\alpha)^{59}_{26}Fe$	3.66	~0.0000125 (f)	~0.09	~0.6	~6	$^{62}_{28}Ni(n,\gamma)^{63}_{28}Ni$ (T = 120 yr) σ = 15 barn $^{58}_{28}Ni(n,\gamma)^{59}_{28}Ni$ (T = 7.5×10^4 yr) isot. abund.: 67.88% σ = 4.4 barn $^{58}_{28}Ni(n,p)^{58}_{27}Co$ (T = 71 d) σ = 0.09 barn $^{58}_{28}Ni(n,\alpha)^{55}_{26}Fe$ (T = 2.6 yr) σ = 0.17 mbarn $^{60}_{28}Ni(n,p)^{60}_{27}Co$ (T = 5.27 yr) isot. abund.: 26.23% σ = ~5 mbarn $^{61}_{28}Ni(n,p)^{61}_{27}Co$ (T = 1.65 h) isot. abund.: 1.19% $^{64}_{28}Ni(n,\gamma)^{65}_{27}Ni$ (T = 2.56 h) isot. abund.: 1.08% σ = 1.52 barn

(th): for thermal neutrons
(f): for fast neutrons
For nuclear data see Refs. [1-6].

The nuclear reaction normally used for the production of ^{59}Fe is the (n, γ) on ^{58}Fe.

For most applications it is necessary to obtain ^{59}Fe preparations with a high specific activity and this can be done (a) from enriched ^{58}Fe irradiated in the form of $^{58}Fe_2O_3$; or (b) using the Szilard-Chalmers effect on potassium ferrocyanide, but this results in a mixture of ^{59}Fe and ^{55}Fe (T = 2.7 yr).

3. APPLICATIONS

3.1. Industrial

^{59}Fe has been used for:

Autodiffusion and migration studies	[7-9]
Wear and corrosion studies	[10-14]
The kinetic study of reactions in the Martin furnace and converters	[15]
Hydrological studies	[16]

In addition to the references given for industrial uses of ^{59}Fe reference may be made to general works [17].

3.2. Medical and biological

Used for diagnosis in the form of chloride or citrate (uses being the same in both forms). ^{59}Fe is used to study: iron metabolism [18-21]; absorption; the role of iron in haematopoiesis; excretion; and particularly plasma iron turnover and the measurement of plasma fixing power.

The activity is of the order of 10 - 25 μCi [20].

In addition to the references already given there are others dealing with the medical uses of ^{59}Fe [22].

4. RADIOLOGICAL PROTECTION

4.1. External exposure

4.1.1. Irradiation doses

The dose delivered by 1 Ci of ^{59}Fe at a distance of 50 cm is:

- for 0.19 MeV γ quanta	0.008 rem/h
- for 1.10 MeV γ quanta	1.344 rem/h
- for 1.29 MeV γ quanta	1.240 rem/h
	2.592 rem/h

4.1.2. Safety measures

Below are shown the tenth-thicknesses[1] for lead and ordinary concrete, which give some idea of the amount of protection needed in handling ^{59}Fe:

	Tenth-thickness (cm)		
	Pb	Ordinary concrete d = 2.3	
For a γ of 1.1 MeV	3.2	17	
For a γ of 1.29 MeV	3.6	19	Ref. [23]

In practice, the following lead thicknesses are needed to reduce the dose to 1 mrem/h at 50 cm:

(cm)	^{59}Fe
4.8 to handle	10 mCi
8.2 to handle	100 mCi
11.7 to handle	1 Ci

4.2. Internal irradiation

Iron-59 is classified as a highly toxic class 2 isotope [24]. Its effective half-life, allowing for both radioactive decay and excretory processes, is:

Organ	(d)	
Whole body	42.7	
Spleen	41.9	
Lungs	44.5	
Liver	41.7	
Bones	43.9	[25]

In the case of internal irradiation (ingestion or inhalation) the maximum permissible concentrations in air and water respectively, for a 40-h exposure, are:

10^{-7} μCi/cm³ and 2×10^{-3} μCi/cm³ (soluble form)
5×10^{-8} μCi/cm³ and 2×10^{-3} μCi/cm³ (insoluble form) [26]

4.3. Decontamination

Except in one or two particular cases, there is no special decontamination method for any given radioisotope. General texts on this subject [27-31] indicate that the following measures are adequate.

[1] The tenth-thickness is the thickness of shielding required to reduce the intensity of a γ-radiation of given energy by a factor of ten.

4.3.1. Skin

Rapid and repeated washing with good-quality soap, warm water and a soft brush. If this is not sufficient, use can be made of detergents or 5-10% solutions of complexing agents of the EDTA (ethylenediamine tetra-acetic acid) type. It is also possible to apply saturated permanganate solutions followed by rinsing with a 5% bisulphite solution to neutralize and remove stain. Abrasive powders should not be used and the addition of entraining agents has proved disappointing.

If any wounds are contaminated, they must be treated rapidly by bleeding, washing with water, decontamination as for the skin and sometimes by additional surgical cleaning.

4.3.2. Hair

If the hair is contaminated, it is important not to take a shower, but merely to wash the head. A normal, good-quality shampoo is usually sufficient. If contamination is persistent, the following solutions can be used:

paraisopropylorthocresol;
lavandin oil;
AC compounded terpene-free lemon;
glycerine diacetin; and
benzoic acid.

Contamination is much easier to remove if the hair is not greasy.

4.3.3. Laboratory equipment

Glasswear is usually cleaned by steeping and this is mainly a radiochemical problem. The use of a specific entraining agent or solutions of complexing agents give good results as also do solutions of chromic acid, concentrated nitric acid, ammonium citrate, pentasodium triphosphate or ammonium bifluoride.

5. SUMMARY OF PRODUCTION METHODS

The problem is to obtain ^{59}Fe solutions of high specific activity. The various methods of doing so are reviewed by Swartout and Rice [32].

5.1. Direct irradiation of iron oxide enriched with ^{58}Fe [33, 34]

$$^{58}Fe(n, \gamma)^{59}Fe$$

The method consists simply of dissolving the target in hydrochloric acid so as to obtain a 1 N hydrochloric acid solution of iron chloride. For medical use, this chloride is transformed into an iron citrate solution in a 12% sodium citrate solution at pH = 5. This is achieved by precipitating the iron hydroxide with concentrated ammonia, after which it is dissolved in citric acid and the pH is adjusted to 4.5 - 5.0 with soda.

5.2. Using cobalt in a (n, p) reaction [35-38]

$^{59}Co(n, p)^{59}Fe$

Kenny, Maton and Spragg [35] dissolve the cobalt target in 3 N nitric acid and then obtain a pH between 4 and 7 with ammonia and ammonium acetate. After adding acetyl acetone, they extract the iron without entraining agent as acetyl acetonate, with xylene. The xylene is then separated out and removed by evaporation (the small amount of residual organic matter is destroyed with perchloric acid). Wahl [36] starts with the oxide Co_3O_4 which he dissolves, after irradiation, in concentrated, hot hydrochloric acid. He adds 10 mg of entraining iron and uses isopropyl ether to extract the iron, which is then re-extracted in water. Molnar [38] has studied Fe III - Co II separation on anion resins in a hydrochloric medium.

5.3. A method often used consists of applying the Szilard-Chalmers effect [39]

5.3.1. On ferrocyanic acid [40]

After irradiation, the ^{59}Fe formed is isolated by extraction in a Soxhlet apparatus with ether containing a small amount of hydrochloric acid, but 50% of the total activity appears to remain in the initial substance.

5.3.2. On magnesium ferrocyanide [41]

This method consists of dissolving in water so as to obtain a 0.1 M magnesium ferrocyanide solution and then separating the water-soluble fraction from the insoluble fraction. The precipitate contains about 80% of the total radioactivity. (The magnesium ferrocyanide of the supernatant solution can be re-crystallized for further irradiation.)

5.3.3. On potassium ferrocyanide (the salt most often used as target) [42-46]

In all cases, the irradiated potassium ferrocyanide is dissolved in water.

Williams [42] and Dewhurst and Miller [43] then co-precipitate the hydroxides by adding an entraining agent, which is generally aluminium.

Henry, Aubertin and Valade [44] have studied a method of separation on ion exchange resins (Dowex 50). They pass the potassium ferrocyanide solution through a K^+-saturated resin column where the Fe^{3+} fixes preferentially on the K^+, after which they elute the K^+ with 1 N HCl and the Fe^{3+} with 6 N HCl.

Hudswell and Taylor [45] and Douis and Valade [46] separate the recoil atoms directly by using ammonia to precipitate the iron hydroxide in the potassium ferrocyanide solution, then they isolate the precipitate by centrifuging or filtering through Grade 4 fritted glass.

Douis and Valade thus obtained an enrichment factor of 400. All these methods of preparing ^{59}Fe by using the Szilard-Chalmers effect give a mixture of ^{59}Fe and ^{55}Fe. If pure ^{59}Fe is wanted, the target must consist of ^{58}Fe with a very low ^{54}Fe content.

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PROCEDURES

ATOMIC ENERGY OF CANADA LTD., CHALK RIVER, CANADA

1. GENERAL

Iron-59 is produced by the irradiation of ferric oxide target Fe_2O_3 enriched to 80% in ^{58}Fe. The irradiated target is processed to $FeCl_3$ and shipped to the pharmaceutical industry for further processing and distribution to the medical profession.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	5 - 10 g ferric oxide Fe_2O_3 enriched to 80% in ^{58}Fe.
Container:	The target is sealed into a small inner aluminium vial, then in a standard reactor capsule.
Irradiation conditions:	Usual yield is from 10 to 15 Ci, depending on the flux and duration of irradiation. An appropriate number of capsules are held under irradiation to provide normal requirements.

Chemical treatment

The chemical process consists of dissolving the irradiated target in HCl. This produces $FeCl_3$ solution which is our standard product.

The irradiated capsule is transferred with extension tongs from a transfer container to the processing equipment. The capsule is opened mechanically and the contents transferred to a tared weighing vessel on a balance by means of which the weight of Fe_2O_3 is determined to the nearest 0.05 mg. A small quantity of concentrated HCl is added. Dissolution is brought about by heating the mixture with an infra-red lamp. Heating is continued until a dried residue is obtained. This residue is redissolved in 1 N HCl, filtered and

made up to a suitable volume with distilled water to yield $FeCl_3$ in approximately 0.5 N HCl.

Equipment

The processing equipment consists of a weighing beaker, glass funnel, volumetric flask, reagent bottles, filter paper, small weighing balance and an infra-red lamp. These are placed in a glove box having 4 in. (10 cm) of lead shielding on all sides. Fitted through the walls are ball joint manipulators and a lead glass window to permit remote viewing and operation. The box is exhausted through absolute filters.

3. ASSAY AND QUALITY CONTROL

Chemical

A small sample is analysed by emission spectroscopy to provide an estimate of metallic impurities. The acidity is checked and the stock accordingly adjusted.

Radiochemical

Specific activity. This is calculated from the weight of the target processed and the measured yield of ^{59}Fe activity.

Activity concentration

The principal radiations measured are the 1.089 and 1.289 MeV gamma rays. The output from a suitable dilution of the active solution is analysed on a 512-channel analyser.

CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production is based on the (n,p) reaction of the cobalt target $^{59}Co(n,p)^{59}Fe$. To enhance the (n, p) reaction and decrease the ^{60}Co activity due to the (n, γ) reaction, the cobalt target is covered with cadmium shielding. After the irradiation, separation is carried out by ion exchange.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Cobalt metal, Johnson Matthey spectrochemically pure. The amount depends on request on order.

Flux:	2×10^{13} n/cm^2 s (th).
Time of irradiation:	120 h.
Container:	Quartz ampoule with ground stopper, wrapped in cadmium foil.

Chemical treatment

After irradiation the target is dissolved in concentrated hydrochloric acid, adding a few drops of hydrogen peroxide, and the solution is fed onto a column of Dowex resin.

Using hydrochloric acid cobalt ions are completely eluted, and after removal of this first fraction, hydrochloric acid of another concentration is applied as eluting agent which quantitatively desorbs carrier-free ^{59}Fe. Finally the solution is diluted to make it isotonic and sterilized.

3. ASSAY AND QUALITY CONTROL

Radiochemical purity is controlled with the aid of a multichannel pulse height analyser for each charge.

pH is determined and sterility is controlled in the usual way.

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Iron-59 is usually produced by the pile irradiation of enriched iron-58. Enriched iron is expensive and is not readily available in a pure form free from ^{54}Fe. For this reason at Trombay ^{59}Fe is produced by the ^{59}Co(n, p)^{59}Fe reaction.

The irradiated cobalt is dissolved in nitric and hydrochloric acids and then converted to the chloride. This chloride solution in 5 M HCl is passed down an anion exchange column. Iron is held up on the resin while the cobalt goes into the effluent. After washing the column free of cobalt, the ^{59}Fe is eluted out with 0.05 M HCl and concentrated.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	100 - 250 g of cobalt metal (rods 40 mm × 5 mm, iron content less than 2 ppm) enclosed in cadmium foil, then loaded into the irradiation container.
In APSARA:	Container type A (screw-capped 1 S aluminium can, 73 mm high, 26.5 mm diam.). 60 g × 1 can. Flux: $2 - 3 \times 10^{12}$ n/cm^{2}s. Irradiation period: 2 months.

Side reactions: When cobalt metal is irradiated in a reactor, the major activity produced is ^{60}Co, resulting from the reaction $^{59}Co(n,\gamma)^{60}Co$. Small amounts of ^{59}Fe are also produced by the threshold reaction $^{59}Co(n,p)^{59}Fe$. By selective neutron shielding using cadmium, the amount of ^{60}Co produced could be considerably reduced.

Chemical treatment

The irradiated cobalt rods are washed with distilled water and then they are dissolved in a mixture of hydrochloric and nitric acids, and the nitrate is converted to chloride by treatment with strong HCl. The chloride is leached out with 6 M HCl and the solution is passed down a 50 cm×1 cm^2 column of Dowex-1 (chloride form, conditioned with 5 - 6 M HCl). The column is washed with 6 M HCl till the effluent is free from cobalt. Finally, the ^{59}Fe is eluted out with 0.05 N HCl, the eluate evaporated to near dryness and the ^{59}Fe is leached out with 100 ml of 5 M HCl.

This solution is again passed down a second 20 cm×1 cm^2 column of Dowex-1, as before, to remove traces of ^{60}Co, and the ^{59}Fe is eluted out with 0.05 M HCl. The eluate is evaporated to dryness, any organic matter is destroyed with concentrated HNO_3 and H_2O_2 followed by strong HCl, and the ^{59}Fe finally leached out with 0.1 M HCl.

3. ASSAY AND QUALITY CONTROL

The activity is assayed by measuring the ion current using an ionization chamber or by gamma scintillation counting using a well-type NaI(Tl) crystal.

The total solids are determined by evaporating a known volume of the stock solution and weighing the residue.

The absence of heavy metal impurities is tested by hydroxide and sulphide precipitation tests.

Radioactive and radiochemical purity: Iron-59 is identified by its 1.1 MeV (56%) 1.29 MeV (49%) photopeaks.

Since the gamma-ray spectrometer cannot differentiate between the gamma emissions of ^{60}Co and ^{59}Fe, a preliminary chemical separation is necessary for detection and identification of any ^{60}Co impurity in the ^{59}Fe. The separation is effected by paper chromatography as follows:

Solvent:	22.5 ml acetone, 2.5 ml 9 M HCl. The solvent will be 0.8 N with respect to HCl.
Spotting:	Cobalt chloride carrier for ^{59}Fe.
Development:	Solvent front up to 15 cm.
Zones:	Cobalt 2-3 cm from point of spotting.
	Iron 10.5-14.5 cm from the point of spotting.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity:	> 5 Ci/g.
Chemical form:	$FeCl_3$ in dilute HCl.

Acidity: 0.1 M HCl.
Radiochemical purity: > 99%.
Radioactive concentration: > 1 mCi/ml.

INSTITUTE OF ATOMIC PHYSICS, BUCHAREST, ROMANIA

1. GENERAL

Production of ^{59}Fe is based on the (n, p) reaction of the cobalt target. Separation of ^{59}Fe is carried out with the aid of concentration by absorption on alumina.

2. EXPERIMENTAL PROCEDURE [1]

Irradiation

Target: Cobalt metal, chemically pure. The amount depends on the request.
Flux: 1×10^{13} n/cm^2 s.
Time of irradiation: 200 h.
Container: Quartz ampoule.

Chemical treatment

After irradiation the target is dissolved in diluted hydrochloric acid (1 : 3) and then evaporated.

After evaporation add distilled water till the concentration in $CoCl_2$ is 1 - 1.5 M.

The solution is heated for 15 min at 80-90°C and is then passed through an alumina column.

The radioactive iron in colloid form is absorbed on the alumina, the cobalt ions being completely eluted.

Hydrochloric acid 1 N is used for the desorption of ^{59}Fe.

Finally the solution is evaporated, diluted with distilled water to make it isotonic, and sterilized for medical use.

3. ASSAY AND QUALITY CONTROL

Radiochemical purity is controlled with the aid of a multichannel pulse height analyser for each charge.

The pH is determined and sterility is controlled in the usual way.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Prepared to order.

REFERENCE

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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Iron, as ferric oxide, electromagnetically enriched in ^{58}Fe (70–80%) is irradiated in a high thermal neutron flux $^{58}Fe(n, \gamma)^{59}Fe$. The oxide is converted to the chloride.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Ferric oxide, EM enriched to 80% in ^{58}Fe.
Amount:	10–15 mg.
Irradiation time:	21 d.
Container:	Sealed silica ampoule, primary; Al container, secondary.
Flux:	10^{14} n/cm^2 s.
Side reactions:	$^{54}Fe(n, \gamma)^{55}Fe$. (The ^{55}Fe content of the product is always less than 1% for the shelf life of the stock).

Chemical treatment

The silica ampoule is crushed in concentrated HCl and the solution filtered and evaporated to dryness. The residue is taken up in 0.1 N HCl.

3. ASSAY AND QUALITY CONTROL

Identification is by γ spectrometry; assay is by scintillation counting against ^{137}Cs reference.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Radioisotope:	Iron-59
Catalogue Code Reference:	IFS. 2.
Preparation:	Ferric ion in sodium citrate solution (1% wt./vol.) made isotonic with sodium chloride. Solution sterilized.
Concentration of radioelement:	Approximately 20 μCi/ml.

Specific activity:	> 500 μCi ^{59}Fe/mg Fe.
Radiochemical purity:	> 99% excluding ^{55}Fe. ^{55}Fe content < 5%.
pH:	6 - 7.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Iron-59 is produced by the (n, γ) reaction in a Fe_2O_3 target, $^{54}Fe(n,\gamma)^{55}Fe$, $^{58}Fe(n,\gamma)^{59}Fe$. During processing of the $^{55,59}Fe$ activity, HNO_3 is added to assure that all of the iron is in the Fe^{3+} state, and the iron extracted after agitation with dichlorodiethyl ether and 9 M HCl. Successive extractions remove the $^{55,59}Fe$. In final steps, organic compounds are destroyed and the volume is adjusted to provide $FeCl_3$ in HCl solution. To produce enriched ^{59}Fe, an oxide target enriched to about 60% ^{58}Fe is irradiated.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Fe_2O_3 or Fe_2O_3 enriched to 60% ^{58}Fe.
Target weight:	Unenriched: 300 mg.
	Enriched: 15 mg.
Neutron flux:	2×10^{14} n/cm^2 s.
Irradiation time:	Unenriched: 7 weeks.
	Enriched: 4 months.
Reactor yield:	Unenriched: ^{55}Fe 250 mCi
	^{59}Fe 55 mCi.
	Enriched: ^{59}Fe 300 mCi.

Chemical treatment

Apparatus

A hot off-gas scrubber unit[1] and an agitation vessel are used in processing. Processing facility and shielding required: manipulator cell, 3-in. lead equivalent.

Processing of $^{55,59}Fe$

Yield: > 95%.

The irradiated target material is placed in a beaker under the hot off-gas assembly, dissolved in a minimum amount of 12 M HCl, and the acid

[1] See Fig. 2 in the section on ^{82}Br provided by ORNL, United States of America.

concentration adjusted to ~ 9 M HCl. A few drops of 16 M HNO_3 is added to assure that all the iron is in Fe^{3+} state. The HCl solution is transferred to an agitator vessel and an equal amount of dichlorodiethyl ether (which has been equilibrated with 9 M HCl) is added. After agitation for 15 min the system is transferred to a separatory funnel. About 5 min are allowed for layers to separate ether and HCl layers. The HCl layer is on top and ether on the bottom. A second extraction is necessary to remove the $^{55,59}Fe$. The ether layers are then transferred to the agitator vessel and 50 ml of distilled water added. Iron goes into the water phase. The mixture is agitated for 15 min, transferred to a separatory funnel, and 5 min allowed for layers to separate. A second water extraction is made if necessary. The water layer is transferred to a clean 150-ml Vycor beaker and the ether layer discarded. The solution in the Vycor beaker is evaporated to near dryness under the hot off-gas assembly, fumed with 16 M HNO_3 to destroy organic compounds, and fumed twice with 12 M HCl to remove nitric acid. The volume is adjusted to 50 ml of 1 M HCl to form a clear yellow product.

Processing of enriched ^{59}Fe

From 10 to 20 ml of 12 M HCl is added to the irradiated target, and the solution heated on hot plate under a hot off-gas scrubber assembly. The solution is adjusted to ~ 100 ml of 9 M HCl solution to prepare for extraction of ^{59}Fe and separation from ^{54}Mn. About 500 ml of dichlorodiethyl ether is equilibrated with 9 M HCl by shaking in a 1-litre separatory funnel for 10 min. The HCl solution is separated and the ether is held for extraction of iron. The 9 M HCl containing iron is transferred into a 250-ml separatory funnel and an equal volume of HCl-washed dichlorodiethyl ether is added. The mixture is agitated and the two phases separated. The extraction is repeated twice to remove the iron from the aqueous solution. Ether fractions are collected and extracted with 50 ml of distilled H_2O. Iron is extracted into the aqueous phase. Water wash is repeated with 10-min agitation periods until the iron is removed from the organic phase. Three extractions are usually sufficient. The wash is collected in a 50-ml Vycor beaker and evaporated to dryness under the hot off-gas assembly. The residue is fumed with 16 M HNO_3 to remove the organic compounds and twice with 12 M HCl to remove HNO_3. The residue is dissolved in 50 ml of 1 M HCl to form a clear yellow product.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for molarity of HCl, total solids, radiochemical purity, and ^{55}Fe and ^{59}Fe concentration according to ORNL Master Analytical Manual (TID-7015), procedure Nos. 9 0733411 and 9 0733222.

Precision and accuracy of the ^{59}Fe assay are:
Calibration by 4π β-γ coincidence counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 5%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity $^{55,59}Fe$ is delivered as $FeCl_3$ in HCl solution on request. Other specifications of interest are:

Acidity:	1 N ± 50%.
Concentration:	> 0.1 mCi of ^{59}Fe per ml.
Ratio of activity of ^{55}Fe to ^{59}Fe:	< 10 : 1.
Specific activity:	≅ 25 mCi of ^{59}Fe per gram Fe.
Radiochemical purity:	> 99%.

Processed, enriched ^{59}Fe is delivered as $FeCl_3$ in HCl solution as a stock item. Other specifications of interest are:

Acidity:	1 N ± 50%.
Concentration:	> 1 mCi ^{59}Fe per ml.
Specific activity:	≅ 10 000 mCi ^{59}Fe per gram Fe.
Radiochemical purity:	> 99% (exclusive of ^{55}Fe).
^{55}Fe:	< 10%.

MAGNESIUM-28

NUCLEAR DATA AND REFERENCES

1. NUCLEAR PROPERTIES

1.1. Half-life [1-5]

20.9 h

1.2. Type of decay and particle energy (MeV) [4-6]

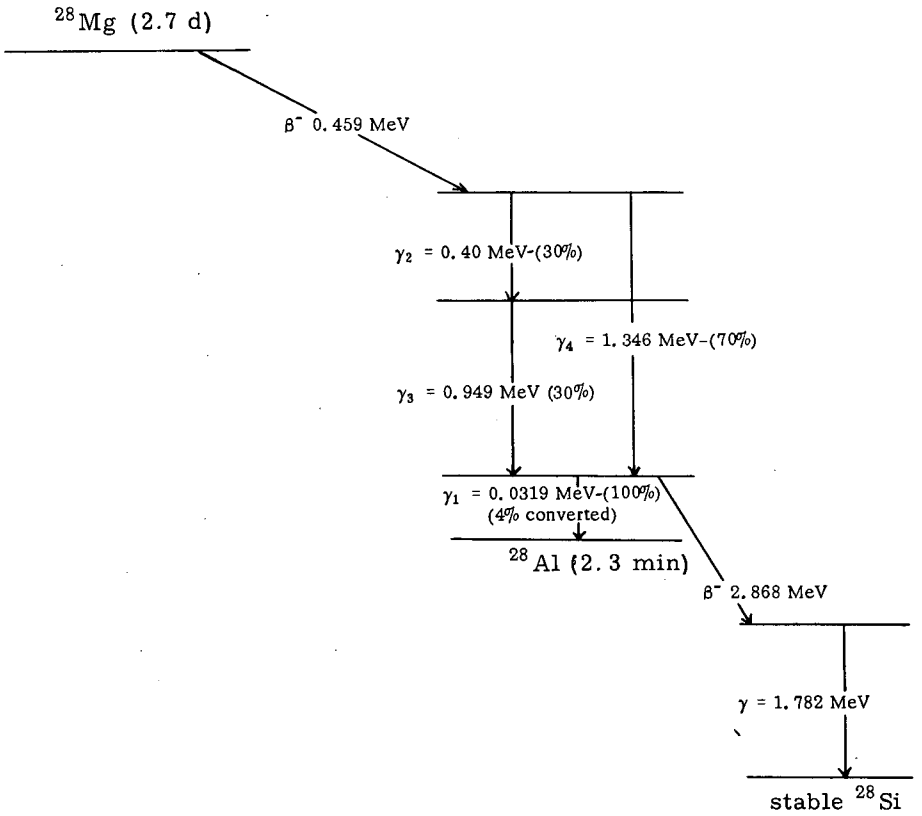
Magnesium-28 decays by beta emission followed by gamma-ray de-excitation to ground state aluminium-28 (half-life 2.3 min).

(a) $E_{max}\beta^-$ = 0.459±0.002

(b) Gamma rays

		(%)
γ_1	0.319	96
γ_2	0.40	30
γ_3	0.949	30
γ_4	1.346	70

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

$^{6}Li(n, t)^{4}He$ followed by $^{26}Mg(t, p)^{28}Mg$ [1, 28, 29]
$^{27}Al(\alpha, 3p)^{28}Mg$ 56 MeV α [4]

^{28}Mg has also been produced in a variety of other nuclear reactions [4,6, 8-10, 12, 13].

3. APPLICATIONS

Magnesium-28, with a half-life of about 21 h, is the only practical isotope of magnesium for tracer studies. A brief survey of published applications is given below.

3.1. Biochemistry and biology

Distribution of magnesium in various body organs of mammals [14-17, 32, 33, 35-37]

3.2. Plant metabolism

Biosynthesis of plant pigment	[18, 19]
Chlorophyll studies	[20, 21]

3.3. Medicine

Determination of body water and electrolytes	[22]
Haematological research	[23]
Determination of magnesium distribution and exchangeable magnesium in man	[17, 24-26, 31, 34]

3.4. Radioisotope generation

^{28}Mg as ^{28}Al-generator	[5, 27]

4. RADIOLOGICAL PROTECTION

The brief summary given below should be read in conjunction with Safe Handling of Radioisotopes, Safety Series No. 1, published by the International Atomic Energy Agency.

4.1. External irradiation

Because of the short half-life of ^{28}Al (2.3 min) a secular equilibrium is quickly established between the parent ^{28}Mg and the daughter ^{28}Al, so that the radiation of both isotopes should be considered.

The maximum range of beta particles from ^{28}Mg is 200 mg/cm^2 Al. For the ^{28}Mg-^{28}Al system the maximum beta range is 1350 mg/cm^2 Al.

For a 100 μCi batch half-an-inch lead shielding is required during production as protection from the gamma radiation of the ^{28}Mg-^{28}Al mixture and from ^{24}Na impurities. Precautions should be taken against tritium contamination.

For transport purposes ^{28}Mg is a group III radioisotope[1]. The radiation from a sample of 100 μCi activity is low enough, so that shipment can be made in a non-returnable unshielded container [29].

5. SURVEY OF PRODUCTION METHODS

The production of magnesium-28 in a reactor is based on the sequence of reactions $^{6}Li(n, t)^{4}He$ and $^{26}Mg(t, p)^{28}Mg$. The 2.73 MeV tritons produced in the primary reaction are utilized to bombard the ^{26}Mg atoms. Carrier-free ^{28}Mg may be obtained in the $^{27}Al(\alpha, 3p)^{28}Mg$ reaction [7].

Spallation reactions of medium-to-heavy nuclides with high energy protons or neutrons carried out in an accelerator also produce ^{28}Mg. The high cost of acceleration and the complex processing procedures necessary for obtaining a high degree of purity make this method uneconomical.

5.1. Targets

Targets reported in the literature for reactor production of ^{28}Mg are Mg-Li alloys. Specific activities obtained with alloys were several times higher than those obtained with mixtures of magnesium and lithium compounds [29].

Lithium enriched to 96% by wt. ^{6}Li (the abundance of ^{6}Li in natural lithium is 7.5% by wt.) is usually used for the target. Removal of ^{7}Li from the target prevents triton energy dissipation in collisions with ^{7}Li atoms, before they can react with ^{26}Mg nuclides. The magnesium component of the alloy is either natural magnesium (11.3% ^{26}Mg) or enriched to ~99% ^{26}Mg [27]. The use of the latter increases the product specific activity thirtyfold [30]; however, the production cost is also increased due to the high price of enriched magnesium. The optimum weight per cent of lithium in the alloy for thin targets is 75% [29].

Thin targets are necessary in order to avoid self-shielding effects which would reduce the yield of ^{28}Mg. Highly purified alloy is required to minimize contamination. The main contaminants are traces of sodium which cannot be completely removed from lithium, and oxygen-16 present as a result of air oxidation. On irradiation in a reactor the oxygen leads to the formation of the undesirable ^{18}F activity through the $^{16}O(t, p)^{18}F$ reaction. Methods for controlling oxidation are mentioned below.

Metallic ^{6}Li and ^{26}Mg in the weight ratio of 3 : 1 are melted together at 650°F in a dry box in an argon atmosphere. The molten alloy is poured into moulds, rapidly cooled to ensure homogeneity and immersed in mineral oil to prevent direct contact between the alloy and the air oxygen. The alloy is rolled to 0.010-in.-thick strips. The prepared foils are placed in alu-

[1] IAEA Safety Series No. 6.

minium cans, in a neon or a helium atmosphere to prevent oxidation. The cans are tightly sealed so as to prevent replacement of helium by air during irradiation [27].

5.2. Chemical processes

Upon removal from the reactor, the target material is dissolved in water or in dilute HCl. Magnesium hydroxide precipitates and the supernate is discarded. Radiochemical impurities present include:

(a) ^{18}F produced by triton reaction with oxygen.
(b) ^{3}H activity of unreacted tritons.
(c) ^{24}Na produced by the reactions: $^{23}Na(n, \gamma)^{24}Na$, $^{25}Mg(t, \alpha)^{24}Na$ and $^{27}Al(n, \alpha)^{24}Na$.

Steps should be taken, prior to irradiation, to avoid the introduction of aluminium impurities.

The high temperatures developed during irradiation may bring about a reaction between the Li-Mg alloy and the aluminium target can. In order to prevent this reaction an 0.001-in. iron foil is placed between the alloy and the aluminium can.

5.2.1. Removal of impurities

5.2.1.1. Removal of ^{3}H

The tritium present in the target after irradiation is removed in two stages:

(a) The magnesium hydroxide precipitate is washed with ice water, slightly alkaline.
(b) The precipitate is dissolved in 0.001 N hydrochloric acid solution and evaporated to dryness. This procedure is repeated twice [27].

5.2.1.2. Removal of ^{18}F impurities

Two methods may be used for the elimination of ^{18}F contamination:

(a) Magnesium hydroxide is dissolved in concentrated hydrochloric acid containing F^- carrier and the solution evaporated [29].
(b) A solution of the $Mg(OH)_2$ in 3 N HCl containing KF carrier is passed through a Dowex 1(X8) ion exchange column (in the Cl^- form). Three quarters of an inch of WOELM natural grade Al_2O_3, preconditioned with 0.5 N NH_4Cl and washed with water, is added to the column. The ^{18}F remains adsorbed on the column.

The relatively short half-life of ^{18}F (110 min) simplifies the problem since complete decay may be allowed before use.

5.2.1.3. Removal of ^{24}Na impurities

Sodium-24 impurities are removed by an exchange between the radioactive ^{24}Na and an added sodium solution, followed by a NaCl precipitation.

The magnesium hydroxide precipitate is dissolved in concentrated hydrochloric acid. Sodium chloride is then added and the solution is evaporated.

Equal volumes of concentrated hydrochloric acid and ethyl alcohol are added. The solution is chilled in an ice bath and the NaCl precipitate which contains the ^{24}Na is discarded [29].

5.2.1.4. Removal of ^{59}Fe impurities

Iron-59 activity is removed by precipitation as ferric hydroxide. Magnesium hydroxide is dissolved in dilute HCl and 2-3 mg Fe^{3+} carrier are added. The solution is made basic to bromcresol green with NaOH. The precipitated $Fe(OH)_3$ is centrifuged and discarded. Small amounts of 45-d ^{59}Fe activity may still be present in the final product [29].

5.2.1.5. Removal of ^{56}Mn, ^{64}Cu, ^{65}Zn and ^{115}Cd impurities

The purification is performed by a sulphide precipitation in the presence of the appropriate carriers. The lithium-magnesium alloy is dissolved in dilute HCl. Carriers of Mn, Cu, Zn and Cd are added. The solution is made basic with ammonium hydroxide. The sulphides are precipitated on the addition of hydrogen sulphide. The precipitate is centrifuged and discarded. This procedure should be repeated three times. The residual liquid is filtered through a fine porosity filter paper [5, 27, 28].

5.2.2. Final purification

After purification from the radiochemical impurities as mentioned above the product ^{28}Mg is further refined by NaOH precipitations. The aqueous phase is discarded and the precipitate washed with ice water. The magnesium hydroxide is dissolved in dilute hydrochloric acid and the procedure is repeated two or three times. The final $Mg(OH)_2$ precipitate may be dissolved in any acid for further use [28, 29].

Unidentified impurities may be removed by adsorption on a Dowex-50 column in the Na^+ form and washing with 1 N sodium hydroxide [27]. This column may be used directly as an ^{28}Al generator yielding ultra-pure ^{28}Al (> 99.999%).

The chemical yields of the reported processes are 90 to 95%. Specific activities of approximately 40 mCi of the equilibrium mixture of ^{28}Mg-^{28}Al/g of stable magnesium are obtained [27].

Residual non-active impurities in the final product include Fe, Al, Cu and Si in less than 0.01% each and 1 to 5% Na [29].

5.3. Carrier-free ^{28}Mg production

Carrier-free ^{28}Mg is produced in the $^{27}Al(\alpha, 3p)^{28}Mg$ reaction. Aluminium targets are bombarded with 41 MeV alpha particles. The target material is dissolved in concentrated sodium hydroxide, and filtered through a fine glass frit. The procedure is based on the fact that carrier-free Mg will form a radiocolloid in basic solution and will be held up on a glass frit. The magnesium hydroxide is washed several times with NaOH and water to remove aluminium and sodium-24 impurities and then dissolved in dilute HCl or HNO_3. The chemical yield of this process is 80% [7].

6. RADIOASSAY

Because of the short half-life of ^{28}Al, transient equilibrium is rapidly established after any separation of magnesium. The comparatively energetic radiation of ^{28}Al permits its detection even in the presence of ^{28}Mg.

Any standard method for beta or gamma counting might be applied to the ^{28}Mg–^{28}Al detection. Beta counting of solid samples is performed with an end-window beta proportional counter or with a plastic beta scintillation counter [5].

Gamma counting of ^{28}Mg is preferred because the sample can be counted both as a liquid or as a solid, and the counting procedure is less dependent on the weight of material in the sample. NaI(Tl) scintillation counters [5, 27] or GM counters [4] are used. Radiochemical purity is determined by gamma spectroscopy and half-life measurements.

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PROCEDURES

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1. GENERAL

The production of ^{28}Mg is based on the irradiation of ^{6}Li–^{26}Mg alloy; $^{6}Li(n, t)^{4}He$, $^{26}Mg(t, p)^{28}Mg$. Magnesium-28 is separated by the processes of precipitation of magnesium hydroxide, followed by the dissolution and ion-exchange method.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Approximately 12 mg of $^{6}Li^{26}Mg$ alloy. Use $^{6}Li^{26}Mg$ approximately 3 : 1 by weight. Use ^{6}Li enriched to 96% and ^{26}Mg enriched to 99%. Prevent air oxidation.

* Extracted from BNL 864 (T-347).

Irradiation conditions: Irradiation of 3 d at the flux of $1.2-1.3\times10^{13}$ n/cm^{2}s.
Reactor yield: 100 Ci $^{28}Mg^{28}Al$.
Chemical yield: 90%.

Chemical treatment

A. Target preparation

Weigh out correct amounts of ^{6}Li and ^{26}Mg metals separately and rapidly on an analytical balance.

Rapidly transfer metal samples into dry box air lock and flush with dry argon; ordinary tank argon is sufficiently dry for this purpose.

Transfer metal samples from air lock into dry box proper. The dry box should already have been filled with argon. The argon flow-rate need only be sufficient to prevent back diffusion of air into box.

Melt samples together in graphite crucible at ~650°F in furnace, stirring with a graphite rod. As soon as all is molten, proceed to next step.

Pour molten alloy into shallow graphite mould; rapid cooling will ensure homogeneity of alloy.

Place ingot under oil for transfer out of box; prevent air oxidation. Mineral oil is satisfactory for this purpose.

Using a suitable small rolling mill, roll to 0.25 mm thickness. If target is too thick, the high σ of ^{6}Li will seriously depress the internal neutron flux, reducing the specific activity of ^{28}Mg.

Cut into suitable strips for irradiation. This cuts easily with ordinary scissors.

Store under oil; prevent air oxidation.

B. Target irradiation

Clean alloy foil with ethyl acetate, weigh and insert in slits in 3/4-in. diam. graphite rod. Solvent removes oil. Rod acts as spacer, holder, and heat sink and has two longitudinal slits, cut about 3/4 of the way through. Dry box not needed if handling is fairly rapid.

Place loaded rod in suitable aluminium can and weld shut. Cap of can should have short length of 1/8-in. diam. tube attached to it.

Evacuate can via tube on cap and fill with helium. Ordinary oil-pump helium is satisfactory. Helium prevents air oxidation and is a good heat transfer agent.

Crimp tube closed. End need not be welded if crimp seal is a good one.

Irradiate in reactor ~3 d. Use cooled hole to prevent sample from melting. Note: If sample melts, thickness will increase and specific activity of ^{28}Mg will decrease; see above.

Open can with remotely-operated opener. Enclosure must be capable of dealing with considerable tritium contamination from $^{6}Li(n,\alpha)^{3}H$.

The following special equipment is needed: low moisture, inert atmosphere glove box ("dry box") with air lock. Remotely-operated can opener. Processing glove box with 1/2-in. lead shielding suitable for handling gross tritium contamination.

C. Post-irradiation processing

Transfer graphite rod and alloy foils to processing glove box. Dry inert atmosphere not required.

Remove foils from rod and dissolve, one at a time, in a minimum of H_2O in a 50-ml plastic centrifuge tube in an ice bath. Reaction is rapid. If foils are added too rapidly, they may ignite. Plastic centrifuge tubes insure against accidental breakage.

Add 3 drops 3 N NaOH and centrifuge. This assures minimum loss of Mg. Centrifuge for 5 min.

Discard supernate. Contains ^{18}F, ^{3}H and ^{24}Na. Fluorine-18 comes from (t, n) reaction on oxide impurities; ^{3}H comes from unreacted tritons; ^{24}Na comes from (n, γ) reaction on sodium impurities, from (t, α) reaction on residual ^{25}Mg, and from (n, α) reaction on Al impurities.

Wash twice with ice water containing 3 drops of 3 N NaOH, discarding supernate. This reduces ^{3}H and ^{24}Na contamination.

Dissolve $Mg(OH)_2$ with concentrated HCl. Use ~0.5 ml HCl/10 mg alloy.

Pour into 50-ml beaker containing stirring bar and place on magnetic mixer. This and the following two steps are necessary only if the original ^{26}Mg becomes contaminated with Al during the reduction to metal.

Add three drops of 0.1% methyl red indicator while stirring. Add 0.1 N NaOH until just yellow. This precipitates $Al(OH)_3$. The end point is critical. $Mg(OH)_2$ will precipitate if the pH goes too high.

Centrifuge and wash precipitate with H_2O. Combine supernate and washes and save. Discard precipitate.

To supernate add 3 mg F^- carrier and 1 drop of 3 N HCl. Use KF for carrier, 30 mg F^- per ml.

Pour supernate onto prepared ion exchange column.

Column preparation: In a 1-in. fritted Büchner funnel settle 3/4 in. of Dowex 1X8 (Cl^- form). Cover with cloth disc and add 3/4 in. of Woelm Al_2O_3 (neutral grade) which has been previously conditioned with 0.5 N HCl and washed twice with H_2O. The column removes the remainder of ^{18}F. This is necessary for subsequent ^{28}Mg assay.

Wash the column with 75 ml of 0.001 N HCl.

Combine the effluent and transfer to the distillation flask. Distil to near dryness. Use glass beads in flask to prevent bumping. Discard the distillate. This step and the following two reduce the volume of the product (residual solution) and ^{3}H contamination in it.

Add ~50 ml 0.001 N HCl and distil to near dryness.

Repeat.

Transfer residual solution from distillation flask to beaker.

Wash the distillation flask at least twice with 0.001 N HCl and combine with the residual solution (the previous step). The final volume should be ~5 ml. The solution should be water clear.

3. ASSAY AND QUALITY CONTROL

Assay by well-type scintillation counter standardized against 4π β counter.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Product composition:	$^{28}MgCl_2$ in dilute HCl containing 1% NaCl.
Radiochemical purity:	95% $^{28}Mg^{28}Al$, 5% ^{3}H, traces of ^{65}Cu, ^{115}Cd as of 24 h following processing.
Specific activity:	40 mCi $^{28}Mg^{28}Al$/g Mg at the time of shipment.

PHOSPHORUS-32

NUCLEAR DATA

1. NUCLEAR PROPERTIES

1.1. Half-life

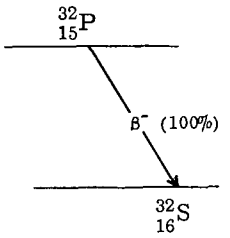
14.45 d

1.2. Type of decay, and energy (MeV)

Pure beta emitter

beta (β^-) 1.71 (100%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{13} n/cm^2 s (mCi/g)			Secondary reactions [a] and half-life of nuclide formed
			1 h	24 h	saturation	
$^{31}P(n,\gamma)^{32}P$	100	0.19 (th)	2.1	48	1020	$^{31}P(n,p)^{31}Si$ (T = 2.62 h)
$^{32}S(n,p)^{32}P$	95.0	0.065 (f)	0.63 [b]	14.8 [b]	318 [b]	$^{34}S(n,\gamma)^{35}S$ (T = 86.7 d) isot. abund.: 4.22% σ = 0.26 $^{33}S(n,p)^{33}P$ (T = 24.6 d) isot. abund.: 0.75% $\sigma_{(f)} \doteq 0.16$, $\sigma_{(th)} = 0.0023$

For nuclear data see Refs. [1-5].

[a] Only side-reactions producing nuclides with half-lives exceeding 1 h are taken into consideration.

[b] The obtainable ^{32}P activity per gram of elementary sulphur depends markedly on the sulphur-uranium-moderator geometry, i.e. on the reactor type.

3. APPLICATIONS

Phosphorus-32 is the only practical radioisotope of phosphorus. Water-soluble phosphates or the free acid are predominant forms in these applications, but many organic labelled compounds have been prepared [6] and some of them are commercially available [7]. A brief classified survey of published applications is given below.

3.1. Biochemistry and biology

Study of ribonucleic [8] and desoxyribonucleic acids [9]
Enzymological studies [10]
Studies of microorganisms [11], viruses and bacteriophages [12, 13]
Muscle physiology studies [14]
Studies of mitochondria metabolism [15]

3.2. Plant metabolism [16, 17]

Investigation of photosynthesis [18]

3.3. Entomology [19]

3.4. Medicine

Diagnosis and therapy of neoplastic diseases [20, 21]
Colloidal chromic phosphate for therapy of tumours [20]

3.5. Analytical chemistry [22]

4. RADIOLOGICAL PROTECTION

4.1. External irradiation

The maximum range of phosphorus-32 beta-particles is 800 mg/cm^2. The formation of bremsstrahlung becomes important as the amount of activity increases. It results from the retardation of the beta-particles in the shielding material. The following equation, based on an empirical relation [23], may be used for estimating S, the number of photons/s so arising.

$$S = 4.07 \times 10^7 \times AZE$$

when

A = activity of the beta source (Ci)

E = maximum beta energy (MeV)

Z = mean atomic number of the shielding material.

It can be seen that low atomic number shielding materials (such as water, plastics, aluminium) give rise to less bremsstrahlung [24].

Only the maximum energy value of photons, 1.7 MeV, is used for shielding calculations [23]. Experimentally the bremsstrahlung spectrum has been shown to have a maximum at 100-300 keV, depending on the atomic number [25].

A practical system of shielding for 1 Ci of ^{32}P would consist of 1 cm of Perspex (to absorb the beta particles), followed by 1 cm of lead (to absorb the bremsstrahlung).

Activities up to 50 mCi can be safely handled behind 1 cm of Perspex only.

Even when handling small activities, say of 1 mCi, some measure of remote handling is necessary, such as short tongs or forceps, because of the high local beta dose on the surface of containers.

4.2. Internal contamination

Phosphorus-32 is classified [26] as a class 3 (moderate toxicity) isotope and has an effective half-life of 14 d [27].

4.3. Decontamination

Phosphorus-32 is more effectively removed from surfaces [28] and from clothing [29] with dilute inorganic acids (at least 0.002 N solutions) than with alkaline or soap solutions. The presence of phosphate carrier increases the efficacy of decontamination. General methods for the treatment of active waste are applicable [30, 31].

5. SURVEY OF PRODUCTION METHODS

The production process is based on the reaction $^{32}S(n, p)^{32}P$. The application of the reaction $^{31}P(n, \gamma)^{32}P$ is limited.

The production processes reported to date can be classified according to the chemical form of the targets and the nature of chemical separation methods.

5.1. Targets

The targets reported in the literature include the following:
(a) Elementary sulphur;
(b) Sulphur compounds, such as sulphates, polysulphides, etc.;
(c) Red phosphorus and phosphorus compounds.

Sulphur: Highly purified sulphur must be used. Purification methods include extraction with acid, treatment with magnesium oxide (removing the organic matter), and distillation [32-34]. Among the impurities arsenic must be strictly controlled, as arsenic follows ^{32}P during processing. Sulphur offers the best exploitation of the reactor space capacity; on the other hand, the separation of ^{32}P is not simple.

Sulphur compounds: The advantage of using a water-soluble sulphur compound as a target lies in the easy conversion of the ^{32}P nuclide to the phosphate form. Most sulphur compounds used possess high thermal stability. The dried Analar grade compounds are used either directly or for the preparation of the target compound (i.e. polysulphides). The sulphur content (22.57, 24.95, 57.7 and 67.9% for sodium sulphate, magnesium sulphate, potassium polysulphide and sodium polysulphide, respectively) is important for neutron economy.

5.2. Chemical processes

Chemical processes can be classified according to the target material used. In each process there are the following steps:
(a) Separation of the ^{32}P from the target;
(b) Purification, if necessary;
(c) Final adjustment of the product.

The following is a brief description of the processes reported in the literature:

5.2.1. For elementary sulphur target

Phosphorus-32 atoms formed exist probably in the form of phosphorus sulphides [35], or are converted to this form during the heating of the irradiated target [36]. Reactions of ^{32}P recoils with impurities have also been reported [37]. On extracting ^{32}P into the aqueous phase, these phosphorus sulphides hydrolyse and produce PO_4^{3-} ions. The chemical processes reported may be classified as follows:

(a) Extraction of ^{32}P from molten sulphur

Extraction with concentrated nitric acid

Molten sulphur is poured into boiling concentrated nitric acid (azeotropic mixture, b.p. 121°C). ^{32}P is extracted into the acid phase in 90-95% yield. Sulphuric acid is also formed [38-40].

Extraction with dilute nitric acid under pressure

The use of dilute nitric acid reduces the amount of sulphuric acid formed during the extraction process. The extraction is carried out with 0.1 N nitric acid at a temperature of 135-138°C in a stationary autoclave overnight [32], or with 0.2 N nitric acid at a temperature of 130°C in a rocking autoclave for 3 h [36, 41-43]. Propeller-type agitation during extraction [44] has been abandoned [32].

These two extraction processes have the disadvantage of simultaneous extraction of corrosion products (Fe^{3+}, Cr^{3+}, Ni^{2+}, etc.) and impurities in the sulphur (Mg^{2+}, Al^{3+}, trace elements, and in some cases arsenic). The following methods have been proposed for further purification and separation from sulphuric acid (containing ^{35}S).

- Co-precipitation of ^{32}P with ferric hydroxide [38-40, 44] or lanthanum hydroxide [32, 36, 43], with subsequent cation exchange treatment to remove the introduced cation; in the former case, solvent extraction by iso-propyl ether is also used;
- Adsorption of ^{32}P on dialysed iron (in acid solution, pH 1-4) [45, 46] or on a specially prepared ferric hydroxide bed [47].

Arsenic can be removed from the ^{32}P as the volatile arsenic tribromide [43]. Organic matter from the exchange resin column can be destroyed by hydrogen peroxide [36]. To avoid the formation of polyphosphates of ^{32}P on local hot areas of the glass surface during the evaporation to dryness of ^{32}P solutions, a special evaporator heated by xylene vapour at 140°C has been used [36, 43]. A total yield of 60-80% is reached using the above processes [43, 48].

Extraction with acetic acid and acetic anhydride mixture (3 : 1).

This process was proposed to minimize the formation of sulphates during the extraction. The extraction conditions are: temperature 120-130°C, extraction for 15 min using air mixing. A yield of 70-85% is reported. Subsequent purification of the ^{32}P is necessary [49, 50].

(b) Extraction of ^{32}P from solid, fine-grained sulphur

Because of the diffusion of ^{32}P in the solid phase, it can be extracted with boiling water in the presence of a small quantity of 2-octanol as a wetting agent [51-54]. The efficiency of the extraction depends greatly on the particle size; for example, 1-2 h extraction yields 90% for a finely

ground target and 76% for sublimed sulphur. No chemical or radioactive impurities are present. Poor stability of the powdered target at higher neutron fluxes (formation of aggregates [55] or melting of the target [56]) sets the limit to this method.

(c) Separation of ^{32}P from sulphur dissolved in an organic solvent

Extraction into an aqueous phase

The irradiated target is dissolved in the organic solvent, and ^{32}P is extracted into the aqueous phase (hydrochloric acid in most cases). The following solvents for the dissolution of sulphur have been proposed: trichloroethylene [33,57], carbon disulphide [33, 57, 58], tetrabromoethane [57], chloroform [33], benzene [33, 59], toluene [59], aniline [33], decaline [60, 61] and tetrachloroethylene [55].

The following solvents have been used for routine production:

Trichloroethylene: 500 ml of the solvent for 50 g sulphur, extraction with 0.1 N hydrochloric acid for 0.5 h, yield of 84-93% [33];

Toluene: 7.6 l. of the solvent for 660 g sulphur, extraction with 300 ml of 0.01 N hydrochloric acid, twice for 25 min, total yield of 90% [59];

Tetrachloroethylene: extraction with 0.1 N hydrochloric acid for several hours [55];

Decaline: extraction with 0.3 N hydrochloric acid for one hour [61].

In some cases subsequent purification processes have been employed including cation exchange treatment [55] and heating with active charcoal [61].

Adsorption on silica gel or alumina

The separation of ^{32}P is done by adsorption on silica gel [62] or on an alumina [63] column from the irradiated sulphur dissolved in carbon disulphide [62] or toluene [63].

(d) Separation of ^{32}P from sulphur by distillation of sulphur

The irradiated sulphur is distilled off in a stream of inert gas (500°C) [64] or under vacuum (5 mmHg, approximately 400°C) [65], when the ^{32}P remains in the residue and is taken up with boiling 0.01 N hydrochloric acid. The yield is nearly 100% and no purification is needed [56, 64, 65].

5.2.2. Sulphur compound as targets

The bulk of ^{32}P atoms is easily changed to phosphate for the majority of soluble sulphates, when dissolved in water; the yield is up to 100% for long irradiation [66-70]. More than 94% of the ^{32}P activity is present in the phosphate form after dissolution of the polysulphides in water [70, 71]. The separation of ^{32}P from the sulphate or polysulphide solution has been achieved by adsorption or co-precipitation. The following gives the pro-

cesses for individual targets, except for carbon disulphide [72-77] which, being insoluble in water and inconvenient as a reactor target, is mentioned here only for completeness.

(a) Sodium sulphate

A ferric-hydroxide bed prepared from a cation exchange resin in the ferric ion form, is used to adsorb ^{32}P from the dissolved target. The elution of ^{32}P is done with sodium hydroxide. Up to 80% yields were obtained [47].

(b) Magnesium sulphate

Adsorption of ^{32}P on alumina

Adsorption on an alumina column from acid solution with subsequent elution with 2.5 N [78] or 0.5 N sodium hydroxide [79] and removal of cations on a cation exchanger gave a total yield of 70% [78].

Adsorption of ^{32}P on magnesia

Adsorption on magnesia from a solution of pH 7.5 under mixing (50 mg of 100-200 mesh powdered magnesia, temperature 60°C, operation time 2 h) with subsequent dissolution of the separated magnesia in acid and the removal of the magnesium by ion exchanger showed a yield of 85-90% [61, 80].

Adsorption of ^{32}P on magnesium metal

Adsorption on magnesium metal from a neutral solution is completed in 2-3 h with mixing at room temperature; 1 mg of magnesium powder of 100-200 mesh per 1 ml of 1 M magnesium sulphate is used. A total yield of 80% is obtained, after magnesium removal on a cation exchanger [81].

Coprecipitation of ^{32}P with magnesium hydroxide

Coprecipitation of ^{32}P with magnesium hydroxide with subsequent cation exchange treatment for the removal of magnesium resulted in a yield of 80% [82]. The precipitation is best carried out in a boiling solution [71].

(c) Sodium or potassium polysulphide

Phosphorus-32 has been coprecipitated with magnesium hydroxide from a boiling water solution of the target. Magnesium ions were then removed on a cation exchange resin. The total yield was reported to be 70-76% [71, 83].

5.2.3. Phosphorus compounds as targets

Elementary phosphorus and some of its compounds can be used as targets if a product of relatively low specific activity is acceptable. The behaviour and stabilization of recoiled ^{32}P in the target depends on irra-

diation conditions and post-irradiation treatment. For example, the ^{32}P activity in irradiated phosphates has been found in the form of nine different compounds after a short irradiation [84], and in two or three compounds after a long irradiation [85-87]. Thermal treatment of the irradiated compound usually increases the activity of ^{32}P in the parent molecule. Chemical processing is therefore necessary in order to obtain a radiochemically pure product.

Phosphorus pentoxide has been used for the production of ^{32}P-labelled phosphoric acid [88]; boiling the dissolved compound with charcoal is necessary to hydrolyse pyrophosphoric acid and to remove insoluble polymeric phosphorus compounds. Various phosphorus halides, such as phosphorus trihalides [88-90], as well as phosphorus pentasulphide [88], phosphorus sulphobromide [89], etc., can be prepared from irradiated red phosphorus. These phosphorus halides and sulphides have been used for syntheses of ^{32}P-labelled compounds.

6. RADIOASSAY

A relative measurement is recommended for routine work. The counting equipment can be calibrated with standardized solutions of ^{32}P. Phosphorus-32 standard solutions are commercially available, their activity usually being determined by 4π absolute counting.

Counting of the product can be carried out using either a liquid-counter or a normal counter under which an aliquot of the solution is placed in a small beaker or planchet. Scintillation counters as well as GM counters can be used for this purpose. Measurement of aliquots of undiluted product can be conveniently carried out using a well-type ionization chamber.

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PROCEDURES

INSTITUTE OF NUCLEAR SCIENCE,
NATIONAL TSING HUA UNIVERSITY,
HSINCHU, TAIWAN, REPUBLIC OF CHINA

1. GENERAL

Phosphorus-32 is prepared by the nuclear reaction $^{32}S(n, p)^{32}P$. Phosphorus is separated from sulphur by dry distillation of sulphur in a nitrogen stream. Finally, phosphorus is extracted from the residue with dilute hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	100 g of elementary sulphur purified by sublimation four times is melted and cast into rods.
Irradiation container:	The target is wrapped with aluminium foil and sealed into the aluminium can 4.7 cm diam. × 9 cm.
Flux:	1.6×10^{12} n/cm^2 s.
Irradiation time:	30 h.

Chemical treatment

The irradiated sulphur is placed in a distillation flask made of quartz. The flask is fitted to a receiver with a ground joint. Pass nitrogen gas through the distillation unit. Switch on the heating system. The internal temperature of the flask reaches ~400°C after 30~40 min. Distillation of sulphur takes place and the sulphur is collected in the receiver for re-use. Sulphur which escapes in the form of vapour is collected in the condenser fitted to the receiver. After the distillation of sulphur is completed, the flask is allowed to cool and the nitrogen stream is cut off. Add 50 ml of 0.1 N hydrogen chloride to the flask, which is then fitted with a condenser and refluxed for two hours to leach out the phosphorus. After cooling the solution is passed into a column of cationic exchanger (Amberite IR-120 conditioned in H^+ form). The effluent is collected and transferred into a concentration vessel to adjust the concentration.

About 95 mCi of phosphorus-32 is obtained.

3. ASSAY AND QUALITY CONTROL

The chemical analysis of the product is carried out according to Oak Ridge National Laboratory Master Analytical Manual 90733601-4. The chemical form of phosphorus-32 is determined by ascending paper chromatography. Pharmaceutical control is carried out according to Minimum Requirements of Radioactive Drugs, Ministry of Health and Welfare, Japan (1962).

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	H_3PO_4 in HCl solution.
Concentration:	2.3 mCi/ml.
Specific activity:	Carrier-free.
Acidity:	0.1 – 0.15 N HCl.
Radiochemical purity:	> 99%.

THE NUCLEAR RESEARCH INSTITUTE, ŘEŽ, CZECHOSLOVAK SOCIALIST REPUBLIC

1. GENERAL

Phosphorus-32 is separated from an irradiated sodium pentasulphide target by co-precipitation with magnesium hydroxide. The subsequent separation of magnesium ions is carried out on a Dowex-50 cation exchange resin. Phosphorus-32 remains in the eluate. The total yield is in the range of 70-76%. Phosphorus-32 is present in the form of phosphate ions. The method is patented [1].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Sodium pentasulphide prepared by melting sodium carbonate (pro analysi) and elementary sulphur (p.a.) in a graphite crucible at 450°C for four hours. The composition of the melt is $3Na_2S_5 + Na_2SO_4$ and the total sulphur content 67.9%. The melt is cast into graphite moulds.
Container:	Aluminium container.
Irradiation conditions:	Irradiation for 160 h (20 h/d, 4 d a week) at a flux of 1×10^{13} n/cm^2 s. Each cylinder of polysulphide is wrapped in aluminium foil of 0.1 mm thickness. Two hundred and seventy grams of target material is sufficient to produce 1.5 Ci.

Chemical treatment

The ninety grams of target material are stored for five days, to allow the ^{24}Na to decay, and then dissolved in 1 litre of hot distilled water. The insoluble residue, if present, is removed by paper filtration and 750 mg of Mg^{2+} are added to the clear solution. The solution is then heated to boiling temperature and the precipitated magnesium hydroxide is separated by decantation and filtration, and washed with water. The precipitate is dissolved in dilute hydrochloric acid, and elementary sulphur, if present, is filtered off. The clear solution is neutralized with 1 N sodium hydroxide (thymol blue; red-yellow) and the resulting precipitate is boiled for 3 min.

After a short cooling period the precipitated magnesium hydroxide is removed with a small paper filter and washed with water. The filter with the precipitate is then transferred into the same flask in which the precipitation was carried out, 30 ml of water and 5 drops of thymol blue are added and the precipitate is dissolved in a 0.3 N solution of hydrochloric acid while being gently heated. The excess of acid is carefully neutralized with a solution of sodium hydroxide to pH 2 (the transition point of the indicator) and the solution is transferred to a cation exchanger column (15 g Dowex-50 in the hydrogen form).

The column is washed with 30 ml of water and the eluate containing the phosphorus-32 and hydrochloric acid is evaporated to dryness. Organic materials are destroyed by heating with 10 ml of 30% hydrogen peroxide and evaporating to dryness. This operation is repeated. The phosphorus-32 is then dissolved in hot 0.01 N hydrochloric acid and the solution is filtered through a glass filter to remove insoluble particles. This solution is used for the production of all ^{32}P phosphate compounds.

The process is carried out in a lead-shielded box. The evaporator is heated with xylene (b.p. 140 - 143°C) to prevent the polymerization of phosphate ions.

3. ASSAY AND QUALITY CONTROL

The ^{32}P content is estimated by liquid counting in a counter which has been calibrated with a standard ^{32}P solution. Phosphorus-32 standards are prepared by 4π counting. The radioactive purity is checked for each batch of the target. A first test for heavy metals is carried out immediately with the sodium sulphide solution (Pharmacopoeia method). If this is negative, the product is dispensed before a complete spectrographic analysis is done.

The amount of ^{32}P as orthophosphate is determined by ascending paper chromatography (isopropanol 75 ml, water 25 ml; trichloroacetic acid 5 g, ammonium hydroxide 0.3 ml) in the presence of carriers of phosphate and pyrophosphates.

4. CHARACTERISTICS OF THE FINAL SOLUTION

A solution of ^{32}P phosphoric acid in 0.01 N hydrochloric acid.
Radioactive concentration: 10-20 mCi/ml.

Radioactive purity:	^{32}P content 99.5%, the rest mainly ^{33}P.
Radiochemical purity:	Orthophosphates at least 95%.
Chemical purity:	Heavy metals content below the sensitivity of sulphide test.
Specific activity:	> 300 mCi/mg P.

REFERENCE

[1] CÍFKA, J., Czechoslovak patent 107306 (Dec. 1961).

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

Irradiation of a natural sulphur target results in the production of ^{32}P by the (n, p) nuclear reaction $^{33}S(n, p)^{32}P$. The most probable chemical state of this phosphorus is the oxide. The conclusion is therefore that the separation sulphur–^{32}P can be effected by fractional distillation.

A method practised in the United Kingdom [1], which has been patented, recommends distillation of sulphur at atmospheric pressure and at a temperature of about 500°C under a stream of gaseous nitrogen. The reported separation yield is 99.9%. Making up the distillation residue with an oxidizing solution gives ^{32}P in the form of orthophosphoric acid.

This method has two appreciable drawbacks: use of a fairly high temperature and, above all, danger of fire during the operation. It is therefore desirable to carry out distillation under 1 mm of mercury at a temperature of about 180°C. Furthermore, final purification of the $H_3{}^{32}PO_4$ solution by passage over an ion exchange resin ensures a very small content of troublesome metallic ions.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Prolabo technical sulphur purified by double distillation; purity over 99%. Irradiation of 10 or 20 capsules, each containing 40 g of sulphur.
Irradiation conditions:	Swimming pool reactors are used because of their high fast neutron flux available. Irradiation in MELUSINE for one month. Fast flux $2-4\times10^{12}$ n/cm^{2}s. Irradiation in SILOE for three weeks. Fast flux about 7×10^{12} n/cm^2 s. Irradiation in TRITON for one month. Fast flux $2-4\times10^{12}$ n/cm^2 s.

Irradiation container:	EL-3 type container:	aluminium capsule, cylindrical, internal diam. 22.5 mm and internal length 65 mm.
	SILOE-type container:	aluminium capsule, internal diam. 19.9 mm and internal length 55 mm.
Side reactions:	The formation of ^{33}P and ^{34}P by the following reactions: $^{33}S(n, p)^{33}P$ and $^{34}S(n, p)^{34}P$. The presence of ^{33}P is of slight importance because of its small cross-section, and ^{34}P soon becomes insignificant because of its very short half-life.	

Chemical treatment

Separation method

After uncrimping the irradiation tubes, the sulphur is poured into a quartz distillation flask. The flask is fitted to a receiver and the vacuum pump and heating system are switched on. Distillation takes place at 180°C and 1 mm of mercury, and at this temperature the sulphur is light orange in colour, becoming dark red if a big rise in temperature occurs.

When distillation is completed the flask is first left to cool, then the vacuum is cut off; 100 ml of N/10 hydrochloric acid, 5 ml of 110 vol. hydrogen peroxide and 30 ml of N/10 hydrochloric acid are added in succession. The flask is fixed under a condenser and heated to boiling with refluxing for two hours. After cooling, the solution is passed over a Dowex-50 resin column. The flask is then rinsed with 20 ml of N/10 hydrochloric acid.

The operation is completed by collecting the purified solution in an evaporator bottle. The solution is evaporated almost to dryness and four portions of N/10 hydrochloric acid from the resin washing are collected. They are evaporated almost to dryness, and then two portions of 2 ml of 110 vol. hydrogen peroxide, followed by two portions of 4 ml of doubly distilled water are added, which are evaporated separately almost to dryness.

Lastly, two portions of 30 ml doubly distilled water are used to make up the final solution of orthophosphoric acid $H_3{}^{32}PO_4$ with a specific activity of 50 to 150 mCi/ml.

Apparatus (Figs. 1, 2, 3)

(a) Sulphur distillation unit: this consists of a mobile quartz flask, which moves on a mechanical trolley and tilts for introduction of the target, and a fixed receiver which collects the distilled sulphur. After one operation the distilled sulphur is run off into a cardboard container by heating and discarded. The flask and the receiver are fitted together by an absolutely flush-ground joint. The movements of the flask are controlled by a manual system which can be locked at will.

(b) Reflux condenser: fitted to the flask by a flush-ground joint.

(c) Dowex 50 resin column: laboratory glassware.

(d) Evaporator vessel: double-jacket reservoir, one containing xylene which, brought to the boil, heats the second containing the solution.

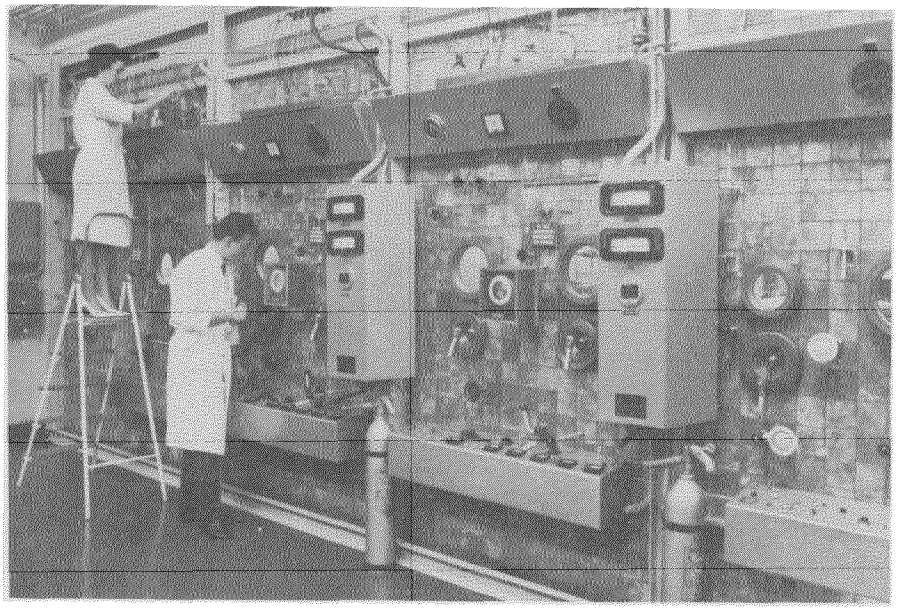


FIG.1. Apparatus for the production of ^{32}P (front-face)

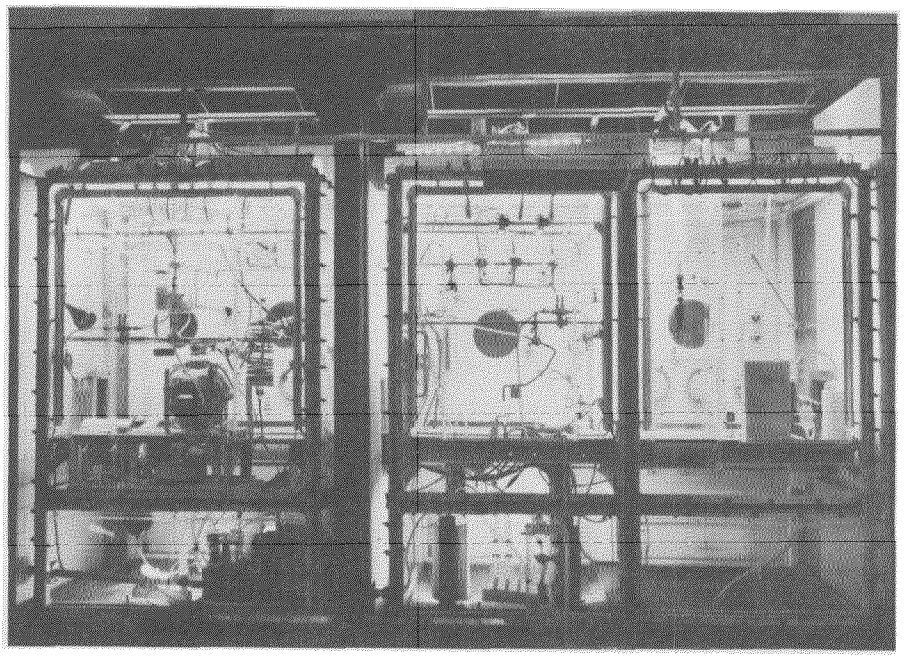
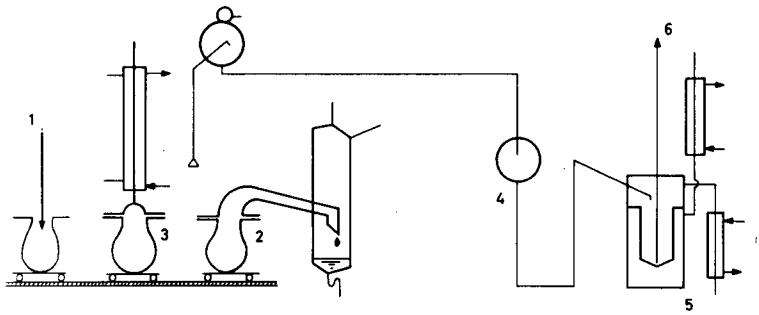


FIG.2. Apparatus for the production of ^{32}P (rear panel removed)

From left to right: Distillation phase
Purification phase
Arrangements for removal



1. Irradiated sulphur load
2. Distillation
3. Dissolution
4. Passage over Dowex-50 resin
5. Evaporation
6. Recovery of $H_3{}^{32}PO_4$ solution for storage

FIG.3. ^{32}P flowsheet

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.

Radioactive control: checks the absence of impurities and γ- and β-emitters.

Chemical purity control: the metallic impurities content must not exceed 10 μg/ml on an average.

Radiochemical purity control: consists of determination of the polyphosphates present in the solution [2]. Paper chromatography is carried out with acid (isopropanol 75 ml, water 25 ml, trichloroacetic acid 5 g, ammonia 0.3 ml) and alkaline (n-propanol 30 ml, ethanol 30 ml, water 30 ml, ammonia 1 ml) baths; it is possible to separate the phosphoric acid from the condensation products: pyrophosphoric, tripolyphosphoric and metaphosphoric acids.

The proportion of polyphosphates is generally lower than 1%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{32}P S-1 – ^{32}P phosphoric acid solution, carrier-free, non-injectable

A sterile solution of phosphoric acid $H_3{}^{32}PO_4$ in about 0.01 N HCl, pH about 2, meeting the following specifications:

Radioactive concentration:	measured to within 5%: 40-50 mCi/ml average; 100 mCi/ml maximum.
Radioactive purity:	^{32}P content > 99.9% (half-life and coefficient of mass absorption characteristic of ^{32}P).
Radiochemical purity:	Orthophosphoric acid content > 95%.
Specific activity:	Above 1 Ci/mg.

No troublesome chemical impurities.

Reference: ^{32}P S-2 - Solution of sodium phosphate ^{32}P, injectable

Aqueous, neutral, isotonic, sterile and pyrogen-free solution of sodium phosphate $Na_2H^{32}PO_4$, meeting the following specifications:

Radioactive concentration, measured to within 5%: 2 mCi/ml.

Radioactive purity: ^{32}P content > 99.9% (half-life and coefficient of mass absorption characteristic of ^{32}P).

Radiochemical purity: Orthophosphate content > 95%.

Composition of the solution: As indicated in the French Pharmacopoeia:

Sodium radiophosphate	unweighable quantity
Anhydrous Na_2HPO_4	450 μg
NaCl	9 mg
Distilled water	1 ml

Sterile.

Pyrogen-free.

REFERENCES

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[2] COHEN, M.Y., Produits pharmaceutiques 17 (Jan. 1962).

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Neutron irradiation of natural sulphur yields carrier-free ^{32}P by the (n, p) reaction. The ^{32}P produced is stabilized in the non-volatile form of phosphate and so, can be separated from sulphur by distilling off the latter. The distillation is carried out under reduced pressure (1-5 mm of Hg) at a temperature of 150-200°C and the ^{32}P is leached out with dilute HCl.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Sulphur, purified by boiling with sulphuric acid and nitric acid, then with repeated washing with distilled water, and finally by the distillation under reduced pressure [1]. Cast into blocks approximately 50 g in weight. The purity is less than 1 ppm of heavy metal impurities and less than 2 ppm of carbon.

Irradiation conditions: Covered with thin aluminium foil, enclosed in cans (Type A, screwed capped 1 S aluminium can of 73 mm height and 26.5 mm diam.), and irradiated in APSARA for 4 weeks at a fast flux of 1×10^{12} n/cm^2 s.

Chemical treatment

After decapping the cans, the contents are transferred into a funnel. The funnel is gradually heated to about 130°C when all the sulphur melts down into the distillation flask. The distillation assembly is then connected to the vacuum pump and the heating furnaces are switched on. The distillation of sulphur takes place at a temperature between 150-200°C at a pressure of 1 - 5 mmHg. After completion of distillation, the system is allowed to cool and the vacuum is released. Fifty millilitres of 0.5 N pure hydrochloric acid is added to the distillation flask and then it is heated to 70°C for an hour to leach out the $H_3{}^{32}PO_4$. The ^{32}P solution is allowed to cool and is then siphoned out into a graduated glass storage bottle.

Recovery of sulphur

It is observed that only traces of the ^{32}P activity are carried over by the distilled sulphur. This sulphur has been formed suitable for re-irradiation. The collected sulphur is melted down, cast into blocks and is sent for irradiation again.

3. ASSAY AND QUALITY CONTROL

The stock solution is assayed for radioactivity by beta counting, using a GM counter.

The total solid content is determined by evaporating a known volume of the stock solution and then weighing the residue.

The absence of heavy metals is confirmed by the hydroxide and sulphide precipitation tests.

The radiochemical purity is determined by paper chromatography using a solvent mixture consisting of isopropanol, ammonia and trichloroacetic acid.

R_f of orthophosphate 0.76
R_f of metaphosphate 0.00
R_f of pyrophosphate 0.40.

The radioactive purity is determined by finding out the range of beta particles in aluminium using a GM counter.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Code P-1

Specific activity:	Carrier-free.
Chemical form:	H_3PO_4 in dilute HCl.
Acidity:	Approx. 0.1 N HCl.
Radiochemical purity:	Orthophosphate content is greater than 95%.
Concentration:	1 - 20 mCi/ml.

Code pHM-2: for medical use

Phosphorus-32 as sodium orthophosphate in isotonic saline solution containing phosphate buffer, pH 7. Solution sterilized.
Phosphate content: 1 mg/ml.
Concentration: 1-2 mCi/ml.

REFERENCE

[1] MURPHY, T.J. et al., J. Res. Natl. Bureau of Stds., 64A (1960) 355.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process is based on the irradiation of a sulphur target, and the separation of phosphorus by the sublimation of sulphur under a nitrogen stream. The phosphorus is extracted from the residue by 0.1 N hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 120 g (60 g × 2 capsules) elementary sulphur purified by sublimation of crystalline sulphur four times (JISGR)[1].
Container: The target is wrapped with aluminium foil, then placed in an aluminium capsule.
Flux: Fast: 1.5×10^{12} n/cm^2 s; thermal: 1.3×10^{12} n/cm^2 s (JRR-1).
Irradiation time: 15 h (5 h × 3 d).
Side reactions: Formations of ^{33}P and ^{35}S.

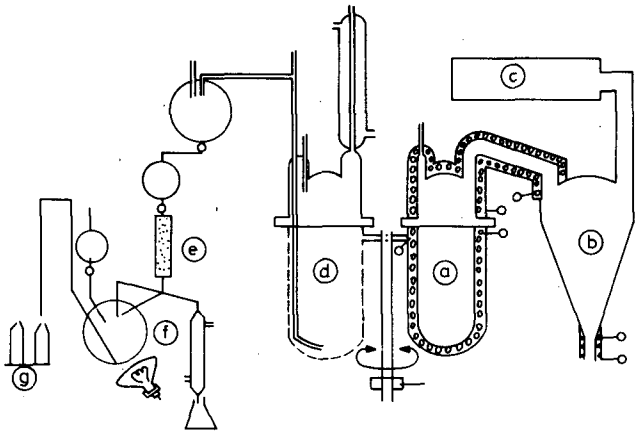
Chemical treatment

Production is based on the sublimation of a sulphur target. The apparatus is shown in Fig. 1.

Remove aluminium foil from the target by the tong-manipulator, then place the target in the sublimation vessel (a).

Fix the cap on the sublimation vessel, then introduce a nitrogen stream at the speed of 2 - 5 bubbles per second.

[1] Japan Industrial Standard Grade Reagent.



(a) Sublimation vessel
(b) Receiver
(c) Condenser
(d) Position of sublimation vessel for extraction
(e) Cation exchange resin column
(f) Evaporator
(g) Bottles of product

FIG. 1. Arrangement of apparatus for ^{32}P production

Heat the sublimation vessel gently; the sublimed sulphur is collected in the receiver (b). Part of the sulphur which escapes in the form of vapour is collected in the condenser (c).

After the sublimation of sulphur, the vessel (a) is rotated to position (d); then fix the cap with the condenser and reagent feed pipe.

Add 60 ml 0.1 N HCl, then boil for four hours to extract ^{32}P.

Pass the solution to the ion exchange resin (e) to remove cations.

Transfer the solution into the concentration vessel; concentrate the solution to 0.3 ml under the infra-red lamp, then dilute with 20 ml distilled water.

Distribute the product solution into the bottle with the rubber and aluminium caps.

3. ASSAY AND QUALITY CONTROL

Total solids, non-volatile materials and heavy metal contents are determined by the following methods:

Total solids:	Evaporate 1 ml to dryness under the infra-red lamp, then heat at 110°C and weigh.
Non-volatile material:	Evaporate 1 ml to dryness, heat at 600°C, then weigh.
Heavy metals:	Compare the colour with the lead standard solution by the addition of hydrogen sulphide.

The aluminium and arsenic contents are determined by a spectrophotometric method by oxine, and by the Gutzeit method respectively.

Routine assay is carried out with a $2\pi\beta$-proportional counter. Calibration is made by a $4\pi\beta$-counter.

The amount of carrier in the product is determined by a spectrophotometric method by molybdenum blue.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	H_3PO_4 in HCl solution; acidity is ~ 0.1 N.
Radiochemical purity:	Over 99% (exclusive of ^{33}P).
Specific activity:	Carrier-free.
Concentration:	> 1 mCi/ml.

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Phosphorus-32 is produced by irradiating finely-ground sulphur [1, 2], $^{32}S(n, p)^{32}P$. The radioactive phosphorus produced, being present mainly as orthophosphate [3, 4], is separated from the target material by extraction with boiling water, with subsequent evaporation to a suitable volume. The process has been patented (Norwegian Patent No. 86832).

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Sulphur, Merck, D. A. B. 6., specially purified and dried, finely ground.
Amount:	400 g.
Time of irradiation:	3 weeks.
Container:	2 aluminium cans.
Flux:	About 2×10^{11} n/cm^2 s (fast neutrons).
Side reactions:	$^{33}S(n, p)^{33}P$ (25 d).
	$^{34}S(n, p)^{34}P$ (14.2 s).

The yield of ^{33}P is only about 0.03% of the yield of ^{32}P, and ^{34}P has a very short half-life. These side reactions have no practical significance.

Chemical treatment

Before irradiation the target material is pretreated by heating it with 2 N hydrochloric acid to 70°C for 1 - 2 h with continuous agitation. It is carefully washed several times with distilled water, and finally dried in vacuum.

The irradiated sulphur powder is extracted with boiling water for one hour; 2-octanol is added as a wetting agent. After extraction the solid and liquid phase are separated by means of filtration, and the ^{32}P solution is concentrated by evaporation and finally re-filtered.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative Geiger-Müller counting.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.

Chemical purity control, emission spectrography.
Radiochemical purity control, radiochromatography.
Specific activity control, phosphorus content (spectrophotometry).
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

FO - orthophosphate in dilute hydrochloric acid solution.

Radioactive concentration:	15-25 mCi/ml.
Isotopic purity:	Greater than 99%.
Radiochemical purity:	100% as orthophosphate.
Specific activity:	1000 mCi/mg P.
pH:	2-3.
Total solids:	Less than 0.5 mg/ml.
Chemical purity:	Metals, spectrographically determined less than 10 μg/ml.

FSI - orthophosphate in isotonic solution containing phosphate buffer, sterilized.

pH:	7.
Total solids:	15 mg/ml.
Phosphorus carrier content:	1 mg/ml.

Other specifications as for FO.

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INSTITUTE OF NUCLEAR RESEARCH, SWIERK NEAR OTWOCK, POLAND

1. GENERAL [1-8]

Phosphorus-32 is obtained from an irradiated elementary sulphur target by distillation. To prevent the ignition of sulphur during distillation the process is carried out at 5 mmHg and 200-240°C. Yield of the process 90-95%.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	High purity elementary sulphur - 30 g.
Flux:	Thermal neutrons 2×10^{13} n/cm^2 s.
	Fast neutrons 1×10^{12} n/cm^2 s.
Time of irradiation:	Two weeks in the reactor working 86 h per week at full power.
Container:	Aluminium capsule treated with hot concentrated nitric acid in order to clean it and reduce sulphur corrosion during irradiation. Closed by welding.
Activity obtained:	800 mCi of ^{32}P.

Chemical treatment

The container is opened with a hand-operated rotary cutter and transferred to a heating device which allows the melting of sulphur; 60 g of liquid sulphur are placed into a quartz distillation flask. The flask is connected by a flat ground joint with a receiver. A vacuum pump is used for lowering the pressure in the apparatus down to 5 mmHg and then the heating system is turned on. The distillation is carried out for approximately 2 h and when sulphur is distilled off, the temperature is raised and maintained at the higher level for another 20 min.

After completing the distillation the apparatus is cooled and the distillation flask is connected by a flat ground joint with a reflux condenser; 15 ml of 0.1 N HCl and 2 ml of 30% H_2O_2 are added. The flask content is then refluxed for 1-2 h. This operation is repeated after the addition of 4 ml 0.1 N HCl and 1 ml of 30% H_2O_2. The resulting mixture is cooled and placed in an evaporator; 1 ml of 30% H_2O_2 is added. After evaporation to dryness the ^{32}P is desorbed by 0.1 N HCl. The evaporator is heated with boiling xylene (b.p. 140-143°C) to prevent polymerization of the final product. The product is filtered through sintered glass and transferred to a receiving vessel. To separate impurities the product is passed through a cation exchanger column.

The orthophosphoric acid solution is used for the preparation of other ^{32}P compounds.

3. ASSAY AND QUALITY CONTROL

The activity of ^{32}P is determined by a comparative method.
The standards are checked by 4π counting.
The chemical purity is determined spectrally.
The radiation purity is analysed by beta and gamma spectrometry.
The radiochemical purity is controlled by paper chromatography.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Solution of phosphoric acid (ortho) in HCl (approx. 0.1 N), pH approx. 1.
Radioactive concentration: Approx. 50 mCi/ml.

Radiation purity:	99.0%.
Radiochemical purity:	99%.
Specific activity:	5-50 mCi/ml.
Impurities:	As, Pb <5 μg/ml.

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INSTITUTE OF ATOMIC PHYSICS, BUCHAREST, ROMANIA

1. GENERAL

The production of ^{32}P is based on the (n, p) reaction of sulphur targets. The separation of ^{32}P is carried out by the method of solvent extraction.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Sulphur crystalline p.a., amount 25-30 g.
Flux:	1×10^{13} n/cm^{2}s.
Time of irradiation:	200 h.
Container:	Aluminium cans.
Activation:	1 Ci.

Chemical treatment

After irradiation the target is introduced in a distillation flask with a refluxing condenser. 100 ml of HCl 0.1 N is then added and is refluxed for one hour. After cooling 150 ml of trichloroethylene is added and is refluxed for one hour. The aqueous layer is separated, heated for 15-20 min and then filtered. 2 ml H_2O_2 30% are added and evaporated. The residue is treated with an isotonic solution of HNa_2PO_4. After measurement of activity the product is sterilized.

3. ASSAY AND QUALITY CONTROL

Radiochemical purity is controlled by paper radiochromatography. The total phosphorus is determined by the spectrophotometrical method. Arsenic, the other metals and pH are controlled in the usual way.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Prepared normally from stock and the packaging is in penicillin type bottle.

REFERENCE

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JUNTA DE ENERGIA NUCLEAR, MADRID, SPAIN

1. GENERAL

The production process is based on the irradiation of elementary sulphur. Phosphorus is separated from the target by distillation of the sulphur. Phosphorus is extracted from the residue with dilute hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material: 120 g of sulphur which has been purified as follows. Boil for three hours with 1% MgO; separate the liquid phase by decantation and boil for 100 h adding 2% MgO every 25 h; distil the sulphur in a slow stream of nitrogen [1]. Analysis of the target material shows the following impurities: Al 0.04 - 0.004 ppm, As < 0.12 ppm, B < 0.08 ppm, Ca 0.4 - 0.02 ppm, Cd < 0.01 ppm, Fe 0.15 - 0.02 ppm, Cr < 0.01 ppm, La < 0.06 ppm, Mg 0.14 - 0.01 ppm, Mn < 0.01 ppm, Ni < 0.04 ppm, Sn < 0.04 ppm, Te < 0.4 ppm, Pb < 0.04 ppm, K 0.02 ppm, Na 0.09 ppm.

Container: Aluminium leak-tight container, 24 × 26 mm diam.

Flux: 1.9×10^{12} n/cm^2 s (JEN-1).

Irradiation time: 4 weeks, equivalent to 138 h of continuous operation at 1 MW. Approximate yield is 200 mCi.

Chemical treatment

Separation method

Sulphur is distilled from the irradiated target under a stream of nitrogen [2]. The diagram of the equipment used is shown in Fig. 1. The process comprises the following steps:

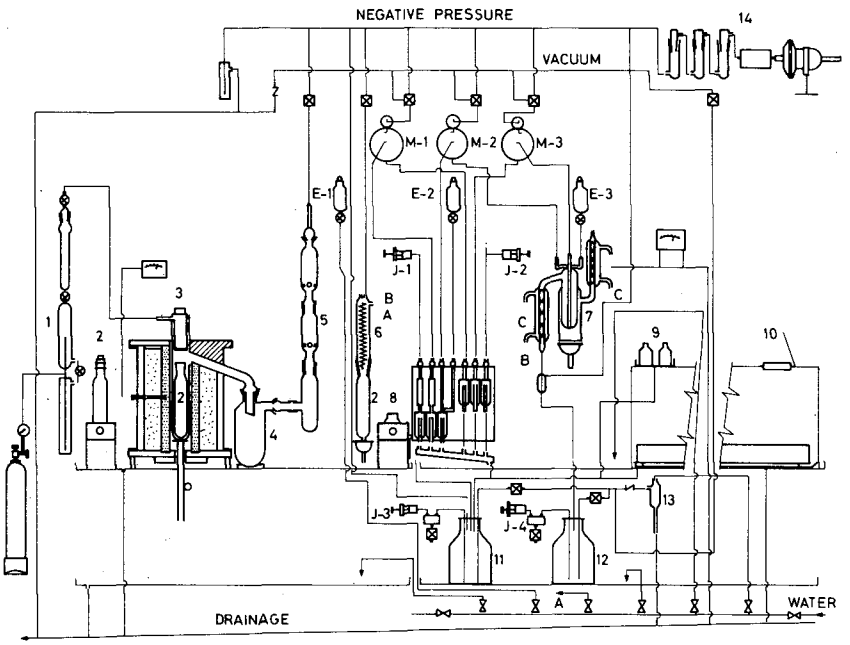

FIG. 1. Phosphorus-32 production process

Cut the irradiation container transversally, then the sulphur, gently heated to melting point, is transferred to a glass flask with a ground conical neck (No. 2).

Place the flask in the furnace (No. 3) which is equipped with an automatically controlled heating system keeping the internal temperature at 480 ± 10°C.

Seal the furnace with the glass plug, and introduce the nitrogen. The furnace is heated until the sulphur is completely distilled into the receiver (No. 4). The distilled sulphur is re-used.

Remove the flask (No. 2) from the furnace and place on the heater. A reflux condenser (No. 6) is fitted into the ground neck of the flask, and 18 ml of 0.1 N HCl is added. Boil for 30 min.

Remove the solution from the flask with a pipette and add 3 ml of a solution, containing 200 g $Na_2HPO_4 . 12H_2O$, 14 g NaCl and 24 g NaOH per litre. This brings the product to pH 7 and makes it isotonic [3]. If the solution is turbid, filtration is necessary.

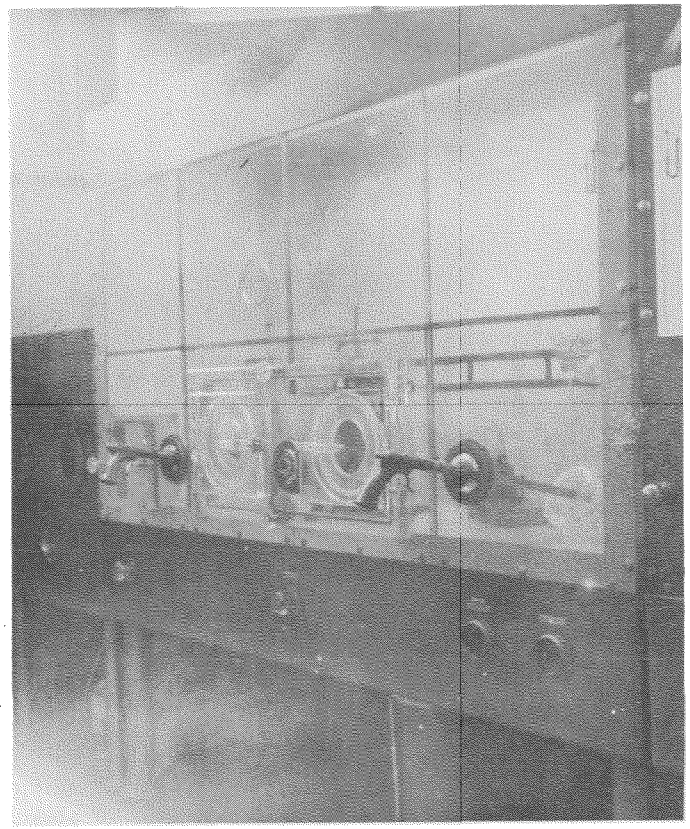

FIG. 2. Cell for ^{32}P samples sealing

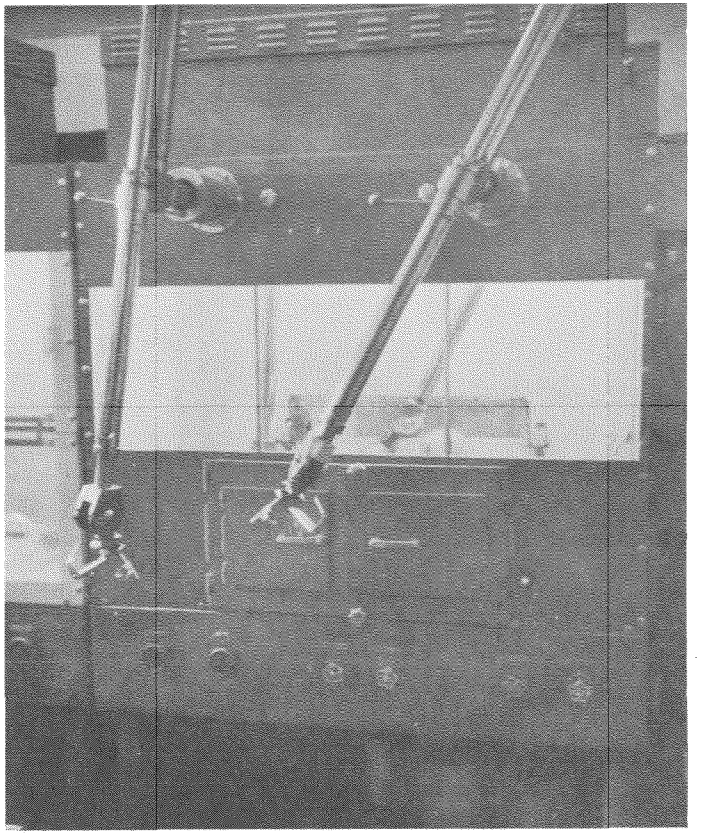

FIG. 3. Cell for ^{32}P separation

Apparatus

Production is carried out in an enclosure 1.90 m high, with side walls of 1.80 and 0.80 m (Figs. 2 and 3), kept at a negative pressure of 20 mm w.c. It comprises a steel frame with 5-mm-thick plexiglass panels as external biological shielding. Besides the equipment pieces already described, the apparatus consists of:

A set-up (No. 1) to prevent nitrogen overpressure and to dry the gas before entering the furnace.

A set of traps (No. 5) to prevent sulphur powder or vapour from entering in the negative pressure line (No. 14).

A distiller (No. 7) to concentrate the product or to carry out the destruction of organic matter, if necessary (never used so far).

Flasks to receive liquid wastes (Nos. 11, 12).

Ancillary elements, such as funnels for the addition of reagents (Nos. E-1, E-2, E-3), vacuum balls to transfer the product (Nos. M-1, M-2, M-3), manual pumps for sampling (Nos. J-1, J-2, J-3, J-4), etc.

3. ASSAY AND QUALITY CONTROL

Determination of chemical purity is made with a Hilger quartz spectrograph (Littrow type, high dispersion) and a JACO "Varisource" generator [4]. The following elements are determined: Al, As, B, Ca, Cd, Cr, Fe, La, Mg, Mn, Ni, Pb, Si, Sn and Te at concentrations of less than 10 μg/ml and with a sensitivity of the order of 0.1 μg/ml. The radioisotopic purity is determined by gamma spectrometry, using a scintillation detector with a 3 × 3-in. crystal and an RCL 256 channel analyser [5]. Because beta emission is involved, beta-absorption and half-life measurement are also carried out. These determinations show that the ^{32}P content is > 99.5%. The determination of chemical form is carried out by electrophoresis and chromatography in conjunction with autoradiography, to localize the distribution of radioactivity on the strips of paper. Lederer electrophoresis technique as modified by Dürrum with paper suspended in the middle is employed [6, 7].

Electrophoresis is performed with 1 N HCl at 10 mA for 18 h. Polyphosphate impurities and ^{35}S can be determined in amounts of less than 1% using autoradiography exposure times of the order of 48 h.

Routine assay is made by comparison with a standard in a well-type ionization chamber (General Radiological Ltd., UK, model NEO14-01) and a micro-microammeter (AVO Ltd., UK, model 1388B). Reasonably accurate ^{32}P determinations can be carried out by the measurement of beta particles (for low activities) or bremsstrahlung. Occasionally absolute measurements are carried out by means of the solid angle technique (defined by diaphragmed Geiger detector). An error of 5-10% in the activity measurements is allowed; in special cases, the error can be less than 5% [8].

4. CHARACTERISTICS OF THE FINAL SOLUTION

^{32}P - Phosphoric acid solution, carrier-free, non-injectable

Phosphoric acid solution in 0.1 N HCl, sterile, meeting the following specifications:

Chemical purity:	Impurities in ^{32}P preparations are (typical analysis) ($\mu g/ml$): Al < 0.2 - 0.7, As < 1, B < 0.1 - 0.7, Ca 1 - 5, Cd < 0.1 - 0.7, Cr < 0.3 - 1.6, Fe < 0.1 - 5, La < 0.3, Mg < 0.1 - 3, Mn < 0.1 - 3, Ni < 0.3, Pb < 0.3, Si < 0.3, Sn < 0.3 - 0.5, Te < 0.3.
Radioactive purity:	^{32}P content > 99.5%.
Radiochemical purity:	Orthophosphoric acid content > 99%.
Radioactive concentration:	Maximum 30 mCi/ml.

Sodium phosphate-^{32}P solution, injectable

Neutral (pH 6-7), isotonic, sterile and pyrogen-free solution of sodium phosphate meeting the following specifications:

Chemical purity:	See above.
Radioactive purity:	^{32}P content > 99.5%.
Radiochemical purity:	Orthophosphate content > 99%.
Radioactive concentration:	1-20 mCi/ml.
Sterility:	Sterilization is carried out in an autoclave at 120°C for about 1 h.
Analysis of pyrogens:	The analysis is carried out occasionally by the General Pharmaceutical Inspectorate, Department of Public Health, Ministry of Interior.
Isotonicity:	Adjusted by means of conductimetric measurements.

PATENT

Spanish patent No. 251.242: Cellini, R.F., de la Cruz, F., Domínguez, G., Suárez, C., Technique for the separation and preparation of radioactive phosphorus (^{32}P) by means of distillation of irradiated sulphur.

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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Phosphorus-32 is produced by the fast neutron irradiation of sulphur, $^{32}S(n, p)^{32}P$.

The radio-phosphorus is separated from the bulk of the sulphur target by high temperature distillation where it is left as a residue in the distillation flask. The ^{32}P is obtained in solution by refluxing the residue with dilute hydrochloric acid.

2. EXPERIMENTAL PROCEDURE (Fig. 1)

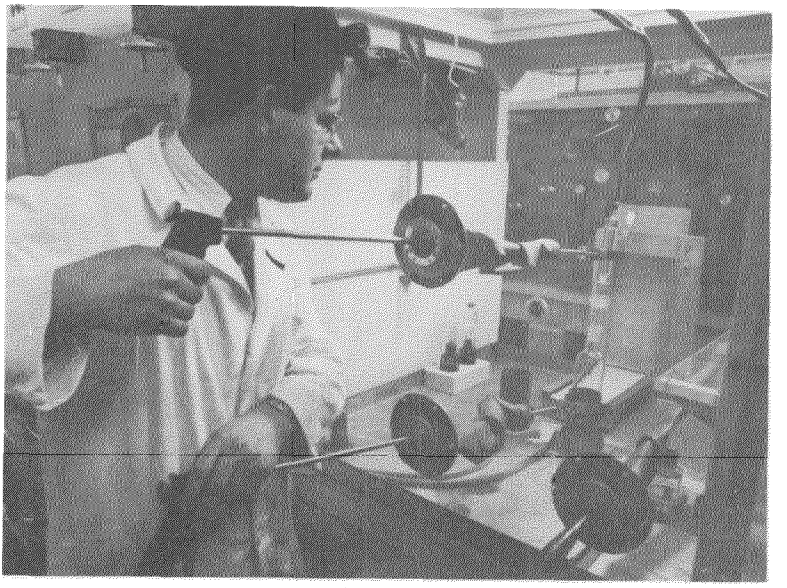


FIG. 1. Plant for the production of ^{32}P.

Irradiation

Target material:	90 g sulphur, redistilled three times.
Irradiation container:	Annular aluminium can into which molten sulphur is poured. Sealing is accomplished by argon arc welding.

Irradiation conditions: Flux ~ 1.5×10^{14} n/cm^{2}s for 24 d. A cluster of cans is inserted into the heavy water moderator which flows around and up the annular cavity and prevents nuclear overheating.

Chemical treatment

The irradiated sulphur is melted out of the can and allowed to run directly into the distillation apparatus. The temperature of the still is raised to 550°C and the sulphur is distilled over in an atmosphere of nitrogen. The active residue is then extracted by refluxing with dilute hydrochloric acid. The solution is finally filtered through a very fine sintered glass frit. Carrier orthophosphate is added to prevent irreversible adsorption of ^{32}P onto the walls of its container (10 atoms ^{31}P atom ^{32}P).

3. ASSAY AND QUALITY CONTROL

The target material is redistilled until no non-volatile residue remains in it. The product is analysed for chemical impurities, As, Pb, Al and SO_4; and for radiochemical impurities (> 99% of the ^{32}P is in the form of orthophosphate). The total dissolved solids are also determined.

British Patent No. 765, 489.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Purified sulphur is irradiated to produce ^{32}P by the (n, p) reaction, $^{32}S(n, p)^{32}P$. Sulphur is distilled away, the remaining solid is dissolved in acid, and leach and rinse solutions heated. As final steps, the product orthophosphoric acid is filtered and samples are analysed.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 35 g sulphur.
Neutron flux: 2×10^{14} n/cm^{2}s (thermal) and $\sim 1 \times 10^{13}$ n/cm^{2}s (fast).
Irradiation time: 8 weeks.
Reactor yield: 30 Ci.

Chemical treatment

Preparing target

Sulphur purification is a difficult and tedious procedure; however, the purity of the final ^{32}P is dependent upon the preparation of very pure sulphur. Repeated distillation from platinum equipment removes traces of magnesium and other impurities.

About 35 g of purified sulphur is melted into an aluminium irradiation capsule, which is closed by welding. The aluminium capsule is treated with hot concentrated nitric acid to clean it and to reduce the possibility of sulphur corrosion during irradiation.

Apparatus

Sulphur distillation equipment (Fig. 1) and melting furnaces (Fig. 2) are used in processing the irradiated target. Processing facility and shielding required: manipulator cell, 6 in. lead equivalent (Fig. 3).

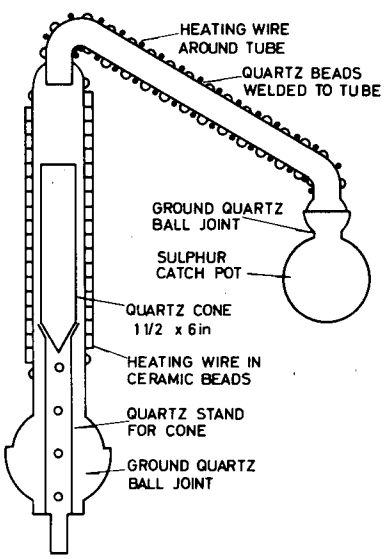


FIG. 1. Sulphur distillation equipment

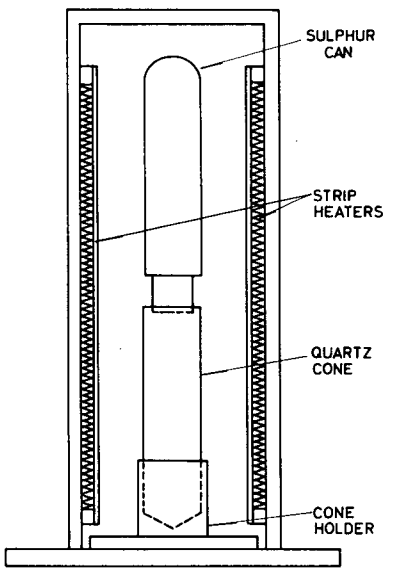


FIG. 2. Sulphur melting furnace, front removed

Processing

Yield: > 95%.

The aluminium capsule is opened with a tubing cutter; then the capsule is positioned between two resistance heaters over a quartz cup. The sulphur is allowed to melt and flow out of the irradiation capsule into the cup. The quartz cup is transferred into the distillation unit, and sulphur distilled from the cup at a temperature of 450 to 475°C for 2–3 h. The distillation equipment is allowed to cool and the quartz cup transferred to a beaker. About 80 ml

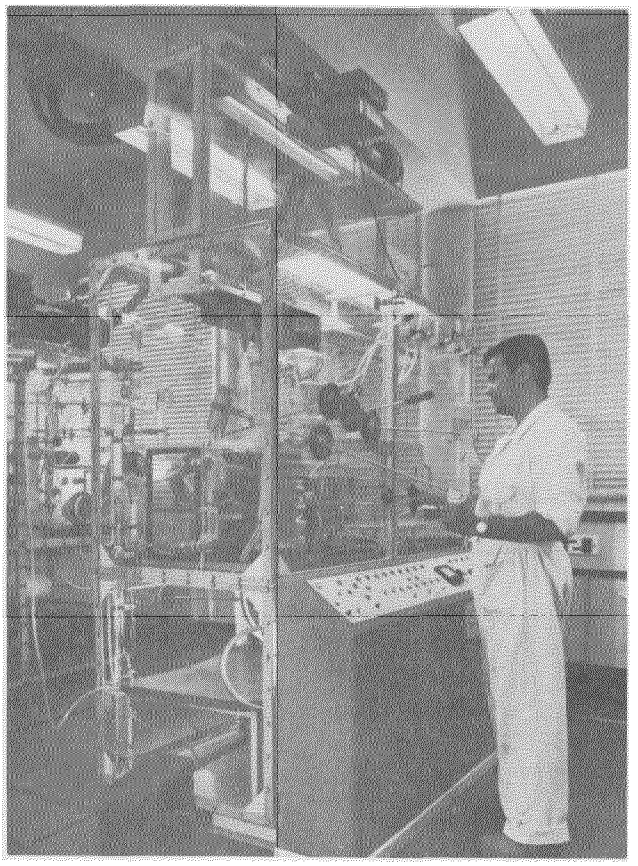


FIG. 3. Unit for the production of ^{32}P

of ~1 M HCl is added to the cup to dissolve $^{32}P_2O_5$, and the cup is leached for 8 to 16 h at 80 to 90°C. Leach solution is poured into a beaker and the cup rinsed with 20 to 30 ml of H_2O. Leach and rinse solutions are heated for 4 h at 90°C. Orthophosphoric acid is formed. The solution is filtered through a fine sintered-glass funnel and adjusted to 100 to 125 ml of 1 M HCl.

3. ASSAY AND QUALITY CONTROL

A sample is analysed for molarity of HCl, heavy metals, ^{32}P concentration, total solids, and radiochemical purity according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733601.

Precision and accuracy of the ^{32}P assay are:

Calibration by 4π β–γ coincidence counter.

Routine assay by windowless 2π proportional counter.

Estimated limit of error in disintegration-rate concentration of routine shipment, 3%.

Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, carrier-free ^{32}P is delivered in the form of H_3PO_4 as a stock item. Other specifications of interest are:

Acidity:	1 N ± 50%
Concentration:	> 5 mCi/ml
Total solids:	< 1 mg/mCi
Precipitate at pH 7-9:	Negligible
Radiochemical purity:	> 99% (exclusive of ^{33}P)

BORIS KIDRIČ INSTITUTE OF NUCLEAR SCIENCES,
VINČA, YUGOSLAVIA

1. GENERAL

Irradiation of sulphur in the form of a magnesium sulphate target gives rise to ^{32}P by the (n, p) reaction.

The method of production is based on the separation of phosphorus-32 from irradiated $MgSO_4$ by adsorption on MgO. It has advantages over some, other methods because it requires fewer chemical operations and does not employ high temperatures [1, 2].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Dehydrated $MgSO_4$ (90 g) prepared by heating reagent grade $MgSO_4 . 7H_2O$ at 400°C for 6 h; 15 g portions are irradiated.
Fast flux:	About 10^{12} n/cm^{2}s in the RA reactor at Vinča.
Irradiation time:	20-40 d.
Irradiation containers:	Cylindrical, aluminium cans with screwed covers, internal length - 70 mm; internal diameter - 25 mm.

After irradiation the target is left to cool for four days to allow for the decay of ^{24}Na produced by the $^{24}Mg(n, p)^{24}Na$ reaction.

Chemical treatment

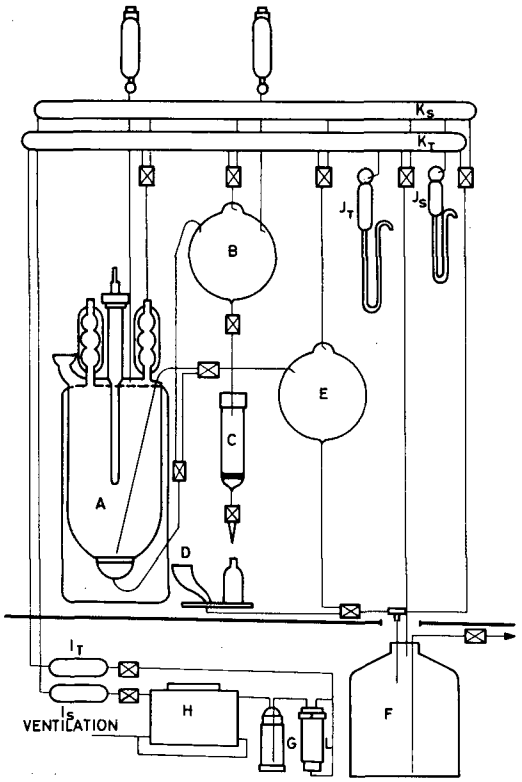
Separation method

Irradiated $MgSO_4$ is dissolved in water at a concentration of about 0.5 M. To this solution 50 mg of powdered magnesia (100-200 mesh) are added. The mixture is maintained at 60°C and mixed by bubbling air through it. The oxide powder, together with the adsorbed ^{32}P, is separated from the solution by filtration and washed with 25 ml of water to remove the SO_4^{2-} anions. It

is then dissolved in 10 ml 0.3 N HCl and the solution is passed through a cation-exchange column (1 g Dowex-50 X8, H^+ form, 100-200 mesh; flow rate 1.9 ml/cm^2 min) to remove quantitatively the MG^{2+} ions. The column is washed with two 15 ml portions of 0.3 N HCl. The effluent is usually collected in three fractions (10, 15, 15 ml), the first containing about 30%, the second 60% and the third 10% of the ^{32}P present. The yield of ^{32}P is 85 - 90%. Up to 10% is adsorbed by the glassware.

Apparatus

The apparatus (Fig. 1) is made of Pyrex glass and placed in a box (Fig. 2) of 10-mm-thick Plexiglass shielded by 20-mm-thick lead plates.



A	Vessel for dissolution	I_T and I_S	Vessels with soda-lime and active charcoal
B	Auxiliary vessel for solution transport	J_T and J_S	Mercury manometers
C	Ion-exchange column	K_T and K_S	Vacuum distributors
D	Vessel for transporting liquids from C to F	H	Vacuum pump
E	Auxiliary vessel for addition of chemicals	G	Rinser
F	Bottle for waste storage	L	Mercury manostat

FIG. 1. Apparatus

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.
Radioactive control.

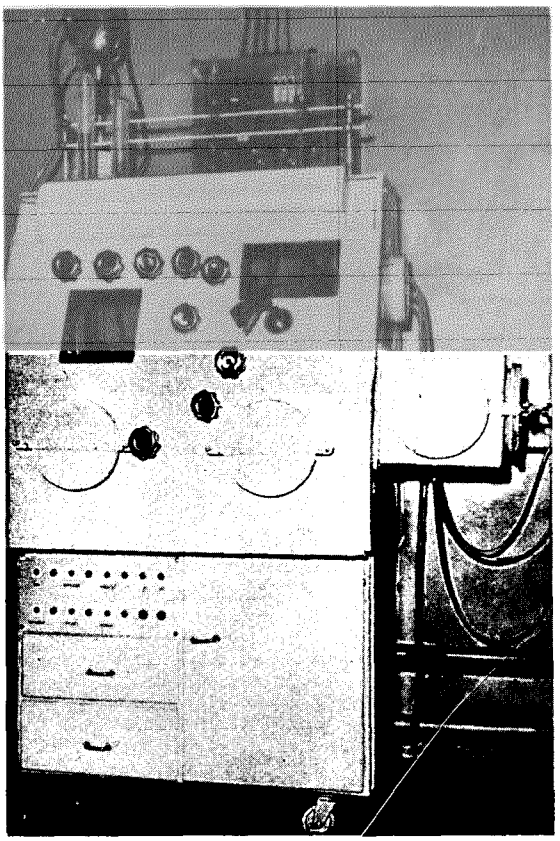


FIG. 2. Glove box for ^{32}P production

pH control of the solution.
Radiochemical purity control. Ascending paper chromatography used [3].
Sterility control [4].
Determination of the total content of solid substance in the solution.

Routine control of each charge includes the first and the third measurements. The other analyses are exceptional, depending on the use of ^{32}P.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVP 32/1X, $H_3{}^{32}PO_4$ in dilute HCl

Radioactive concentration measured to within 10%: 0.5–5 mCi/ml.
Radioactive purity: ^{32}P content more than 99%.
Radiochemical purity: Orthophosphate content more than 99%.
Total content of solid substance in the solution less than 0.5 mg/ml.

Reference: YVP 32/2X, Sodium phosphate in 0.9% NaCl solution (isotonic)

Radioactive concentration measured to within 10%: 0.5–5 mCi/ml.
Radioactive purity: ^{32}P content more than 99%.

Radiochemical purity: Orthophosphate content more than 99%.
Total content of solid substance in the solution less than 10 mg/ml.
Sterile.
pH 6-8.
Isotonic.

Reference: YVP 32/3X, Potassium phosphate in 1.2% KCl solution (isotonic)

Radioactive concentration measured to within 10%: 0.5-5 mCi/ml.
Radioactive purity: ^{32}P content more than 99%.
Radiochemical purity: Orthophosphate content more than 99%.
Total content of solid substance in the solution less than 10 mg/ml.
Sterile.
pH 6-8.
Isotonic.

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POTASSIUM-42

NUCLEAR DATA

1. NUCLEAR PROPERTIES

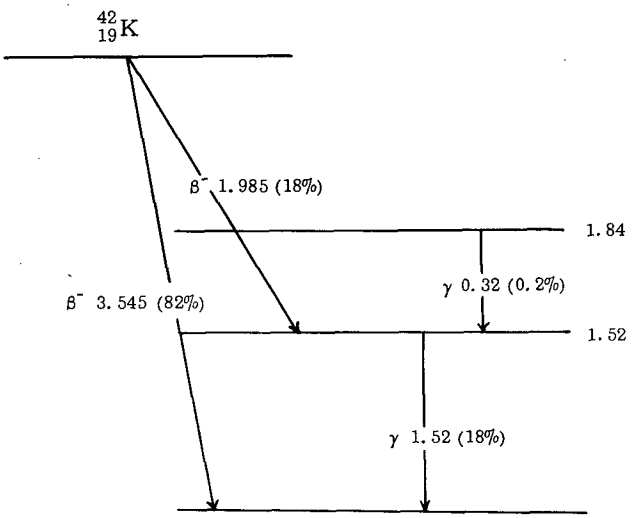
1.1. Half-life

12.5 h

1.2. Type of decay, and energy (MeV)

beta (β^-)	1.985 (18%)	gamma	0.32 (0.2%)
	3.545 (82%)		1.52 (18%)

1.3. Decay scheme



$^{42}_{20}Ca$ stable

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm^2 s (mCi/g)			Secondary reactions and half-life of radionuclide formed
			1 h	24 h	saturation	
$^{41}_{19}K(n,\gamma)^{42}_{19}K$	6.88	1.3 (th)	2	27	36	$^{41}_{19}K(n,\alpha)^{38}_{17}Cl$ (T = 37.3 min)
$^{42}_{20}Ca(n,p)^{42}_{19}K$	0.64	unknown (f)				$^{43}_{20}Ca(n,p)^{43}_{19}K$ (T = 22 h) σ unknown $^{44}_{20}Ca(n,\gamma)^{45}_{20}Ca$ (T = 165 d) isot. abund.: 2.06% σ = 0.72 barn $^{44}_{20}Ca(n,p)^{44}_{19}K$ (T = 22 min) $^{46}_{20}Ca(n,\gamma)^{47}_{20}Ca$ (T = 4.7 d) isot. abund.: 0.033% σ = 0.25 barn $^{48}_{20}Ca(n,\gamma)^{49}_{20}Ca$ (T = 8.8 min) isot. abund.: 0.185% σ = 1.1 barn
$^{45}_{21}Sc(n,\alpha)^{42}_{19}K$	100	< 0.005 (f)	< 0.1	< 1.3	< 1.8	$^{45}_{21}Sc(n,\gamma)^{46}_{21}Sc$ (T = 85 d) σ = 22.3 barn $^{45}_{21}Sc(n,p)^{45}_{20}Ca$ (T = 165 d) σ unknown

(th): thermal neutrons.
(f): fast neutrons.
For nuclear data see Refs. [1,2].

The nuclear reaction normally used for the production of ^{42}K is the (n,γ) on ^{41}K.

The target is potassium carbonate (K_2CO_3) or potassium chloride (KCl). In the second case, ^{36}Cl, ^{38}Cl, ^{35}S and ^{32}P occur also from the irradiation of chlorine.

$^{35}_{17}Cl(n,p)^{35}_{16}S$ (87.1 d)

$^{35}_{17}Cl(n,\gamma)^{36}_{17}Cl$ (2.5×10^5 yr)

$^{35}_{17}Cl(n,\alpha)^{32}_{15}P$ (14.45 d)

$^{37}_{17}Cl(n,\gamma)^{38}_{17}Cl$ (37.8 min)

3. APPLICATIONS

3.1. Industrial

Potassium-42 has hardly any applications, but it has been used in the glass and cement industries [3].

3.2. Medical and biological

It is used in the activation analysis of biological samples.

3.2.1. Diagnostic

It is used in studying potassium exchanges [4, 5] such as: permeability of the cellular membrane and permeability of the chloroid plexus and spinal fluid. The activity used is of the order of 100 μCi.

3.2.2. Therapeutic

It is used in the treatment of malignant tumours [6-9], the dose being of the order of 500 μCi [5]. The medical uses of ^{42}K are also mentioned in other works [10].

4. RADIOLOGICAL PROTECTION

4.1. External exposure

4.1.1. Irradiation doses

The dose delivered by 1 Ci of ^{42}K at a distance of 50 cm is 0.52 rem/h [11].

4.1.2. Safety measures

The tenth-thickness[1] for lead and ordinary concrete gives some idea of the amount of protection needed in handling ^{42}K, namely,

	Tenth-thickness (cm)		
	Pb	Ordinary concrete d = 2.3	
For a γ of 1.52 MeV	4	22	Ref. [11]

[1] The tenth-thickness is the thickness of shielding required to reduce the intensity of a γ-radiation of given energy by a factor of ten.

In practice the following lead thicknesses are needed to reduce the dose to 1 mR/h at 50 cm: 3.5 cm to handle 10 mCi of ^{42}K; 7.5 cm to handle 100 mCi of ^{42}K; and 12 cm to handle 1 Ci of ^{42}K.

4.2. Internal irradiation

Potassium-42 is classified as a moderately toxic, class 3 isotope [12]. Its effective half-life, allowing for both radioactive decay and excretory processes, is 0.52 d [13].

For internal irradiation (ingestion or inhalation) the maximum permissible concentrations in air and water, respectively, for a 40-h exposure, are:

2×10^{-6} μCi/cm^3 and 9×10^{-3} μCi/cm^3 (soluble form)
10^{-7} μCi/cm^3 and 6×10^{-4} μCi/cm^3 (insoluble form) [14]

4.3. Decontamination

Except in one or two particular cases, there is no special decontamination method for any given radioisotope. Some general texts on this subject [15-19] report that the following measures are adequate.

4.3.1. Skin

Rapid and repeated washing with good-quality soap, warm water and a soft brush. If this is not sufficient, use can be made of detergents or 5-10% solutions of complexing agents of the EDTA (ethylenediamine tetraacetic acid) type. It is also possible to apply saturated permanganate solutions followed by rinsing with a 5% bisulphite solution to neutralize and remove stain. Abrasive powders should not be used and the addition of entraining agents has proved disappointing.

If any wounds are contaminated they must be treated rapidly by allowing them to bleed, washing with water, followed by decontamination, as for the skin, and sometimes by additional surgical cleaning.

4.3.2. Hair

If the hair is contaminated it is important not to take a shower but merely to wash the head. A normal, good-quality shampoo is usually sufficient. If contamination is persistent the following solutions can be used:

paraisopropylorthocresol,
lavandin oil,
AC-compounded terpene-free lemon,
glycerine diacetin, or
benzoic acid.

Contamination is much easier to remove if the hair is not greasy.

4.3.3. Laboratory equipment

Glassware is usually cleaned by steeping, and this is mainly a radiochemical problem. The use of a specific entraining agent or solutions of

complexing agents gives good results, as do solutions of chromic acid, concentrated nitric acid, ammonium citrate, pentasodium triphosphate or ammonium bifluoride.

5. SUMMARY OF PRODUCTION METHODS

Potassium-42 is generally prepared by irradiating a potassium salt (KCl, or more usually K_2CO_3) with thermal neutrons, followed by solution in hydrochloric acid [20-22]. This process gives ^{42}K with a low specific activity.

It can also be prepared carrier-free by using the (n, p) reaction on ^{42}Ca [23, 24].

In this case the target is calcium carbonate. Irradiated $CaCO_3$ is suspended in boiling water containing traces of KCl. After filtration, the ^{42}K is present in the water as KOH or K_2CO_3.

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PROCEDURES

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

The method consists of the irradiation of potassium carbonate, $^{41}K(n,\gamma)^{42}K$, and simple dissolution of the irradiated target in order to obtain an isotonic final solution (12 mg KCl/ml).

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Potassium carbonate (Johnson Matthey).
Irradiation conditions and yield:	500 mg of potassium carbonate irradiated for 3 d at a flux of 1.9×10^{13} n/cm^2 s; yield of about 120 mCi with a specific activity of 0.3 mCi/mg potassium chloride. Two capsules each containing 2 inner capsules of 500 mg are generally irradiated. 100 to 400 mCi can thus be obtained.

Chemical treatment

500 mg irradiated potassium carbonate is dissolved in 44 ml of N/7 hydrochloric acid.

If no loss has occurred, this quantity should exactly neutralize the potassium carbonate. A solution of pH 7 containing 12 mg of potassium chloride is thus obtained.

If loss has occurred, the pH is adjusted with soda or 0.1 N hydrochloric acid.

No special equipment is needed for this treatment; all that is necessary are beakers, pipettes and a pH meter.

3. ASSAY AND QUALITY CONTROL

The activity of two 1-ml samples is measured with an ionization chamber and an analysis for radiochemical purity is carried out (presence of 1.51 MeV γ line).

Biological tests are applied to check the sterility and absence of toxicity of the product.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{42}K S-1 - injectable

A neutral, isotonic, sterile and pyrogen-free solution of potassium chloride, meeting the following specifications:

Radioactive concentration, measured to within 5%: 0.5-5 mCi/ml.

Radioactive purity: ^{42}K content > 99.9% (gamma spectrum characteristic of ^{42}K).

Specific activity: 40-400 mCi/g of KCl.

KCl content: 12 mg/ml.

CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

The production of ^{42}K is based on the nuclear reaction $^{41}K(n,\gamma)^{42}K$.

Processing consists of dissolving the irradiated target in the corresponding dilute acid and adding inactive salt when preparing isotonic solution. When specially requested the product is sterilized.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Potassium carbonate, Merck analytical grade; amount variable, depending on order.
Flux:	10^{13} n/cm^2 s.
Time:	25 h.
Container:	Quartz ampoule with ground stopper.

Chemical treatment

No special separation or purification is carried out. Different compounds are produced by dissolving the irradiated target in the corresponding dilute acid.

3. ASSAY AND QUALITY CONTROL

The purity of the inactive target is previously checked by spectrometric methods.

Radiochemical purity is controlled with a multichannel pulse height analyser for each charge.

The pH is determined in the usual way by measuring aliquot samples.

Pharmaceutical control regarding sterility is carried out only in the case of products for medical use.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Radioactive purity:	> 99%.
Specific activity:	50 mCi/g.
Chemical form:	Potassium carbonate, white tablets.
	Potassium chloride, isotonic sterilized solution.

MINISTRY OF DEFENCE, ATOMIC ENERGY COMMISSION,
SOREQ RESEARCH ESTABLISHMENT, YAVNE, ISRAEL

PRODUCTION OF ^{42}K AS KCl ISOTONIC SOLUTION

1. GENERAL

The irradiation of K_2CO_3 produces ^{42}K by the (n,γ) reaction. The irradiated sample is dissolved in the required amount of 0.5 N hydrochloric acid to obtain an isotonic solution of pH = 7.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Potassium carbonate (AR). Target amount (mg) is 10.6 × the required solution volume (ml).

Irradiation in the Israel Research Reactor 1 (IRR-1): Thermal neutron flux of 10^{13} n/cm^2 s ("rabbit") or 3×10^{13} n/cm^2 s (pool).

Irradiation time is calculated from the simple formula $t = 5\ A/F$

where t = required irradiation time, (min)
A = required specific activity of the solution (calculated to irradiation's end time) (μCi/ml)
F = flux, expressed in units of 10^{12} n/cm^2 s.

This formula holds for short irradiations. For pool irradiation, the target is sealed into a silica ampoule, which is in turn put into an aluminium irradiation container.

For "rabbit" irradiation, the sample is sealed into a polyethylene vial.

Chemical treatment

Transfer irradiated sample into cell.
Wash silica ampoule with acetone.
Break ampoule. Transfer contents to beaker containing required amount of 0.15 N HCl.
After potassium carbonate is dissolved, check pH (it should be 7).
Filter through grade "F" sintered glass plate.
Take an aliquot; calibrate activity.
Deliver required amounts into penicillin bottles. Close bottles.
Sterilize to 120°C for one hour.

3. ASSAY AND QUALITY CONTROL

Radioactive purity is ascertained by γ-ray spectrography.
Note: Pyrogen-free distilled water is used throughout.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE, TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process is based on the irradiation of a potassium carbonate target, and dissolution in dilute hydrochloric acid. The process is similar to that for the production of ^{24}Na.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	20 g K_2CO_3 (JISGR[1]) for JRR-1.
	8 g for JRR-2.
Container:	Sealed in a polyethylene sheet, then placed in a polyethylene capsule (JRR-1).
	Placed in a polyethylene bottle, then in a capsule (JRR-2).
Flux:	$\sim 3 \times 10^{11}$ n/cm^2 s (JRR-1).
	$\sim 2 \times 10^{13}$ n/cm^2 s (JRR-2 pneumatic tube).
Irradiation time:	10 h (5 h $\times$ 2 d) for JRR-1.
	20 min for JRR-2.

Chemical treatment

The apparatus[2] used for the production of ^{42}K is the same as that for the production of ^{24}Na.

Place the target in the dissolving vessel (b), fix the cap, then add the following reagent from the reagent feed pipe (c) with magnetic stirring:

8.8 ml $\sim$ 1.6 $\underline{N}$ HCl/g K_2CO_3 (irradiation with JRR-1);

6 ml $\sim$ 2.4 $\underline{N}$ HCl/g K_2CO_3 (irradiation with JRR-2).

Exhaust gases and bubblings are trapped in the trap (d).

Adjust the pH of the dissolved solution to 7-8.5. Then move the dissolving vessel (b) to the place where the remote control burette (f) is operated. The product solution is distributed in the sample bottles placed on the rotary table (g).

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[1] Japan Industrial Standard Grade Reagent.

[2] See Fig. 1 of the section on ^{24}Na provided by the Japan Atomic Energy Research Institute, Japan.

The inner rubber cap and outer aluminium cap are fixed on the sample bottle with the capping machine (f).

3. ASSAY AND QUALITY CONTROL

The same as for ^{24}Na.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	KCl in neutral solution (pH 7.0-8.5)
Radiochemical purity:	> 98%.
Specific activity:	~ 1.3 mCi/g K (product of JRR-1); 6.0 mCi/g K (product of JRR-2).
Concentration:	~ 0.08 mCi/ml (product of JRR-1); 0.5 mCi/ml (product of JRR-2).

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Potassium-42 is produced by irradiating potassium carbonate in a thermal neutron flux, $^{41}K(n,\gamma)^{42}K$. After irradiation the potassium carbonate is converted to potassium chloride by reaction with hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	3 g K_2CO_3, Merck, p.a., dehydrated.
Time of irradiation:	2-3 d.
Container:	Aluminium can, with sealed polyethylene inner container.
Flux:	About 1.5×10^{12} n/cm^2 s.
Side reactions:	None.

Chemical treatment

The irradiated potassium carbonate is dissolved in dilute hydrochloric acid. After completion of the reaction the solution is evaporated to dryness and the chloride is dissolved in water.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative ionization chamber measurements.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control, emission spectrography.
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

KS - potassium chloride in neutral solution, sterilized.

Radioactive concentration:	2 mCi/ml.
Isotopic purity:	Greater than 99.9%.
Specific activity:	About 30 mCi/g K.
pH:	6-7.
Chemical purity:	Metals, spectrographically determined, less than 10 μg/ml.
KCl content:	11.5%.

KSI - potassium chloride in neutral isotonic solution, sterilized.

Radioactive concentration:	0.2 mCi/ml.
KCl content:	1.15%.

Other specifications as for KS.

INSTITUTE OF NUCLEAR RESEARCH, SWIERK NEAR OTWOCK, POLAND

1. GENERAL [1-5]

Potassium-42 is obtained from K_2CO_3 irradiated in the reactor. The product is used mostly in the form of chloride which is prepared by dissolution of K_2CO_3 in HCl. The yield of the process is approximately 90%.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	1 g of anhydrous K_2CO_3, analytical grade, powder in sealed quartz tube wrapped in aluminium foil.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	18 h.
Container:	Aluminium capsule closed by welding.
Activity obtained:	200 mCi/g.

Chemical treatment

The capsule containing 1 g of irradiated target is placed in a dry-box for opening. The aluminium capsule is removed. The quartz tube with the target material is opened with a special cutter. The tube content is transferred to a 150-ml beaker and 88 ml N/7 HCl is added. The beaker is placed in a fume box and heated with a special device for 10 min to remove CO_2. The acidity of the resulting isotonic solution which should be in the pH range 7 - 8.5 is checked after cooling on a pH meter. The solution is filtered through a sintered-glass filter and then dispensed into penicillin-type vials. Closed vials are sterilized at 2.5 atm for 25 min. "For injection" preparations are obtained by the use of pyrogen-free water and pyrogen-free reagents. Pyrogen-free water is also used for rinsing the glass equipment. All operations are carried out in a box with 10-cm-thick lead shields.

3. ASSAY AND QUALITY CONTROL

The activity of the product is measured with an ionization chamber against standard ^{42}K.
The chemical purity is checked spectrally.
The radiation purity is determined by gamma spectrometry.
The sterility is checked with the use of the culture media.
Test for pyrogens is carried out on rabbits.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Potassium chloride-42 for injections

Radioactive concentration:	0.5-5 mCi/ml. (Accuracy of activity determinations ± 5%.)
Radiation purity:	99.9%.
Specific activity:	20-40 mCi/g K.
Dry residue:	12 mg/ml.

Sterile, pyrogen-free.

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THE RADIOCHEMICAL CENTRE,
AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Potassium-42 is prepared as a sterile isotonic solution of its chloride. The nuclear reaction utilised is $^{41}K(n,\gamma)^{42}K$. Irradiated potassium bicarbonate, in pellet form, is converted to potassium chloride by reaction with hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	$KHCO_3$, pellet, Burroughs Wellcome, analytical reagent grade, low Br and Na content.
Irradiation container:	Doubly encapsulated in aluminium screw top containers.
Irradiation conditions:	Flux 1.2×10^{12} n/cm^2 s for 4 days. ^{82}Br and ^{24}Na impurities are kept to a minimum by careful selection of target material.

Chemical treatment

The irradiated target material is dissolved in water and titrated against hydrochloric acid using methyl orange indicator. Dissolved CO_2 is removed and methyl orange destroyed by boiling with hydrogen peroxide. The pH is then adjusted to 7 and checked by pH meter and the total volume of solution is corrected for isotonicity. After dispensing each consignment is sterilised by autoclaving.

3. ASSAY AND QUALITY CONTROL

The target material is subjected to activation analysis.

The product undergoes examination by γ-spectrometry for ^{24}Na and ^{82}Br, and for anionic impurities by ion exchange.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity (at time of dispensing):	~ 20 mCi ^{42}K/g K.
Radioactive concentration (at time of dispensing):	~ 0.1 mCi ^{42}K/ml.
Radioisotopic purity (at time of dispensing):	$^{24}Na < 0.05\%$ $^{82}Br < 0.005\%$.
Radiochemical purity:	^{42}KCl 100%.
Total solids:	11.5 mg KCl/ml (to give isotonic solution)
pH:	6-8.

OAK RIDGE NATIONAL LABORATORY,
TENN., UNITED STATES OF AMERICA

1. GENERAL

Potassium-42 is produced by the (n,γ) reaction in a K_2CO_3 target, $^{41}K(n,\gamma)^{42}K$, and is prepared as KCl in HCl solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 3 g K_2CO_3.
Neutron flux: $\sim 1.3 \times 10^{14}$ n/cm^2 s.
Irradiation time: 61 h.
Reactor yield: 700 mCi.

Chemical treatment

Apparatus

A hot off-gas scrubber unit[1] is used in processing. Processing facility and shielding required: manipulator cell 4-in lead equivalent.

Processing

Yield: > 95%.

The irradiated target is dissolved in a minimum amount of 12 M HCl added dropwise. The volume is adjusted to 50 ml of 1 M HCl.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for molarity of HCl, total solids, ^{42}K concentration, and radio-chemical purity according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733641.

The precision and accuracy of the ^{42}K are:
Calibration by $4\pi\,\beta$-γ coincidence counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 5%.
Precision, 3%.

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[1] See Fig. 2 of the section on ^{82}Br provided by ORNL, Tenn., United States of America.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity ^{42}K is delivered as KCl in HCl solution as a stock item. Other specifications of interest are:

Acidity:	1 N ± 50%.
Concentration:	> 1 mCi/ml.
Specific activity:	> 200 mCi/g K.
Radiochemical purity:	> 99%.

BORIS KIDRIČ INSTITUTE OF NUCLEAR SCIENCES, VINČA, YUGOSLAVIA

1. GENERAL

Potassium carbonate is used for the production of an isotonic solution of ^{42}KCl. The irradiated carbonate is dissolved in H_2O, the solution neutralized with HCl and evaporated to dryness. The ^{42}KCl is finally dissolved in water to obtain an isotonic solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	0.557 g Merck's reagent grade K_2CO_3.
Irradiation containers:	Cylindrical, with screwed covers; internal length: 70 mm, internal diam.: 25 mm.
Thermal flux:	1.5×10^{13} n/cm^2 s (RA Reactor at Vinča).
Irradiation time:	1-36 h.

Chemical treatment

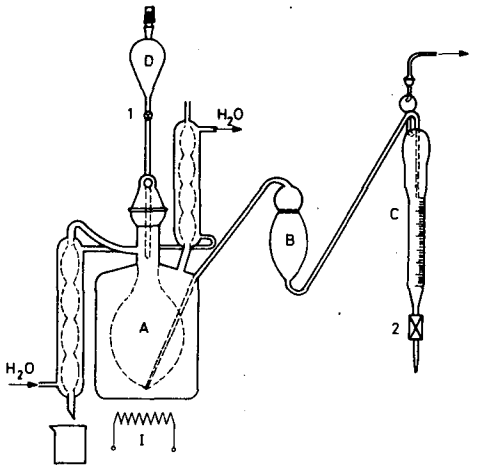
Separation method

A sample of irradiated carbonate is put into a vessel for dissolution (A) and from a vessel for adding chemicals (D) 10 ml of twice distilled water is added. After dissolving the target, 20.1 ml of 0.4 N HCl is added and finally 10 ml of water to rinse the HCl remaining in the tube. The neutral liquid obtained is heated to remove CO_2 and evaporated to dryness. This is necessary as, to obtain an isotonic solution, the concentration of salt should be precisely adjusted. After complete evaporation the heater is switched off and vessel (A) is allowed to cool down. The chloride is dissolved with the addition of 49.5 g doubly distilled water. The sodium chloride solution is percolated through the G-5 sintered glass of the filtration vessel (B) and transferred to burette (C) for weighing. In this case vacuum

is used. If double amounts are taken, 100 ml of the solution can be produced with the same apparatus.

Apparatus

An apparatus of Pyrex glass is used for the production of isotonic solutions of $^{24}NaCl$ and ^{42}KCl (Fig.1).



A. Vessel for dissolution;
B. Vessel for filtration;
C. Burette;
D. Vessel for reagent addition;
I. Heater

FIG.1. Apparatus for the production of isotonic solutions of $^{24}NaCl$ and ^{42}KCl

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.
Radioactive purity control.
pH control.
Sterility control.
A pyrogenity control of doubly distilled water used for preparing a radioactive solution.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVK42/1, sterile isotonic potassium chloride solution, pH 6-7

Radioactive concentration:	measured to within 10%; 0.2 - 3 mCi/ml.
Radioactive purity:	^{42}K content more than 99%.
Specific activity:	1 Ci/g K.
Isotonic solution:	1.2% KCl.
Pyrogen-free.	

SODIUM-24

NUCLEAR DATA

1. NUCLEAR PROPERTIES

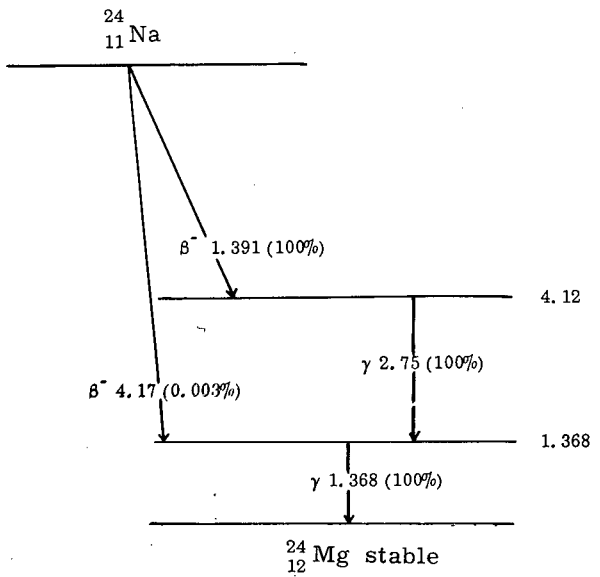
1.1. Half-life

15 h

1.2. Type of decay, and energy (MeV)

beta(β^-)	1.391	(100%)	gamma	1.368	(100%)
	4.17	(0.003%)		2.75	(100%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm²s (mCi/g)			Secondary reactions and half-life of nuclide formed
			1 h	24 h	sat.	
$^{23}_{11}Na(n,\gamma)^{24}_{11}Na$	100	0.525 (th)	16	260	380	
$^{24}_{12}Mg(n,p)^{24}_{11}Na$	78.7	0.001 (f)	0.025	0.44	0.66	$^{26}_{12}Mg(n,\gamma)^{27}_{12}Mg$ (T = 9.5 min) σ = 27 mb
$^{27}_{13}Al(n,\alpha)^{24}_{11}Na$	100	0.0006 (f)	0.015	0.27	0.40	$^{27}_{13}Al(n,\gamma)^{28}_{13}Al$ (T = 2.3 min) σ = 210 mb; $^{27}_{13}Al(n,p)^{27}_{12}Mg$ (T = 9.5 min) σ = 2.8 mb

(th): for thermal neutrons.
(f): for fast neutrons.
For nuclear data see Refs. [1-3].

The nuclear reaction normally used for the production of ^{24}Na is the (n,γ) reaction on natural sodium.

The target is sodium carbonate (Na_2CO_3) or sodium chloride (NaCl). In the second case, ^{36}Cl, ^{38}Cl, ^{35}S and ^{32}P occur also from the irradiation of the chlorine.

$^{35}_{17}Cl(n,p)^{35}_{16}S$ (87.1 d)

$^{35}_{17}Cl(n,\gamma)^{36}_{17}Cl$ (2.5×10^5 yr)

$^{35}_{17}Cl(n,\alpha)^{32}_{15}P$ (14.3 d)

$^{37}_{17}Cl(n,\gamma)^{38}_{17}Cl$ (37.3 min)

3. APPLICATIONS

3.1. Industrial

Sodium-24 is the short-lived isotope most used in tracer work, for such applications as:

Location of losses from underground piping [4,5].
Discharge measurements (pipes and rivers) [6].

Study of industrial circuits: mixers [7, 8].
Determination of retention and storage times of industrial materials [9-11].

It is also used in activation analysis, particularly in graphite and high-nuclear-grade aluminium [12], in hydrocarbons [13] and in glass [12, 14].

In addition it is used in the glass industry for structure and surface investigations [15] and in hydrology [16].

In addition to the references given for industrial uses of ^{24}Na reference may be made to general works [17].

3.2. Medical and biological

In these fields it is used in the form of chloride.

3.2.1. Diagnostic: ^{24}Na is used for:

Sodium exchange studies [18-20] concerning

Permeability of hair.
Permeability of digestive mucosa.
Measurement of extra-cellular fluids (doses of the order of 1 μCi/kg) [21].

Urinary excretion studies [18].

Cardiovascular studies [18-20, 22-26] (doses of the order of 200 μCi [21]) regarding:

Measurement of circulation rate.
Measurement of the mixing rate of labelled blood and the blood circulating in various organs.
Heart output measurements.
Peripheral circulation.

Location of the placenta [20].

3.2.2. Therapeutic: ^{24}Na is used in the treatment of animal and human leukaemias [20, 27-29]. The dose administered in each treatment is between 20 and 30 mCi [20]. Besides the references given there are others dealing with medical uses of ^{24}Na [30].

4. RADIOLOGICAL PROTECTION

4.1. External exposure

4.1.1. Irradiation doses

The dose delivered by 1 Ci of ^{24}Na at a distance of 50 cm is:

- for 1.368 MeV γ quanta (100%) 2.60 rem/h
- for 2.75 MeV γ quanta (100%) 4.20 rem/h

6.80 rem/h [31]

4.1.2. Safety measures

The following tenth-thicknesses[1] for lead and ordinary concrete give some idea of the amount of protection needed in handling ^{24}Na:

	Tenth-thickness (cm)		
	Pb	Ordinary concrete d = 2.3	
For a γ of 1.368 MeV	3.8	20	
For a γ of 2.75 MeV	5.5	30	Ref. [31]

In practice, to get a dose of 1 mrem/h at 50 cm one can handle:
- 10 mCi of ^{24}Na with 9 cm of lead shielding.
- 100 mCi of ^{24}Na with 14.5 cm of lead shielding.
- 1 Ci of ^{24}Na with 20 cm of lead shielding.

4.2. Internal irradiation

Sodium-24 is classified as a moderately toxic, class 3, isotope [32]. Its effective half-life, allowing for both radioactive decay and excretory processes, is 0.60 d [33].

In the case of internal irradiation (ingestion or inhalation), the maximum permissible concentrations in air and water, respectively, for a 40-h exposure, are:

10^{-6} μCi/cm^3 and 6×10^{-3} μCi/cm^3 (soluble form)

10^{-7} μCi/cm^3 and 8×10^{-4} μCi/cm^3 (insoluble form) [34]

4.3. Decontamination

Except in one or two particular cases there is no special decontamination method for any given radioisotope. Some general texts on this subject [35-39] indicate that the following measures are adequate:

4.3.1. Skin

Rapid and repeated washing with good-quality soap, warm water and a soft brush. If this is not sufficient, use can be made of detergents or 5-10% solutions of complexing agents of the EDTA (ethylenediamine tetra-acetic acid) type. It is also possible to apply saturated permanganate solutions followed by rinsing with a 5% bisulphite solution to neutralize and remove

[1] The tenth-thickness is the thickness of shielding required to reduce the intensity of a γ-radiation of given energy by a factor of ten.

stain. Abrasive powders should not be used and the addition of entraining agents has proved disappointing.

If any wounds are contaminated, they must be treated rapidly by bleeding, washing with water, decontamination as for the skin and sometimes by additional surgical cleaning.

4.3.2. Hair

If the hair is contaminated, it is important not to take a shower, but merely to wash the head. A normal, good-quality shampoo is usually sufficient. If contamination is persistent, the following solutions can be used:

paraisopropylorthocresol;
lavandin oil;
AC-compounded terpene-free lemon;
glycerine diacetin;
benzoic acid;

Contamination is much easier to remove if the hair is not greasy.

4.3.3. Laboratory equipment

Glassware is usually cleaned by steeping and this is mainly a radiochemical problem. The use of a specific entraining agent or solutions of complexing agents gives good results and so do solutions of chromic acid, concentrated nitric acid, ammonium citrate, pentasodium triphosphate or ammonium bifluoride.

5. SUMMARY OF PRODUCTION METHODS

Sodium-24 is generally prepared by bombarding a sodium salt with thermal neutrons, followed by solution in hydrochloric acid. The salt used may be sodium carbonate [40-42] or sodium chloride [43,44]. In both cases, ^{24}Na is obtained with an entraining agent.

Some authors have described methods of preparing ^{24}Na without carrier by using the Al(n, α) and Mg(n, p) reactions [45-48].

Govaerts [45] treats the target – magnesium carbonate or aluminium oxide – with water to which a trace of sodium chloride has been added to facilitate the entrainment of radioactive sodium. This passes into solution as sodium carbonate or sodium. He separates the sodium from the magnesium carbonate or insoluble aluminium hydroxide by filtration.

Kimura, Shibata and Shikata [47] adopt the ion-exchange method of chemical separation. The specific activity is 300 times greater than that obtained by the $^{23}Na(n,\gamma)^{24}Na$ reaction.

Parker, Bildstein and Getoff [48] irradiate MgO or $Mg(OH)_2$ in water; the ^{24}Na isotope extracted in solution with water is then purified by ion exchange. This method is suitable up to activities of the order of one curie.

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PROCEDURES

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

The method consists of the irradiation of a sodium carbonate target and the simple dissolution of the irradiated target in order to obtain an isotonic final solution (9 mg NaCl/ml).

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Sodium carbonate (Johnson Matthey).

Irradiation conditions and yield: Irradiation of 500 mg of sodium carbonate for 1 week at a flux of 2×10^{12} n/cm^2 s yields about 100 mCi with a specific activity of 0.2 - 0.3 mCi/mg of NaCl.

Two capsules each containing two inner capsules of 250 mg of sodium carbonate are generally irradiated. An activity of between 50 and 200 mCi can thus be obtained according to requirements.

Chemical treatment

Five hundred milligrams of sodium carbonate are dissolved in 58 ml of N/6 hydrochloric acid. If no loss of sodium carbonate has occurred, this quantity should permit its exact neutralization and yield a solution at 9 mg/ml of sodium chloride and pH 7.

The pH is adjusted if necessary with 0.1 N soda or 0.1 N hydrochloric acid.

No special equipment is needed for this treatment; all that is necessary are beakers, pipettes and a pH meter.

3. ASSAY AND QUALITY CONTROL

The activity of two 1-ml samples is measured with an ionization chamber, and a gamma spectrum analysis to check the radiochemical purity is carried out.

Biological tests to check sterility and the absence of toxicity are also made.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{24}Na S-1-injectable

A sterile, neutral, isotonic and pyrogen-free solution of sodium chloride, meeting the following specifications:

Radioactive concentration, measured to within 5%:	0.5-5 mCi/ml.
Radioactive purity:	^{24}Na content > 99.9% (gamma spectrum characteristic of ^{24}Na).
Specific activity:	50 - 500 mCi/g NaCl.
NaCl content:	9 mg/ml.

CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

The production of ^{24}Na is based on the nuclear reaction $^{23}Na(n,\gamma)^{24}Na$. Processing consists of dissolving the irradiated target in the corresponding dilute acid and adding inactive salt when preparing an isotonic solution. At special request the product is sterilized.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: Sodium carbonate, Merck analytical grade; amount variable, depending on order.

Flux: 10^{13} n/cm^2 s.
Time: 15 h.
Container: Quartz ampoule with ground stopper.

Chemical treatment

No special separation or purification is carried out. Different compounds are produced by dissolving the irradiated target in the corresponding dilute acid.

3. ASSAY AND QUALITY CONTROL

The purity of the inactive target is previously checked by spectrometric methods.

Radiochemical purity is controlled with a multichannel pulse height analyser for each charge.

The pH is determined in the usual way by measuring aliquot samples.

Pharmaceutical control regarding sterility is carried out only in the case of products for medical use.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity: 212 mCi/g

Chemical form:

Sodium carbonate, white tablets.
Sodium chloride, isotonic sterilized aqueous solution.

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Sodium-24 and Potassium-42 are produced by irradiating the respective carbonates with neutrons in a nuclear reactor. The irradiated carbonate is dissolved in hydrochloric acid and the chloride is supplied as sterile isotonic solution at pH 7 for medical use.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: For ^{24}Na very pure Na_2CO_3 or for ^{42}K pure K_2CO_3 (sodium content < 10 ppm).

Container: 200 mg in can-type "A" (screw-capped 1S aluminium can of 73 mm height and 26.5 mm diam.) or type "C" (cold-welded 2S aluminium can of 44 mm height and 22 mm diam.).
Flux: 10^{12} n/cm^2 s.
Irradiation time: 12-24 h.

Chemical treatment

The glassware to be used for the production is washed several times with doubly distilled water and after covering with brown paper, dry-sterilized at 150°C for 2 h.

The irradiation can containing 200 mg of Na_2CO_3 (or K_2CO_3) is opened and the contents are transferred into a beaker containing 10 ml of pyrogen-free water. The pH is adjusted to 7 by adding dilute hydrochloric acid and the solution is boiled for a few minutes. After cooling, the pH is adjusted again to 7, and the solution is filtered, collecting the filtrate in a graduated storage bottle. The volume is made up to 25 ml in the case of ^{24}Na (for ^{42}K the volume is diluted to 21 ml). The solution is stirred well and an aliquot is assayed for activity in an ion chamber. The rest of the solution is distributed into various vials and autoclaved along with a bacterial culture sample (to test the sterilizing conditions).

3. ASSAY AND QUALITY CONTROL

The activity assay is done by measuring the ion current of 1 ml of the sample in a calibrated ion chamber.

Estimation of NaCl or KCl in stock solution: The chloride is estimated by the Volhard's method.

Radioactive purity: The gamma spectrum of the sample is taken and is compared with the known standard spectrum.

To confirm the absence of pyrogens in the active solutions, a simulated dummy-run is carried out with every batch and the dummy product is tested for pyrogens on rabbits.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Code N AM - 1

Sodium-24 as sodium chloride in isotonic solution, sterilized, pH 7. Specific activity: 50 mCi/g Na.

Code K AM - 1

Potassium-42 as potassium chloride in isotonic solution, sterilized, pH 7. Specific activity = 50 mCi/g K.

MINISTRY OF DEFENCE, ATOMIC ENERGY COMMISSION,
SOREQ RESEARCH ESTABLISHMENT, YAVNE, ISRAEL

A. PRODUCTION OF ^{24}Na AS NaCl ISOTONIC SOLUTION

1. GENERAL

Irradiation of $Na_2CO_3 \cdot H_2O$ produces ^{24}Na by the (n,γ) reaction. The irradiated sample is dissolved in the required amount of 0.15 N hydrochloric acid to get an isotonic solution of pH 7.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material is sodium carbonate monohydrate (AR). Target amount (mg) is 9.3 × required solution volume (ml). Irradiations are made in the Israel Research Reactor 1 (IRR-1) at a thermal flux of 10^{13} n/cm^2 s (rabbit) or 3×10^{13} n/cm^2 s (pool).

Irradiation time is calculated from the simple formula $t = A/F$ where:

t = required irradiation time (min)
A = required specific activity of the solution (calculated to irradiation's end time) in μCi/ml
F = flux, expressed in units of 10^{12} n/cm^2 s.

This formula holds for short irradiations.

For pool irradiation, the target is sealed into a silica ampoule, which is in turn put into an aluminium irradiation container. For rabbit irradiation, the sample is sealed into a polyethylene vial.

Chemical treatment

Transfer irradiated sample into cell.
Wash silica ampoule with acetone.
Break ampoule. Transfer contents to beaker containing required amount of 0.15 N HCl.
After sodium carbonate is dissolved check pH (it should be 7).
Filter through grade "F" sintered glass plate.
Take an aliquot; calibrate activity.
Deliver required amounts into penicillin bottles. Close bottles.
Sterilize to 120°C for one hour.
Note: Pyrogen-free distilled water is used throughout.

3. ASSAY AND QUALITY CONTROL

Radioactive purity is ascertained by γ-ray spectrography.

B. PRODUCTION OF ^{24}Na IN AQUEOUS SOLUTION IN THE CURIE ACTIVITY RANGE [1]

1. GENERAL

A special small aluminium container, holding about 1 g sodium carbonate is irradiated, and then dissolved in HCl. All the processing is done in a lead-shielded plastic container as explained below.

2. EXPERIMENTAL PROCEDURE

Irradiation

Sodium carbonate (AR) is put into a special aluminium container of 1 cm^3 capacity, tightly closed by means of a screw-on cap and polyethylene gasket. This is irradiated at a thermal neutron flux of 2.5×10^{13} n/cm^2 s (pool irradiation). The polyethylene gasket will withstand up to one hour irradiation. After irradiation and a half-hour cooling time have elapsed, the lead-shielded plastic container shown in Fig. 1 is lowered into the pool by a crane.

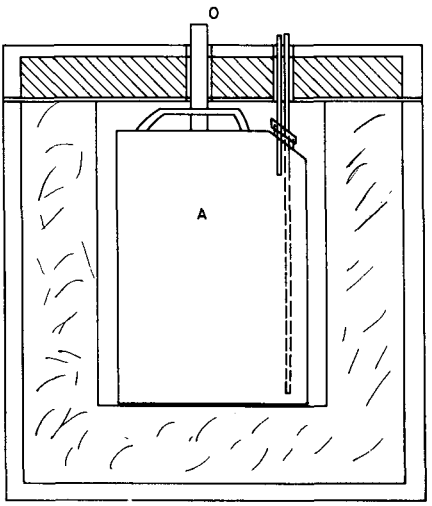


FIG. 1. Apparatus for the chemical processing of ^{24}Na solution in the curie activity range

[1] In collaboration with the Industrial Applications Unit.

Chemical treatment

Put the irradiated sample into container 'A'. Cut the aluminium wire above the irradiated sample.

Raise the container above the pool. Close opening 'O'. Apply air pressure for drawing the pool water out of the container.

Lower the container onto the truck. Take it out of the reactor hall.

Dissolve the aluminium container and sodium carbonate by adding 2 litres 5 N hydrochloric acid through a tube.

Add 2 litres of 5 N sodium hydroxide.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process of ^{24}Na is based on the irradiation of a sodium carbonate target and the subsequent dissolution in dilute hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	3.0 g Na_2CO_3 (JISGR[1]) for JRR-1; 0.8 g for JRR-2.
Container:	JRR-1: sealed in the polyethylene sheet and placed in the polyethylene capsule.
	JRR-2: placed in the polyethylene bottle, then in the polyethylene capsule.
Flux:	$\sim 3 \times 10^{11}$ n/cm^2 s (JRR-1).
	$\sim 2 \times 10^{13}$ n/cm^2 s (JRR-2 pneumatic tube).
Irradiation period:	10 h (5 h/d) in JRR-1; 20 min in JRR-2.

Chemical treatment

The apparatus for the chemical processing is shown in Figs. 1 and 2.

Cut the polyethylene inner capsule by the cutter (a).

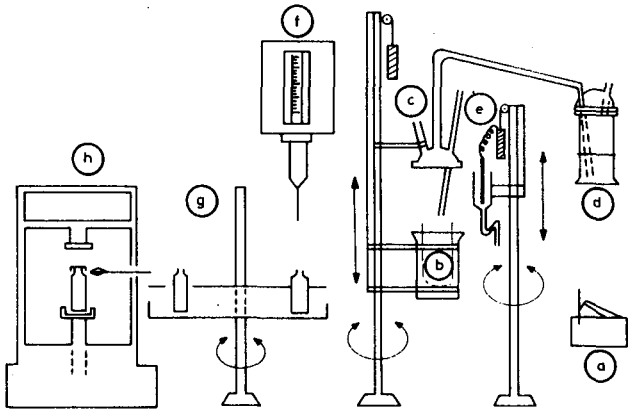
Transfer the target into the dissolving vessel (b). After fixing the cap of the vessel, add the following amount of hydrochloric acid from the reagent feed pipe (c) with magnetic stirring.

$\sim$ 6 ml 3 N HCl/g Na_2CO_3 (irradiations in JRR-1).

$\sim$ 21 ml 0.8 N HCl/g Na_2CO_3 (irradiations in JRR-2).

The gases and bubblings are trapped in the trap (d).

[1] Japan Industrial Standard Grade Reagent.



a. Polyethylene capsule cutter
b. Dissolving vessel
c. Reagent feed pipe
d. Trap for exhausting fume
e. Electrode for pH measurement
f. Remote pipetter for dispensing
g. Rotary table
h. Encapsulator

FIG.1. Arrangement of apparatus for ^{24}Na production

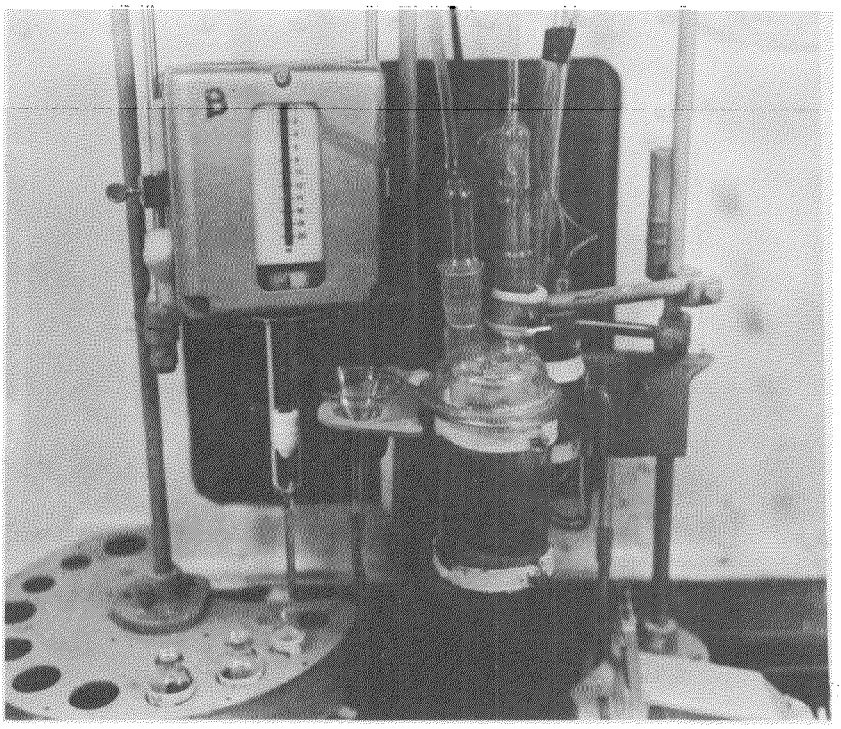


FIG.2. Apparatus for the production of ^{24}Na

Adjust the pH of the dissolved solution to 7-8.5. Place the dissolving vessel (b) under the remote pipette (f), suck the ^{24}Na solution into the pipette, then distribute into the bottles placed on the rotary table (g).

A rubber cap and an aluminium cap are fixed on the bottle with the encapsulator (h) (Fig. 3).

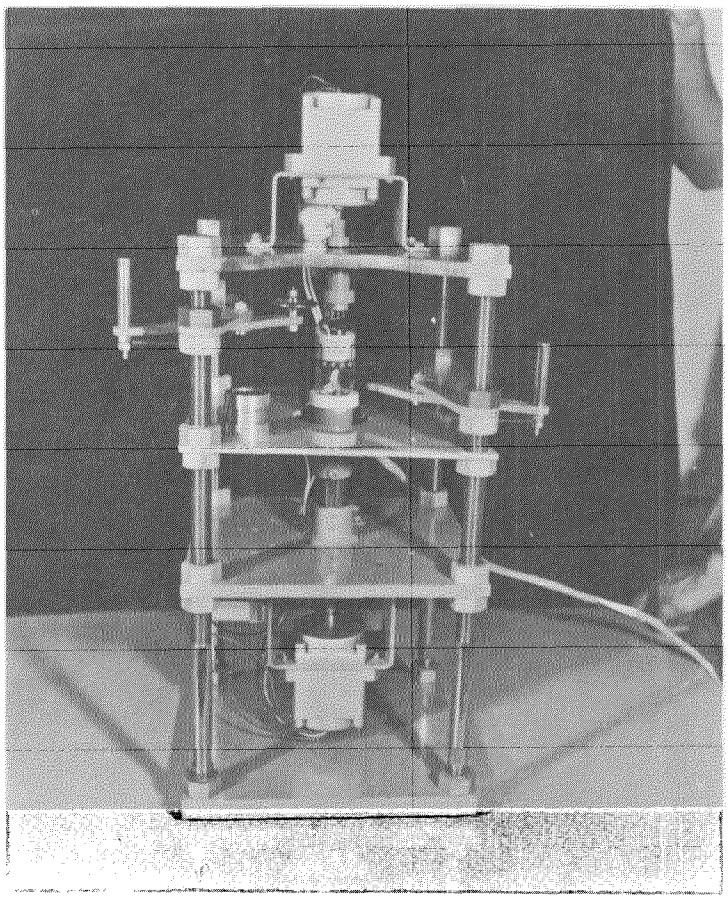


FIG. 3. Encapsulator for the product bottle

3. ASSAY AND QUALITY CONTROL

The analysis of heavy metals is carried out by the comparison of colour development with the standard lead solution on the addition of hydrogen sulphide gas.

Routine assay is carried out by the well-type ionization chamber, and for the calibration a 4π β-γ coincidence counter is employed.

In addition, a routine check of pH is carried out.

4. CHARACTERISTICS OF THE FINAL SOLUTION

The specifications of the product ^{24}Na are as follows:

Chemical form:	NaCl in neutral solution (pH 7.0 - 8.5)
Radiochemical purity:	Over 99%
Specific activity:	~ 13 mCi/g Na (Product of JRR-1);
	~ 60 mCi/g Na (Product of JRR-2).
Concentration:	~ 0.8 mCi/ml (Product of JRR-1);
	~ 1.0 mCi/ml (Product of JRR-2).

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Sodium-24 is produced by irradiating sodium carbonate in a thermal neutron flux, $^{23}Na(n,\gamma)^{24}Na$. After irradiation the sodium carbonate is converted to sodium chloride by reaction with hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	200 mg Na_2CO_3, Merck, p.a. dehydrated.
Time of irradiation:	2-3 d.
Container:	Aluminium can, with sealed polyethylene inner container.
Flux:	About 1.5×10^{12} n/cm^2 s.
Side reactions:	None.

Chemical treatment

The irradiated sodium carbonate is dissolved in dilute hydrochloric acid. After completion of the reaction the solution is evaporated to dryness, and the chloride is dissolved in water.

3. ASSAY AND QUALITY CONTROL

Radioactivity, relative ionization chamber measurements.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control, emission spectrography.
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

NSI – sodium chloride in neutral isotonic solution, sterilized.

Radioactive concentration:	1-2 mCi/ml.
Isotopic purity:	Greater than 99.9%.
Specific activity:	300-500 mCi/g Na.
pH:	6-7.
Chemical purity:	Metals, spectrographically determined, less than 10 μCi/ml.
NaCl content:	0.9%.

INSTITUTE OF NUCLEAR RESEARCH, SWIERK NEAR OTWOCK, POLAND

1. GENERAL [1-5]

Sodium-24 is obtained from Na_2CO_3 irradiated in the reactor. The product is usually distributed as chloride which is formed after the dissolution of Na_2CO_3 in HCl.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	140 mg of anhydrous Na_2CO_3, analytical grade, powder, in a sealed quartz tube wrapped in aluminium foil.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	18 h.
Container:	Aluminium capsule closed by welding.
Activity obtained:	Approximately 180 mCi/g.

Chemical treatment

The irradiated capsule is placed in a dry-box for opening. The quartz tube with the target material is opened with a special cutter. The tube content is placed in a 50-ml beaker and 16.5 ml of 6 N HCl is added. The beaker is placed in a fume box and heated with a special device for 5-8 min to remove remaining CO_2. Pyrogen-free water is used for the preparation of all solutions as well as for rinsing the glass equipment used. The acidity of the resulting solution which should be in the pH range 7-8 is checked, after cooling, on a pH meter. The concentrations of Na_2CO_3 and HCl are calculated so that the neutralization leads to the formation of the isotonic ^{24}NaCl solution. The ^{24}NaCl solution is divided into portions by pipetting

into penicillin vials. The solutions prepared for injections are produced by the use of pyrogen-free water and pyrogen-free reagents and after stoppering are sterilized at 2.5 atm for 25 min. All operations are carried out in a box with 10-cm-thick lead shields.

3. ASSAY AND QUALITY CONTROL

The activity of the product is measured in an ionization chamber against standard.
The chemical purity is checked spectrally.
The radiation purity is checked by gamma spectrometry.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Sodium chloride-24 for injection

Radioactive concentration:	0.5-5 mCi/ml.
Radiation purity:	99.9%.
Specific activity:	50-250 mCi/g Na.
Dry residue:	9 mg/ml.

Sterile, pyrogen-free.

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THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Sodium-24 is prepared as a sterile isotonic solution of its chloride. The nuclear reaction utilized is $^{23}Na(n,\gamma)^{24}Na$. Irradiated sodium bicarbonate, in pellet form, is converted to sodium chloride by reaction with hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	$NaHCO_3$, pellet, Burroughs Wellcome, analytical reagent grade, low Br and K content.
Irradiation container:	Doubly encapsulated in aluminium screw-top containers.
Irradiation conditions:	Flux 1.2×10^{12} n/cm^2 s for 4 d. ^{82}Br and ^{42}K impurities are kept to a minimum by careful selection of target material.

Chemical treatment

The irradiated target material is dissolved in water and titrated against hydrochloric acid, using methyl orange indicator. Dissolved CO_2 is removed and methyl orange destroyed by boiling with hydrogen peroxide. The pH is then adjusted to 7 and checked by pH meter and the total volume of the solution is corrected for isotonicity. After dispensing each consignment is sterilized by autoclaving.

3. ASSAY AND QUALITY CONTROL

The target material is subjected to activation analysis.

The product undergoes examination by γ-spectrometry for ^{42}K and ^{82}Br and for anionic impurities by ion exchange.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity (at time of dispensing):	~ 300 mCi ^{24}Na/g Na.
Radioactive concentration (at time of dispensing):	~ 1 mCi ^{24}Na/ml.
Radioisotopic purity (at time of dispensing):	^{42}K < 0.005%. ^{82}Br < 0.005%.
Radiochemical purity:	^{24}NaCl 100%.
Total solids:	9 mg NaCl/ml (to give isotonic solution).
pH:	6-8.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Sodium-24 is produced by the (n,γ) reaction in a Na_2CO_3 target, ^{23}Na(n,γ)^{24}Na, and is prepared as NaCl in a water solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 250 mg Na_2CO_3.
Neutron flux: 1×10^{13} n/cm^2 s.
Irradiation time: 60 h.
Reactor yield: 250 mCi.

Chemical treatment

Apparatus

A hot off-gas scrubber unit[1] is used in processing. Processing facility and shielding required: manipulator cell, 6-in. lead equivalent.

Processing

Yield: > 90%

The irradiated target is transferred into a beaker under the hot off-gas scrubber assembly, and 12 M HCl is added dropwise (to minimize effervescing) and heated until all target material is dissolved. The solution is evaporated to complete dryness to remove excess HCl. The residue is dissolved in ~ 20 ml of distilled H_2O and again evaporated to dryness to remove traces of HCl. Finally, the volume is adjusted to 50 ml of distilled H_2O to give a product solution that is water-white, pH ~ 7.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for pH, total solids, ^{24}Na concentration, and radiochemical purity according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733792.

Precision and accuracy of the ^{24}Na assay are:
Calibration by 4π β-γ coincidence counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 3%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity ^{24}Na is delivered as NaCl in water solution as a stock item. Other specifications of interest are:
pH: 7.0 - 8.5.

[1] See Fig. 2 of section on ^{82}Br provided by ORNL, Tenn., United States of America.

Concentration: > 1 mCi/ml.
Specific activity: ≅ 10 000 mCi/g Na.
Radiochemical purity: > 99%.

BORIS KIDRIČ INSTITUTE OF NUCLEAR SCIENCES,
VINČA, YUGOSLAVIA

1. GENERAL

Sodium carbonate is used for the production of the isotonic solution of $^{24}NaCl$.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 0.408 g Merck's reagent grade Na_2CO_3.
Thermal flux: 1.5×10^{13} n/cm^2 s (RA reactor at Vinča).
Irradiation time: 1-36 h.
Irradiation containers: Cylindrical with screwed covers, internal length 70 mm, internal diam. 25 mm.

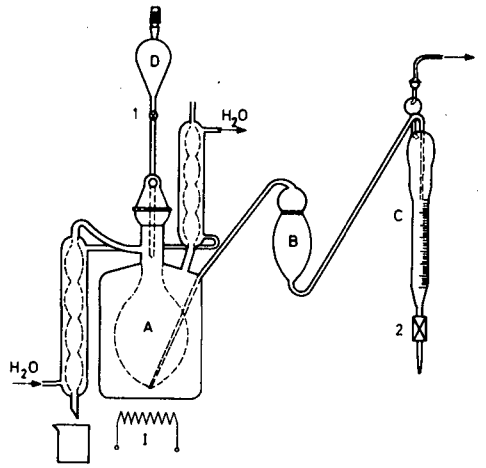
Chemical treatment

Separation method

A sample of irradiated carbonate is put in a dissolution vessel (Fig. 1) (A) and, from a vessel for adding chemicals (D), 10 ml of doubly distilled water is added. After dissolving the target 19.2 ml of 0.4 N HCl is added and finally 10 ml of water to rinse the HCl remaining in the tube. The neutral liquid obtained is heated to remove the CO_2 and evaporated to dryness. This is necessary as, to obtain an isotonic solution, the concentration of salt should be precisely adjusted. The evaporation of the solution is regulated by switching on the adjustable heater (I). After complete evaporation the heater is switched off and vessel (A) is left to cool down. The chloride is dissolved with the addition of 49.5 g of doubly distilled water. Sodium chloride is dissolved and eluted from the vessel. It is percolated through the G-5 sintered glass of the filtration vessel (B) and transferred to burette (C) for weighing. In this case vacuum is used. If double amounts are taken 100 ml of the solution can be produced with the same apparatus.

Apparatus

An apparatus of Pyrex glass is used for the production of isotonic solutions of $^{24}NaCl$ and ^{42}KCl (Fig. 1).



A. Vessel for dissolution
B. Vessel for filtration
C. Burette
D. Vessel for reagent addition
I. Heater

FIG.1. Apparatus for the production of isotonic solutions of $^{24}NaCl$ and ^{42}KCl

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.
Radioactive purity control.
pH control.
Sterility control.
Pyrogenity control of doubly distilled water used for preparing a radioactive solution.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVNa24/1, sterile isotonic sodium chloride solution, pH≈6-7.
Radioactive concentration: Measured to within 10%; 1-15 mCi/ml.
Radioactive purity: ^{24}Na content more than 99%.
Specific activity: 1 Ci/g Na.
Isotonic solution.
Pyrogen-free.

SULPHUR-35

NUCLEAR DATA

1. NUCLEAR PROPERTIES

1.1. Half-life

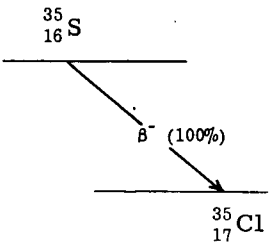
87 d

1.2. Type of decay, and energy (MeV)

Pure beta emitter

beta (β^-) 0.167 (100%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{13} n/cm^{2}s (mCi/g)			Secondary reactions and half-life of nuclide formed
			1 h	24 h	sat.	
$^{34}S(n,\gamma)^{35}S$	4.22	0.27	0.019	0.47	58	$^{32}S(n,p)^{32}P$ (T = 14.3 d) isot. abund.: 95.0% $^{33}S(n,p)^{33}P$ (T = 24.6 d) isot. abund.: 0.75%
$^{35}Cl(n,p)^{35}S$	75.529	0.35[a]	0.42	9.7	1220	$^{35}Cl(n,\gamma)^{36}Cl$ (T = 2.5×10^5 yr) isot. abund.: 75.4% σ = 33 barn $^{35}Cl(n,\alpha)^{32}P$ (T = 14.3 d) $\sigma_{(f)}$ = 0.0145 barn, $\sigma_{(th)}$ = 0.08 mbarn

[a] The mean of nine reported values [3-12].
Only the side-reactions producing nuclides with half-lives exceeding 1 h are taken into consideration.
For nuclear data see Refs. [1-13].

3. APPLICATIONS

Sulphur-35 has found wide application, mainly as a tracer. Sulphur-35-labelled inorganic sulphate, as well as sulphide or elementary sulphur, are used either as such, or as starting material for further syntheses of compounds. Many ^{35}S-labelled compounds have been prepared [14], some of them by exchange reactions [15, 16].

Some references to the main applications are given below.

3.1. Biochemistry and biology

Metabolism of proteins	[17]
Sulphur metabolism in microorganisms	[18]
viruses and bacteriophages	[19]
Sulphur metabolism in bones and teeth	[20]
Genetic studies	[21]
Immunology	[22]

3.2. Plant physiology [23]

4. RADIOLOGICAL PROTECTION

4.1. External irradiation

The maximum range of ^{35}S beta particles is 35 mg/cm^2; thus chemical glassware is quite sufficient for shielding. The resulting bremsstrahlung (for calculation see [29]) has a maximum energy of 0.16 MeV; the experimentally determined spectrum of the bremsstrahlung shows a maximum in the 15–40 keV interval of energy [30] depending on the atomic number of the absorber. If ^{35}S has been prepared by the (n, γ) reaction, ^{32}P will also be present. Appropriate parts of apparatus must therefore be shielded with 1 cm of Perspex and, for large ^{32}P activities, with lead. Remote handling is necessary as well, if ^{32}P is present in significant quantities.

4.2. Internal contamination

Sulphur-35 is classified [28] as a class 3 (moderate toxicity) isotope and has an effective half-life of 18 d [31].

4.3. Decontamination

^{35}S-sulphate can be removed from surfaces by dilute inorganic acids [32]; washing with water is sufficient for glass, Polythene, Plexiglass and linoleum [33]. A dilute carrier solution containing saponates is suitable for removal from clothing [33].

^{35}S-sulphide contamination should be removed with an alkaline solution of an oxidizing agent (hydrogen peroxide). Acid solutions must not be used to avoid the release of volatile hydrogen sulphide. For the same reason, an alkaline solution of an oxidizing agent must be employed in traps closing apparatus in which the labelled hydrogen sulphide may be formed. The wastes containing ^{35}S-sulphide should be thoroughly oxidized.

General methods for the treatment of active waste are applicable [34]; adsorption columns have been recommended [35].

5. SUMMARY OF PRODUCTION METHODS

The production of carrier-free ^{35}S is based on the nuclear reaction $^{35}Cl(n, p)^{35}S$. The application of the $^{34}S(n, \gamma)^{35}S$ reaction is very limited [36].

After chemical processing ^{35}S is present as sulphate. The methods for the preparation of ^{35}S-labelled sulphide or elementary sulphur are also reviewed.

5.1. Targets

The following targets are reported in the literature:
Sodium or potassium chloride.
Anhydrous ferric chloride.
Carbon tetrachloride.

Carefully dried Analar grade sodium or potassium chloride should be used. Ferric chloride is purified by sublimation [37]. Carbon tetrachloride is unsuitable for pile irradiation; this target was used for the preparation of ^{35}S, using radium-beryllium neutron sources [38-43] and is mentioned here for completeness only.

5.2. Chemical processes

5.2.1. Preparation of ^{35}S-sulphate

Sodium or potassium chlorides are the main targets used for the production of ^{35}S. Sulphur-35 formed in these targets is found as sulphate ion on dissolving the target in water and no additional oxidation is necessary. Sulphur-35-sulphide may also be expected [44-46] but is found only in slightly irradiated crystals [47-48], in contrast to highly irradiated ones used for production. Phosphorus-32 atoms arising in these targets react with water to give phosphates; compounds in lower oxidation states are formed under the conditions mentioned for ^{35}S-sulphides [49-51].

In all separation methods the short-lived activity (especially that of ^{24}Na or ^{42}K) is allowed to decay before the target is processed. Chlorine-36, which arises together with sulphur-35, is often processed as a valuable by-product [46, 52, 53].

The production methods reported are:

(a) Removal of cations from the dissolved targets

Cations are removed after dissolving the target in hydrochloric acid which is then evaporated, leaving ^{35}S-sulphate in the residue.

Removal of cation on cation exchange resin

The solution of the target is adjusted for concentration and passed through a column [46, 52, 54-59]. A column, 30-mm diam., containing 300 g of Amberlite IR-120, is used for processing 20 g of potassium chloride [57, 58]. Continuous [46] or vacuum [59] evaporation of hydrochloric acid may be employed.

Precipitation of cation

Hydrogen chloride gas is passed into a concentrated solution of the target which is cooled to -10°C. After saturation, the precipitated crystals of

potassium or sodium chloride are removed, the filtrate evaporated and the whole process repeated. The last traces of cations are removed on a small cation exchange column [36, 37, 60].

Extraction of cations

Irradiated ferric chloride is dissolved in concentrated hydrochloric acid in the presence of hydrogen peroxide. After dilution with water to 6 N hydrochloric acid, the ferric ions are repeatedly extracted with isopropyl-ether, when the ^{35}S remains in the aqueous phase [37].

In all the above processes the ^{32}P has to be removed either on a column of aluminium shavings [46, 59] or by co-precipitation with ferric hydroxide in alkaline solution [56-58].

(b) Isolation of ^{35}S from the dissolved targets

Sulphur-35-sulphates are adsorbed on appropriate materials leaving cations and chlorides in solution

Adsorption on alumina

The solution of the irradiated target in 0.5 N hydrochloric acid is passed through an alumina column. After washing with water the ^{35}S-sulphate is quantitatively eluted with 1 N ammonia, while 96% of the ^{32}P activity remains on the column. The ^{35}S-solution is then evaporated and cations removed on a small ion exchanger column [61]. Some improvements have been proposed (elution of ^{35}S by 0.1 N ammonia [62] or 0.05 N sodium bicarbonate [63], removal of aluminium traces by precipitation [64], etc.) and designs of production apparatus have been developed [33, 62-67].

Separation on anion exchanger resin

The 0.1 M solution of the target is passed through an Amberlite IRA-400 column. Phosphorus-32 is collected in the first fractions, when eluted by 0.1 M hydrochloric acid, and the pure ^{35}S-sulphate in the next fraction [68].

Adsorption on other materials

Barium sulphate columns [69] and iron hydroxide columns [70] have also been proposed for the separation of ^{35}S.

Co-precipitation of ^{35}S with barium chromate

Barium chromate is precipitated from a solution of the irradiated potassium chloride. The precipitate containing ^{35}S is dissolved in hydrochloric acid, the chromate ions reduced and the cations removed on a cation exchanger [53]. In the second process [71, 72], the barium chromate precipitate is dissolved in a warm solution of potassium carbonate, and the solu-

tion containing ^{35}S is evaporated with phosphoric acid and powdered copper. Sulphur-35-labelled sulphate is reduced to ^{35}S-sulphur dioxide at the end of evaporation and trapped in hydrogen peroxide solution as ^{35}S-sulphate.

Precipitation of ^{35}S in the presence of sulphate carrier

Barium sulphate is precipitated from a solution of the target containing sulphate carrier. The precipitate is then reduced to barium sulphide and the released hydrogen sulphide oxidized to sulphate [44, 73].

(c) Isolation of ^{35}S from the solid targets

The irradiated crystals of the alkali chloride are heated at 770°C in a stream of hydrogen. The ^{35}S-hydrogen sulphide is trapped in bromine water [74, 75]. Phosphorus-32 remains in the crystals.

5.2.2. Preparation of ^{35}S-sulphide

^{35}S-sulphide is usually prepared from separated ^{35}S-sulphate, although direct processing of irradiated targets has also been reported. The ^{35}S-sulphide is usually prepared with added carrier. All operations with water solutions of sulphide or hydrogen sulphide gas must be carried out in an inert atmosphere to prevent oxidation. Methods available for the reduction of ^{35}S-sulphate can be essentially classified as dry or wet ones, according to the conditions.

(a) Reduction of ^{35}S-sulphate in the solid state

Sulphur-35-labelled barium sulphate is mostly used as the starting material in the dry processes. The following reducing agents were reported:

Elementary carbon

For low activity samples [39, 41, 43, 76].

Hydrogen

Heating at temperatures of 850-1000°C for several hours [73, 77, 78]. See also Refs. [74, 75].

Metallic potassium

Heating in a sealed tube at 500°C for 2-3 min [79].

Aluminium powder

For low activity samples [80].

(b) Reduction of ^{35}S sulphate in solution

The wet reduction methods, proposed and worked out for use in analytical chemistry [81-86], have been applied to the preparation of ^{35}S-sulphides. The isotope effect has been observed in the reduction of sulphate, independent of the reduction mixture used [87, 88]. The heavier isotopes of sulphur are concentrated in the residue; it is therefore necessary to prolong the reduction for some time, even though the chemical yield has already reached 95%. The following mixtures were reported for ^{35}S-sulphate reduction:

Hydroiodic acid and formic acid [89]

Hydroiodic acid, formic acid and sodium hypophosphite

Heating at 80-90°C for 0.5 h [90]. This mixture is also applied directly for the solution of the irradiated target [91].

Phosphoric acid, potassium iodide, and sodium hypophosphite.

This mixture is used for direct processing of the target [56].

Hydroiodic acid, formic acid and red phosphorus

Heating at 90-150°C for 4 h [92]. A temperature of 150°C for 2 h is recommended for direct processing of the target [93, 94].

Phosphoric acid containing stannous ions

Heating at 200-250°C for 45 min [91, 95]. No volatile compounds except hydrogen sulphide have been observed during the reduction.

The processing of the ^{35}S-hydrogen sulphide obtained by one of the above methods depends on the product required. The absorption of ^{35}S-hydrogen sulphide in an aqueous solution of alkali hydroxide [90, 92, 95] or carbonate [56], in an ethanolic solution of alkali hydroxide [93], or in an ethanolate [56] were reported for the preparation of alkali sulphide; solutions of appropriate salts were used for preparing other metal sulphides [93].

5.2.3. Preparation of ^{35}S-elementary sulphur

^{35}S-elementary sulphur can be prepared by oxidation of ^{35}S-sulphide. Iodine in an acid solution [73, 78] or potassium ferricyanide in alkaline solution [39, 91, 92, 94] are used for oxidation. The direct introduction of ^{35}S-hydrogen sulphide into an oxidizing solution has been described [89, 94], but dropwise oxidation in the presence of a benzene layer with stirring was recommended to obtain the crystalline sulphur (after separation and evaporation of the benzene layer) [92].

6. RADIOASSAY

Relative measurement is recommended for routine work. To avoid discrepancies due to self-absorption losses, counting of the sulphur-35 activity in aqueous solutions is recommended. The counting equipment can be calibrated with standard solutions of sulphur-35, which are commercially available, their activity being estimated by 4π absolute counting.

The relative counting of the diluted product can be carried out using a thin window GM counter, or a scintillation counter. The presence of ^{32}P will of course cause erratic results.

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PROCEDURES

ATOMIC ENERGY OF CANADA LTD., CHALK RIVER, CANADA

1. GENERAL

Sulphur-35 is a beta emitter with a half-life of 87 d. It is produced in the reactor by the irradiation of a chloride target, $^{35}Cl(n, p)^{35}S$.

After irradiation, the sulphur-35 is chemically separated from the target, analysed and shipped as required.

2. EXPERIMENTAL PROCEDURE

Irradiation

Each irradiation consists of 18-20 g of potassium chloride sealed in a standard reactor capsule. The normal irradiation time is six months. The

usual yield is 12 to 15 Ci from each capsule, depending on the neutron flux. An appropriate number of capsules are held under irradiation to provide our normal and standby requirements.

Chemical treatment

The irradiated target is cooled for several days to allow the high energy ^{42}K to decay and is then entered to a glove box for processing. The capsule lid is removed and the contents poured into a small glass vessel where they are dissolved in approximately 100 ml warm distilled water. This solution is applied to a Dowex-50 cation exchange column at a flow-rate of about one drop per second. The column retains the potassium ion. The effluent contains the sulphur-35 and the chloride-35,-36 ions. This effluent is transferred to a distillation and condenser assembly where it is distilled to near dryness. The distillate contains the chlorine-35,-36 ions in HCl. The sulphur-35 remains in the distillation flask. This is treated with a small quantity of fuming nitric acid to destroy any organic material present, which is subsequently distilled off as waste material. The remaining residue is refluxed in a few millilitres of concentrated HCl, which is also distilled off to waste. The residue is dissolved in distilled water and drawn off as H_2SO_4 in dilute HCl, which is the final product.

Equipment

The equipment is enclosed in a lucite box fitted with rubber gloves since no additional shielding is required. The decayed capsule is transferred with extension tongs from the storage container to the first compartment in the box. The capsule is placed into a manually operated capsule opener located above a small dissolution vessel. The capsule contents are poured into this vessel where the initial dissolution step begins. The remainder of the equipment is a sealed glassware system consisting of the ion exchange column, distillation and condenser assembly and a burette for product dispensing. Reagents are added as required through header vessels located on top of the box. Liquids are transferred by means of small vacuum pumps and appropriate glass piping. Stopcocks are manually operated, using the rubber gloves. The box is exhausted via absolute filters. Waste solutions are collected inside the box in glass bottles.

3. ASSAY AND QUALITY CONTROL

Chemical

Small samples of the product are removed and analysed for total solids, non-volatile solids, oxidizing materials and metals. The acidity is adjusted to the appropriate normality. An archive sample is kept for record purposes.

Radiochemical

A 0.167 MeV beta particle is the only radiation emitted in the disintegration process. A suitable dilution of the active solution is made so

that a small quantity of activity can be dried on a stainless-steel counting disc.. This activity is then measured on a beta electroscope. The radiochemical purity is checked using a 512-channel analyser.

INSTITUTE OF NUCLEAR SCIENCE,
NATIONAL TSING HUA UNIVERSITY,
HSINCHU, TAIWAN, REPUBLIC OF CHINA

1. GENERAL

Sulphur-35 is prepared by the nuclear reaction $^{35}Cl(n, p)^{35}S$. Potassium chloride is used as the target. After irradiation, potassium chloride is converted to hydrogen chloride by passing through a cation exchange column. The hydrogen chloride is then removed by distillation. Sulphur-35 is obtained from the residue by leaching with dilute hydrochloric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	50 g of potassium chloride purified by recrystallization twice.
Irradiation container:	The target is wrapped with aluminium foil, and placed in the aluminium can 4.7 cm diam. × 9 cm.
Flux:	2.2×10^{12} n/cm^{2}s.
Irradiation time:	30 h.

Chemical treatment

The irradiated potassium chloride is allowed to cool for about a week before chemical processing. The target is dissolved in 1 litre of distilled water and the solution is passed through an ion exchange column. (4.0 cm diam. × 55 cm, Dowex 50 X12, 50 ~ 100 mesh conditioned in H^+ form.) The column is washed with an additional 200 ml of distilled water. The effluent is then transferred to the distillation unit to distil off the hydrogen chloride to dryness. After cooling, 100 ml of hydrogen peroxide (1 : 10) are added to the distillation flask and re-distilled to dryness again. One hundred millilitres of distilled water are then added to the flask to leach out the sulphur-35 from the residue. The leaching solution is then passed through an ion exchange column (1.2 cm diam. × 15 cm. Dowex 50 X12 conditioned in Fe^{3+} form). The effluent is condensed to appropriate concentration for use. About 80 mCi of sulphur-35 is obtained.

3. ASSAY AND QUALITY CONTROL

The chemical analysis of the product is carried out according to Oak Ridge National Laboratory Master Analytical Manual 90733811-5. The chemical form of sulphur-35 is determined by paper chromatography.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	$SO_4^=$ in HCl solution.
Concentration:	8.7 mCi/ml.
Specific activity:	Carrier-free.
Acidity:	0.03 N.
Radiochemical purity:	> 99%.

NUCLEAR RESEARCH INSTITUTE, ŘEŽ, CZECHOSLOVAK SOCIALIST REPUBLIC

1. GENERAL

The irradiated potassium chloride target is dissolved in dilute hydrochloric acid and poured onto an alumina column where the ^{35}S and ^{32}P are adsorbed. Sulphur-35 is then eluted with dilute ammonia and the cations are removed on a cation exchanger. The total yield is in the range of 80-83%. The process is based on the Yugoslav method [1]. This method has been used in Czechoslovakia since 1959. The product, ^{35}S-sulphuric acid, is used for the preparation of ^{35}S-compounds. The reduction of sulphates is carried out by a wet method using a reduction mixture prepared from stannous chloride and phosphoric acid [2].

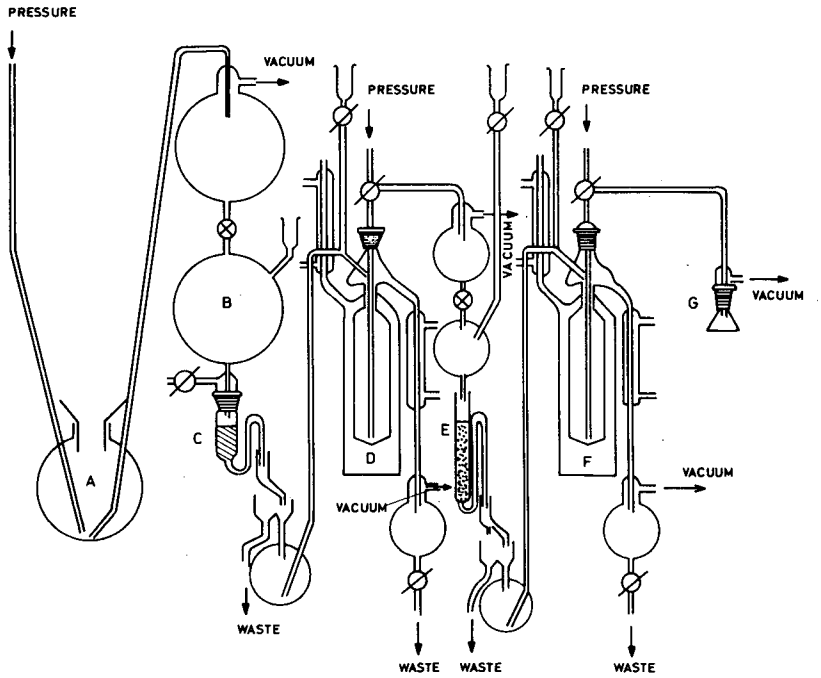
2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	KCl (R.G.) dried at 140°C for 10 h, 200 g for each irradiation.
Irradiation container:	Sealed aluminium container.
Irradiation conditions:	Irradiation for 480 h (over a period of 3 months) at a flux of 1×10^{13} n/cm^2 s; 200 g of the target will yield 3-4 Ci.

Chemical treatment

Two hundred grams of the irradiated target material are stored for 2 months for the ^{32}P to decay and then dissolved in 3 litres of 0.5 N hydrochloric acid, Fig. 1 (Flask A). This solution is transferred into the reservoir (B) and then passed through a chromatographic column (C) filled with 20 g of alumina. The column is washed with 1.5 litres of distilled water. The ^{35}S-sulphate fixed on the alumina is eluted by 100 ml of 0.2 N solution of ammonia and this solution is evaporated (evaporator D) almost to dryness. After dilution with 50 ml of 0.01 N hydrochloric acid, cations are removed on an ion-exchanger column (E) (10 g Dowex-50 in hydrogen form). The



A. Dissolving vessel for the irradiated target
B. Reservoir
C. Chromatographic column filled with alumina
D.F. Evaporator
E. Ion exchange column
G. Storage vessel.

FIG. 1. System for the routine production of ^{35}S

effluent is evaporated to dryness (evaporator F). To destroy organic compounds, 10 ml of 30% hydrogen peroxide (sulphate free) are added and evaporated. This operation is repeated. The ^{35}S-sulphate is washed out with 30-50 ml of distilled water and transferred into the storage vessel (G).

The alumina is prepared for use in the following manner. Alumina (for chromatographic purposes) is mixed with water and small particles are removed by decantation. The remaining larger particles are washed successively with 0.5 N hydrochloric acid, water, 1 N ammonia, water, and 0.5 N hydrochloric acid. The slurry of the alumina is then poured onto the column.

All the processes are carried out in a closed apparatus which is placed in a Perspex-shielded box. Transfer of the solutions is done by vacuum. The evaporators are heated with xylene (b.p. 140-143°C) to prevent overheating [3]).

3. ASSAY AND QUALITY CONTROL

The content of ^{32}P in the product of ^{35}S-sulphate is determined by the absorption of beta rays in aluminium. The content of ^{35}S is determined by

liquid counting, the counting assembly being calibrated with a standard solution of ^{35}S.

The ^{35}S-standards are prepared by 4π counting. Metallic impurities are determined by spectroscopic analysis, the sum of heavy metals is estimated by a sulphide test (Pharmacopoeia method).

4. CHARACTERISTICS OF THE FINAL SOLUTION

A solution of ^{35}S-sulphuric acid in weak hydrochloric acid (pH 3-4).

Radioactive concentration:	80-120 mCi/ml. For dispensing diluted to 20 mCi/ml.
Radioactive purity:	^{35}S content 99.9%, ^{32}P content 0.02%.
Radiochemical purity:	100%.
Chemical purity:	Heavy metals content below the sensitivity of sulphide test.
Specific activity:	> 2 Ci/mg S.

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CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

Sulphur-35 is formed by the (n, p) reaction on a KCl target, $^{35}Cl(n, p)^{35}S$. The recoil energy released during the reaction causes oxidation of the sulphur nucleus formed [1] and dissolution of the KCl target in water causes its hydration to H_2SO_4.

The separation between Cl^- and SO_4^{--} is carried out by the Rupp method [2, 3] consisting of the fixation of all the potassium on a cation exchange resin. The H_2SO_4-HCl mixture thus obtained is separated by distillation. After elimination of all the HCl, the residue contains $H_2{}^{35}SO_4$.

Irradiation of the targets in swimming-pool reactors in high fast-neutron fluxes leads to the formation of ^{32}P by the (n, α) reaction, $^{35}Cl(n, \alpha)^{32}P$. The method has therefore been subjected to a slight modification consisting of separation of ^{32}P mainly in the form of H_3PO_4 by absorption on a ferric hydroxide precipitate.

The advantage of this separation lies in the fact that it is unnecessary to await the disappearance of ^{32}P by decay.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: High purity potassium chloride powder (Johnson Matthey); impurity content less than 0.1%.

Irradiation conditions: Swimming pool reactors are preferred for the irradiation, owing to their substantial fast neutron flux. Targets are usually irradiated for three months.

Irradiation in MELUSINE: fast neutron flux of about $2\text{-}4\times10^{12}$ n/cm^{2}s.

Irradiation in TRITON: fast neutron flux of about $2\text{-}4\times10^{12}$ n/cm^{2}s.

Irradiation in SILOE: fast neutron flux of about $7\text{-}8\times10^{12}$ n/cm^{2}s.

Container: The same type as that for the irradiation of TeO_2, and the same dimensions.

Side reactions: $^{35}Cl(n, \alpha)^{32}P$
$^{35}Cl(n, \gamma)^{36}Cl$
$^{37}Cl(n, \gamma)^{38}Cl$.

Activity produced: For a fast flux of 10^{13} n/cm^{2}s the formation of ^{35}S per gram of KCl target is given below:

Irradiation (d)	^{35}S activity (mCi/g)	^{32}P activity (mCi/g)
30	55	2
60	99	3.7
90	130	4.8
saturation	261	9.6

Chemical treatment

Chemical separation

After the KCl target is placed in a dissolving flask, 200 ml of distilled water are poured in, and bubbling is caused in this solution by circulating a stream of nitrogen. The bubbling is stopped when the powder is wholly dissolved. The solution is then transferred to a co-precipitation vessel by means of a siphon connection.

Two millilitres of 110 vol. hydrogen peroxide, 3 drops of 4 N HCl and 5 ml of the water used for rinsing the piping are added and the solution is heated until boiling begins. It is left to cool and 1.5 ml of a 1% ferric nitrate solution are added. After stirring, a solution of 5 N soda is added drop by drop until total precipitation of $Fe(OH)_3$ has occurred. The solution is stirred, heated and filtered by suction through a fritted glass up to a siphon connection. The precipitate is washed with 3 portions of 20 ml of water.

The solution and the washing water are collected in a neutralization vessel into which a solution of 4 N HCl is poured drop by drop until a neutral pH is attained.

The solution is passed over two Dowex-50 columns. Each column is then washed with 1 litre of distilled water. The quantity of liquid is then reduced by boiling in a concentrator vessel.

The use of an evaporator enables the solution to be reduced almost to dryness (about 1 to 2 ml). One millilitre of 110 vol. hydrogen peroxide and 1 ml of water are added three times, and each time they are evaporated almost to dryness. Lastly, the solution is made up with two portions of distilled water in order to yield a final volume of 100 ml.

A solution of $H_2{}^{35}SO_4$ in a solution of HCl of pH ~ 2 is thus obtained.

Apparatus (Figs. 1, 2)

This consists solely of small laboratory glassware.

Evaporation vessel: this has a fritted glass in its lower part permitting both the passage of a nitrogen stream and the filtration of the solution.

Neutralization and co-precipitation vessels: graduated every 10 ml; they are emptied by introducing a fritted glass plunger linked to a siphon connection.

Dowex-50 resin columns - made of glass.

Concentrator and evaporator: heated by an infra-red heater.

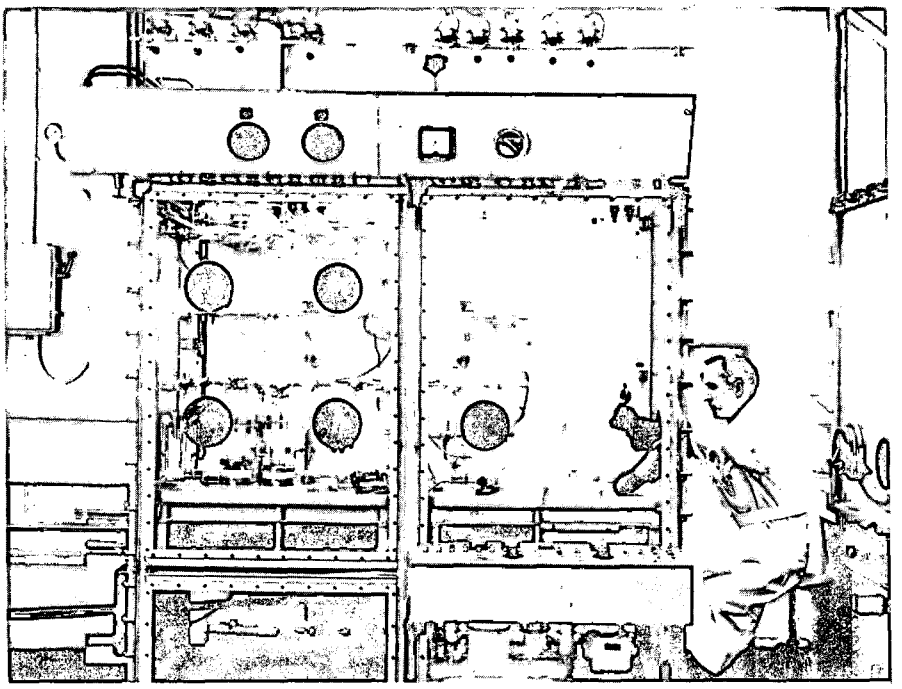
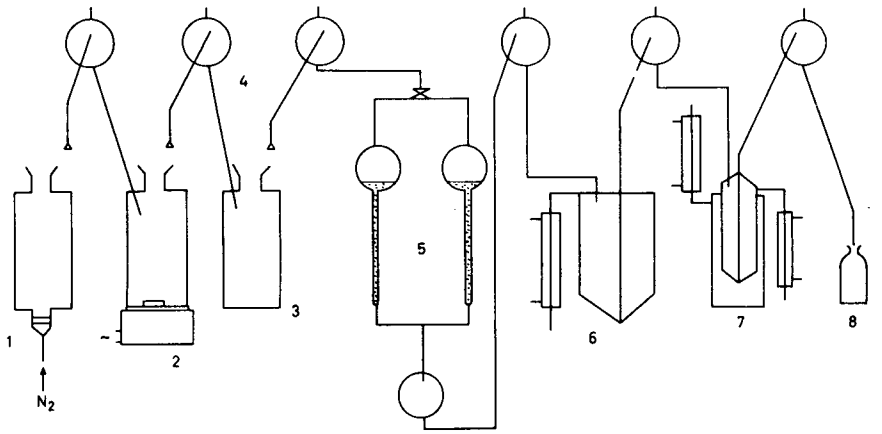


FIG. 1. Apparatus for the production of ^{35}S



1. Dissolving vessel
2. Precipitation vessel
3. Neutralization vessel
4. Siphon connections with fritted plate mobile plunger
5. Dowex-50 resin columns
6. Concentrator vessel
7. Evaporator vessel
8. Bottle for storage of $H_2{}^{35}SO_4$

FIG.2. ^{35}S flowsheet

Investigation of chemical forms

Activity per unit volume and the absence of impurities are determined by radioactive measurements. In particular the ^{32}P content must be less than 0.01%.

Determination of the dry extract, whose weight must not exceed 1 mg/ml.

A γ-spectrum analysis to determine the absence of γ-emitting impurities.

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ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

The irradiation of crystalline potassium chloride in a reactor gives rise to ^{35}S by (n, p) reaction on ^{35}Cl. The other isotopes produced in the target are ^{32}P, ^{42}K, ^{36}Cl and ^{38}Cl. A post-irradiation cooling of one week ensures the complete decay of the short-lived activities of ^{42}K and ^{38}Cl. The ^{35}S is separated by selective adsorption on an alumina column, from which it is then eluted out with dilute ammonia solution. The cationic impurities like aluminium are then removed by precipitation as hydroxides.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	60 g of reagent grade potassium chloride.
In APSARA:	Container type "A" can (screw-capped 1 S aluminium can of 73 mm height and 26.5 mm diam.).
	Flux: 3×10^{12} n/cm^2 s.
	Irradiation period: 3 months.
Target:	60 g of reagent grade potassium chloride.
In APSARA:	Container type "A" can (screw-capped 1 S aluminium can of 73 mm height and 26.5 mm diam.).
	Flux: 3×10^{12} n/cm^2 s.
	Irradiation period: 3 months.
In CIR:	Container type "C" can (cold-welded 2 S aluminium can of 44 mm height and 22 mm diam.).
	Flux: 4-6 $\times 10^{13}$ n/cm^2 s.
	Irradiation period: 3 months.

Chemical treatment

The irradiated KCl is allowed to cool for one week and then it is dissolved in 0.1 N HCl. The solution is passed down an alumina column (1 cm^2 × 6 cm length, in the chloride form, washed with 0.1 M HCl) and the effluent is collected and set aside for ^{36}Cl processing. The column is washed with 100 ml of 0.1 M HCl followed by 100 ml of distilled water.

The ^{35}S is then eluted with 25 ml of 1 M ammonia. To the eluate 1.5 ml of 9 M HCl is added and the solution is evaporated to a small volume, allowed to cool and filtered through a fine sintered-glass filter. The filtrate is evaporated to the point of dryness. The residue is treated with strong nitric acid to destroy ammonium chloride. After evaporation, the mixture is digested with strong HCl and again evaporated to near dryness. Finally the ^{35}S activity is leached out with 0.1 M HCl solution.

For the recovery of ^{36}Cl, the effluent potassium chloride solution from the alumina column is distilled with the requisite amount of 6 M H_2SO_4 through a small rectifying column, and the ^{36}Cl is recovered as the approximately 20% constant boiling HCl solution.

3. ASSAY AND QUALITY CONTROL

(a) The activity is assayed by using a liquid scintillation counter having a known efficiency.

(b) The absence of heavy metal impurities is confirmed by the hydroxide and sulphide precipitation tests and also by spot tests.

(c) The radiochemical purity is ascertained as follows:

The aluminium absorption curve for the test sample is compared with that of the standard.

Aliquots of the stock solution are taken. The ^{35}S is precipitated as

$BaSO_4$, the ^{36}Cl as AgCl and the precipitates are filtered and the filtrates are assayed for other activities, if any.

(d) The acidity is determined by titration against standard alkali.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity:	Carrier-free.
Chemical form:	$H_2{}^{35}SO_4$.
Acidity:	0.1 M HCl.
Radiochemical purity:	Greater than 99% as sulphate.
Radioactive concentration:	1 - 200 mCi/ml.

MINISTRY OF DEFENCE, ATOMIC ENERGY COMMISSION,
SOREQ RESEARCH ESTABLISHMENT, YAVNE, ISRAEL

PRODUCTION OF ^{35}S AS CARRIER-FREE $H_2{}^{35}SO_4$

1. GENERAL

Irradiation of KCl produces ^{35}S by the $^{35}Cl(n, p)^{35}S$ reaction. Other activities produced are ^{32}P, ^{36}Cl, ^{42}K. The ^{35}S is adsorbed on activated alumina, together with the ^{32}P which is present as phosphate. Chlorine and potassium are not adsorbed. The ^{35}S is then eluted with a 0.2 N NH_4OH solution. The method is based on the process developed at the Boris Kidrič Institute in Yugoslavia [1].

2. EXPERIMENTAL PROCEDURE

Irradiation

The target material is KCl (AR) dried overnight at 110°C. The target amount is 20 g, distributed in three silica ampoules of approximately 12 cm^3 each. The ampoules are sealed, put into aluminium irradiation cans and irradiated for 100 h at a flux of 2.5×10^{13} $n/cm^2 s$ in the Israel Research Reactor 1, and allowed to decay for 1 week.

Chemical treatment

This is done in a glove-box provided with tongs.

Preparation

Prepare two 1.5 cm high, 0.6 cm diam. alumina columns (Fluka alumina, 100-200 mesh, activity 1, can be used).

Pass 100 ml 1 N HCl through each column. Wash with distilled water. Pass 50 ml 1 N NH_4OH. Wash with distilled water. Pass 100 ml 0.5 N HCl.

Prepare a 0.6 cm diam., 5-cm-long Dowex-50 (50-100 mesh) column.

Pass 200 ml 3 N HCl through a Dowex-50 column. Adjust the pH with water.

Processing

(a) Transfer irradiated samples to glove-box.
(b) Crush ampoules under 50 ml water. Heat gently to dissolve.
(c) Pass solution to beaker. Rinse crusher with 10 ml water and add to beaker. Repeat rinsing.
(d) Add 67 ml of 1 N HCl to beaker and 0.2 mg of phosphate ion.
(e) Pass solution through alumina column, at a flow-rate of up to 4 ml/min.
(f) Pass 50 ml of 0.5 N HCl, then wash twice with 100 ml H_2O each time. Eluates from the last two steps go to waste.
(g) Pass 20 ml of 0.2 N NH_4OH.
(h) Take a sample from the eluate. Check the ^{32}P to ^{35}S ratio. If no further purification is necessary, follow steps (m) to (s) below. If further phosphorus/sulphur separation is required:
(i) Add 28 ml 1 N HCl to ammonia eluate.
(j) Pass through the second alumina column.
(k) Wash twice with 100 ml H_2O.
(l) Pass 20 ml 0.2 N NH_4OH.
(m) Receive into 25 ml of 0.2 N HCl.
(n) Pass through a Dowex-50 column.
(o) Wash with 25 ml H_2O. Take a sample for calibration.
(p) Add 300 mg NaCl.
(q) Neutralize to pH 7.
(r) Dispense into bottles.
(s) Sterilize at 120°C for one hour.

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JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process for ^{35}S is based on the irradiation of a potassium chloride target. After irradiation, ion exchange treatment is used to remove the potassium and phosphate ions.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	10 g KCl (JISGR[1]).
Container:	Cold-welded-type aluminium capsule.
Flux:	$\sim 2 \times 10^{13}$ n/cm^2 s (Reactor JRR-2).
Irradiation time:	130 h.
Side reactions:	Formation of ^{32}P, ^{42}K, ^{38}Cl and ^{36}Cl.

Chemical treatment

The apparatus for the production is shown in Figs. 1 and 2.
Cut the aluminium capsule.

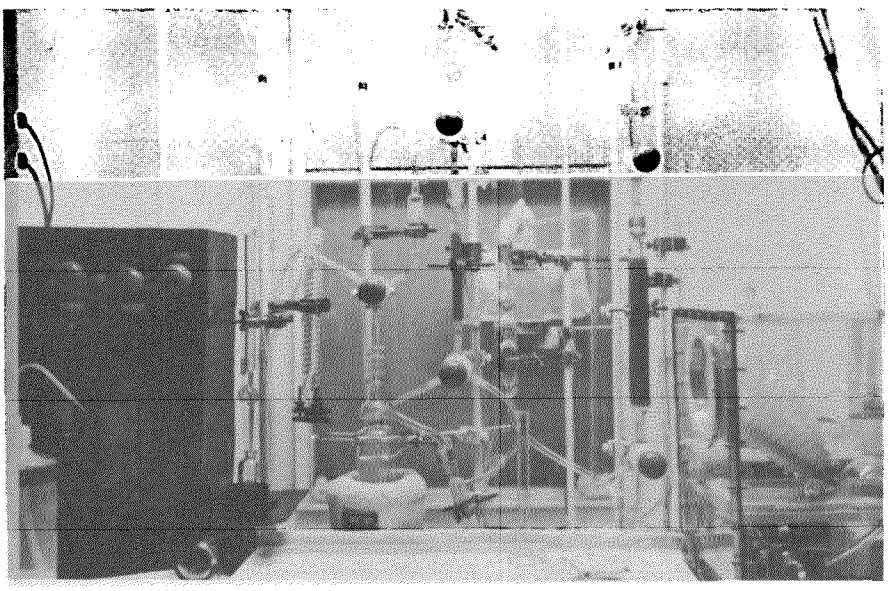


FIG. 1. Apparatus for the production of ^{35}S

Place the irradiated target into the dissolving vessel (a), Fig. 2, then add 150 ml distilled water to dissolve the target by gentle heating.

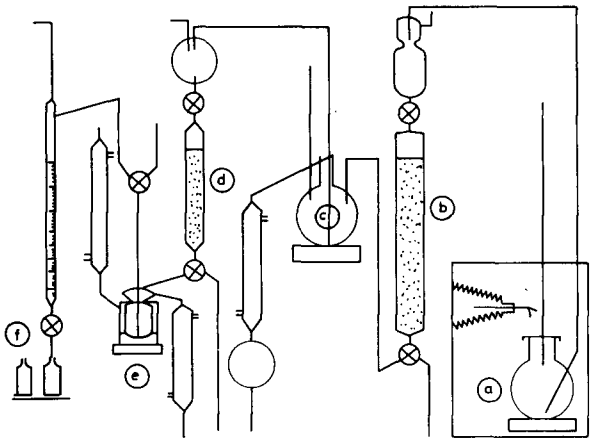
Pass the dissolved solution through the cation exchange resin (b) to remove K^+ ions.

Concentrate the effluent in the evaporator (c), then add hydrogen peroxide to decompose the organic materials.

Pass the solution through the anion exchange resin in the iron form (d) to remove PO_4^{3-} ions.

Concentrate the effluent in the evaporator (e), then add hydrogen peroxide to decompose the organic materials.

[1] Japan Industrial Standard Grade Reagent.



a. Dissolving vessel
b. Cation exchange resin column
c. Evaporator 1
d. Cation exchange resin column of Fe^{3+} form
e. Evaporator 2
f. Bottles of product

FIG.2. Arrangement of apparatus for ^{35}S production

Add 20 ml 0.1 N HCl and warm gently.

Distribute the solution into the sample bottles with a rubber inner cap and aluminium outer cap.

3. ASSAY AND QUALITY CONTROL

The routine determination of total solids, non-volatile materials and heavy metals is carried out by the following procedures:

Total solid:	Weighing after the evaporation and heating to 110°C of 1 ml sample solution.
Non-volatile materials:	Weighing after the evaporation and heating to 600°C of 1 ml sample solution.
Heavy metals:	Comparison of colour development with lead standard by the addition of hydrogen sulphide.

Routine assay is carried out with a $2\pi\beta$ proportional counter, and the calibration is made by a $4\pi\beta$ counter.

The amount of carrier in the product is made by the spectrophotometric method by methylene blue.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	H_2SO_4 in HCl solution; acidity ~0.1 N.
Radiochemical purity:	Over 99%.
Specific activity:	Carrier-free.
Concentration:	> 1.0 mCi/ml.

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Sulphur-35 is produced by irradiating potassium chloride in a fast neutron flux, $^{35}Cl(n, p)^{35}S$. The target material is dissolved in water, and potassium is removed by means of cation exchange resin. Any excess of hydrochloric acid produced during the ion exchange process is removed by evaporation.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	KCl, Merck, p.a.
Amount:	20 g.
Time of irradiation:	3 months.
Container:	Aluminium can.
Flux:	Fast neutron flux $1-2\times10^{11}$ n/cm^2 s.
Side reactions:	$^{35}Cl(n, \alpha)^{32}P$ (14.2 d).
	$^{35}Cl(n, \gamma)^{36}Cl$ (3×10^5 yr).
	$^{37}Cl(n, \gamma)^{38}Cl$ (37.3 min).
	$^{41}K(n, \gamma)^{42}K$ (12.4 h).

The target is stored a few days before processing to remove foreign activity due to ^{38}Cl and ^{42}K.

Chemical treatment

The irradiated potassium chloride is dissolved in water and transferred to a column filled with Dowex-50 cation exchange resin. Sulphur-35 present as SO_4^{--} (together with small amounts of ^{32}P and ^{36}Cl), passes through, and the solution is evaporated to dryness. The excess of hydrochloric acid, together with ^{36}Cl is then removed. After dissolution in water ^{32}P can be removed by passing the solution through a column packed with aluminium shavings.

3. ASSAY AND QUALITY CONTROL

Radioactivity: Geiger-Müller counting of samples evaporated on polyethylene foils.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control: emission spectrography, dry matter content (evaporation).
Radiochemical purity control, radiochromatography.
Toxicity and pyrogen control, test on animals.

All products are subject to individual inspection and approval by pharmaceutical personnel.

4. CHARACTERISTICS OF THE FINAL SOLUTION

SO - sulphate in neutral solution.

Radioactive concentration:	10-15 mCi/ml.
Isotopic purity:	Greater than 99%.
Specific activity:	Greater than 100 mCi/mg S.
pH:	5-7.
Total solids:	Less than 1 mg/ml.
Chemical purity:	Metals, spectrographically determined, less than 10 μg/ml.

SSI - sulphate in neutral isotonic solution, sterilized.
Total solids: About 10 mg/ml.
Other specifications as for SO.

INSTITUTE OF NUCLEAR RESEARCH, SWIERK NEAR OTWOCK, POLAND

1. GENERAL [1-15]

Sulphur-35 is isolated from an irradiated KCl target. The isolation is carried chromatographically on two columns. The first is filled with Al_2O_3 and allows ^{35}S and ^{32}P to be separated from Cl and ^{42}K and the main part of KCl. The second column, filled with a cation exchange resin, allows purification of the final product; on this column the remaining K^+ and other metallic impurities are separated. The overall yield of the process is approximately 85-97%. The final product gives carrier-free sulphuric acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	20 g KCl, analytical grade.
Flux:	2×10^{13} n/cm^2 s.
Time of irradiation:	6 weeks (reactor working 86 h/week at full power).
Container:	Aluminium capsule closed by welding.
Activity obtained:	500 mCi ^{35}S.

Chemical treatment

Twenty grams of irradiated KCl target are dissolved in 0.1 N HCl to obtain 1 N solution in respect to KCl. This solution is introduced to an Al_2O_3

column (diam. 9 mm, length 100 mm, containing 3.5 g Al_2O_3) at a rate of 1 ml/min. The column is then washed with 10 ml of deionized water. This volume of water allows potassium to be removed from the column. The column is then washed with 15 ml of NH_4OH solution, pH 11.0 and with 10 ml of deionized water. A fraction of between 1/6 and 1/12 ml eluate is collected. This fraction contains practically the whole amount of sulphur (in the form of $^{35}SO_4$) and K^+ (0.49 - 0.70 mg/ml). The fraction is introduced to an Amberlite IR 120 column H^+ form, 9 mm diam., 10 cm long, flow-rate 1 ml/min. Then the column is washed with 10 ml of deionized water and the whole eluate is transferred to a flask equipped with a reflux condenser. One millilitre of 10% H_2O_2 is added and the mixture is refluxed for 2 h to destroy traces of organic substances eluted from the column. After cooling the solution is transferred to a vessel equipped with a dosing pipette. The product gives $H_2{}^{35}SO_4$ in hydrochloric acid, pH 2-3.

3. ASSAY AND QUALITY CONTROL

The activity is measured in a well-type scintillation counter N. S. T. against a standard prepared by 4π counting. The chemical purity is checked spectrally and, for K, by flame photometry.

The radiation purity is checked by beta and gamma spectrometry.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity: 20 mCi/ml.
Radiation purity: 99.9%.
Impurities: As, Pb 5 μg/ml.

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INSTITUTE OF ATOMIC PHYSICS, BUCHAREST, ROMANIA

PRODUCTION OF CARRIER-FREE ^{35}S IN THE FORM OF SO_4^{2-}

1. GENERAL

The production of ^{35}S is based on the (n, p) reaction of the KCl target. Radiosulphur in the form of bisulphate is absorbed over 99% on an alumina column. Finally ^{35}S is eluted with ammonia 1 M.

2. EXPERIMENTAL PROCEDURE [1-3] (Fig. 1)

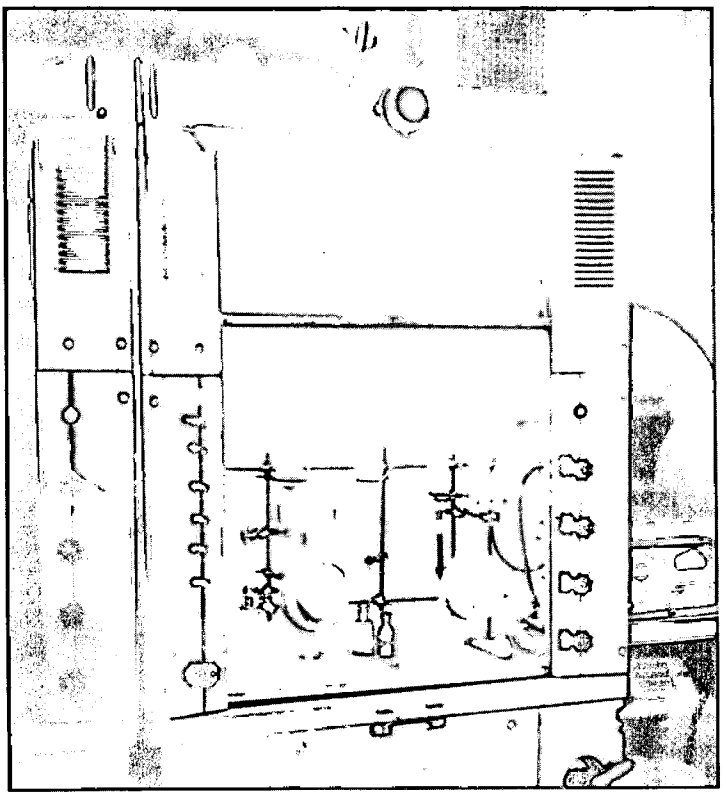

FIG. 1. Cell for ^{35}S separation

Irradiation

Target:	KCl p. a. The amount depends on the request.
Flux:	1×10^{13} n/cm^{2}s.
Time of irradiation:	400 h.
Container:	Aluminium cans.

Chemical treatment

After irradiation the target is dissolved in distilled water and is acidified with hydrochloric acid, HCl 0.5 M. It is then passed through an activated acid alumina-column at the standard speed of 12 cm^3/cm^2 min.

After the column is washed with distilled water, ^{35}S is eluted with ammoniac 1 M.

For the production of $H_2{}^{35}SO_4$, the ammoniacal solution is neutralized with HCl to obtain a pH of about 1 and passed through an Amberlite IR. 120 column. For the production of alkaline sulphates the solution eluted is neutralized with alkaline hydroxides.

For the production of $Na_2{}^{35}S$, $Na_2{}^{35}SO_4$ is reduced with a mixture of H_3PO_4 and $SnCl_2$.

3. ASSAY AND QUALITY CONTROL

Radiochemical purity is controlled by paper radiochromatography.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Prepared to order.

PRODUCTION OF ELEMENTARY ^{35}S

1. GENERAL

The production of elementary ^{35}S is based on the (n, p) reaction of chlorine targets. The separation of ^{35}S is carried out by trichloroethylene extraction.

2. EXPERIMENTAL PROCEDURE [4]

Irradiation

Target:	KCl dried and degassed.
Flux:	1×10^{13} $n/cm^2 s$.
Time of irradiation:	400 h.
Container:	Quartz ampoule sealed in vacuum.

Chemical treatment

After irradiation the target of KCl is heated for 4 h at 500°C. The target is then refluxed with trichloroethylene for 6 h in a Soxhlet apparatus.

^{32}P is removed by washing the trichloroethylene solution with HCl 0.1 N.

3. ASSAY AND QUALITY CONTROL

The radiochemical purity is controlled by paper radiochromatography.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Prepared to order.

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JUNTA DE ENERGIA NUCLEAR, MADRID, SPAIN

1. GENERAL

The production process of ^{35}S is based on the irradiation of a potassium chloride target and co-precipitation on barium chromate. Carrier-free $^{35}SO_2$ is then distilled in the presence of phosphoric acid and powdered copper [1].

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	60 g potassium chloride, of analytical-grade quality.
Container:	Leak-tight aluminium container, 24×26 mm diam.
Flux:	5×10^{11} n/cm^{2}s (JEN-1).
Irradiation time:	Depends on requirements; at least 8 weeks; possible yield is 250 mCi.

Chemical treatment

Separation method

The ^{32}S is co-precipitated from the irradiated potassium chloride, then $^{35}SO_2$ is distilled. The apparatus for the production of ^{35}S is shown in Figs. 1 and 1a. The process comprises the following steps.

Dissolve 30 g irradiated KCl in 150 ml of distilled water in the vessel (A). The solution is heated with the epiradiators EP-1 and EP-2, while air is injected under pressure through the filter (P) to stir the solution.

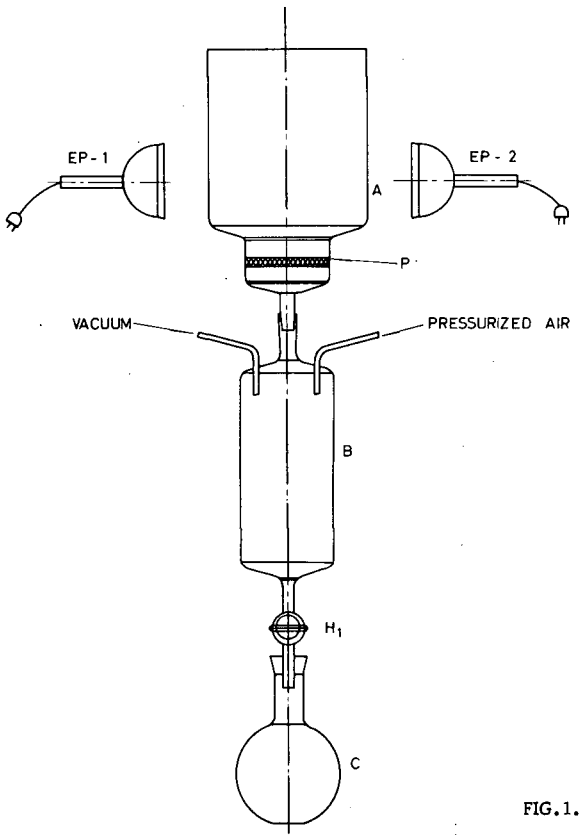

FIG. 1. Apparatus for the production of ^{35}S

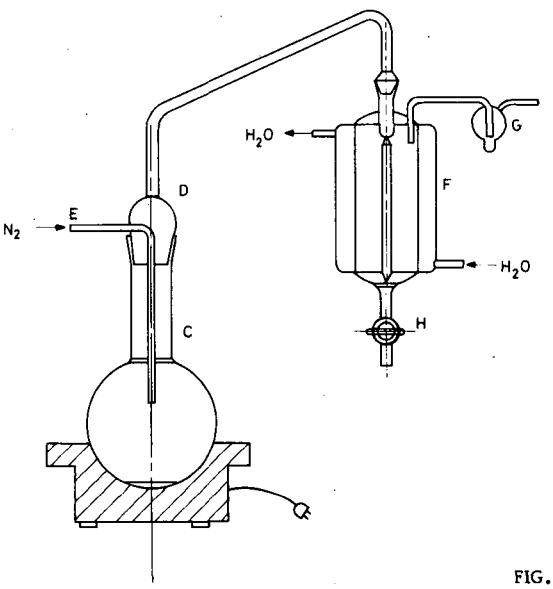

FIG. 1a. Apparatus for the production of ^{35}S

Add 5 g $BaCl_2$ and 0.3 ml 5% K_2CrO_4 aqueous solution while the solution is still being stirred. Heat the solution for 15 min, then allow to cool for 45 min. Filter the solution under vacuum.

Wash the precipitate three times with 50 ml 96% ethyl alcohol. Apply vacuum for 15 min to remove alcohol.

Replace the collector (B) by an identical fresh, clean and dry collector. The $BaCrO_4$ precipitate is washed with 10 ml of a warm 3 N K_2CrO_3 solution, applying compressed air for the stirring. Filter the solution after 5 min under vacuum, and wash the precipitate with 20 ml distilled water. Repeat this operation three times. The solution, with a final volume of 90 ml, is slowly decanted into the flask (C) which contains the reducing mixture.

Preparation of the reducing mixture. Before the above solution is added, 15 ml of phosphoric acid (85%) and 5 g of powdered copper are heated in the flask (C) until the fumes of phosphorous pentoxide appear.

Heat the flask (C) containing the reducing mixture and 90 ml of the active solution to expel some of the water and all of the CO_2. Flask (C) is then connected to the collector (F), and the distillation is continued under a weak nitrogen stream; 20 ml of 1% hydrogen peroxide are placed in the collector (F). When the fuming of phosphorous pentoxide begins in the flask (C), stop heating, but continue the nitrogen stream until complete cooling of the flask is reached.

Any excess of hydrogen peroxide present in the solution in the collector (F) is removed by boiling. Add hydrochloric acid to bring the solution to 0.1 N.

If ^{35}S is collected in the form of sulphite, 20 ml 1 N NaOH are placed in the collector (F).

If an isotonic solution of pH 7 is desired, the hydrochloric acid solution is neutralized with a suitable buffer such as that used for ^{32}P.

Apparatus

The operation is carried out in an ordinary glove box where the equipment shown in Figs. 1 and 1a is contained.

3. ASSAY AND QUALITY CONTROL

Determination of chemical purity is made by emission spectrography as in the case of ^{32}P preparations. Radioactive purity is also determined as for ^{32}P. The chemical form of the product is determined by electrophoresis [2] by the technique described in the section on ^{32}P.[1] Autoradiography of the paper subjected to electrophoresis is performed by the Duncombe technique [3].

Measurement of activity is made by comparison with standards. For a product of relatively high activity, the ionization chamber described in the section on ^{32}P [1] is used. For activities of less than 1 mCi a liquid scintillation counter, an ionization chamber or a Geiger-Müller counter (in the gaseous phase) is employed. The latter two methods are used more frequent-

[1] Provided by the Junta de Energía Nuclear, Madrid.

ly for labelled compounds. An error of less than 10% in the activity measurements is allowed.

4. CHARACTERISTICS OF THE FINAL SOLUTION

^{35}S - Sulphuric acid solution, carrier-free, non-injectable

Sulphuric acid solution in 0.1 N HCl meeting the following specifications:

Chemical purity:	The results of a typical analysis are: Elements not detected (sensitivity 0.2 μg/ml): As, Cd, Cr, Fe, La, Mn, Ni, Pb, Sn and Te. Elements with a concentration of less than 1 μg/ml: Al, B, Si. Ditto between 0.5 and 10 μg/ml: Mg. Ditto between 4 and 20 μg/ml: Ca. Dry residue: less than 0.5 mg/ml.
Radioactive purity:	^{35}S content > 99.5%.
Radiochemical purity:	Sulphuric acid content > 99%.
Radioactive concentration:	Maximum 25 mCi/ml.

Sodium sulphate - ^{35}S solution, injectable

Neutral (pH 7), isotonic, sterile and pyrogen-free solution of sodium sulphate meeting the following specifications:

Chemical purity:	See above.
Radioactive purity:	^{35}S content > 99.5%.
Radiochemical purity:	Sulphate content > 99%.
Radioactive concentration:	1-10 mCi/ml.
Sterility:	Sterilization is carried out in an autoclave at 120°C for about 1 h.
Analysis of pyrogens:	See the Section on ^{32}P.[1]
Isotonicity:	Adjusted by means of conductimetric measurements.

PATENT

Sulphur-35

Spanish patent No. 278.692: ORTEGA, J., Technique for the preparation of carrier-free radioactive sulphate and sulphite (^{35}S).

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1. GENERAL

Sulphur-35 is produced by the (n, p) reaction in a KCl target, $^{35}Cl(n,p)^{35}S$. Radioisotopes of potassium and chlorine are also produced in the target by the (n, γ) reaction, and are removed by ion exchange and distillation. Processed carrier-free or high-specific-activity ^{35}S is prepared as either H_2SO_4 in HCl solution, BaS in $Ba(OH)_2$ solution, or as elementary sulphur in benzene.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: KCl.

Chemical treatment

Apparatus

Glass distillation equipment (2 to 3 litres), an ion exchange column, tube furnace assembly, and conversion equipment (Figs. 1-4) are used in processing. Processing facility and shielding required: hot hood.

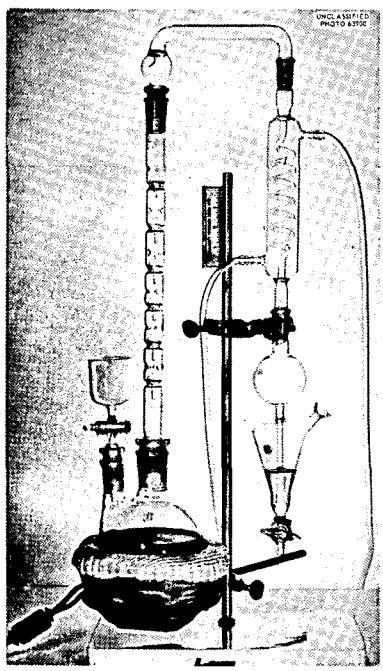

FIG. 1. Glass distillation equipment with reflux condenser

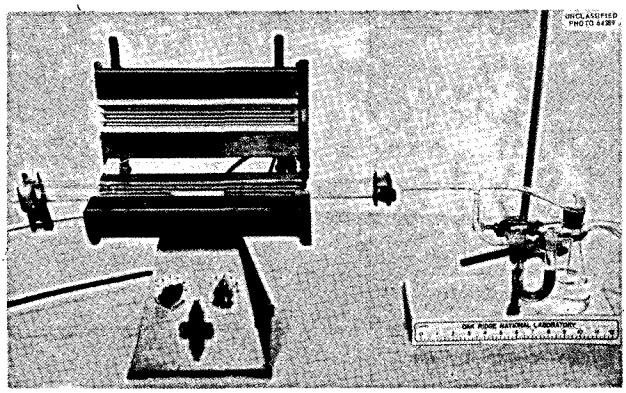

FIG. 2. Tube furnace assembly with scrubber

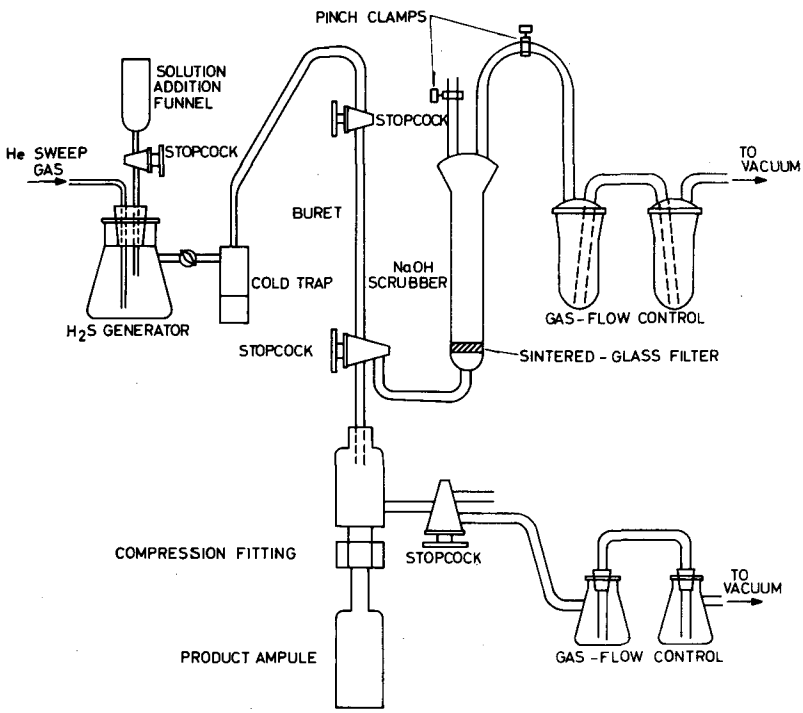

FIG. 3. Sulphur-35 barium-sulphide conversion equipment

Processing of ^{35}S for H_2SO_4 form

The irradiated target is dissolved in 200 ml of distilled water and diluted to 1 litre. An ion exchange column is prepared with Amberlite IR-120 resin by washing the column with 6 M HCl followed by a water wash until the column effluent is neutral. The column should contain ~ 50% excess capacity. The KCl-H_2O solution is transferred into the head flask and the

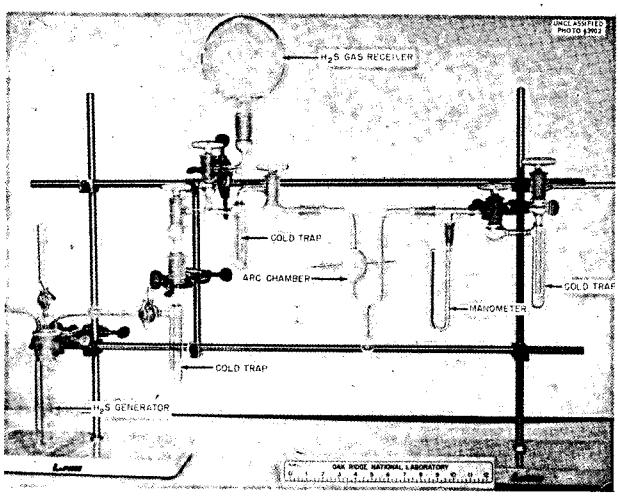

FIG. 4. Elemental ^{35}S conversion equipment

column flow rate is adjusted to ~1 ml/min. Potassium ions remain on the column; ^{36}Cl and ^{35}S pass through the column as H_2SO_4 and HCl. The column is washed with 1 litre of water to ensure complete removal of ^{36}Cl and ^{35}S. Effluents are distilled, and distillates discarded until HCl appears (in distillate). The removal of HCl is determined by testing with litmus paper. After acid appears in distillate, distillation is continued until no more than 0.5 ml remains in the flask. Removal of the last traces of HCl without loss of H_2SO_4 is accomplished in this step. The flask, therefore, is not permitted to become dry. Sulphur is recovered from the distillation residue after the removal of ^{36}Cl. About 10 ml of 16 M HNO_3 is added to the boiling solution. This step is repeated three times to remove organic material. About 10 ml of 12 M HCl is added and fumed. This step is repeated three times to remove nitric acid. As a final step, the volume is adjusted to 50 ml with water.

Processing of ^{35}S for BaS form

Two curies of ^{35}S as H_2SO_4 in HCl are treated with $BaCl_2$ solution to yield $BaSO_4$. Barium sulphate is filtered on a fine filter paper and washed with water. The filtrate is discarded. The filter paper containing precipitate is placed in a platinum boat and heated in a quartz tube under a stream of hydrogen for ~16 h at red heat. This step converts $BaSO_4$ to BaS. The platinum boat containing BaS is transferred to a gas-generation flask and sufficient concentrated H_3PO_4 is added to cover the boat. The H_2S generated is swept from the flask with a stream of nitrogen at a flow-rate of ~1 cm^3/min into a scrubber containing $Ba(OH)_2$ solution. The system is protected from air at all times to prevent conversion of the sulphide to sulphate or formation of $BaCO_3$ in the scrubber solution. When H_2S generation is complete, as shown by the cessation of bubbles from the platinum boat, the gas generator is swept with nitrogen for an additional hour and the scrubber system is valved off. The solution in the scrubber is held as a storage container for the ^{35}S product, which is eventually packaged in sealed ampoules evacuated and filled under nitrogen atmosphere.

Processing of ^{35}S for elementary sulphur product

Yield: 80%

Barium sulphide is loaded into a reaction flask and enough concentrated H_3PO_4 is added to the reaction flask to cover it. The flask is swept with helium at a flow-rate of ~ 1 cm^3/min. The H_2S generated is transferred to a cold trap maintained at a liquid-nitrogen temperature, where the H_2S is collected. The reaction flask is valved off at the completion of the H_2S generation, and the cold trap isolated. The H_2S gas receiver and warm trap are evacuated to release H_2S to the gas receiver. The residual H_2O and H_3PO_4 remain in the trap. Hydrogen sulphide is recycled.

(Conversion to elementary sulphur is made by decomposition of the H_2S in a glow discharge formed between two platinum electrodes in a low-pressure chamber. A Tesla coil is used as a high-voltage power supply. The chamber is maintained at low pressure by pumping with a high vacuum pump. A cold trap is installed between the pump and chamber to recover H_2S that is not decomposed in the arc chamber. Elementary sulphur collects on the sides of the arc chamber and on the electrodes. Hydrogen sulphide gas collected in the cold trap between the chamber and pump is recycled back to the gas receiver by evacuating the receiver and warming the cold trap.)

The recycle is repeated until all the H_2S is decomposed to elementary sulphur. Elementary sulphur is washed from the arc chamber and electrodes with warm benzene and transferred to a product bottle.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for total solids, molarity of HCl, radiochemical purity, ^{35}S concentration, nonsulphide sulphur, and molarity of $Ba(OH)_2$, according to ORNL Master Analytical Manual (TID-7015) procedure No. 9 0733811.

The precision and accuracy of the ^{35}S assay are:

Calibration by 4π β-γ coincidence counter.

Routine assay by liquid scintillation counter.

Estimated limit of error in disintegration-rate concentration of routine shipment, 10%.

Precision, 3%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed ^{35}S in various forms is delivered as stock items, and the specifications of interest are:

Chemical form:	H_2SO_4 in HCl solution.
Acidity:	~ 0.1 N.
Concentration:	> 1 mCi/ml.
Total solids:	< 1 mg/mCi.
Specific activity:	Carrier-free.
Radiochemical purity:	> 99%.
^{32}P:	< 0.1%.

Chemical form:	BaS in $Ba(OH)_2$ solution.
Basicity:	~ 0.15 N.
Concentration:	> 5 mCi/ml.
Specific activity:	≅ 10 000 mCi/g of S.
Radiochemical purity:	> 99%.
^{32}P:	Negligible.
Nonsulphide S:	< 30%.

Chemical form:	Elementary sulphur in benzene solution.
Concentration:	> 2 mCi/ml.
Specific activity:	> 1000 mCi/g of S.
Radiochemical purity:	> 99%.

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CARRIER-FREE SULPHUR-35

1. GENERAL

A new procedure for the production of carrier-free ^{35}S has been developed [1, 2]. The method is based on the separation of ^{35}S, ^{32}P and ^{36}Cl on alumina from irradiated KCl, $^{35}Cl(n, p)^{35}S$ reaction. Al_2O_3 has proved to be very suitable for the separation of ^{35}S of high specific activity. The method has the following advantages: small amounts of the adsorbent are required; work is possible with highly concentrated solutions; volumes of the solutions are small, so the time required for treating the irradiated target is also short, not longer than 2 or 3 hours; considerable changes of the working conditions do not affect the yield, nor the chemical and the radiochemical purities; as distinct from some other procedures, work is carried out only with two phases, avoiding the gaseous phase; high chemical and radiochemical purity of the product is achieved.

2. EXPERIMENTAL PROCEDURE

Irradiation

Irradiations are made under the following conditions:

Target:	20 g reagent-grade KCl in tablet form. The formation of isotopes ^{32}P and ^{36}Cl by the reactions; $^{35}Cl(n, \alpha)^{32}P$ and $^{35}Cl(n,\gamma)^{36}Cl$ should be noted. Other isotopes formed: ^{42}K and ^{38}Cl are practically allowed to decay by cooling the irradiated sample for 7-10 d.
Fast flux:	About $1\text{-}2 \times 10^{12}$ n/cm^2 s (RA reactor, Vinča).

Irradiation time: 4-5 d.
Irradiation containers: Cylindrical, aluminium cans with screwed covers: internal length - 70 mm; internal diam. - 25 mm.

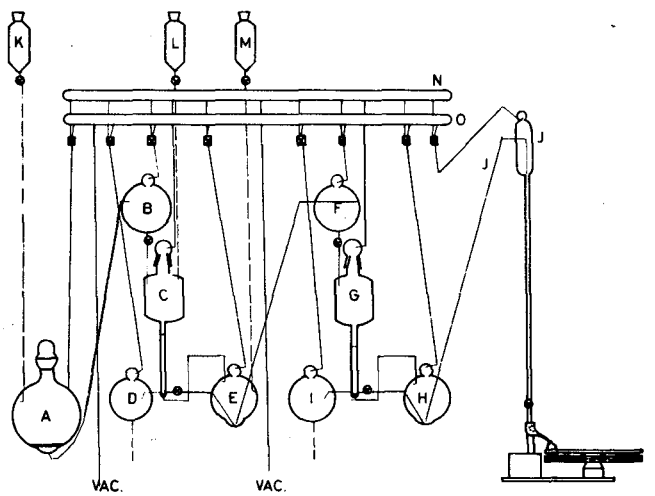
Chemical treatment

Separation method

A solution of irradiated KCl in 0.5 N HCl is passed through an acid activated alumina column on which only ^{35}S, ^{32}P and part of ^{36}Cl are adsorbed. The column is then washed with 0.5 N HCl to remove ^{36}Cl by isotopic exchange; ^{35}S is eluted from the column with 0.2 N NH_4OH, the eluent acidified with 0.2 N HCl and finally allowed to pass through a cation-exchange column to remove NH_4 and some other impurities from the solution. By this procedure $H_2{}^{35}SO_4$ in a 0.05 N solution of HCl is obtained. The high selectivity of alumina makes possible the separation of curie activities of ^{35}S from irradiated KCl with radiochemical purity better than 99.9% [3].

Apparatus

The procedure is carried out in an apparatus made of Pyrex glass (Fig. 1). The reduced pressure required in the apparatus is maintained by



A	Flask for potassium chloride dissolution
B, F, D, I	Vessels for solution transfer
C	Al_2O_3 column
G	Dowex-50 column
J	Burette
O, N	Vacuum systems
K, L, M	Vessels for reagent addition
E	Vessel for effluents from Al_2O_3 column
H	Vessel for effluents from Dowex-50 column

FIG. 1. Apparatus for the production of carrier-free ^{35}S

a small diaphragm pump. Filters of activated carbon and soda-lime are placed between the apparatus and the pump. The apparatus is connected to the diaphragm pump over a manostat.

A reduced pressure of about 15 cm Hg for liquid transfer is maintained in system O. System N is used for maintaining a constant reduced pressure in the apparatus (about 10 mm H_2O). The apparatus is placed in a protective box made of 10-mm-thick Plexiglass. During work a reduced pressure of about 20 mm H_2O is maintained in this box. This is achieved by a tornado-type aspirator. The ventilation system of the box is connected over an absolute filter to the main ventilation system.

3. ASSAY AND QUALITY CONTROL

Radioactive measurement of the solution.
Radioactive control - check the absence of β and γ impurities.
Chemical purity control.
Radiochemical purity control. Only if the material is used for medical purposes.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: YVS35/1x - ^{35}S sulphuric acid solution, carrier-free, non-injectable

A solution of sulphuric acid $H_2{}^{35}SO_4$ in about 0.05 N HCl, meeting the following specifications:

Radioactive concentration:	Measured to within 10%: 40 mCi/ml.
Radioactive purity:	^{35}S content more than 99.9%.
Radiochemical purity:	Sulphuric acid content more than 99.9%.
Specific activity:	1 Ci/mg S.

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YTTRIUM-90

NUCLEAR DATA

1. NUCLEAR PROPERTIES

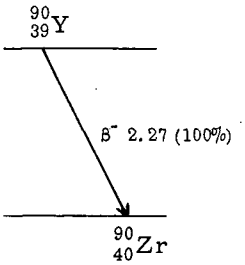
1.1. Half-life

64.3 h

1.2. Type of decay and energy (MeV)

Pure beta emitter
beta (β^-) 2.27 (100%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Abundance of target nuclide	Cross-section (barn)	Activity per g of element at 10^{12} n/cm^2 s (mCi)			Side reactions
			24 h	7 d	saturation	
$^{89}Y(n,\gamma)^{90}Y$	100%	1.3	53	192	230	None

For nuclear data see [1].

^{90}Y can also be produced via ^{90}Sr by uranium fission: $U(n,f) \longrightarrow {}^{90}Sr \xrightarrow[28\ yr]{} {}^{90}Y$. Fission yield: 5.9%.

3. APPLICATIONS

Yttrium-90 has found application in solutions, suspensions and in solid form. A brief survey of published applications is given below.

3.1. Medicine

Yttrium-90 is widely used in medical applications, mostly as seeds or rods of yttrium oxide, Y_2O_3, as carrier-free solutions in nitric, citric or hydrochloric acid or in colloidal suspensions [2-10, 17-25, 31, 38].

3.2. Biological research [11, 12, 16, 26].

3.3. Tracer applications [15].

3.4. Radiography [13, 14].

4. RADIOLOGICAL PROTECTION

4.1. External radiation

Yttrium-90 is a pure β-emitter. The maximum range of the 2.27 MeV β-ray is about 1100 mg/cm^2. The thickness of shielding required to stop the β-radiation completely is: copper 1.3 mm, Pyrex glass 5 mm, Perspex 9 mm or water 11 mm. Some remote-handling equipment, e.g. short tongs or forceps, should be used always, even for handling small activities, to avoid high local β doses.

Bremsstrahlung are formed in the shielding material from the retardation of β-particles. The bremsstrahlung become significant when handling large amounts (more than 100 mCi) of yttrium-90. The necessary lead shield thickness to reduce the ^{90}Y bremsstrahlung by a factor of 10 is about 2.1 cm [41].

4.2. Internal radiation

Yttrium-90, together with its "parent" isotope strontium-90, has been classified as a class 1, very high toxicity nuclide [36]. Yttrium-90 alone, arising from thermal neutron irradiation of yttrium oxide, has not been included in the Classification List in [36]; [42] classifies yttrium-90 in the medium toxicity group, lower sub-group B.

The biological excretion of yttrium-90 is too slow, 38.3 yr [40] to be significant compared to the radioactive decay.

4.3. Decontamination

The radionuclide yttrium-90 represents no special decontamination problem. It is effectively removed from working surfaces, benches, etc. with dilute mineral acid ($\sim$ 0.002 N) or detergent solutions. Detailed instructions for decontamination of personnel, equipment and working surfaces are given in [36].

5. SUMMARY OF PRODUCTION METHODS

5.1. Irradiation of yttrium compounds

The usual target material for ^{90}Y production is Y_2O_3. For the preparation of YCl solutions the irradiated oxide is dissolved in hydrochloric acid and converted to the chloride. Excess of acid is evaporated, and the residual chloride is taken up in distilled water.

Yttrium oxide or hydroxide pellets, seeds, rods, etc. are pressed and sintered beforehand and irradiated in that form for use.

Colloidal forms of the isotope may be prepared from yttrium chloride solutions [26, 37].

5.2. Preparation from strontium-90

Strontium-90 is separated from fission products and yttrium-90, the "daughter" isotope, is formed by decay; ^{90}Y can be separated from the "parent" isotope by precipitation of the Sr from a nitric acid solution [28, 31, 32]. The yttrium is recovered from the filtrate.

Other methods for the separation of Sr and Y are chromatography and electrolysis [31, 32]. A so-called "cow" system is prepared by fixing the strontium ions to a cation exchange resin bed and eluting this with a solution which selectively releases the yttrium ions produced by decay [33, 35].

6. RADIOASSAY

See section 6 of Part I.

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ATOMIC ENERGY ESTABLISHMENT, TROMBAY, BOMBAY, INDIA

1. GENERAL

Yttrium-90 is produced by the neutron irradiation of pure Y_2O_3, and is supplied in the form of yttrium chloride in hydrochloric acid solution. Carrier-free ^{90}Y can be separated from its parent ^{90}Sr, which is extracted from fission products.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Spec-pure Y_2O_3. 25-50 mg in type "C" can (cold-welded 2 S aluminium can, 44 mm high and 22 mm diam.)
Flux:	1×10^{13} n/cm^2 s.
Irradiation period:	1 week.

Chemical treatment

After irradiation, the can is opened and the yttrium oxide powder is tranferred into a two-necked 250-ml flask. Excess of 2-3 hydrochloric acid is added and the contents of the flask are boiled till complete dissolution of the oxide; the excess acid is distilled off. After cooling, the ^{90}Y activity is leached out with dilute hydrochloric acid and transferred into a stock bottle.

3. ASSAY AND QUALITY CONTROL

Activity assay is done by absolute beta counting.

Radiochemical purity is determined by taking a beta absorption spectrum in aluminium and finding out the range of the beta particles.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity:	1-2 Ci/g.
Chemical form:	YCl_3 in HCl solution.
Radioactive concentration:	> 10 mCi/ml.
Radioactive purity:	> 99%.

JAPAN ATOMIC ENERGY RESEARCH INSTITUTE,
TOKAI, IBARAKI, JAPAN

1. GENERAL

The production process is based on the irradiation of yttrium oxide target and dissolution in hydrochloric acid.

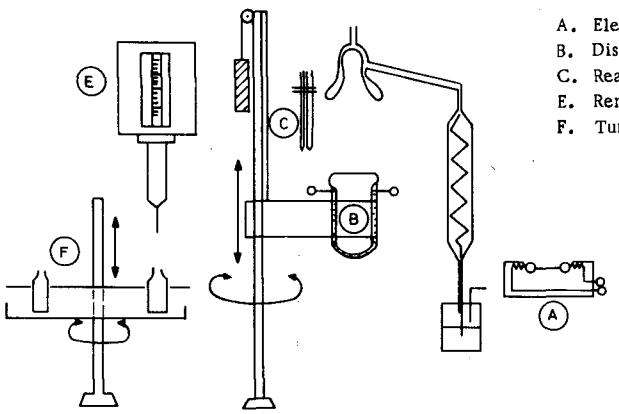
2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	4.0 g Johnson Matthey spec-pure yttrium oxide (Y_2O_3) for JRR-1; 1.0 g for JRR-2.
Container:	Placed in the polyethylene bottle, then in the polyethylene capsule.
Flux:	$\sim 3 \times 10^{11}$ n/cm^2 s (JRR-1). $\sim 2 \times 10^{13}$ n/cm^2 s (JRR-2).
Irradiation time:	10 h (5 h × 2 d) for JRR-1; 20 min for JRR-2.

Chemical treatment

The irradiated target is dissolved in 6 N HCl by heating, evaporated to dryness, then redissolved in 1 N HCl. The apparatus is shown in Fig. 1.



A. Electric polyethylene capsule cutter
B. Dissolving vessel
C. Reagent feed pipes
E. Remote pipetter for dispensing
F. Turret of bottles

FIG. 1. Arrangement of the apparatus for ^{90}Y production

Cut the inner capsule by the electric cutter (a).

Place the target in the dissolving vessel (b), add 5 ml 6 N HCl, fix the cap, dissolve by heating, and evaporate to dryness.

Add the following reagent to redissolve the residue:
10 ml 1 N HCl/g of Y_2O_3 for irradiation in JRR-1.
20 ml 1 N HCl/g of Y_2O_3 for irradiation in JRR-2.
The product solution is dispensed in the sample bottles.

3. ASSAY AND QUALITY CONTROL

The routine assay is carried out with a 2π β ionization chamber. The calibration is made with a 4π β counter. The heavy metal content is determined by comparison of the colour development with a lead standard by the addition of hydrogen sulphide.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Chemical form:	YCl_3 in HCl solution; acidity ~1 N.
Radiochemical purity:	> 99%.
Specific activity:	~ 3.2 mCi/g of Y (JRR-1 product).
	~ 14 mCi/g of Y (JRR-2 product).
Concentration:	~ 0.2 mCi/ml (JRR-1 product).
	~ 1.0 mCi/ml (JRR-2 product).

INSTITUTT FOR ATOMENERGI, KJELLER, NORWAY

1. GENERAL

Yttrium-90 is produced by irradiating yttrium oxide in a thermal neutron flux $^{89}Y(n,\gamma)^{90}Y$. The oxide is dissolved and converted to yttrium chloride.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	200 mg Y_2O_3, spectral pure, Johnson, Matthey & Co.
Time of irradiation:	4 d.
Container:	Aluminium can with a sealed polyethylene inner container.
Flux:	~ 2×10^{12} n/cm^2 s.
Side reactions:	None.

Chemical treatment

The oxide is dissolved in 1 ml concentrated hydrochloric acid. The solution is evaporated to dryness, and the residue is dissolved in water.

3. ASSAY AND QUALITY CONTROL

Radioactivity, Geiger-Müller counting.
Isotopic purity control, β-absorption analysis, γ-spectrography.
pH.
Chemical purity control, emission spectrography.

4. CHARACTERISTICS OF THE FINAL SOLUTION

YT-yttrium chloride in aqueous solution.

Radioactive concentration:	1.5 mCi/ml.
Specific activity:	150 mCi/g Y.
pH:	5-7.
Chemical purity:	Metals, spectrographically determined (except Y), less than 10 μg/ml.

THE RADIOCHEMICAL CENTRE,
AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Yttrium as Y_2O_3 is irradiated in a thermal neutron flux, $^{89}Y\ (n,\gamma)^{90}Y$. The oxide is converted to the chloride.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Johnson Matthey spec-pure yttrium oxide.
Amount:	Up to 1 g.
Irradiation time:	1 week.
Container:	Primary and secondary screw-top Al containers.
Flux:	10^{12} n/cm^2 s.
Side reactions:	None.

Chemical treatment

The target is dissolved in 6 N hydrochloric acid, evaporated to dryness and taken up in water.

3. ASSAY AND QUALITY CONTROL

Impurities by γ-spectrometry; assay against ^{90}Sr standard by Geiger counting; pH by Capillator.

OAK RIDGE NATIONAL LABORATORY,
TENN., UNITED STATES OF AMERICA

1. GENERAL

Yttrium-90 is produced by fission and is separated from ^{90}Sr by solvent extraction using di-2(ethylhexyl)phosphoric acid, $^{90}Sr \xrightarrow[28\ yr]{\beta^-} {}^{90}Y$. Fission yield: 5.9%. The isotope is further purified by successive washes and separations with HCl, dried, fumed with concentrated HNO_3 to destroy organic material, and prepared as YCl_3 in HCl solution.

2. EXPERIMENTAL PROCEDURE

Chemical treatment

Apparatus

Processing facility and shielding required: manipulator cell, 6-in. lead equivalent.

Processing

Twenty-five millilitres of di-2(ethylhexyl)phosphoric acid (HDEHP) (10 ml HDEHP and 15 ml Amsco 120) is equilibrated with 25 ml of 0.1 M HCl by manually shaking them together in a separatory funnel. This step adjusts the acidity of HDEHP to ~ 0.1 M HCl. The organic phase is saved and the aqueous phase discarded. A total of 25 ml of 0.1 M HCl solution of ^{90}Sr-^{90}Y is added to the 25 ml of organic phase in a separatory funnel. The mixture is manually shaken, then for ~ 5 min the phases are allowed to settle out. Yttrium-90 extracts into the organic phase and ^{90}Sr into the aqueous phase. The bottom phase (aqueous) is drained into a clean bottle and saved. The organic phase, which contains ^{90}Y and some ^{90}Sr contamination, is washed four times with 25 ml of 0.1 M HCl each time and the funnel shaken. After settling, the aqueous phase is strained off each time and saved. Washing removes most of the ^{90}Sr contaminant. (The bottle containing the original separation and all washes is saved; this material is used two to three weeks later for another ^{90}Y separation after ^{90}Y appears again.) A total of 25 ml of 6 M HCl is added to the funnel and shaken for ~ 5 min. The aqueous phase is drawn off after the phases settle. The aqueous solution contains most of the ^{90}Y. This step is repeated to remove the remaining ^{90}Y. The aqueous solution is boiled to dryness to remove acid, and the volume is adjusted to 25 ml with 0.1 M HCl to reduce the ^{90}Sr contaminant even more, extractions being repeated in new glassware. The resulting residue is fumed twice with 25 ml of concentrated HNO_3 to destroy organic matter, and twice with concentrated HCl to convert ^{90}Y to $^{90}YCl_3$ and to remove HNO_3. The volume is adjusted to 25 ml with 1.0 M HCl.

3. ASSAY AND QUALITY CONTROL

A sample is analysed for ^{90}Y and ^{90}Sr concentrations, total solids, molarity of HCl, and heavy metals, according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733960.

The precision and accuracy of the ^{90}Y assay are:
Calibration by $4\pi\beta$-γ coincidence counter.
Routine assay by windowless 2π proportional counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 5%.
Precision, 3%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, carrier-free ^{90}Y is delivered in the form of YCl_3 in HCl solution on request. Other specifications of interest are:

Acidity:	1 $\underline{N}$ ± 50%.
Concentration:	> 5 mCi/ml.
Total solids:	< 1 mg/mCi.
Radiochemical purity:	99.9%.

ZINC-65

NUCLEAR DATA

1. NUCLEAR PROPERTIES

1.1. Half-life

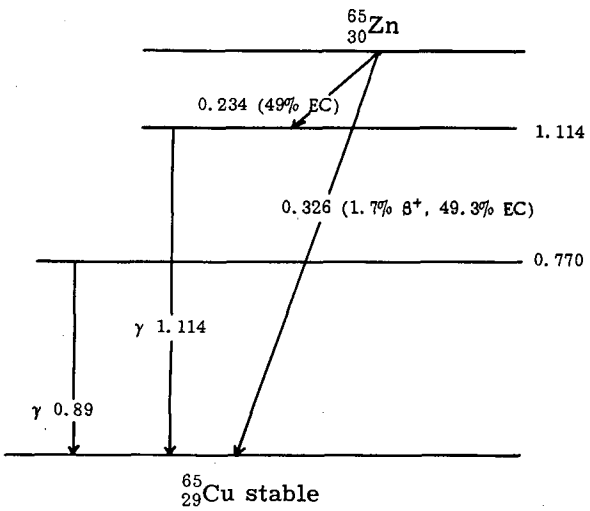
245 d

1.2. Type of decay, and energy (MeV)

beta (β^+) 0.326 (1.7%) gamma 0.51 from β^+
1.11 (45%)

EC (98.3%)

1.3. Decay scheme



2. NUCLEAR REACTIONS AND PRODUCTION

Reaction	Isotopic abundance of the nuclide (%)	Cross-section (barn)	Activity of element at 10^{12} n/cm^2 s (mCi/g)			Secondary reactions and half-life of nuclide formed
			1 week	4 weeks	saturation	
$^{64}_{30}Zn(n,\gamma)^{65}_{30}Zn$	48.89	0.47 (th)	1.2	3.2	58.3	$^{64}_{30}Zn(n,p)^{64}_{29}Cu$ (T = 12.8 h) σ = 35 mbarn $^{66}_{30}Zn(n,\alpha)^{63}_{28}Ni$ (T = 120 yr) isot. abund.: 27.8% σ = 0.02 mbarn $^{67}_{30}Zn(n,p)^{67}_{29}Cu$ (T = 61.6 h) isot. abund.: 4.11% σ = 43 mbarn $^{68}_{30}Zn(n,\gamma)^{69m}_{30}Zn$ (T = 13.9 h) isot. abund.: 18.57% σ = 0.097 barn ↓ I. T. $^{68}_{30}Zn(n,\gamma)^{69}_{30}Zn$ (T = 55 min) σ = 1 barn $^{68}_{30}Zn(n,\alpha)^{65}_{28}Ni$ (T = 2.56 h) $^{70}_{30}Zn(n,\gamma)^{71m}_{30}Zn$ isot. abund.: 0.62%

(th): for thermal neutrons.
For nuclear data see Refs. [1,2].

The target irradiated is usually zinc oxide (ZnO). Zinc-65 of high specific activity can be obtained using the Szilard-Chalmers reaction on zinc phthalocyanine.

3. APPLICATIONS

3.1. Industrial

Zinc-65 has been used:
For measurements of diffusion [3], friction, lubrication [4] and wear [5].

In the metallurgy of copper [6].
In geology [7].
In hydrology [8, 9].
In studying reaction kinetics [10].
In the glass industry [11].
General references on this subject are available [12].

3.2. Medical and biological

The chloride is used in diagnosis:
For studying zinc metabolism (absorption and elimination), especially in diabetic studies [13].
For labelling red blood cells.
In urology, for diagnosing cancer of the prostate [14].
Other general works [15] can be consulted.

4. RADIOLOGICAL PROTECTION

4.1. External exposure

4.1.1. Irradiation doses

The dose delivered by 1 Ci of zinc-65 at a distance of 50 cm is:
for 0.511 MeV γ quanta (3.5%) 0.038 rem/h
for 1.11 MeV γ quanta (45%) $\frac{0.9704}{1.0084}$ " " [16]

4.1.2. Safety measures

The following tenth-thicknesses[1] for lead and ordinary concrete give an idea of the amount of protection needed in handling zinc-65.

	Tenth-thickness (cm)		
	Pb	Ordinary concrete d = 2.3	
For a γ of 0.511 MeV	1.4	11.5	
For a γ of 1.11 MeV	3.2	17	Ref. [16]

[1] The tenth-thickness is the thickness of shielding required to reduce the intensity of a γ-radiation of given energy by a factor of ten.

In practice, the following lead thicknesses are needed to reduce the dose to 1 mR/h at 50 cm:

3.1 cm to handle 10 mCi of ^{65}Zn
6.3 cm to handle 100 mCi of ^{65}Zn
9.5 cm to handle 1 Ci of ^{65}Zn.

4.2. Internal irradiation

Zinc-65 is classified as a moderately toxic (Class 2) isotope [17]. Its effective half-life, allowing for both radioactive decay and excretory processes, is:

(d)	for
194	whole body
13	prostate
206	bones
93	kidney
218	muscle
66	liver
23	pancreas
128	testicles
74	ovaries

In the case of internal irradiation (ingestion or inhalation), the maximum permissible concentrations in air and water respectively, for a 40-h exposure, are:

10^{-7} $\mu Ci/cm^3$ and 3×10^{-3} $\mu Ci/cm^3$ (soluble form)
6×10^{-8} $\mu Ci/cm^3$ and 5×10^{-3} $\mu Ci/cm^3$ (insoluble form) [19]

4.3. Decontamination

Except in one or two particular cases, there is no special decontamination method for any given radioisotope. General texts on this subject [20-24] indicate that the following measures are adequate.

4.3.1. Skin

Rapid and repeated washing with good-quality soap, warm water and a soft brush. If this is not sufficient, use can be made of detergents or 5-10% solutions of complexing agents of the EDTA (ethylenediamine tetra-acetic acid) type. It is also possible to apply saturated permanganate solutions followed by rinsing with a 5% bisulphite solution to neutralize and remove the stain. Abrasive powders should not be used and the addition of entraining agents has proved disappointing.

If any wounds are contaminated, they must be treated rapidly by allowing them to bleed, washing with water, decontamination as for the skin and sometimes by additional surgical cleaning.

4.3.2. Hair

If the hair is contaminated, it is important not to take a shower, but merely to wash the head. A normal, good-quality shampoo is usually sufficient. If contamination is persistent, the following solutions can be used:

paraisopropylorthocresol;
lavandin oil;
AC compounded terpene-free lemon;
glycerine diacetin; or
benzoic acid.

Contamination is much easier to remove if the hair is not greasy.

4.3.3. Laboratory equipment

Glassware is usually cleaned by steeping and this is mainly a radiochemical problem. The use of a specific entraining agent or solutions of complexing agents gives good results and so do solutions of chromic acid, concentrated nitric acid, ammonium citrate, pentasodium triphosphate or ammonium bifluoride.

5. SUMMARY OF PRODUCTION METHODS

(a) Zinc-65 can be prepared by (n, γ) reaction on metallic zinc [25]; the target is dissolved in dilute hydrochloric acid (1 to 2 M), finishing with 1 M HCl.

(b) To obtain zinc-65 of high specific activity, use is made of the Szilard-Chalmers effect on zinc phthalocyanine. In this case there are two methods of extracting the "recoil zinc":

- By dissolving the irradiated phthalocyanine in concentrated sulphuric acid, followed by reprecipitation of the phthalocyanine by dilution and filtration [26, 27];
- By stirring the phthalocyanine in dilute sulphuric acid (4 N H_2SO_4) [28, 29].

The process is followed by filtration and dilution of the 4 N sulphuric solution, which is then passed through a resin ion-exchange column to fix the metallic atoms. Elution follows, using 6 N hydrochloric acid. After evaporation and taking up with water, zinc chloride is obtained in a hydrochloric acid solution. In this way, enrichment factors of 1000 to 3000 can be obtained.

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PROCEDURES

CENTRE D'ETUDES NUCLEAIRES DE SACLAY, FRANCE

1. GENERAL

Formerly, high-specific-activity ^{65}Zn was prepared [1] by the Szilard-Chalmers effect on zinc phthalocyanine, based on the $^{64}Zn(n, \gamma)^{65}Zn$ reaction.

Specific activities as high as those obtained in Szilard-Chalmers processes, and even higher, are now achieved by direct irradiation of a zinc oxide target at a high flux.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	500 mg of zinc oxide (Johnson Matthey).
Irradiation conditions:	Irradiated for 8 months at 2×10^{13} n/cm^{2}s or for 9 weeks at 7×10^{13} n/cm^2 s.
Yield:	400 mCi are obtained with a specific activity of 1 mCi/mg.

Side reactions: $^{68}Zn(n, \gamma)\, ^{69*}Zn \xrightarrow[14\ h]{I.T.} {}^{69}Zn$ (55 min)

$^{70}Zn(n, \gamma)\, ^{71*}Zn \xrightarrow[3\ h]{I.T.} {}^{71}Zn$ (2.2 min)

The product is allowed to decay for 8 d to eliminate the ^{69}Zn and ^{71}Zn formed.

Chemical treatment

Preparation

Five hundred milligrams of zinc oxide are dissolved in 20 ml of hot concentrated hydrochloric acid. The solution is evaporated to one drop and taken up with 20 ml of 1 N hydrochloric acid; 0.2 N hydrochloric acid may also be used for this purpose, followed by neutralization with 0.2 N soda, to pH = 4.5, to obtain the isotope in an isotonic solution for medical purposes.

Apparatus

This consists merely of a dissolving apparatus in two parts: a cylindrical vessel closed in its upper part by a ground joint and a condenser jointed into the first vessel.

3. ASSAY AND QUALITY CONTROL

Ionization chamber measurements are made of the activity of two samples, the zinc carrier content of which is then determined.

The radiochemical purity is demonstrated by γ spectrometry.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Reference: ^{65}ZnS

A hydrochloric acid solution of zinc chloride.

Radioactive concentration, measured to within 5%: 10-20 mCi/ml.

Specific activity: 200-1000 mCi/g.

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CENTRAL INSTITUTE FOR PHYSICS, BUDAPEST, HUNGARY

1. GENERAL

Production is based on the thermal-neutron-induced nuclear reaction on zinc metal. Processing consists of the dissolution of irradiated metal in the corresponding acid.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Zinc metal (BDH). Amount depending on the request.
Flux:	2×10^{13} n/cm^{2}s.
Time of irradiation:	50 d.
Container:	Quartz ampoule with ground stopper.

Chemical treatment

No special separation or purification is carried out; different compounds are produced by dissolving the irradiated metal in the corresponding dilute acid. A cooling period of 6 d is necessary for the elimination of ^{69m}Zn and ^{71}Zn activities.

3. ASSAY AND QUALITY CONTROL

The purity of the target is previously checked by routine spectrometric method.

Radiochemical purity is controlled with a multichannel pulse height analyser for each charge.

The pH of the solutions is determined in the usual way by measuring aliquot samples. As the products are not used for medical purposes, no pharmaceutical control is carried out.

4. CHARACTERISTICS OF THE FINAL SOLUTION

		Specific activity (mCi/g)
Zn	grey powder	~70
$ZnCl_2$	in aqueous solution	~30
$ZnSO_4$	in aqueous solution	~15
$Zn(NO_3)_2$	in aqueous solution	~20

ATOMIC ENERGY ESTABLISHMENT TROMBAY, BOMBAY, INDIA

1. GENERAL

Zinc-65 is produced by the neutron irradiation of pure ZnO in a nuclear reactor. Other isotopes produced, namely ^{69m}Zn (13.8 h), ^{69}Zn (51 min) are both short-lived and are allowed to decay. Zinc-65 of high specific activity is prepared by Szilard-Chalmers enrichment using the phthalocyanine as the target.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	5 g ZnO (E. Merck G.R. grade) per can type "C" (cold-welded 2 S aluminium can, 44 mm high and 22 mm diam.)
Flux:	$4\text{-}6 \times 10^{13}$ n/cm^{2}s.
Irradiation period:	6 months.

Chemical treatment

After unloading the irradiated can it is cooled for about 2-3 weeks to allow the short-lived activities of zinc to decay. Then the can is cut open and the irradiated ZnO is transferred into a two-necked 250-ml round-bottomed flask fitted with a distillation condenser. Excess of 2-3 N HCl is added and the solution is boiled until the complete dissolution of ZnO. Then the excess acid is removed by distillation. After allowing the flask to cool, the zinc-65 activity is leached out with dilute hydrochloric acid to give a zinc chloride solution.

3. ASSAY AND QUALITY CONTROL

The activity assay is done by measuring the ion current of a known volume of the stock solution in a calibrated ion-chamber.

The radionuclide is identified by the photo-peak of ^{65}Zn (1.11 MeV 45%).

The radioactive purity is determined by comparing the gamma-ray spectrum of the test sample with that of the standard spectrum for pure ^{65}Zn.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Specific activity:	> 50 mCi/g.
Chemical form:	$ZnCl_2$ in dilute hydrochloric acid solution.
Concentration:	> 1 mCi/ml.
Radiochemical purity:	> 99%.

INSTITUTE OF NUCLEAR RESEARCH,
SWIERK NEAR OTWOCK, POLAND

1. GENERAL [1-5]

The production of ^{65}Zn is based on the (n, γ) reaction of ZnO or Zn target material irradiated with neutron flux in the reactor. For isolation of the radioisotope the target is dissolved in an appropriate solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target:	Zinc oxide or zinc amount corresponding to the requirements.
Flux:	2×10^{13} n/cm^{2}s.
Irradiation time:	2-3 months (reactor working 86 h per week at full power).
Container:	Aluminium capsule closed by welding.

Chemical treatment

Zinc-65 in the form of inorganic compounds is obtained by dissolution of the irradiated target material in HCl, HNO_3 or H_2SO_4. The resulting solution is concentrated to a small volume and then diluted with water to the required concentration; the target material is left for 6 d after irradiation for the decay of the short-lived isotopes ^{69m}Zn and ^{71}Zn.

3. ASSAY AND QUALITY CONTROL

The chemical purity of the target material is checked by a routine spectral method.

The radiation purity is controlled by gamma spectrometry.

The activity of the final product is determined by an ionization chamber calibrated with a standard.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Zinc chloride in aqueous solution

Specific activity:	100-500 mCi/g Zn.
Radiochemical purity:	Not less than 99%.

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[5] VALLEE, B.L., The metabolic role of zinc, JAMA 163 (1956) 1053.

THE RADIOCHEMICAL CENTRE, AMERSHAM, BUCKS., UNITED KINGDOM

1. GENERAL

Metallic zinc is irradiated in a high thermal neutron flux $^{64}Zn(n, \gamma)^{65}Zn$. The metal is converted into chloride in solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target material:	Johnson Matthey spec-pure zinc metal.
Amount:	200 mg.
Irradiation time:	21 d.
Container:	Sealed silica tube primary; aluminium tube secondary.
Flux:	10^{14} n/cm^2 s.
Side reactions:	$^{68}Zn(n, \gamma)\,^{69m}Zn/^{69}Zn$.
	Product stored for two weeks before use.

Chemical treatment

The target is dissolved in 6 N hydrochloric acid, evaporated to dryness and taken up in water.

3. ASSAY AND QUALITY CONTROL

Identity by γ-spectrometry, assay by scintillation count against ^{137}Cs reference. pH by Capillator.

OAK RIDGE NATIONAL LABORATORY, TENN., UNITED STATES OF AMERICA

1. GENERAL

Zinc-65 is produced by the (n, γ) reaction in a zinc metal target, $^{64}Zn(n, \gamma)^{65}Zn$, and is prepared as $ZnCl_2$ in HCl solution.

2. EXPERIMENTAL PROCEDURE

Irradiation

Target: 1 g zinc metal.
Neutron flux: 2×10^{14} n/cm^2 s.
Irradiation time: 2.5 yr.
Reactor yield: 13 Ci.

Chemical treatment

Apparatus

A hot off-gas scrubber unit[1] is used in processing. Processing facility and shielding required: manipulator cell, 4 in. lead equivalent.

Processing

Yield: > 95%.

The irradiated sample is placed in a beaker containing 10 ml of distilled water, and about 10 ml of 1 to 2 M HCl is added. The beaker is placed under the hot off-gas scrubber unit and heated gently until all zinc is dissolved. The volume is adjusted to 50 ml of 1 M HCl for the final product.

3. ASSAY AND QUALITY CONTROL

Samples are analysed for molarity of HCl, total solids, ^{65}Zn concentration, and radiochemical purity according to ORNL Master Analytical Manual (TID-7015), procedure No. 9 0733971.

The precision and accuracy of the ^{65}Zn assay are:
Calibration by X ray - γ coincidence counter.
Routine assay by ionization chamber and well-type scintillation counter.
Estimated limit of error in disintegration-rate concentration of routine shipment, 5%.
Precision, 2%.

4. CHARACTERISTICS OF THE FINAL SOLUTION

Processed, high specific activity ^{65}Zn is delivered in the form of $ZnCl_2$ in HCl solution as a stock item. Other specifications of interest are:

Acidity: 1 N ± 50%.
Concentration: > 1 mCi/ml.
Specific activity: ≅ 500 mCi/g of Zn.
Radiochemical purity: 99%.

[1] See Fig. 2 of Section on ^{82}Br provided by ORNL, Tenn., United States of America.

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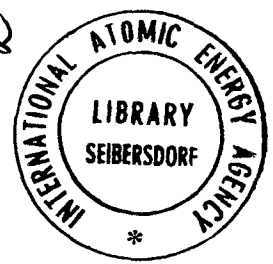

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