Nuclear Development

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Beneficial Uses and Production of Isotopes

2000 Update

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NUCLEAR ENERGY AGENCY
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

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Pursuant to Article 1 of the Convention signed in Paris on 14th December 1960, and which came into force on 30th September 1961, the Organisation for Economic Co-operation and Development (OECD) shall promote policies designed:

- to achieve the highest sustainable economic growth and employment and a rising standard of living in Member countries, while maintaining financial stability, and thus to contribute to the development of the world economy;
- to contribute to sound economic expansion in Member as well as non-member countries in the process of economic development; and
- to contribute to the expansion of world trade on a multilateral, non-discriminatory basis in accordance with international obligations.

The original Member countries of the OECD are Austria, Belgium, Canada, Denmark, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, Turkey, the United Kingdom and the United States. The following countries became Members subsequently through accession at the dates indicated hereafter: Japan (28th April 1964), Finland (28th January 1969), Australia (7th June 1971), New Zealand (29th May 1973), Mexico (18th May 1994), the Czech Republic (21st December 1995), Hungary (7th May 1996), Poland (22nd November 1996) and the Republic of Korea (12th December 1996). The Commission of the European Communities takes part in the work of the OECD (Article 13 of the OECD Convention).

NUCLEAR ENERGY AGENCY

The OECD Nuclear Energy Agency (NEA) was established on 1st February 1958 under the name of the OEEC European Nuclear Energy Agency. It received its present designation on 20th April 1972, when Japan became its first non-European full Member. NEA membership today consists of 27 OECD Member countries: Australia, Austria, Belgium, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Japan, Luxembourg, Mexico, the Netherlands, Norway, Portugal, Republic of Korea, Spain, Sweden, Switzerland, Turkey, the United Kingdom and the United States. The Commission of the European Communities also takes part in the work of the Agency.

The mission of the NEA is:

- to assist its Member countries in maintaining and further developing, through international co-operation, the scientific, technological and legal bases required for a safe, environmentally friendly and economical use of nuclear energy for peaceful purposes, as well as
- to provide authoritative assessments and to forge common understandings on key issues, as input to government decisions on nuclear energy policy and to broader OECD policy analyses in areas such as energy and sustainable development.

Specific areas of competence of the NEA include safety and regulation of nuclear activities, radioactive waste management, radiological protection, nuclear science, economic and technical analyses of the nuclear fuel cycle, nuclear law and liability, and public information. The NEA Data Bank provides nuclear data and computer program services for participating countries.

In these and related tasks, the NEA works in close collaboration with the International Atomic Energy Agency in Vienna, with which it has a Co-operation Agreement, as well as with other international organisations in the nuclear field.

FOREWORD

Radioactive and stable isotopes are widely used in many sectors including medicine, industry and research. Practically all countries in the world are using isotopes in one way or another. In many cases, isotopes have no substitute and in most of their applications they are more effective and cheaper than alternative techniques or processes. The production of isotopes is less widespread, but more than fifty countries have isotope production or separation facilities operated for domestic supply, and sometimes for international markets.

In spite of the importance of isotopes in economic and social terms, comprehensive statistical data on volumes or values of isotope production and uses are not readily available. This lack of information led the NEA to include the topic in its programme of work. The study carried out by the NEA, in co-operation with the International Atomic Energy Agency (IAEA), aimed at collecting and analysing information on various aspects of isotope production and uses in order to highlight key issues and provide findings and recommendations of relevance, in particular, for governmental bodies involved.

This report provides data collected in 1999, reviewed and analysed by a group of experts nominated by Member countries. The participating experts and the NEA and IAEA Secretariats endeavoured to present consistent and comprehensive information on isotope uses and production in the world. It is recognised, however, that the data and analyses included in the report are by no means exhaustive. The views expressed in the document are those of the participating experts and do not necessarily represent those of the countries concerned. The report is published under the responsibility of the Secretary-General of the OECD.

EXECUTIVE SUMMARY

The present report is based on a study undertaken under the umbrella of the Nuclear Energy Agency (NEA) Committee for Technical and Economic Studies on Nuclear Energy Development and the Fuel Cycle (NDC) within its 1999-2000 programme of work. The study was carried out jointly by the NEA and the International Atomic Energy Agency (IAEA) with the assistance of a Group of Experts nominated by NEA Member countries. The core of the report and its annexes are essentially an update of the publication on *Beneficial Uses and Production of Isotopes* issued in 1998 by the OECD. It includes statistical data and analyses of key issues in the field of isotopes demand and supply.

The main objectives of the study were to provide Member countries with a comprehensive and up-to-date survey of isotope uses and production capabilities in the world, to analyse trends in supply/demand balance, and to draw findings and recommendations for the consideration of interested governments. Although their importance was recognised by the group, issues related to regulation were excluded since they are dealt with in a number of publications from the IAEA, the International Organisation for Standardisation (ISO) and the International Commission on Radiological Protection (ICRP). The production of isotopes used in nuclear power plant fuels is also excluded since it is part of nuclear power industries and analysed as such in many specific studies. Information on isotope production was collected by the NEA and the IAEA Secretariats. This information was completed by data on isotope uses provided by members of the Expert Group. The Group reviewed and analysed the information with the assistance of an NEA Consultant.

The information collected for the present study and its analysis highlight the important role of governments and public sector entities in isotope production and uses. The direct responsibilities of governments in the field of isotopes include establishment of safety regulations and control of compliance with those regulations. Given the importance of beneficial isotopes for science and human welfare, governments may consider supporting to a certain extent the production and non-commercial uses of isotopes in the framework of their sustainable development policies.

There are many isotope applications in various sectors of the economy and in nearly all countries of the world. Isotopes have been used routinely in medicine for several decades. This sector is characterised by a continued evolution of techniques and the emergence of new procedures requiring the production of new isotopes. Globally, the number of medical procedures involving the use of isotopes is growing and they require an increasing number of different isotopes. In the industry, isotope uses are very diverse and their relative importance in various sectors differs. Generally, isotopes occupy niche markets where they are more efficient than alternatives or have no substitute. Food irradiation may deserve specific attention in the light of the size of its potential market, although regulatory barriers remain to be overcome in many countries to allow its broader deployment. The multiple applications of isotopes in research and development are essential for scientific progress especially in biotechnology, medicine, environmental protection and material research.

The 1998 survey and the present study showed that beneficial uses of isotopes remain a current practice in many sectors of economic activities. The present study confirmed the lack of comprehensive information including qualitative and quantitative data on the use of isotopes in different sectors, covering the whole world. In particular, a robust assessment of the overall economic importance of beneficial uses of isotopes remains to be done. The overview on isotope uses included in this report mainly provides qualitative information. While it was recognised by the expert group that a comprehensive quantitative review of isotope uses could be valuable, the collection of reliable data raised a number of methodological and fundamental issues such as consistency between sectors and countries and commercial confidentiality.

Isotopes are produced for domestic and/or international markets in more than sixty countries, including 25 OECD Member countries. Radioactive isotopes are produced mainly in research reactors, accelerators and separation facilities. Except for research reactors, OECD countries operate a majority of the isotope production facilities in service today. While most research reactors are producing isotopes as a by-product, accelerators are generally dedicated to isotope production. Research reactors are ageing, especially in OECD countries where around one half of them are more than 20 years old. However, a number of new reactors are being built or projected in several countries including Australia, Canada and France. The number of accelerators producing isotopes is growing steadily and those machine are generally recent.

The ownership of isotope production facilities varies. Public entities own and operate almost all the research reactors, large-scale accelerators and chemical separation facilities being used for isotope production. Through public-owned facilities, governments offer infrastructures for isotope production and provide education and training of qualified manpower required in the field. There is, however, a trend to privatisation and, for example, two privately owned reactors dedicated to isotope production are being built in Canada. A number of medium-size cyclotrons producing major isotopes for medical applications are owned and operated by private sector enterprises for their exclusive uses. Regarding such facilities, the role of governments is limited to the implementation of safety regulations and controls.

Trends in isotope uses vary from sector to sector but globally there is an increasing demand for many isotopes. A number of emerging applications gain importance, thereby requiring more isotopes, and innovative applications are introduced calling for the production of “new” isotopes, i.e., isotopes that had no significant beneficial uses previously. While the benefits of using isotopes are recognised by users, especially in the medical field but also in many industrial sectors, public concerns about radiation are a strong incentive to search for alternatives. Past trends illustrate this point and show that isotopes are not the preferred choice whenever alternatives are available. Therefore, isotopes should remain significantly more efficient and/or cheaper than alternatives in order to keep or increase their market share in any application.

Trends in isotope production vary according to the type of production facility and the region. In particular, trends are different for facilities dedicated to isotope production, such as cyclotrons producing isotopes for medical applications, and for facilities that produce isotopes only as a side activity such as most research reactors. Recent additions to the isotope production capabilities in several regions show a trend to the emergence of private producers in response to increasing demand and the potential threat of shortage for some major isotopes such as ^{99}Mo. It seems that now security of supply for major isotopes used in the medical and industrial fields is not an issue for the short or medium term. However, it is important to ensure a redundancy mechanism in order to secure, in each country, supply to users of critical short half-life radioisotopes such as ^{99}Mo, irrespective of technical (e.g. facility failure) or social (e.g. strike) problems that producers may encounter.

The present study confirmed that governments and public entities play an important role in the field. National policy, on research and development and medical care for example, remains a key driver for isotope demand and, although to a lesser extent, for their production. However, an increasing involvement of private companies was noted as well as a shift to a more business like and commercial management of the activities related to isotope production and uses. Government policies in the field of isotope production and uses are likely to be re-assessed in the context of economic deregulation and privatisation of industrial sectors traditionally under state control. It might be relevant to investigate whether changes in policies might affect the availability and competitiveness of isotopes and, thereby, the continued development of some isotope uses.

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1. INTRODUCTION

1.1 Background

The present report is the result of a study carried out jointly by the OECD Nuclear Energy Agency (NEA) and the International Atomic Energy Agency (IAEA). This study was approved by the Nuclear Development Committee (NDC) within the 1999-2000 programme of work of the NEA. The Committee found it relevant for NEA to undertake jointly with the IAEA an update of the first study on beneficial uses and production of isotopes published by the OECD in 1998. It was recommended that the new study go beyond updating statistical information and put emphasis on analysing key issues in the field to draw findings and conclusions for the attention of governmental bodies and other interested parties.

1.2 Objectives and scope

The main objectives of this report are:

- To provide Member countries with a comprehensive and up to date survey of isotope uses and production capabilities around the world.
- To analyse trends in isotope demand and supply.
- To draw findings and conclusions of interest to governments and other interested parties.

The study is based upon data and factual information; it focuses on technical and statistical aspects but endeavours to draw some findings and conclusions from the analysis of data and trends. The scope covers all peaceful applications of radioactive and stable isotopes in various economic sectors. However, the production of isotopes used for nuclear power plant fuel fabrication, which is a very specific activity closely linked with the nuclear power industry, that has been thoroughly analysed in the literature about nuclear power and the fuel cycle, is not dealt with in the present document.

Commercial aspects that do not fall under the responsibilities (and are not part of the mandates) of inter-governmental organisations such as the NEA and the IAEA, are not addressed in the study. Issues related to regulation, including radiation protection and waste disposal, are excluded from the study since they are comprehensively dealt with in a number of IAEA, ISO or ICRP publications.

The report includes a survey of the main uses of isotopes in different economic sectors, and data on isotope production capacities in the world by type of facility and by region. The data and analyses presented reflect the information available to members of the Group and the Secretariat. Efforts were made to obtain comprehensive and up to date information covering all geopolitical areas of the world. However, the reliability and detail of the data vary from region to region and even from country to country within a given region.

The report presents issues related to trends in the sector and provides some elements of analysis dealing with supply demand balance. It offers some findings, conclusions and recommendations to stakeholders. It elaborates on ways and means to take advantage of international organisations such as the NEA and the IAEA for enhancing information exchange between countries and regions, and promoting a more efficient international co-operation in the field of isotope production and uses.

1.3 Working method

The study was carried out by a Group of Experts from NEA Member countries. The NEA Secretariat, in co-operation with the IAEA Secretariat and assisted by an NEA Consultant, was responsible for co-ordinating the work, including compilation of information and harmonisation of drafting materials prepared by members of the Group.

Data on radioisotope production in research reactors and on stable isotope production was collected through questionnaires designed by the Secretariat under the guidance of the Expert Group. Three questionnaires, addressing respectively radioisotope production in research reactors, isotope processing facilities and stable isotope production (see Annex 9, Questionnaires on isotope production), were sent to relevant institutes from OECD Member countries by the NEA Secretariat, and to those of non-member countries by the IAEA Secretariat.

Information on isotope production in accelerators was derived mainly from the previous NEA report and the IAEA-TECDOC on cyclotrons for isotope production; complementary information was obtained on an ad-hoc basis from a number of manufacturers and operators of accelerators.

Information on isotope uses was provided mainly by members of the Group and compiled by the Secretariat. The information was compiled, harmonised and analysed by the Secretariat with the assistance of a Consultant. It was reviewed and complemented whenever relevant by the Expert Group. The outcomes were discussed and agreed upon in the framework of the preparation of the present publication. The members of the Group are listed in Annex 2.

2. ISOTOPE USES

Isotopes are used in many sectors including medicine, industry, agriculture, food processing, and research and development. The following chapter does not intend to provide an exhaustive list of isotope applications but rather to illustrate by way of examples, some of the main uses of isotopes in different sectors. Isotopes used for nuclear reactor fuels (i.e., uranium and plutonium) or non-civil applications are not covered in the present study.

2.1 Medical applications

Isotopes have been used routinely in medicine for over 30 years and the number of applications in this field is increasing with the development and implementation of new technologies and processes. Over 30 million critical medical procedures involving the use of isotopes are carried out every year.

Radiopharmaceuticals account for the principal application of radioisotopes in the medical field. In nuclear medicine imaging for diagnosis of common diseases, such as heart disease and cancer, gamma rays emitted by radioisotopes are detected by means of gamma cameras. The newer technique of positron emission tomography (PET) cameras detects two gamma emissions caused by positron annihilation.

2.1.1 Nuclear diagnostic imaging

Nuclear medicine diagnostic imaging is a unique technique which provides functional information about a range of important medical conditions. Nuclear imaging techniques are powerful non-invasive tools providing unique information about physiological and biochemical processes. They complement other imaging methods, such as conventional radiology (X-rays), nuclear magnetic resonance and ultrasound, which provide excellent physical and structural information. Additionally, nuclear diagnostic imaging is able to provide information at the cellular level reflecting the local biochemistry of diseased or damaged tissues.

Nuclear diagnostic imaging has an important role in the identification and management of conditions such as heart disease, brain disorder, lung and kidney functions, and a broad range of cancers. The high sensitivity and specificity of nuclear diagnostic imaging techniques offer the important advantages of being able to identify diseases at an early stage, to track disease progression, to allow for accurate disease staging and to provide predictive information about likely success of alternative therapy options.

In the case of cancers for example, nuclear diagnostic imaging is effective in assessing responses to treatment and detecting at an early stage any recurrence of the disease. Such information allows a precise and accurate management of the disease and may significantly alter medical decisions, for example surgical intervention.

2.1.1.1 Gamma imaging

There are some than 8 500 nuclear medicine departments in the world using gamma cameras to detect diseases of various organs including heart, brain, bone, lung and the thyroid. A total of some 20 000 gamma cameras are in use. Gamma imaging activities represent a global annual turnover greater than 1 billion USD and the demand for material in this sector is growing by more than 5% per year. Some 70% of the gamma imaging procedures rely on the use of ^{99m}Tc. For the remainder of the applications the most frequently used radioisotopes are ^{67}Ga, ^{81m}Kr, ^{111}In, ^{123}I, ^{131}I, ^{133}Xe and ^{201}Tl. Those radioisotopes are produced either by accelerators (^{67}Ga, ^{81m}Kr, ^{111}In, ^{123}I and ^{201}Tl) or by reactors (^{99m}Tc, ^{131}I and ^{133}Xe). Most of the supply is ensured essentially by a dozen private companies and a few public bodies.

The main applications of nuclear diagnostic imaging using gamma cameras are summarised in Table 1.

Table 1. **Main isotopes used for diagnostic purposes**

Organs	**Isotopes used**	**Disease investigated**
Lung	^{81m}Kr, ^{99m}Tc, ^{133}Xe	Embolisms, breathing disorders
Bone	^{99m}Tc	Tumours, infection, bone fracture
Thyroid	^{99m}Tc, ^{123}I, ^{131}I	Hyper/hypothyroidism, tumours
Kidney	^{99m}Tc, ^{111}In, ^{131}I	Renal function
Brain	^{99m}Tc, ^{123}I, ^{133}Xe	Embolisms, blood flow, tumours, neurological disorders
Liver, pancreas	^{99m}Tc, ^{111}In	Tumours
Abdomen	^{67}Ga, ^{99m}Tc	Tumours
Blood	^{111}In, ^{99m}Tc	Infection, blood volume and circulation
Heart	^{82}Rb, ^{99m}Tc, ^{201}Tl	Myocardial function and viability
All	^{67}Ga, ^{99m}Tc, ^{111}In, ^{201}Tl	Tumours

A number of modality-specific immuno-diagnostic agents are in various phases of development. Combinations of radioisotopes (essentially ^{99m}Tc) and monoclonal antibodies or peptides (about 10 products already marketed and many under development) for use in oncology, infection imaging, movement disorders and detection of deep vein thrombosis are under development. Also, a number of companies are developing post-surgical probes to find isotopic markers linked to specific antibodies or other biomolecules as a means to verify the effective removal of cancer cells after surgery.

The calibration of nuclear imaging instruments is based on the use of sealed gamma sources, with energy peaks similar to those of the radiopharmaceuticals, these sources include large area flood sources, point sources and anatomical phantoms.

Additionally, a recent new development has been the use of a transmission source fitted to the gamma camera that compensates for the attenuation of the radioactive signal in the body tissue; this technique of so called “attenuation correction” can provide improved image quality. Since 1995, the Food and Drug Administration (FDA) in the United States, and regulatory bodies in some other countries, have authorised systems incorporating a number of attenuation correction sources in gamma cameras. The radioisotopes used are ^{57}Co, ^{153}Gd and ^{241}Am.

Other applications in this field include the use of ^{57}Co, ^{133}Ba and ^{137}Cs as standard sources for activity meters or other instruments. Marker pens, rigid or flexible radioactivity rulers are used for delineating the anatomy of the patients.

2.1.1.2 Positron emission tomography (PET)

There are about 180 PET centres in the world operating a total of some 250 PET cameras. They are used mainly for the diagnosis and staging of cancer. The annual turnover of this sector represents around 100 million USD and is growing by more than 15% per year. This high growth rate results from the recognition of clinical benefits from PET.

The most commonly used radiopharmaceutical in clinical PET is the ^{18}F labelled compound fluoro-deoxy-glucose (FDG) which behaves in a similar way to ordinary glucose in the body. Some 90% of the PET procedures use FDG and this application is growing very rapidly in particular for detecting cancer cells metabolism. The radio-labelling of drugs or biologically active molecules with PET isotopes such as ^{11}C, ^{13}N and ^{15}O are used to a lesser extent.

PET imaging is characterised presently by the very short half lives of the isotopes which require use within close proximity of the point of production. The maximum distribution range is of the order of 2 hours. Approximately 70% of the sites produce their own radioisotopes. Only 30% of the PET centres obtain their radioisotopes from other sites. With the recent growth in the clinical use of PET isotopes the commercial supply from dedicated production cyclotrons is increasing rapidly in Australia, Europe, Japan and the United States.

PET cameras use isotopes such as ^{68}Ga as a calibration source. Systems using ^{57}Co, ^{68}Ge/^{68}Ga, ^{133}Ba and ^{137}Cs sources may be added to PET cameras for attenuation correction.

The development of other PET isotopes, such as ^{64}Cu, ^{86}Y and ^{124}I is underway as potential diagnostic agents and markers of disease.

2.1.1.3 Bone density measurement

Systems to determine bone density are used in radiology centres. A total of some 500 units are in operation using ^{125}I, ^{153}Gd or ^{241}Am sources. This demand is decreasing because X-ray tube devices tend to replace isotope based systems and only existing machines are still in use. The sources are supplied by three private companies, including two European companies.

2.1.1.4 Gastric ulcer detection

Urea labelled with ^{14}C is used as a marker for the presence of Helicobacter Pylori which can be responsible for gastric ulcers. This technique is growing rapidly but faces some competition from the alternative approach using a stable isotope, ^{13}C, combined with mass spectrometry. This type of product was initially developed by an Australian scientist and has been commercialised by private companies.

2.1.2 Radioimmunoassay

Radioimmunoassay is a technique used in immunology, medicine and biochemistry for quantifying very small amounts of biological substances such as enzymes, hormones, steroids and vitamins in blood, urine, saliva or other body fluids. Radioimmunoassay is commonly used in hospitals to help diagnose diseases such as diabetes, thyroid disorders, hypertension and reproductive problems.

Radioimmunoassay requires radioisotopes incorporated in a radioactively labelled sample of the substance to be measured and an antibody to that substance. The high specificity of immunoassay is provided by the use of immunoproteins. The high sensitivity of the method, combined with advanced instrumentation, allows the measurement of very low concentrations of these products. Typically, radioimmunoassay tests use immunoproteins labelled with radioisotopes such as tritium (^{3}H), ^{57}Co and ^{125}I.

World-wide, in vitro diagnostic radioimmunoassay tests represent an annual turnover of some 350 million USD, but market is not growing since radioisotopes are progressively replaced by alternative technologies, such as methods involving chemoluminescence, fluorescence or enzymes.

2.1.3 Radiotherapy with radiopharmaceuticals

Nuclear medicine uses radiotherapy with pharmaceuticals mainly for the treatment of hyperthyroidism, synovitis and cancers. An additional use is palliative care of pain associated with secondary cancers.

2.1.3.1 Therapy applications

For the ablation of thyroid tissue in hyperthyroidism or thyroid cancer, ^{131}I is the treatment of choice since it is superior to any available surgical technique. Other isotopes, ^{32}P, ^{90}Y and ^{169}Er are used for the treatment of synovitis and arthritic conditions. The demand is growing at a projected rate of 10% per year.

An increasing number of commercial companies are involved in the development of therapeutic substances for radiotherapy with radiopharmaceuticals and also many research organisations are active in the field. Development is targeted at the treatment of various cancers which have poor prognosis and are difficult to treat and cure by other techniques. Clinical tests are performed using products that combine radioisotopes, such as ^{90}Y, ^{131}I, ^{153}Sm and ^{213}Bi, with monoclonal antibodies, antibody fragments and smaller molecules such as peptides.

2.1.3.2 Palliative care

Recent developments for the care of pain arising from secondary metastasis derived from spread of breast, prostate and lung cancers include the use of ^{32}P, ^{89}Sr, ^{153}Sm and ^{186}Re. The use of such techniques is growing steadily because of the quality of life improvements provided to the patients. Other agents based on ^{117m}Sn, ^{166}Ho and ^{188}Re are under development. The present use of radioisotopes for palliative care represents an annual turnover of some 40 million USD.

2.1.4 Radiotherapy with sealed sources

2.1.4.1 Remotely controlled cobalt therapy

World-wide, some 1 500 units using ^{60}Co sources are in operation in about 1 300 radiotherapy centres for remotely controlled cobalt therapy aiming at destroying cancer cells. Around 70 new machines are installed every year, including the replacement of obsolete units. This application represents an annual turnover (in terms of value of cobalt sources) of around 35 million USD but demand is declining since ^{60}Co is being replaced by electron accelerators.

Gamma-Knife surgery is a relatively recent development of cobalt therapy. The Gamma-Knife is used to control benign and malignant brain tumours, obliterate arteriovenous malformations and relieve pain from neuralgia. This new process of radiosurgery is developing rapidly and some 140 Gamma-Knife systems dedicated to brain tumour treatment are in service. Nine companies, including three in North America, are active suppliers in this sector.

2.1.4.2 Brachytherapy

Brachytherapy is a medical procedure for the treatment of diseases by internal radiation therapy with sealed radioactive sources using an implant of radioactive material placed directly into or near the tumour. Globally, brachytherapy is used in some 3 000 specialised oncology centres in operation world-wide providing several hundred thousands of procedures every year. The demand is growing steadily at more than 10% per year.

The brachytherapy implant is a small radiation source that may be in the form of thin wires, capsules or seeds. An implant may be placed directly into a tumour or inserted into a body cavity with the use of a catheter system. Sometimes, the implant is placed in the area left empty after a tumour has been removed by surgery, in order to kill any remaining tumour cells. The main radioisotopes used for brachytherapy are ^{103}Pd, ^{125}I, ^{137}Cs, ^{192}Ir and to a lesser extent ^{106}Ru and ^{198}Au.

Brachytherapy implants may be either low dose rate (LDR) or high dose rate (HDR) implants. HDR implants are normally removed after a few minutes whereas LDR implants are left in place for at least several days and, for some cancer sites, permanently. HDR can be referred to as remote after-loading brachytherapy since the radioactive source is sent by a computer through a tube to a catheter placed near the tumour. One of the advantages of HDR remote therapy is that it leaves no radioactive material in the body at the end of the treatment. It has been used to treat cancers of the cervix, uterus, breast, lung, pancreas, prostate and oesophagus.

Recently the permanent implantation of LDR brachytherapy seeds (^{125}I and ^{103}Pd) has become extremely successful for early stage prostate cancer treatment. The demand for these radioisotopes has increased at a rapid rate. Private companies, including one in the United States, have announced the addition of several (nearly 15) cyclotrons dedicated to ^{103}Pd production as well as the construction of a facility dedicated to the production of ^{103}Pd in a reactor. In the United States alone, almost 57 000 patients were treated for prostate cancer using LDR brachytherapy seed implants during the year 1999; this alone represented an annual turnover exceeding 140 million USD.

2.1.5 Irradiation of blood for transfusion

About 1 000 irradiators are used in blood transfusion laboratories. Irradiating blood is recognised as the most effective way of reducing the risk of an immunological reaction following blood transfusions called Graft-Versus-Host Disease (GVHD). Irradiation of blood bags at very low dose is used for immuno-depressed patients, as is the case for organ transplants or strong chemotherapy. It is carried out in self-shielded irradiators using, for example, one to three ^{137}Cs sources of about 10 TBq[1] each, delivering doses of 25-50 Gy. This radiation dose is sufficient to inactivate the transfused donor lymphocytes. Other methods presently available in blood banks to physically remove the lymphocyte cells through washing or filtration do not provide effective protection against GVHD.

This is a stable market. Demand for new units is about 70 per year, supplied by four industrial firms. The annual turnover of this sector of activity is about 25 million USD. Some companies are developing irradiators that use an X-ray source instead of an isotope source. These units are intended to be competitive with the isotope-based machines.

2.2 Industrial applications

Industrial use of radioisotopes covers a broad and diverse range of applications relying on many different radionuclides, usually in the form of sealed radiation sources. Many of these applications use small amounts of radioactivity and correspond to “niche” markets. However, there are some large market segments that consume significant quantities of radioactivity, such as radiation processing and industrial radiography.

The uses of radioisotopes in industry may be classified under four main types of applications: nucleonic instrumentation systems; radiation processing, including sterilisation and food irradiation; technologies using radioactive tracers; and non-destructive testing.

Nucleonic instrumentation includes analysis, measurement and control using sealed radioactive sources (incorporated into instrumentation) and non-destructive testing equipment (gamma radiography apparatus). The sources used may be emitters of alpha or beta particles, neutrons, or X-ray or gamma photons. Typically, the sources used have activities varying from some 10 MBq to 1 TBq. A relatively large number of radioisotopes are used for these technologies that constitute the major world-wide application of radioisotopes in terms of the number of industrial sectors concerned, the number of equipment in operation and the number of industrial companies manufacturing such equipment.

Radiation processing uses high intensity gamma photon emitting sealed sources, such as for example ^{60}Co in industrial irradiators. Typically, the activity of those sources is in the 50 PBq range. It is the largest world-wide application in terms of total radioactivity involved, yet a limited number of end-users and manufacturers are concerned.

An important issue, regarding nucleonic instrumentation and radiation processing, is the limited number of companies that manufacture the required sealed sources, in particular for alpha or neutron emitters (such as ^{241}Am or ^{252}Cf) or fission products (such as ^{90}Sr/^{90}Y or ^{137}Cs).

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[1] 1 TBq = 10^{12} Bq. The becquerel (Bq) is the unit of radioactivity equal to one disintegration per second. 1 Bq = 27 picocurie (pCi) = 27×10^{-12} Ci.

Radioactive tracers (mainly beta or gamma emitters), as unsealed sources in various chemical and physical forms, are used to study various chemical reactions and industrial processes. Typically, the activity of those tracers range between some 50 Bq and 50 MBq. This category is widely spread in a large number of sectors, including agronomy, hydrology, water and coastal engineering, and oil and gas industry. Radioactive tracers are used also in research and development laboratories in the nuclear or non-nuclear fields. However, this type of application has less economic significance than the nucleonic instrumentation or radiation processing.

2.2.1 Nucleonic instrumentation

Nucleonic instrumentation systems are integrated as sensors and associated instrumentation in process control systems. The major fields of application are: physical measurement gauges; on-line analytical instrumentation; pollution measuring instruments; and security instrumentation.

Gauges of density, level and weight, by gamma absorptiometry, are employed in most industries for performing on-line non-contact and non-destructive measurement. They incorporate ^{60}Co, ^{137}Cs or ^{241}Am sealed sources. For those applications, isotopes are in competition with non ionising technologies such as radar, and their market share tends to decrease. However, emerging applications include multi-flow metering in oil exploration.

Gauges of thickness and mass per unit area, by beta particle or gamma photons absorptiometry, are used mainly in steel and other metal sheet making, paper, plastics and rubber industries. They use radioisotopes such as ^{85}Kr, ^{90}Sr/^{90}Y, ^{137}Cs, ^{147}Pm, and ^{241}Am. Demand in this sector is stable, but isotopes face competition with technologies based on the use of X-ray generators.

Gauges for measuring thickness of thin coatings, by beta particles back-scattering, incorporating ^{14}C, ^{90}Sr/^{90}Y, ^{147}Pm or ^{204}Tl sealed sources are used essentially for measurements on electronic printed circuits, precious metal coatings in jewellery or electrical contacts in the electromechanical industry. The demand is stable in this area.

Different sealed sources are incorporated in various on-line analytical instrumentation. Sulphur analysers with ^{241}Am sources are used in oil refineries, power stations and petrochemical plants, to determine the concentration of sulphur in petroleum products. The demand for this type of device is stable. Systems with ^{252}Cf sources are used in instrumentation for on-line analysis of raw mineral materials, mainly based on neutron-gamma reactions. Such systems are used for various ores, coal, raw mineral products and bulk cement. The demand for those applications is relatively limited but growing. Very few manufacturing firms are involved. Some chemical products, like pollutants, pesticides and PCBs may be detected by gas phase chromatography, coupled with electron capture sensors incorporating ^{63}Ni beta sources.

One of the applications in the field of pollution measure instruments is the use of beta particles for absorptiometry of dust particles collected on air filters in order to measure particulate concentration in air. The radioisotopes involved are ^{14}C and ^{147}Pm.

Security instrumentation systems generally based on neutron-gamma reactions using ^{252}Cf sources are used to detect explosives and/or drugs mainly in airports, harbours and railway stations. Those systems are very reliable and demand from public security authorities is expanding. Only a few companies are developing those systems. Tritium (^{3}H) is used to make luminous paints for emergency exit signs.

Laboratory or portable systems, including X-ray fluorescence analysers, sensors and well-logging tools, constitute a stable demand for various isotopes. X-ray fluorescence analysers are used in mines and industrial plants to analyse ores, to determine the nature of alloys and for inspecting or recovering metals (for example, they are used for analysing old painting aiming at finding traces of heavy metals). The radioisotopes used are ^{55}Fe, ^{57}Co, ^{109}Cd, and ^{241}Am. Humidity/density meters for on-site measurements are used in agronomy and civil engineering. Humidity meters are also used in steel making. These sensors, based on neutron diffusion, sometimes coupled with gamma diffusion, may use ^{241}Am-Be sources (and sometimes ^{137}Cs and ^{252}Cf). Well-logging tools, used by oil and gas prospecting companies for example, are very important in those sectors of activity. Sources of isotopes such as ^{137}Cs, ^{241}Am-Be, and ^{252}Cf are used for measuring parameters like density, porosity, water or oil saturation of the rocks surrounding the exploration wells.

Smoke detectors using ^{241}Am sources in general are installed in a large number of public areas such as hospitals, airports, museums, conference rooms, concert halls, cinemas and aeroplanes as well as in private houses. They are so widely spread that they represent the largest number of devices based on radioisotopes used world-wide. The demand in this field is stable.

2.2.2 Irradiation and radiation processing

Irradiation and radiation processing is one of the major uses of radioisotopes that requires high activity levels particularly of ^{60}Co. Radiation processing includes four main types of applications:

- Radiation sterilisation of medical supplies and related processes such as sterilisation of pharmaceutical or food packaging. These processes are by far the most important uses of dedicated and multipurpose ^{60}Co irradiators.
- Food irradiation, mainly to improve the hygienic quality of food. Currently most treated food is in the dry state (e.g., spices, dried vegetables) or in the deep frozen state (e.g., meat, fish products).
- Material curing, mostly plastic by cross-linking.
- Pest control (Sterile Insect Technique/SIT).

There are a few other treatments or activities related to radiation processing, such as irradiation for radiation damage study, or sludge irradiation, which have a rather limited economic significance. There are about 180 gamma irradiators in operation world-wide. Some of them are dedicated to radiation sterilisation while others are multipurpose facilities dealing mostly with radiation sterilisation yet irradiating food or plastics as complementary activities.

In practice low specific activity ^{60}Co is the only radioisotope used for radiation processing although ^{137}Cs could also be considered. Typically, sources ^{60}Co for industrial applications have low specific activities, around 1 to 4 TBq/g, and very large total activities, around 50 PBq. In this regard, they differ from ^{60}Co sources for radiotherapy that have higher specific activities, around 10 TBq/g.

The ^{60}Co gamma irradiators offer industrial advantages because they are technically easy to operate and able to treat large unit volumes of packaging (up to full pallets). Such gamma irradiators are in competition with electron accelerators using directly the electron beam or via a conversion target using Bremstrahlung X-rays. Currently, ^{60}Co source irradiators represent the main technology for food irradiation and sterilisation. On the other hand, most plastic curing involving large quantities of product and high power is carried out with accelerators.

Radiation sterilisation is growing slowly but steadily. The technical difficulty in controlling the alternative process (ethylene oxide sterilisation) and the toxicity of the gas involved in that process are incentives for the adoption of radiation sterilisation. However, the cost of the radiation sterilisation process (investment and validation) is a limiting factor for its deployment.

Food irradiation has a very large potential market for a broad variety and large quantities of products. At present, the quantities treated every year amount to about 0.5 million tonnes. A real breakthrough of this technology could lead to a demand exceeding the present capacities of ^{60}Co supply. Food irradiation has been endorsed as a means to improve the safety and nutritional quality of food available by reducing bacterial contamination levels and spoilage. Food irradiation has been endorsed by a number of international governmental organisations such as the World Health Organisation (WHO), the Food and Agriculture Organisation (FAO) and the International Atomic Energy Agency (IAEA), and by national organisations such as, in the United States, the US Food and Drug Administration.

World-wide, an increasing number of food suppliers are seriously considering the use of food irradiation in their processes and the number of countries allowing food irradiation is growing continuously. Nevertheless, growth in demand for ^{60}Co is likely to be relatively slow in the short-term and a market penetration breakthrough might not occur for some years.

In the future, competition from accelerator facilities will become stronger and stronger, owing to both technical and economic progress of accelerator technology, and because accelerators (and the products processed by accelerators), that do not involve radioactivity, are accepted better by the public than isotopes and irradiated products.

2.2.3 Radioactive tracers

A tracer is a detectable substance, for instance labelled with a beta or gamma emitter, which has the same behaviour in a process (e.g., chemical reactor, ore grinder, water treatment plant) as the substance of interest.

The main areas of use are to study:

- Mode and the efficiency of chemical reactions (in chemical synthesis research laboratories).
- Mass transfer in industrial plants (e.g., chemistry, oil and gas, mineral products transformation, metallurgy, pulp and paper, water treatment, waste treatment).
- Behaviour of pollutants (dissolved or suspended) in rivers, estuaries, coastal shores, aquifers, waste dumping sites, oil, gas or geothermal reservoirs.

A large number of radioisotopes produced by reactors and accelerators in various chemical or physical forms are required for such applications and studies to check performance, optimise process, calibrate models or test pilot, prototype or revamped installations. Also, tracers are increasingly used in the oil exploration and exploitation industries.

2.2.4 Non-destructive testing

Gamma radiography is used for non-destructive testing in a variety of fields including petroleum and gas industry, boiler making, foundry, civil engineering, aircraft and automobile industries. The value of this type of non-destructive testing is principally to ensure the safety and security of critical structures, for example the integrity of an aircraft turbine blade. The world-wide turnover of this activity is around 20 million USD per year and is roughly stable. More than 90% of the systems use ^{192}Ir sources. The other radioisotopes concerned are ^{60}Co, ^{75}Se and ^{169}Yb. Neutron radiography is also applied using ^{252}Cf.

2.2.5 Other industrial uses of radioactive isotopes

The start-up of nuclear reactors, for power generation, research or ship propulsion, necessitates the use of start-up sources emitting neutrons like ^{252}Cf. The demand is driven by the rate of reactor construction, including commercial, research and naval units. There are five suppliers for those finished sources.

Radioisotopic power sources, called RTG (Radioisotopic Thermoelectric Generators) are now restricted to power supply for long term and long range space missions. They are based on heat thermoelectric conversion and use high activity sealed sources of ^{238}Pu. Russia and the United States are the only current producers in this area.

Calibration sources are required for nuclear instrumentation including all health physics instrumentation, nuclear detectors and associated electronics, and instrumentation used in nuclear medicine. Those sources include a large number of isotopes with small activities adapted to the different measurement conditions. The various users of these sources are the manufacturers of nuclear instruments, nuclear medicine and radiotherapy departments of hospitals, nuclear research centres, the nuclear fuel cycle plants and the operators of power producing reactors.

Paper, plastic, graphic, magnetic tape and paint industries are the principal users of systems using ^{210}Po to eliminate static electricity that builds up during the process.

2.3 Scientific/research applications

Three types of unique characteristics come into play when isotopes are used in research work:

- Radioisotopes emit a range of particles with varying characteristics (types of interaction, penetration, flux etc.). The way in which they interact with matter gives information about the latter. This means that a range of radiometric instruments can be used which improve the way in which various phenomena are observed.
- Radioisotopes, or stable isotopes, have exactly the same chemical and physical properties as the natural elements to which they correspond and are easy to detect; in the case of radioisotopes, detection is possible in the absence of any contact and at extremely low concentrations, making them unrivalled tools as tracers.
- The particles emitted make it possible to deposit energy in matter in a highly controlled manner and to make chemical and biological alterations which would be impossible using any other method.

A rapid survey of current or recent research work involving isotopes, or results which were only made possible by the use of isotopes, points to the wide variety of isotopes used and to the uncertain and ever-shifting boundary between R&D and applications, particularly in the medical field.

The very wide range of isotopes involved makes it difficult to group them into general homogeneous categories. Furthermore, there are examples of one isotope being used for a unique application, e.g., ^{51}Cr as a reference source for the emission of neutrinos. The shift from R&D to application may be illustrated by PET procedures that currently are used routinely for medical care in some hospitals but remain a tool for research in the fields of neurology and psychiatry.

2.3.1 Research on materials

Mössbauer spectroscopy employs ^{57}Co, ^{119m}Sn, ^{125m}Te and ^{151}Sm. Demand is low and stable, and there are only a few private suppliers along with governmental organisations involved. ^{22}Na is used as positron source for material science studies.

2.3.2 Research in the field of industrial processes

Radioactive tracers continue to be a powerful tool for developing and improving processes in the field of process engineering. They are used to closely monitor the behaviour of solid, liquid and gaseous phases in situ. This makes it possible to optimise the operation and validate operational models for a wide range of equipment. It should be remembered that until a model has been validated, it is no more than a working hypothesis.

In the field of mechanical engineering, radioactive tracers are the most effective and accurate way of measuring wear phenomena in situ, without having recourse to dismantling. It is also used to devise the most appropriate technical solutions to ensure that an item of equipment complies with its specification. In most cases, the tracer is generated by irradiation of parts of the component to be studied in a cyclotron.

2.3.3 Research in the field of environmental protection

Some characteristics of radioisotopes make them among the most effective tracers for studies involving the environment. The period during which a radioisotope can be detected depends on its half-life and the choice of the isotope can be adapted to the specific problem investigated. The radioisotope and its chemical form can be selected from a wide range of elements and compounds. The detection of radioisotopes is possible at very low concentrations.

Radioisotopes constitute the perfect tool for carrying out a whole range of environmental studies including:

- Subterranean and surface hydrology studies: measurement of velocity, relative permeability and pollutant migration, identification of protection boundaries around lines of catchment, instrumentation of rivers and location of leaks from dams.
- Dynamic sedimentology studies: the transfer of sediment in the marine environment, studies of catchment areas.

The most common radioisotopes used in this field of applications are ^{46}Sc, ^{51}Cr, ^{113}In, ^{147}Nd, ^{182}Ta, ^{192}Ir and ^{198}Au.

However, society has been less and less willing to accept the use of radioisotopes in the natural environment and their use now tends to be limited to cases where there is practically no alternative. Hydrology and river sedimentology studies almost exclusively make use of chemical or fluorescent tracers, or even radioactivable tracers (which can be made radioactive), with the exclusion of those occurring naturally.

2.3.4 Medical research

Medical research is of strategic social and economic importance. It has an impact on the long-term performances of national health systems, including quality of life and life expectancy, and health care efficiency and costs. The outcomes of medical research may have significant economic consequences in the medical sector (manufacture of equipment and products). In this domain, radioisotopes and stable isotopes have a unique and often irreplaceable role.

The boundary between research and application is evolving very rapidly in the medical field and the need for isotopes is changing rapidly also. It should be stressed that differences between countries are very significant in this area.

Current research in this field falls roughly into four categories aiming primarily to enhancing medical care procedures (see Section 2.1 above) already used:

- Radioimmunotherapy, where a radioisotope is associated with an antibody or biological molecule with a specific affinity for the cancerous cells to be destroyed.
- Metabolic radiotherapy, characterised by the injection of a radiopharmaceutical which selectively focuses on the target tissue and irradiates it in situ.
- Treatment of pain caused by cancers.
- Brachytherapy for the treatment of prostate cancer using ^{103}Pd and ^{125}I.
- Functional imagery using ^{18}F within fluoro-deoxy-glucose.

Finally, endovascular brachytherapy is potentially a very effective preventive treatment of coronary artery restenosis. This application is under active clinical development. A large number of private companies and university teams are developing radioactive stents (devices positioned in blood vessels to prevent vessel collapse) or radioactive source systems to prevent restenosis of blood vessels following therapy technique known as balloon angioplasty. The radioisotopes being investigated include ^{32}P, ^{90}Y, ^{188}Re and ^{192}Ir. The number of patients that could be treated by this method exceeds 150 000 persons and the potential turnover of the activity is estimated to some 350 million USD per year.

2.3.5 Biotechnologies

Radioisotopes continue to be a reference tool for a large range of research work in the fields of biology and biotechnology, from the most fundamental research to developments that can practically be classed as industrial research. This work includes plant biology and research into photosynthesis, agronomy (studies of fertilisers containing nitrogen) and biochemistry. The main radioisotopes used are ^{3}H, ^{14}C, ^{32}P and ^{35}S.

2.4 Stable isotopes

Stable isotopes are frequently used as precursors for the production of cyclotron and reactor produced radioisotopes. In this sector, demand requiring very high enrichment levels is growing. Table 2 illustrates by some selected examples the use of stable isotopes for producing radioisotopes in reactors or accelerators.

Table 2. **Selected enriched stable isotopes and derived radioisotopes**

Stable isotope target	**Radioisotope product**	
	Produced in reactors	**Produced in accelerators**
^{13}C		^{13}N
^{15}N		^{15}O
^{18}O		^{18}F
^{33}S	^{33}P	
^{50}Cr	^{51}Cr	
^{58}Ni	^{58}Co	^{57}Co
^{76}Ge	^{77}As	
^{68}Zn		^{67}Ga, ^{67}Cu
^{88}Sr	^{89}Sr	
^{102}Pd	^{103}Pd	
^{112}Cd		^{111}In
^{124}Xe	^{125}I	^{123}I
^{152}Gd	^{153}Gd	
^{152}Sm	^{153}Sm	
^{168}Yb	^{169}Yb	
^{176}Lu	^{177}Lu	
^{185}Re	^{186}Re	
^{186}W	^{188}W	^{186}Re
^{198}Pt	^{199}Au	
^{203}Tl		^{201}Tl

2.4.1 Medical applications

Table 3 provides a detailed list of stable isotopes used for medical applications including the direct use of stable isotopes, such as ^{10}B for Boron Neutron Capture Therapy (BNCT) in cancer treatment and the use of hyper polarised ^{3}He and ^{129}Xe for magnetic resonance medical imaging. Stable isotopes used as precursors for producing radioisotopes used in medical applications are not included in this table.

Table 3. **Selected examples of stable isotope uses in biomedical research**

Stable Isotopes	**Uses**
^{10}B	* Extrinsic food label to determine boron metabolism * Boron neutron capture therapy for cancer treatment
^{42}Ca, ^{46}Ca, ^{48}Ca	* Calcium metabolism, bioavailability, and absorption parameters during bed rest, and space flight * Osteoporosis research and bone turnover studies * Role of nutritional calcium in pregnancy, growth and development, and lactation * Bone changes associated with diseases such as diabetes and cystic fibrosis
^{13}C	* Fundamental reaction research in organic chemistry * Molecular structure studies * Fundamental metabolic pathway research, including inborn errors of metabolism * Extrinsic labelling of food for determination * Non-invasive breath tests for metabolic research and diagnosis * Biological substrate oxidation and turnover * Elucidation of metabolic pathways in inborn errors of metabolism * Amino acid kinetics * Fatty acid metabolism * Air pollution and global climatic changes effects on plant composition
^{35}Cl, ^{37}Cl	* Environmental pollutant toxicity studies
^{53}Cr, ^{54}Cr	* Non-invasive studies of chromium metabolism and human requirements * Adult onset diabetes mechanism
^{63}Cu, ^{65}Cu	* Non-invasive studies of copper metabolism * Studies of congenital disorders and body kinetics in gastrointestinal diseases * Investigation of role in maintaining integrity of tissue such as myocardium
^{3}He	* In vivo magnetic resonance studies
^{2}H	* Vitamin research * Chemical reaction mechanisms
^{54}Fe, ^{57}Fe, ^{58}Fe	* Metabolism, energy expenditure studies * Conditions for effective iron absorption and excretion * Research to develop successful interventions for anaemia * Metabolic tracer studies to identify genetic iron control
^{78}Kr, ^{80}Kr, ^{82}Kr, ^{84}Kr, ^{86}Kr	* Diagnosis of pulmonary disease

Table 3. **Selected examples of stable isotope uses in biomedical research (cont.)**

Stable Isotopes	**Uses**
^{204}Pb, ^{206}Pb, ^{207}Pb	* Isotope dilution to measure lead levels in blood
^{6}Li	* Sodium and renal physiology * Membrane transport * Psychiatric diseases
^{25}Mg, ^{26}Mg	* Non-invasive studies of human requirements, metabolism and absorption * Kinetic studies of heart disease and vascular problems
^{94}Mo, ^{96}Mo, ^{97}Mo, ^{100}Mo	* Extrinsic labelling of food for determination of human nutrition requirements
^{58}Ni, ^{60}Ni, ^{61}Ni, ^{64}Ni	* Non-invasive measurement of human consumption and absorption
^{15}N	* Large-scale uptake studies in plants * Whole body protein turnover, synthesis, and catabolism * Amino acid pool size and turnover * Metabolism of tissue and individual proteins
^{17}O	* Studies in structural biology; Cataract research
^{18}O	* Non-invasive, accurate, and prolonged measurement of energy expenditures during everyday human activity * Lean body mass measurement * Obesity research * Comparative zoology studies of energy metabolism
^{85}Rb, ^{87}Rb	* Potassium metabolism trace * Mental illness research
^{74}Se, ^{76}Se, ^{77}Se, ^{78}Se, ^{80}Se, ^{82}Se	* Bioavailability as an essential nutrient
^{33}S, ^{34}S	* Human genome research and molecular studies * Nucleotide sequencing studies
^{51}V	* Diabetes, bioavailability, and metabolism * Brain metabolism studies
^{129}Xe	* Magnetic resonance imaging
^{64}Zn, ^{67}Zn, ^{68}Zn, ^{70}Zn	* Non-invasive determination of human zinc requirements * Metabolic diseases, liver disease, and alcoholism * Nutritional requirements and utilisation studies

2.4.2 Industrial applications

Industrial applications of stable isotopes represent an annual turnover of around 30 million USD per year. They usually require larger amounts and lower enrichment levels than biomedical applications and they are cheaper. Therefore, gas centrifuge production is often the preferred production method for the heavier isotopes, whilst distillation is generally chosen for the lighter isotopes; electromagnetic separation is used for some of the stable isotopes used in industry. The main industrial sectors using stable isotopes are the nuclear power and laser industries.

The nuclear power industry uses isotopes such as ^{10}B for neutron absorption and depleted ^{64}Zn as an additive to cooling water of nuclear power plants in order to reduce radiation levels from unwanted radioactive isotopes of cobalt and zinc (^{65}Zn and ^{67}Co) and reduce stress corrosion cracking. These are large-scale applications using up several tonnes of isotopes per year.

In the laser industry, even numbered cadmium isotopes are used for performance boosters in HeCd lasers. The quantities involved are in the range of some kilograms per year, although this application is diminishing with the replacement of HeCd lasers with solid state lasers.

Other industries are currently investigating various uses of stable isotopes. For example, stable isotopes may be used to enhance thermal conductivity or to improve ion implantation in semiconductor applications, to enhance efficiency in lighting, as identification tags (e.g., in explosives) or in high accuracy timing devices.

2.4.3 Scientific/research applications

Although medical and industrial uses of stable isotopes probably constitute the largest physical and monetary volumes of stable isotope uses, research applications represent the largest number of uses. Many of the medical applications of stable isotopes listed on Table 3 may be classified also in the category of medical or biomedical research applications.

All stable isotopes of the same element have the same chemical and physical properties (with minor exceptions) and, therefore, are excellent tracers and compound labelling tools. Analysis of stable isotope content and their relative abundance forms the basis for a considerable amount of research in the field of ecology and environmental protection. The variations in isotopic content in stable isotopes are used to study a wide variety of phenomena occurring in the biosphere and in the field of life sciences. Many studies are underway and are giving promising results. A number of these rely on natural differences in the relative abundance of various stable isotopes, others use separated or enriched isotopes as tracers.

A number of stable isotopes can be used in a variety of high-energy physics experiments such as the use of ^{48}Ca bullets in building super heavy elements.

Compounds labelled with stable isotopes, such as ^{2}H, ^{13}C, ^{15}N and various isotopes of calcium, can be integrated into a number of different biological cycles. This allows various studies to be performed, for example on: production processes in the field of plant biology, the use of fertilisers and irrigation processes; structural dynamics of proteins using NMR spectrometry; biotechnological processes (e.g. fermentation) using substrates enriched with ^{13}C; calcium metabolism, osteoporosis research; and energy balance studies.

3. ISOTOPE PRODUCTION

This focuses on isotope production facilities information on which was provided, by the institutes or companies operating them, in response to questionnaires circulated by the NEA and the IAEA. Data refer to the situation as of 1st January 1999, except when indicated otherwise. The most common radioisotope production facilities, i.e., reactors, accelerators and radioisotope separation facilities, are described in Sections 3.1, 3.2 and 3.3 respectively; stable isotope production is presented in Section 3.4. A number of reactors and accelerators producing isotopes have on the same site processing facilities including hot cells that allow some preliminary treatment and packaging of the isotopes that they produce. Also, there are processing facilities operated independently from isotope production reactors or accelerators.

The production of radioisotopes requires a series of steps leading to a product ready for end-uses (see Figure 1). Generally, the entire process is not carried out in a single plant but rather in several different facilities, as illustrated on Figure 1. This report focuses on the nuclear part of the process, i.e., production of the desired isotope per se. Therefore, the radioisotope production facilities described below include only reactors, accelerators and processing facilities used to produce radioisotopes. Neither the upstream part of the process, i.e., selection and preparation of the target material, nor the downstream, i.e., chemical processing, packaging and control of the isotopes leading to a commercial product ready for final use, are described in this report.

Table 4 summarises the main radioisotope production facilities included in the present survey and their geographic distribution. For the purpose of this report, countries have been grouped in six regions (see Annex 4). According to the present survey, some sixty countries, including 25 OECD Member countries, are producing some stable or radioactive isotopes, however, in many of those countries the isotope production is essentially dedicated to domestic uses.

Table 4. **Main isotope production facilities**

Type of facility	Number of units in the world (in OECD countries)
Research reactors	73 (30)
of which high flux reactors	*6 (3)*
Accelerators	255 (219)
cyclotrons dedicated to medical isotopes	*59 (47)*
cyclotrons dedicated to PET	*167 (151)*
non-dedicated accelerators	*29 (21)*
Heavy stable isotope production facilities	11 (6)

Figure 1. **Flow of radioisotope production, manufacturing, applications and waste management**

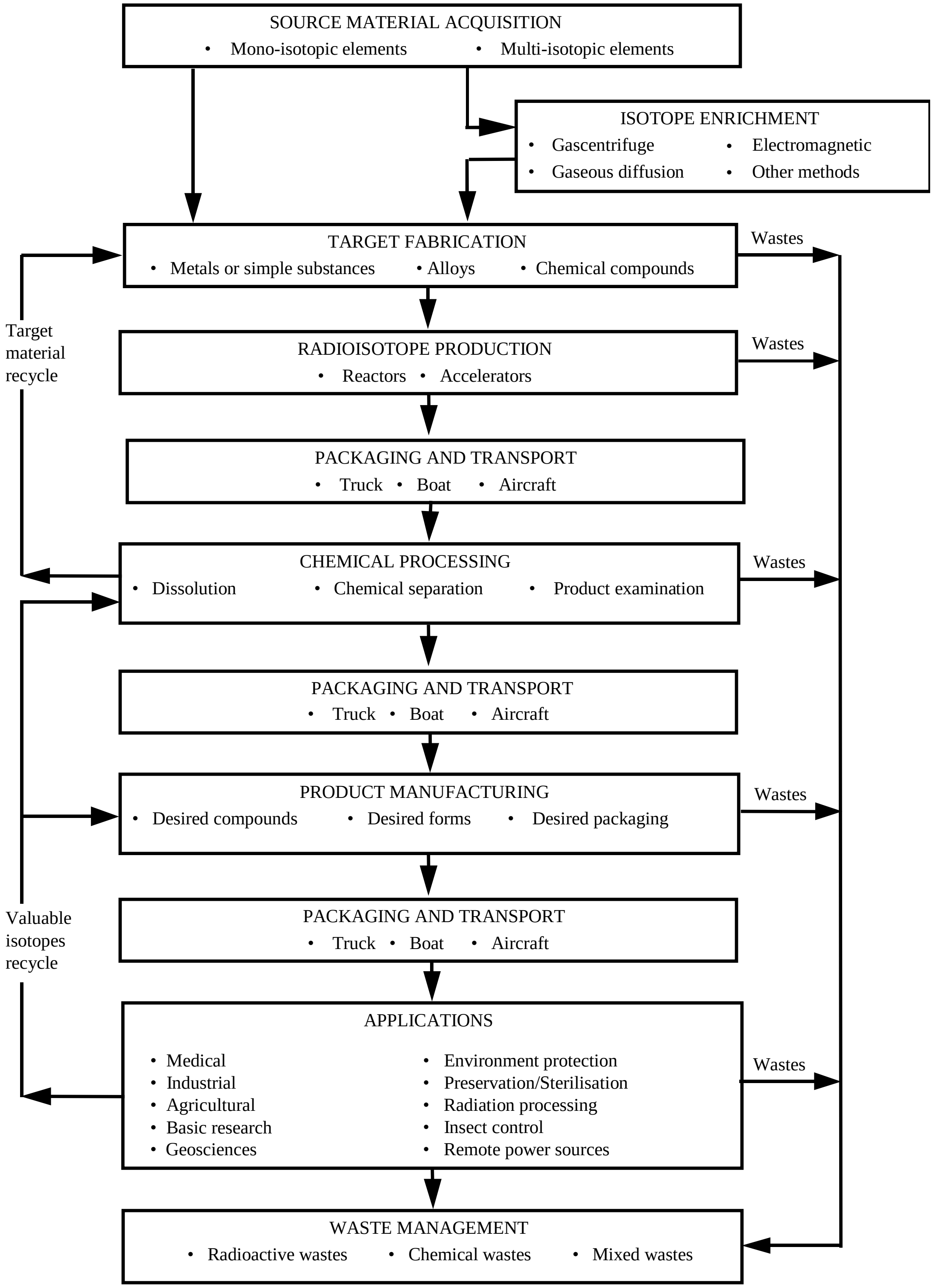
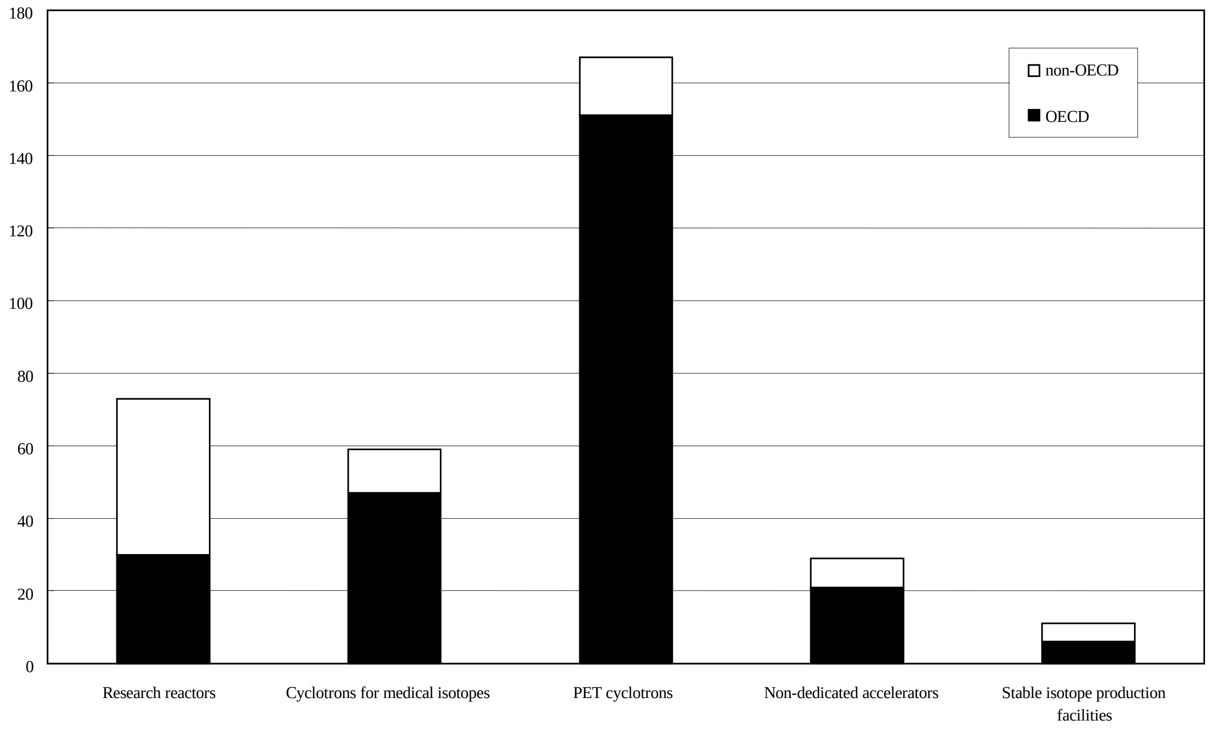


Figure 2 displays the number and types of the main isotope production facilities in operation in the world as of January 1999, as identified within the present study; it shows that, except for research reactors, a majority of those facilities, are located in OECD countries.

Figure 2. **Number of isotopes production facilities in the world**



3.1 Reactors

Reactors generally are used to produce neutron-rich isotopes by neutron irradiation. A list of the main isotopes produced by reactors is included in Annex 3. Most of the reactors used for producing isotopes are research reactors, however, some radioisotopes (mainly ^{60}Co) are produced in nuclear power plants. Two reactors dedicated to isotope production are now in the process of being built and commissioned in Canada.

3.1.1 Research reactors

The research reactors considered in this study are those that produce a significant amount of isotopes. These devote at least 5% of their capacity to radioisotope production. For the purpose of the present study, neutron activation analysis is not considered as part of isotope production activities. Generally, reactors producing isotopes have a power level greater than 1 MW. Using this definition, of a total of some 300 research reactors in operation world-wide[1], nearly 75 produce radioisotopes. Table 5 gives the distribution of the research reactors included in the present survey by range of power level and by region. A detailed geographical distribution by country of research reactors producing

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[1] Source: IAEA, RDS n° 3, Nuclear Research Reactors in the World, December 1996 Edition, Vienna (1996) and update on the IAEA Web site.

isotopes is given in Annex 6. In addition to the research reactors included in Table 5 and Annex 6, there are two reactors in operation in Russia with particularly high fast neutron flux that can offer an alternative route for producing ^{89}Sr.

Table 5. **Geographical distribution of research reactors producing isotopes**

Region (country)	**Number of reactors**			
	< 5 MW	5 to 30 MW	> 30 MW	Total
OECD Europe	5	8	4	17
OECD North America	2	2	3	7
OECD Pacific	1	4	1	6
Non-OECD Eastern Europe & FSU	1	11	4	16
Non-OECD Asia & the Middle East	7	7	3	17
Non-OECD Africa & South America	4	6	0	10
Total	**20**	**38**	**15**	**73**

Figure 3. **Geographical distribution of research reactors producing isotopes (number of units)**

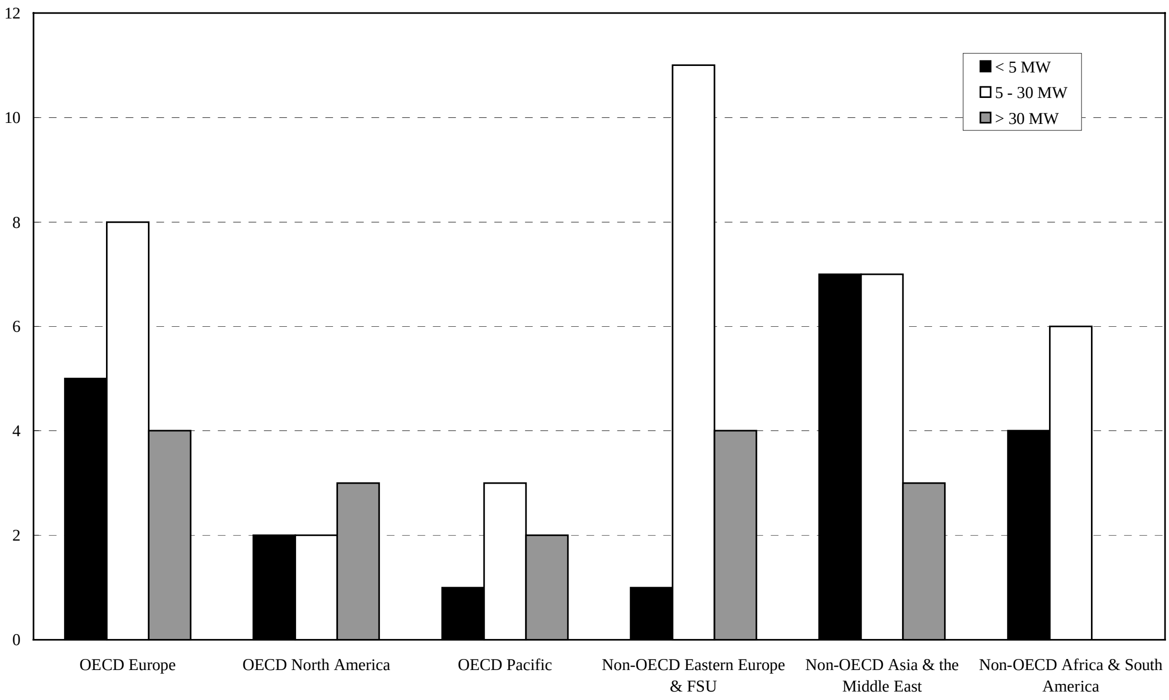


Table 5 and Figure 3 show that, at present, research reactors producing isotopes are rather evenly distributed in the world, and between OECD and non-OECD countries, although in Africa and South America there is no isotope producing reactor in the power range above 30 MW. Three regions, OECD Europe, non-OECD Eastern Europe & the Former Soviet Union, and non-OECD Asia & the

Middle East, have each around one quarter of the isotope producing research reactors, while each of the remaining regions have around 10% of those reactors.

Nearly one third of the research reactors producing isotopes are in the power range between 1 and 5 MW, more than half are in the range 5 to 30 MW and the rest (only 20%) are in the range above 30 MW.

Neutron flux is a key parameter for the isotope production capabilities of reactors. Practically all the research reactors producing isotopes have a thermal neutron flux higher than 1×10^{13} neutrons per cm^2 per second ($n/cm^2.s$). Around one third of the reactors for which the information was provided have a thermal neutron flux below 9×10^{13} $n/cm^2.s$. They include mainly university and research centre machines operated primarily for scientific research that produce isotopes generally as a side activity and for in-house or domestic purposes. More than a half of the reactors for which the information was provided have a thermal neutron flux in the range 1 to 5×10^{14} $n/cm^2.s$. These multi-purpose machines carry out R&D in support to nuclear power programmes and produce isotopes mainly for local and regional markets.

High neutron flux reactors (i.e., with a thermal neutron flux over 5×10^{14} neutrons per cm^2 per second) are needed to produce some radioisotope products with sufficiently high specific activity such as ^{60}Co (high specific activity), ^{75}Se, ^{188}W and ^{252}Cf. Five such high flux reactors, included in the total numbers indicated in Table 5, are in operation in Belgium, China, Russia and the United Stated as shown in Table 6.

Table 6. **Geographical distribution of high flux reactors (total 5)**

Country	Number of units	Name (location)
Belgium	1	BR2 (Mol)
Russia	2	SM3 (Dimitrovgrad) MIR-M1 (Dimitrovgrad)
United States	1	HFIR (Oak Ridge)
China	1	HFETR (Chengdu)

The age profile and shut down schedule of research reactors producing isotopes is a key issue in assessing future security of supply. According to the responses received, around half of the isotope producing research reactors are some 30 to 40 years old and very few reactors are less than 10 years old. In OECD countries, the proportion of older reactors (20 years or more) exceeds 50% and a significant share of those reactors is in the power range above 30 MW. Nearly one third of reactor operators have just completed a refurbishment or are planning an upgrade within the next 5 years. The planned shut down of reactors for refurbishment will reduce temporarily isotope production capacity (normally for 6 months to a year), but upgrades will contribute to enhance security of supply in the long term. Three reactors are planned to be shut down permanently before 2002. They are expected to be replaced by new, generally more powerful machines. In July 2000, Australia signed a contract to construct a replacement reactor with a thermal neutron flux greater than 3×10^{14} $n/cm^2.s$. In the second half of the decade, France is planning to replace an old reactor by a new machine.

The importance of isotope production in the overall operation of research reactors varies widely. As far as responses to the questionnaire provide a reliable image of the situation, it seems that the weight of isotope production, in operation time and in income, is lower in OECD countries than in non-member countries. Generally, isotope production has a lower weight in high power reactors than in low and medium power machines.

All the isotope producing research reactors are owned by public entities (state-owned), with two exceptions. Private companies own and operate two research reactors producing isotopes, one in the Czech Republic and one in Sweden. In the Netherlands and the United States, three state-owned reactors are operated by private companies. There is a trend, in OECD countries in particular, towards more involvement of the private sector in the field. The two reactors dedicated to isotope production under construction in Canada are privately owned.

A majority of the research reactors producing isotopes are equipped with facilities dedicated to the storage, conditioning and/or pre-processing of the raw isotope material produced by the reactor, before its transportation and delivery to a processing facility or end-use customer. A large majority of research reactors producing isotopes have radioisotope storage capacities at or near the reactor site, as well as hot cells. The capacity for loading/unloading during operation is available at around half of the reactors.

3.1.2 Nuclear power plants

Nuclear power plants are used to produce radioisotopes in some countries, including Argentina, Canada, Hungary, India and Russia. The only significant isotope produced in power plants is ^{60}Co. In Canada, tritium (^{3}H) is recovered from the heavy water coolant of the power plants.

3.2 Accelerators

Generally, accelerators are used to obtain neutron deficient isotopes by proton bombardment. Some accelerators, including high-energy machines, are operated essentially for research purposes and produce isotopes only with excess or surplus beam capacity. Other machines are dedicated to medical isotope production for either the Single Photon Emission Computed Tomography (SPECT) or Positron Emission Tomography (PET) applications. For the purpose of the present study, isotope producing accelerators are classified within 3 categories: dedicated to medical radioisotope production (mainly SPECT); PET cyclotrons; and non-dedicated accelerators. Annex 7 provides details on the main isotopes producing accelerators, listed by category and by country of location.

3.2.1 Accelerators dedicated to medical radioisotope production

More than 200 accelerators (cyclotrons) are operated exclusively for the production of radioisotopes used mainly for medical applications. This includes 170 cyclotrons dedicated to the production of isotopes for PET cameras and operated in connection with PET centres.

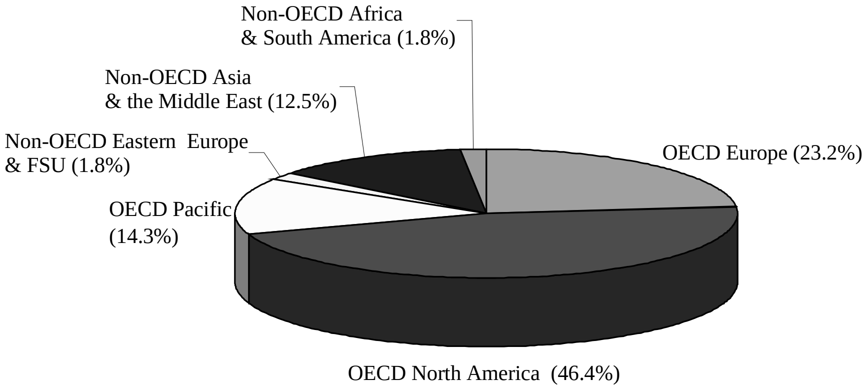
3.2.1.1 Cyclotrons producing isotopes for medical applications (mainly SPECT)

There are nearly 60 cyclotrons dedicated to the production of radioisotopes for medical applications in operation in 20 countries, including 11 OECD countries. These machines are operated mainly in OECD North America – nearly half – and in OECD Europe – nearly a quarter – with less than 10 machines of that type in operation in non-OECD countries (see Table 7 and Figure 4). Some countries have chosen to implement such machines owing to the size of their domestic demand and/or the lack of sufficient foreign supply sources of the radioisotopes that are required in the medical sector. The main isotopes produced by those cyclotrons are ^{67}Ga, ^{111}In, ^{123}I and ^{201}Tl. In most instances these cyclotrons also produce the PET isotopes, if needed.

Table 7. **Geographical distribution of cyclotrons dedicated to medical isotopes**

Region (country)	Number of machines		
	Total	Private	Public
OECD Europe	13	12	1
OECD North America	26	26	0
OECD Pacific	8	6	2
Non-OECD Eastern Europe & FSU (Russia)	1	0	1
Non-OECD Asia & the Middle East	8	0	8
Non-OECD Africa & South America	3	0	3
Total	**59**	**44**	**15**

Figure 4. **Geographical distribution of cyclotrons dedicated to medical applications**



Practically, all the cyclotrons producing isotopes for medical applications are built by a small number of commercial companies. About 75% of those machines are operated by private companies and five companies control half of the total. However, public-owned machines are in operation in some countries.

The demand for the current, 3rd generation, of classic negative ion cyclotrons is reaching a plateau. However, there is a demand arising from the need to the replace ageing machines and it is estimated that between 1 and 3 of this type of cyclotron are built every year.

3.2.1.2 Cyclotrons for specialised applications

There is an increasing demand for cyclotrons dedicated to the production of individual isotopes, such as ^{103}Pd. This is due to the technical nature of the production requirements for some isotopes, that need either a very high current or a combination of other factors that would make a multi-purpose machine (suited for producing several isotopes) too expensive to manufacture and operate. The machines of this type already in operation by the end of 1999 are included in Table 7.

3.2.1.3 Cyclotrons producing isotopes for PET applications

Often, cyclotrons producing isotopes for positron emission tomography are built and operated close to PET centres. The cyclotrons have to be close to PET facilities owing to the short half-lives of the isotopes used by PET cameras. The main radioisotopes produced by those cyclotrons are those needed to operate PET cameras, i.e., ^{11}C, ^{13}N, ^{15}O and ^{18}F.

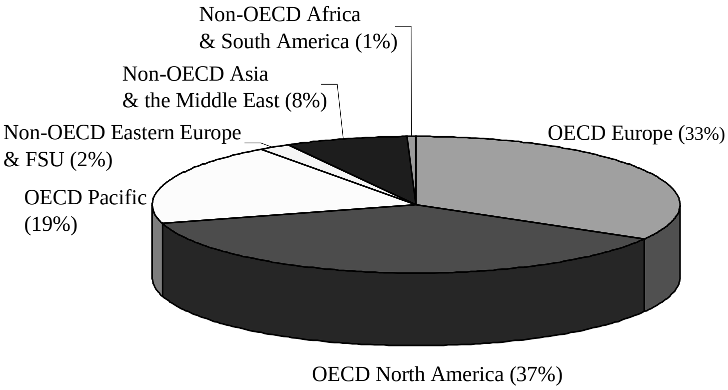
There are nearly 170 machines of this type in operation in 23 countries world-wide including 18 OECD countries; their geographical distribution is shown in Table 8 and Figure 5. Around 90% of the PET cyclotrons are operated in OECD countries. The limited number of PET centres in non-member countries results mainly from the slow adaptation of their health care systems to advanced technologies.

Table 8. **Geographical distribution of PET cyclotrons**

Region (country)	**Number of units**
OECD Europe	56
OECD North America	62
OECD Pacific	33
Non-OECD Eastern Europe & FSU (Russia)	3
Non-OECD Asia & Middle East	12
Non-OECD Africa & South America	1
Total	**167**

A large share of the PET cyclotrons is operated by state-owned companies within the framework of PET centres owned by public entities. However, there is a trend to move this type of equipment as well as more generally medical care infrastructure and services to the private sector. Today, PET technology is well established and there are no large financial and institutional barriers to the implementation of PET centres. Although the role of governments remains essential in terms of regulation and health care support system, the private sector is becoming more active in the field as the demand for PET centre services is growing, at least in some countries. It is estimated that around ten to fifteen cyclotrons for Positron Emission Tomography are built annually in the world. The demand for this type of machine is expected to increase significantly over the next few years.

Figure 5. **Geographical distribution of PET cyclotrons**



3.2.2 Accelerators not dedicated to medical isotope production

Accelerators that produce isotopes although they are not dedicated to this activity include high-energy accelerators (between 180 and 800 MeV) and medium energy accelerators (between 25 and 130 MeV). The high-energy accelerators are used mainly for ^{64}Cu, ^{67}Cu, ^{82}Sr and ^{127}Xe production, because they offer the most effective means of producing those isotopes. Two of those machines are operated in the United States, one in Canada and one in Switzerland. A list of the main isotopes produced by high-energy accelerators is included in Annex 3.

Although dedicated mainly to research activities, a number of cyclotrons rated between 25 and 130 MeV, produce isotopes (see list of main isotopes produced by those accelerators in Annex 3). The geographical distribution of those cyclotrons is given in Table 9.

Table 9. **Geographical distribution of non-dedicated accelerators producing isotopes**

Region	Number of units
OECD Europe	15
OECD North America	4
OECD Pacific	2
Non-OECD (Brazil, India, Kazakhstan, Russia, South Africa)	8
Total	**29**

3.3 Radioactive isotope separation

3.3.1 Separation of isotopes from fission products

The most important isotope produced by separation from fission products is ^{99}Mo a parent isotope for ^{99m}Tc generators which are used widely in nuclear medicine procedures. Since today's users require high specific activity ^{99}Mo, its production is achieved mainly by separation from fission products resulting from the irradiation of ^{235}U targets in reactors. There are facilities in operation world-wide that produce ^{99}Mo from fission product on a large scale in several countries including

Belgium, Canada, the Netherlands and South Africa. Additionally, there are a number of other medium size producers in Australia and non-OECD Europe. Some of these facilities also produce other isotopes such as ^{131}I and ^{133}Xe. A new facility for the production of ^{99}Mo has been constructed in the United States but remains in standby condition without having been commissioned.

Also, seven facilities including hot cells produce isotopes such as ^{85}Kr and ^{137}Cs from nuclear power plant irradiated fuel. Five of those facilities are operated in Russia, one in India and one in the United States. Recently, in the United States, the production of ^{90}Y (derived from ^{90}Sr contained as a fission product in spent fuel) is gathering increasing attention and a stock of ^{90}Sr together with a production process has been transferred to a private company. Other companies elsewhere in the world have similar "^{90}Y generator" technology.

3.3.2 Separation of transuranium elements and alpha emitters

These plants produce a number of heavy radioisotopes for various applications. The technology required is rather complex and the volume of output is fairly low in comparison with the stocks treated. Their geographical distribution is given in Table 10.

Table 10. **Geographical distribution of plants producing transuranium elements and α emitters**

Region (countries)	Number of facilities	Main isotopes produced
OECD Europe (Germany, United Kingdom)	2	^{213}Bi, ^{225}Ac, ^{241}Am, ^{243}Am, ^{244}Cm
OECD North America (United States)	3	^{225}Ac, ^{229}Th, ^{235}U, ^{236}U, ^{238}U, ^{239}Pu, ^{240}Pu, ^{241}Pu, ^{242}Pu, ^{241}Am, ^{243}Am, ^{249}Bk, ^{252}Cf
Non-OECD Europe (Russia)	4	^{235}U, ^{236}U, ^{252}Cf, ^{241}Am, ^{244}Cm,
Total	**9**	

The demand for alpha emitting isotopes, in particular the ^{225}Ac/^{213}Bi and ^{212}Bi systems, may increase depending on the development and market penetration of some promising applications. Their production currently does not require the availability of existing research reactors, but is limited by the availability of starting source materials. In the case of the ^{225}Ac/^{213}Bi, it is the supply of the source material ^{229}Th, derived from ^{233}U or produced by the irradiation of ^{226}Ra, that is a limiting factor. For the ^{212}Bi system, the supply of the parent material ^{228}Th (derived from ^{232}U) determines the availability of the desired isotope. Limited quantities of source materials for those two systems are currently available and additional quantities will be necessary to ensure future security of supply.

3.4 Stable isotope production

Approximately 300 different stable isotopes of some 60 elements have been produced by a number of separation technologies. Generally these stable isotopes are classified as either heavy (sulphur and above in atomic number) or light. Both the separation technologies and the financial and institutional barriers differ greatly for each of these groups. Separation technologies applicable to heavy stable isotopes can, and have, been used to separate fissile materials and thus are subjected to strict international controls. Technologies to separate light stable isotopes are easier to implement and less sensitive.

3.4.1 Heavy stable isotopes

Two production technologies for heavy stable isotopes are currently in use. These are the highly versatile but older electromagnetic separation process, using dedicated mass spectrometers called calutrons, and the modern and more efficient gas centrifuge process. The latter can only be used for elements that form suitable gaseous compounds. Both technologies are quite complicated and the entry barriers for potential new producers are very high. The number of heavy stable isotope producers is very limited. These are generally government owned facilities except for the enrichment plant in Netherlands, which does have some limited government investment. Table 11 presents the geographic distribution of the heavy isotope production facilities.

Table 11. **Geographical distribution of stable isotope production facilities**

Region (Country)	Operator	Technology
OECD Europe		
Netherlands	Urenco	Centrifuge
OECD North America		
United States	Isotec Inc. Oak Ridge Nat. Lab./DOE	Liquid thermal diffusion Electromagnetic separation
Non-OECD		
China	CIAE	Electromagnetic separation
Russia	Centrotech ECP, St. Petersburg	Centrifuge
	ECP Zelenogorsk, Krasnoyarsk	Centrifuge
	Kurchatov Institute, Moscow	Electromagnetic sep., Centrifuge
	SCC Siberian Group, Tomsk	Centrifuge
	EKPC, Sverdlovsk	Electromagnetic separation
	OKB GAZ, Nizny Novgorod	Centrifuge
	VNIIEF, Nizny Novgorod	Centrifuge

The electromagnetic producers of stable isotopes rely on relatively old and expensive to operate, facilities with the associated risks related to reliability of supply. The centrifuge producers have the advantage of more modern, cheaper equipment. However this technology is less versatile and cannot produce a broad range of stable isotopes. Additional concerns are raised by the importance of Russian producers in the world supply since financial and organisational problems in that country create a potential risk regarding their ability to ensure adequate levels of production.

Other technologies for the production of heavy stable isotopes that have been, and are being explored include laser technologies, a variety of plasma separation processes, and even a few chemical separation schemes.

3.4.2 Light stable isotopes

A number of light isotopes (below Na in the periodic table) have a wide range of applications in medicine and research. Various isotopes of oxygen, nitrogen, carbon and others are currently used. Different technologies may be used to separate stable isotopes. Electromagnetic separation, performed in the past for a number of such elements, is rather inefficient and tends to be replaced by more efficient methods including thermal diffusion and cryogenic distillation. Light isotopes are easier to produce than heavy isotopes and technological or institutional barriers to their production are minor. The main producers of light stable isotopes are the United States, Russia and Israel. The companies involved are mainly private. Facilities producing these isotopes are not covered in the report since there is no key supply issue with regard to light stable isotopes.

4. TRENDS IN ISOTOPE USES AND PRODUCTION

The present study and the survey carried out in 1998 have identified some key features characterising the general evolution in the field of beneficial uses and production of isotopes. It should be stressed, however, that neither the 1998 survey nor the present enquiry were exhaustive and, therefore, some aspects may have been overlooked in particular at the regional level.

Regarding uses, trends vary from sector to sector but globally there is an increasing demand for many isotopes. A number of emerging applications gain importance, thereby requiring more isotopes, and innovative applications are introduced calling for the production of "new" isotopes, i.e., isotopes that had no significant beneficial uses previously.

On the production side, the evolution is rather slow owing to the lead times necessary to put into operation, modify or refurbish most major production facilities. For example, the construction, licensing and commissioning of research reactors or heavy stable isotope production facilities take several years. Cyclotrons dedicated to the production of radioisotopes used in medical applications may be implemented more rapidly but, globally, the adaptation of isotope production capacities is a lengthy process.

4.1 Trends in isotope uses

Trends in isotope uses are not generic and vary from sector to sector as well as from region to region.

In the medical field as a whole, isotopes are increasingly used in a wide range of applications. Radioactive and stable isotopes are essential in many medical procedures for diagnosis and therapeutic purposes. They offer some unique characteristics as compared to alternatives and it has been assessed over time that they contribute significantly to human health care by providing cost efficient means to detect and/or cure a large number of diseases. However, trends vary for each specific application, from progressive decrease, e.g., remotely controlled cobalt therapy, to sharp increase, e.g., brachytherapy. The development of new applications, such as palliative care, create additional demand for isotopes currently used as well as for new isotopes.

In the therapeutic field, new developments include increasing demand for brachytherapy implants and growing use of radioisotopes for palliative care. The use of several isotopes traditionally used in the medical field, such as ^{90}Y, ^{125}I, ^{131}I and ^{192}Ir is expanding. As well, demand for new isotopes, such ^{103}Pd, ^{117m}Sn or ^{166}Ho has been created. There is no serious concern, however, about supply of isotopes used for therapeutic purposes since the existing production capabilities are adequate or easily adaptable. Production costs are not a key issue in this field owing to the small share of the raw material cost in the total price of medical procedures. However, prices will likely contribute to determining market shares of different producers.

In the field of nuclear imaging high growth has been experienced for PET and this trend is expected to continue. The demand for ^{18}F as the radioactive component of FDG is increasing since it has proven to be an efficient tool for the staging of various cancers. For gamma imaging, there is a sustained demand of ^{99}Mo (parent isotope of ^{99m}Tc). The future growth in demand for isotopes used in imaging, however, will depend largely on government policies regarding preventive medical procedures in general and nuclear medicine in particular. Comprehensive cost/benefit analyses generally demonstrate the economic advantage of prevention over treatment (e.g., productivity of work force), besides the obvious social benefit of improved quality of life. The recognition of nuclear imaging procedures by social security, i.e., reimbursement of corresponding expenses, is a major milestone for the development of those procedures. Situations in this regard differ from country to country and may continue to be contrasted. In particular, it is likely that nuclear imaging procedures will become current practice at a slower pace in developing countries than in OECD countries.

For industrial applications as a whole, the demand for isotopes is relatively stable. In many industrial sectors, however, even where their use is a well established practice, isotopes are facing competition with other techniques such as X-rays, ultra-sound, laser and radar. Some specific applications, such as some types of nucleonic gauges, show decreasing trends while other types of gauges enjoy increasing market opportunities.

The sector of food irradiation deserves some attention since the evolution of demand could change dramatically within a few years. The potential demand for food preservation is enormous worldwide and the market for a reasonably cheap and easy to use technology would be huge provided it will be licensed by health protection regulators and accepted by consumers. The barriers to the use of isotopes in this field are national regulations that, in many countries, do not authorise the distribution and consumption of irradiated food products. The recent moves towards alleviating restrictions, in the United States in particular, could facilitate the penetration of food irradiators on the market and create an additional demand for large volumes of low specific activity ^{60}Co sources.

For scientific applications, isotope demand is linked with the evolution of basic research programmes. This sector is characterised by its diversity and frequent changes in the type of isotopes required, as well as by the small volumes needed; the future demand is, therefore, difficult to predict. The continued role of isotopes in scientific research will depend on the availability to local and regional laboratories of a wide range of isotopic elements.

The demand for enriched stable isotopes for biomedical, industrial and scientific uses is growing and could increase further for already existing and new emerging or “dormant” applications. Stable isotopes used as starting materials to produce radioisotopes follow the trends of demand for radioisotopes. In addition, stable isotopes themselves are increasing being used in medicine, and research in biology and life sciences in particular. Moreover, there are many promising opportunities for expanded applications of stable isotopes that could be developed when and if reliable supply would be made available at affordable prices.

While the benefits of using isotopes are recognised by users, especially in the medical field but also in many industrial sectors, public concerns about radiation are a strong incentive to search for alternatives. Past trends illustrate this point and show that isotopes are not the preferred choice whenever alternatives are available. Therefore, isotopes should remain significantly more efficient and/or cheaper than alternatives in order to keep or increase their market share in any application. It should be recognised that the use of sealed radioactive source and/or irradiators requires a stringent safety and radiation protection framework in order to ensure adequate protection of human health and the environment. Repeated incidents, and a few largely publicised accidents, that have occurred in both OECD and non member countries may contribute to increased public reluctance to accept beneficial uses of isotopes.

Additionally, the transport and distribution of isotopes, both locally and in particular internationally, raises some legislative and commercial issues that may create a barrier to continued reliable and secure supply of isotopes. Container and transport regulations, although based common principles, are not universally accepted around the world and may vary from country to country. Increased efforts at the legislative level will help to minimise risk of disruption to international isotope supply that may result from this lack of harmonisation in norms and standards. With the complexities and associated costs of international shipment and in particular for those radioisotope products with a relatively short half-life (e.g. less than 3 days), then smooth distribution as well as a broad global spread of manufacturing facilities become increasingly important factors for guaranteed continuous supply.

4.2 Trends in isotope production

Trends in isotope production vary according to the type of production facility and the region. In particular, trends are different for facilities dedicated to isotope production, such as cyclotrons producing isotopes for medical applications, and for facilities that produce isotopes only as a side activity such as most research reactors. Also trends differ depending on the degree of governmental involvement in the construction and operation of various isotope production facilities. As far as research reactors are concerned, since generally they are operated for scientific purposes and isotopes are only "by-products", the trends mainly result from policies on nuclear research.

Production of some radioisotopes require specific facilities that are operated in a limited number of countries and their production trend depends mainly on policies in those countries, upon which the world's supply relies. It is the case of ^{252}Cf and high specific activity ^{60}Co for medical applications, produced only in high neutron flux reactors.

For neutron rich isotopes produced in reactors, trends and issues tend to be region specific. In OECD Europe three reactors (Astra, in Austria, Osiris, in France and FRM in Germany) will be shut down in the next decade and replaced by machines more powerful but not specifically designed for isotope production.

In Asia, where demand is growing, new reactors are being built and commissioned. However, those reactors are multi-purpose machines and cannot be expected to produce large quantities of isotopes on a regular basis. Therefore, they are likely to provide supply only in the country where they are operated or at most in the region.

In North America, research reactors are ageing and their replacement is not always planned. However, the two new 10 MW reactors dedicated to isotope production that are expected to come into operation in Canada in 2000 should contribute to future security of supply. Each of these two units, which are privately owned, can produce significant quantities of ^{99}Mo (several times the current world demand according to the plant owner) and can produce as well ^{125}I, ^{131}I and ^{133}Xe.

The trend in non-OECD Europe and the Former Soviet Union is difficult to assess because few countries in the region responded to the questionnaire and published data on current and future production and/or capabilities in the region are scarce. In Russia, a third of the reactors producing isotopes at present are likely to be shut down by 2005 owing to ageing and high operating costs, and it is not clear whether new investments will be made for isotope production in the region.

The number of high neutron flux reactors in operation is low enough to raise some concern on their ability to supply the isotopes that cannot be produced by other reactors and are essential for a number of non commercial applications.

For neutron deficient isotopes produced by accelerators, the adaptation of production capacity to demand is easier since accelerators are more rapid to build and commission than reactors. Cyclotrons producing isotopes for medical applications may be ordered and put into operation within two years to respond to increasing demand. Investors are attracted in this field by the prospect of a growing market for medical procedures relying on the use of radiopharmaceuticals. The demand, however, depends on the health care system in place in each country (social security coverage). In many industrialised countries, where nuclear imaging is reimbursed by health insurance, the demand is growing steadily and production increases accordingly as cyclotrons can be operated on a commercial basis by private enterprises. In other countries, the construction of cyclotrons may depend essentially on the implementation of health care programmes covering medical procedures relying on the use of radiopharmaceuticals.

In the field of PET, production trends are in line with the surge in demand. Wide spread adoption of PET in a country depends mainly on governmental policies regarding research in the medical field and upon health care system reimbursement for the procedure. Further developments would be necessary in order to go beyond the present research and prototype level and bring PET cameras to the level of being a commonly used medical practice uniformly used throughout developed countries.

The tritium production programme of the United States ensures short-term security of supply with regards to isotopes produced by linear accelerators if the accelerator route is chosen as the preferred option. Also, tritium can be obtained in bulk from a Canadian facility processing heavy water used as coolant for Candu reactors.

The production of high specific activity ^{60}Co for medical applications might become a problem as the three production facilities in operation in Western Europe and North America are expected to be shut down shortly (within the next three years).

The production of some isotopes, such as ^{137}Cs and ^{90}Sr, that are obtained by separation from fission products, raise important concerns regarding access to source materials, i.e., dedicated separation processes of high level waste at spent fuel reprocessing plants. There is, however, no major concern regarding short and medium term supply.

The production of light stable isotopes is carried out in a rather large number of facilities distributed in several countries. Additional capacity may be added rapidly if and when needed. On the other hand, the production of heavy stable isotopes rely on very few facilities and countries. Furthermore, a large share of heavy stable isotope demand is satisfied by drawing from inventories rather than through actual separation. This raises medium term concerns regarding the future availability of key heavy stable isotopes.

The emergence of private producers is a key trend in the isotope production field. Recent additions to the isotope production capabilities in several regions show that the commercial sector has reacted to increasing demand and the potential threat of shortage for some major isotopes such as ^{99}Mo. It seems that now security of supply for major isotopes used in the medical and industrial fields is not an issue for the short or medium term. However, it is important to ensure a redundancy mechanism in order to secure, in each country, supply to users of critical short half-life radioisotopes such as ^{99}Mo, irrespective of technical (e.g. facility failure) or social (e.g. strike) problems that producers may encounter.

5. FINDINGS, CONCLUSIONS AND RECOMMENDATIONS

5.1 Findings

The enquiries and analysis that support the present study focused on key issues in the field of isotope uses and production already identified by the first NEA survey published in 1998. In particular, efforts were made to update and complete factual information and to highlight trends in the various applications of isotopes as well as in the isotope production sector. Responses to the questionnaire showed some interest from the producers in participating in an international enquiry but also a reluctance to provide detailed information on actual production. A consensus was reached within the participating experts and organisations on the relevance of periodic reviews in the field of beneficial uses and production of isotopes. The pace of evolution in the sector would call for an update of the review every three to four years.

The present study confirmed that governments and public entities play an important role in the field. National policy, on research and development and medical care for example, remains a key driver for isotope demand and, although to a lesser extent, for their production. However, an increasing involvement of private companies was noted as well as a shift to a more business like and commercial management of the activities related to isotope production and uses.

International co-operation was identified as an important dimension for optimising the use of production capabilities and ensuring security of supply. In this context, it was found that international governmental organisations could assist both in ensuring adequate information exchange and strengthening international co-operation. Some consideration may be given to harmonisation of standards and regulation applicable to transport of irradiated targets and separated isotope products world-wide in the light of the role of international exchanges for guaranteeing adequate supply in all regions of the world.

5.1.1 Isotope uses

The two successive surveys showed that beneficial uses of isotopes remain a current practice in many sectors of economic activities. The present study confirmed the lack of comprehensive information including qualitative and quantitative data on the use of isotopes in different sectors, covering the whole world. In particular, a robust assessment of the overall economic importance of beneficial uses of isotopes remains to be done.

While uses of isotopes evolve continuously, the opportunities for stakeholders to discuss trends in their respective sectors are limited for most applications, with the notable exception of the medical field. In most industrial sectors, isotope applications are occupying niche markets and represent small volumes of activity even when they have a key role in individual processes. Continuously, some applications may decline due to the replacement of isotopes by other technologies that prove to be more efficient and/or cheaper while new applications are emerging as science and technology progress. A systematic collection and harmonisation of data and indicators on isotope uses at the international level could assist in analysing global trends and assessing the viability of specific applications.

5.1.2 Isotope production

Although isotopes are produced in a large number of plants and workshops all over the world, it has proven reasonably easy to establish a fairly complete list of isotope production facilities. Quantitative data on isotope production, on the other hand, has proven difficult to obtain according to the experience acquired through the two enquiries carried out in 1997 and 1999 by the NEA and the IAEA.

The IAEA maintains a data base of research reactors in operation in the world that provides a sound basis for enquiring about their isotope production. However, since isotopes are often by-products of research reactors, it has not been always possible to identify and contact directly the persons responsible for isotope production in those reactors. The isotope producer is often independent of the reactor operator, and may receive services, (i.e. target irradiation for isotope production), from different reactors. Moreover, even when responses to the questionnaire were returned they were often incomplete and did not cover by far the whole scope of information requested. Therefore, while collecting information on research reactors producing isotopes proved to be reasonably easy, assessing the actual isotope production level of those reactors has been less straightforward.

The enquiry did not cover the production of low specific activity ^{60}Co for gamma-ray irradiation plants that is carried out on a large scale by nuclear power plants, especially heavy water reactors, nor details on light stable isotope production that does raise major security of supply issues.

Likewise, high-energy accelerators are used mainly for research purposes and information on their isotope production, being a secondary activity, is generally not easily available. Still, low and medium energy accelerators, mostly cyclotrons, are dedicated exclusively to isotope production. Nevertheless, since they are operated essentially on commercial bases, commercial confidentiality makes it hard to get data.

Data are published by some countries on national isotope production annually. These publications may serve as a basic framework for collecting similar data world-wide through an international inquiry and by compiling the results.

International co-operation could be considered as an efficient means to ensure adequate supply of some isotopes, in particular for scientific applications that do not offer an attractive commercial market.

5.1.3 Role of governments

The information analysed in the study highlights the important role of the public sector in isotope production and, to a lesser extent, in isotope uses. Also, in all countries, governments are responsible for establishing regulations and norms regarding production, transport and uses of isotopes.

Public entities own and operate almost all the research reactors, large-scale accelerators and chemical isotope separation facilities for isotope production as well as facilities for extended uses of isotopes in medical and scientific fields. Governments perform the role of funding an infrastructure for effective isotope production and their beneficial uses. In particular, governments have an important role to play in ensuring availability at reasonable cost of new isotopes desired by the research community that cannot be supplied by commercial producers. Governments also provide opportunities for education and training of qualified manpower required for these activities.

Concerning the production of major isotopes used in medical applications, a number of medium-size cyclotrons are owned and operated by private companies for their exclusive use. The role of governments in such cases is to ensure that activities are carried out in compliance with safety regulations.

5.1.4 Role of international exchanges

Nearly all countries depend on imports at least for some isotopes that are not domestically produced, though half lives of some isotopes limit their distribution globally. Many isotope producers rely on target irradiation services provided by reactors operated in foreign countries. Some isotopes are supplied only by a few producers serving a large number of foreign users. Therefore, international exchanges are essential to ensure adequate supply, together with the availability of comprehensive information on existing and projected production capabilities.

At present, most of the isotope production facilities are operated in OECD countries and they also are the main users. Demand is increasing in non-OECD countries and their production capabilities might not increase as fast as their demand.

5.1.5 Costs and prices

Facilities dedicated to isotope production, such as cyclotrons producing isotopes for medical applications, are managed on a commercial basis and prices in that case reflect full cost recovery. For some research reactors and high-energy accelerators that are not dedicated to isotope production, only the marginal additional cost associated to isotope production per se is generally accounted for in prices of isotopes from these sources. In these cases, the overall cost of the facilities, including investment, safety, maintenance, fuel, waste management and decommissioning are borne by the main users, i.e., research programmes. However, some reactors and accelerators not dedicated to isotope production are operated on a more commercial setting.

Since economic conditions differ according to region, costs and prices for isotopes produced with the same technology may vary greatly depending on the country where they are produced. This has led users to seek supply preferably from some regions where prices tend to be low. Supply of some isotopes as raw materials has shifted progressively from North America and Western Europe to Eastern Europe and, to a lesser extent, to China, because of the lower prices that those regions can offer owing to their low costs and/or highly subsidised operating modes.

5.2 Conclusions

The present report is the second edition of a general survey on isotope uses and production in the world carried out jointly by the NEA and the IAEA. The information collected and presented aims at providing experts and policy makers in the field with factual data that may be used to identify potential gaps in supply for a given application and over capacity of production for some isotopes.

Further effort may be undertaken at the national and international levels to collect reliable data on isotope demand covering all sectors and countries concerned. The regulatory framework in place in each country for licensing isotope uses may offer the opportunity to access information. On the supply side, existing databases on research reactors and accelerators in operation provide a significant share of the information required. However, additional data and evaluations are needed to provide a full overview of isotope production capabilities.

For some isotopes, particularly those with short lives or with special types of specifications, the supply demand balance is a regional issue. Production capabilities of very short half-life isotopes must match demand at regional level. This is the case for PET isotopes that generally have to be produced close to the end-user's site. For other isotopes, that may be transported over long distances and require highly specialised machines and/or facilities for their production, world supply may be ensured by a limited number of facilities located in a few countries. International co-operation and exchanges are important for adequate security of supply. In all countries, domestic supply relies at least partly on imports. In particular, supply demand balance at national level requires exchange between OECD and non-OECD countries.

Owing to the development of new applications on the one side and to the progressive phase out of some uses on the other, radioactive isotope demand is evolving. On the production side, adaptation to demand requires rather long lead-times. Most production facilities require several years to be built and commissioned (e.g. around two years for dedicated cyclotrons and eight years for research reactors). Monitoring projected demand and planned production capacities at world level is essential to alleviate the risk of inadequate supply in the future.

The demand for stable isotopes is increasing as they are essential for existing and arising applications. The production of economically attractive stable isotopes in large quantities is likely to be ensured as long as industrial enrichment plants using gaseous centrifuge technology will continue to operate. However, the continued production of stable isotopes that cannot be produced by gas centrifuge and of those used for scientific (R&D) applications may raise concerns.

The study has shown that beneficial uses of isotopes are important for economic and social welfare world-wide. Its findings and conclusions highlight the role of governments in the field and the need for enhanced information exchange and international co-operation to ensure adequate supply of all the isotopes needed in various sectors. International organisations, such as the NEA and the IAEA, could assist in enhancing international information exchange and co-operation.

5.3 Recommendations

Recognising both the importance of isotopes for medical, industrial and scientific applications and the present and potential future roles that they could play in enhancing welfare world-wide, it is recommended that governments consider maintaining or implementing policies favouring adequate supply of isotopes taking into account present and foreseeable future demands. Governmental measures in this field may complement market mechanisms in particular for isotopes needed in scientific research and innovative emerging applications. Intergovernmental organisations, such as the NEA and the IAEA, could assist in this process by collecting and compiling in a database relevant information on demand and supply of isotopes and by providing analyses, including projections, on supply and demand issues.

In the light of the continuing changes in isotope uses and geographic distribution of production capabilities, it seems relevant for intergovernmental organisations to analyse global and regional trends on a regular basis, e.g. every third or fourth year. Such analyses could help to assess whether adequate supply could be ensured in the short, medium and long term. They may support identifying specific actions and measures that governments could consider to facilitate international exchange of isotopes between OECD and non-OECD countries and to optimise production capabilities globally.

Some isotopes, such as ^{99}Mo and ^{192}Ir, have key medical and/or industrial applications. Although the production of those isotopes is generally ensured by the private sector and large government owned authorities, the consequences of supply shortages would have drastic consequences that call for governments' attention. It is recommended that governments consider adequate policy measures to complement market mechanisms in order to guarantee continued supply of the isotopes that are essential in the medical and/or industrial field.

The production of some isotopes especially useful in medical care requires high neutron flux reactors and/or special facilities. The present situation does not raise concern in this regard since there are enough high neutron flux reactors either in operation or planned to be commissioned in the short or medium term. However, it is recommended to be attentive to long term supply through both maintaining in operation the existing reactors and facilities that can be used for this purpose and making timely plans for their replacement at the end of their lifetime.

Adequate supply of diverse isotopes, generally in small quantities for each isotope, is essential for basic medical, physical and life science research that support scientific, technical and social progress. Recognising that the production of isotopes for research is unlikely to be a commercially profitable activity, it is recommended that governments support the infrastructure, equipment and staff, necessary for a secure a continued supply of those isotopes at the country and/or regional level.

The supply of stables isotopes increasingly used for traditional and emerging applications does not raise concern in the near term since industrial enrichment plants using gaseous centrifuge technology are expected to continue operating to supply enriched uranium for the power sector. It is recommended, however, that countries, in particular OECD countries, pursue the development of new technologies and plants to separate stable isotopes that cannot be obtained from centrifuge technology and eventually to substitute gaseous diffusion plants.

Given the importance of international exchanges in ensuring adequate isotope supply world-wide, it is recommended that governments endeavour to harmonise regulations and norms for isotope production, transport and uses, in order to facilitate these exchanges.

Government policies in the field of isotope production and uses are changing in the context of economic deregulation and privatisation of industrial sectors traditionally under state control. Like in other sectors, economic deregulation is expected to enhance efficiency and reduce costs. The social dimension of development, especially relevant in the case of some research applications of isotopes, should be integrated in the decision-making framework according to the overall national policy goals.

In the past, isotope production facilities partly supported by governments in the framework of global scientific and social development policies have been instrumental in promoting the unique isotope technology and making it available for the advancement of human society. The role of governments in this field should be assessed against this background. While it would be fair to consider pricing policies reflecting marginal costs of isotope production, full cost recovery applied to facilities producing isotopes as a by-product might jeopardise the development of a number of beneficial uses of isotopes in particular for science and medicine.

On the other side, in many areas and sectors – such as the supply of medical isotopes – the demand for isotopes is regular and large enough to justify the operation of dedicated facilities and ensure their effectiveness. Market mechanisms are already fully in force in those sectors and have proven to be effective in providing competitively priced products.

The overview on isotope uses included in this report mainly provides qualitative information. While it was recognised by the expert group that a comprehensive quantitative review of isotope uses could be valuable, the collection of reliable data raised a number of methodological and fundamental issues such as consistency between sectors and countries and commercial confidentiality.

Therefore, it is recommended to pursue a regular review of isotope uses through literature surveys and to promote exchange of information on the topic through ad-hoc meetings, seminars or conferences covering in so far as feasible a broad range of isotope applications as well as production means and facilities.

Annex 1

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Annex 2

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Annex 3

MAJOR RADIOISOTOPES PRODUCED IN REACTORS AND ACCELERATORS

Reactor produced radioisotopes	**Accelerator produced radioisotopes**	**High energy accelerator produced radioisotopes**
^{3}H	^{11}C	^{26}Al
^{14}C	^{13}N	^{28}Mg
^{32}P	^{15}O	^{32}Si
^{33}P	^{18}F	^{67}Cu
^{35}S	^{22}Na	^{82}Sr
^{51}Cr	^{57}Co	^{148}Gd
^{59}Fe	^{67}Ga	^{172}Hf
^{60}Co	^{81}Rb	^{200}Pb
^{64}Cu	^{103}Pd	
^{89}Sr	^{111}In	
^{90}Y	^{123}I	
^{99}Mo	^{201}Tl	
^{125}I		
^{131}I		
^{133}Xe		
^{153}Sm		
^{159}Gd		
^{186}Re		
^{188}W		
^{192}Ir		
^{198}Au		
^{204}Tl		
^{252}Cf		

Annex 4

COUNTRIES AND REGIONAL GROUPINGS

OECD Europe [19 countries*]

- Austria
- Belgium
- Czech Republic
- Denmark
- Germany
- Finland
- France
- Greece
- Hungary
- Italy
- Netherlands
- Norway
- Poland
- Portugal
- Spain
- Sweden
- Switzerland
- Turkey
- United Kingdom

OECD North America [3 countries*]

- Canada
- Mexico
- United States

OECD Pacific [3 countries*]

- Australia
- Japan
- Korea (Republic of)

Non-OECD Eastern Europe and Former Soviet Union [9 countries*]

- Bulgaria
- Kazakhstan
- Latvia
- Romania
- Russia
- Slovenia
- Ukraine
- Uzbekistan
- Yugoslavia

Non-OECD Asia and the Middle East [12 countries*]

- Bangladesh
- China
- Chinese Taipei
- India
- Indonesia
- Iran
- Israel
- Korea (DPRK)
- Malaysia
- Pakistan
- Saudi Arabia
- Viet Nam

Non-OECD Africa and South America [9 countries*]

- Algeria
- Argentina
- Brazil
- Chile
- Congo (Dem. Rep. of)
- Egypt
- Libya
- Peru
- South Africa

* Number of countries included in the study

Annex 5

RADIOISOTOPE PRODUCTION RESEARCH REACTORS AND ACCELERATORS IN OECD COUNTRIES

Country	Research reactors	Cyclotrons dedicated to medical isotopes	Cyclotrons dedicated to PET	Non-dedicated accelerators
EUROPE	**17**	**13**	**56**	**15**
Austria	1	0	1	0
Belgium	1	4	5	3
Czech Republic	1	1	1	0
Denmark	1	0	2	0
Finland	0	0	2	2
France	2	2	4	0
Germany	1	1	20	3
Greece	1	0	0	0
Hungary	1	0	0	1
Italy	1	0	5	1
Netherlands	2	3	3	1
Norway	1	0	0	1
Poland	1	0	0	0
Portugal	1			0
Spain	0	0	2	0
Sweden	1	0	2	0
Switzerland	0	0	2	1
Turkey	1	0	0	0
United Kingdom	0	2	7	2
NORTH AMERICA	**7**	**26**	**62**	**4**
Canada*	2	2	6	1
Mexico	1	0	0	0
United States	4	24	56	3
PACIFIC	**6**	**8**	**33**	**2**
Australia	1	1	1	0
Japan	4	6	30	2
Korea (Rep. of)	1	1	2	0

* Not including the 2 Maple reactors to be commissioned in 2000.

Annex 6

GEOGRAPHICAL DISTRIBUTION OF RESEARCH REACTORS PRODUCING ISOTOPES

OECD Europe (17 reactors in 15 countries)

Country	Reactor name	Location	Power (MW)	Main producers
Austria	ASTRA	Seibersdorf	10	
Belgium	BR 2	Mol	100	**X**
Czech Republic	LWR-15 REZ	Rez	10	**X**
Denmark*	DR-3	Roskilde	10	
France	ORPHEE OSIRIS	Saclay Saclay	14 70	 **X**
Germany	FRM	Garching	4	
Greece	DEMOKRITOS (GRR-1)	Attiki	5	
Hungary	BRR	Budapest	10	**X**
Italy	TRIGA RC-1	Santa Maria di Galeria	1	
Netherlands	HOR HFR	Delft Petten	2 45	 **X**
Norway	JEEP II	Kjeller	2	
Poland	MARIA	Swierk	30	**X**
Portugal*	RPI	Sacavem	1	
Sweden	R-2	Nyköping	50	**X**
Turkey	TR-2 TURKISH REACTOR 2	Istanbul	5	

OECD North America (7 reactors in 3 countries)

Country	Reactor name	Location	Power (MW)	Main producers
Canada**	NRU	Chalk River	135	**X**
	MNR McMaster University	Hamilton	5	**X**
Mexico	TRIGA MARK III	Salazar	1	
United States	ATR	Idaho Falls ID	250	**X**
	HFIR	Oak Ridge TN	100	**X**
	ACRR	Albuquerque NM	2	
	MURR Univ. of Missouri RR*	Columbia MO	10	**X**

OECD Pacific (6 reactors in 3 countries)

Country	Reactor name	Location	Power (MW)	Main producers
Australia	HIFAR	Menai	10	**X**
Japan	KUR	Ibaraki-ken	5	
	JRR-3M	Ibaraki-ken	20	**X**
	JRR-4	Ibaraki-Ken	3.5	**X**
	JMTR	Ibaraki-Ken	50	**X**
Korea (Rep. of)	HANARO	Taejeon	30	

Non-OECD Eastern Europe & Former Soviet Union (16 reactors in 7 countries)

Country	Reactor name	Localisation	Power (MW)	Main producers
Bulgaria*	IRT		2	
Kazakhstan*	WWR-K		10	
Romania	TRIGA II	Pitesti	14	
Russia*	SM-3	Dimitrovgrad	100	**X**
	MIR/M1	Dimitrovgrad	100	**X**
	RBT-6	Dimitrovgrad	6	
	RBT-10	Dimitrovgrad	10	
	WWR-TS	Obninsk	12	
	AM-2	Obninsk	10	
	WWR-M	Gatchina	18	
	IR-8	Moscow	8	**X**
		Mayak	>30	**X**
		Mayak	>30	**X**
Ukraine*	WWR-M		10	
Uzbekistan*	WWR-CM		10	**X**
Yugoslavia*	RA		6.5	

Non-OECD Asia & Middle East (17 reactors in 11 countries)

Country	Reactor name	Localisation	Power (MW)	Main producers
Bangladesh*	TRIGA MARK II		3	
China	HWRR-II* HFETR SPR IAE SPRR-300* MJTR*	 Chengdu Centre Beijing Chengdu Centre Chengdu Centre	15 125 3.5 3.7 5	**X** **X** **X**
Chin. Tapei*	THOR		1	
DPRK*	IRT-DPRK		5	
India	CIRUS* DRHUVA	Trombay Trombay	40 100	 **X**
Indonesia	TRIGA II GAS MPR	Bandung Serpong	1 30	 **X**
Iran	TRR	Tehran	5	
Israel*	IRR-1	Yavne	5	
Malaysia	TRIGA PUSPATI	Bangi	1	
Pakistan*	PARR-1	Islamabad	9	**X**
Thailand	TRR-1/M1	Bangkok	2	

Non-OECD Africa & South America (10 reactors in 9 countries)

Country	Reactor name	Localisation	Power (MW)	Main producers
Algeria*	ES-SALAM NUR	W. Djelfa	15 1	
Argentina	RA-3	Buenos Aires	5	**X**
Brazil	IEA-R1	Sao Paulo	10	**X**
Chile	RECH-1	Santiago	2	
Egypt*	ETRR-1	Cairo	5	
Libya*	IRT-1		2	
Peru*	RP-10	Lima	10	
South Africa	SAFARI-1	Pretoria	20	**X**
Congo (D. R.)*	TRICO II		1	

* Information from previous enquiries.
** Not including the 2 Maple reactors to be commissioned in 2000.

Annex 7

GEOGRAPHICAL DISTRIBUTION OF ACCELERATORS PRODUCING ISOTOPES

CYCLOTRONS DEDICATED TO MEDICAL ISOTOPES (total 59 in 20 countries)

OECD Europe (total 13 in 6 countries)

Country	Operator	Type	Number of units
Belgium	IBT MDS Nordion MDS Nordion	CYCLONE 18 (2) CGR 930 S CYCLONE 30	4
Czech Republic	NRI	U-120	1
France	CIS BIO CIS BIO	CGR 40 MeV CYCLONE 30	2
Germany	FZK	TCC-CP-42	1
Netherlands	Vrije Amsterdam University Mallinckrodt Mallinckrodt	PHILIPS PHILIPS CYCLONE 30	3
United Kingdom	Nycomed Amersham Nycomed Amersham	TCC-CP-42 MC-40	2

OECD North America (total 26 in 2 countries)

Country	Operator	Type	Number of units
Canada	MDS Nordion MDS Nordion	TCC-CP-42 TR-30	2
United States	Amersham Amersham Amersham Amersham Dupont Dupont Dupont Dupont Mallinckrodt Mallinckrodt Mallinckrodt Theragenics	CGR 70 MC-40 (2 units) TCC-CS-22 (2 units) CYCLONE 30 TCC-CS-22 TCC-CS-30 (3 units) MC-30 CYCLONE 30 MC-40 Cyclone 30 TCC-30 (2 units) CYCLONE 18 (8 units)	24

OECD Pacific (total 8 in 3 countries)

Country	Operator	Type	Number of units
Australia	NMC/ANSTO	CYCLONE 30	1
Japan	Daiichi RL Daiichi RL Nihon Medi-Physics Nihon Medi-Physics	CYCLONE 30 MC-40 CYCLONE 30 (2 units) TCC-CS-30 (2 units)	6
Korea (Republic of)	IRI/KAERI	MC-50	1

Non-OECD Eastern Europe & Former Soviet Union (total 1 in 1 country)

Country	Operator	Type	Number of units
Russia	Radium Institute	MGC-20	1

Non-OECD Asia & the Middle-East (total 8 in 5 countries)

Country	Operator	Type	Number of units
China	IAE INR BNU/IAC IMP	CYCLONE 30 CYCLONE 30 TCC CS-30 69 MeV	4
Chinese Taipei	INER	TR 30/15	1
Indonesia	Batan	TCC-CS-30	1
Iran	NRC	CYCLONE 30	1
Korea (DPRK)	Nuclear Energy Institute	MGC-20	1

Non-OECD Africa & South America (total 3 in 3 countries)

Country	Operator	Type	Number of units
Argentina	CNEA	CP-42	1
Brazil	IPEN CNEM	CYCLONE 30	1
Egypt	Nuclear Research Center	MGC-20	1

CYLOTRONS DEDICATED TO PET (total 167 in 23 countries)

OECD Europe (total 56 in 13 countries)

Country	Operator	Type	Number of units
Austria	AK Hospital	PETTRACE	1
Belgium	Liege University (Ulg) Liege University (Ulg) Erasmus (ULB) Gasthuisberg (KUL) UCL	CGR-520 CYCLONE 18/9 CYCLONE 30 CYCLONE 10/5 CYCLONE 30	5
Czech Republic	Na Hom Hospital	CYCLONE 18/9	1
Denmark	RIGS Hospital Aarhus Hospital	MC-32 PETRACE	2
Finland	Turku University University Helsinki	CYCLONE 3 CYCLONE 10/5	2
France	SHFJ CERMEP CHU Toulouse CYCERON	CGR-30 CYPRIS 325 CYCLONE 10/5 CYPRIS 325	4
Germany	Bonn University DKFZ Essen University Euro-PET FZ Julich FZ Julich FZ Rossendorf Herzzentrum HMI Humbolt MHH MPI Rhoen Clin RWT Tech. University Munich Tübingen University UKRW UKE-Cyclotron Ulm University West. Wilhelms University	RDS-112 MC-32 CYCLONE 18/9 PETTRACE JSW BC1710 PETTRACE CYCLONE 18/9 CYCLONE 18/9 SPC-120 RDS-112 MC-35 MC-17 RDS-111 RDS-111 RDS-112 PETTRACE CYCLONE 3 PHILIPS 140-IV CYCLONE 18/9 RDS-111	20
Italy	Istituto S. Raffaele Milano Ospedale Castelfranco Ven. Istituto Naz. Tumori Milano CNR-ICP Pisa Istituto Naz. Tumori Napoli	RDS-112 RDS-112 MC-17F PETTRACE MC-17	5

OECD Europe (total 56 in 13 countries) (cont.)

Country	Operator	Type	Number of units
Netherlands	Univ. Hospital Groningen Vrije Amsterdam Univ. Vrije Amsterdam Univ.	MC-17 CYCLONE 18/9 RDS-111	3
Spain	Clinic Univ. Navarre Madrid	CYCLONE 18/9 ISOTRACE	2
Sweden	Karolinska Institute UN. PET CENTRE	MC-17 MC-17	2
Switzerland	HCU Geneva USZ Zurich	CYCLONE 18/9 PETTRACE	2
United Kingdom	Aberdeen University Aberdeen University Cambridge University Hammersmith Hammersmith London Inst. of Neurology St. Thomas Hospital	TCC-CS-30 RDS 111 PETTRACE CYCLONE 3 MC-40 CYCLONE 3 RDS-112	7

OECD North America (total 62 in 2 countries)

Country	Operator	Type	Number of units
Canada	CUSE Clark Institute Heart Institute McGill University McMaster Triumf	TR-19 MC-17 RDS-111 CYCLONE 18/9 RDS-112 TR-13	6
United States			56

OECD Pacific (total 33 in 3 countries)

Country	Operator	Type	Number of units
Australia	Austin Hospital	CYCLONE 10/5	1
Japan			30
Korea (Republic of)	Samsung Medical Centre Seoul National University	PETTRACE TR-13	2

Non-OECD Eastern Europe & Former Soviet Union (total 3 in 1 country)

Country	Operator	Type	Number of units
Russia	Bakulev Institute Inst. Human Brain NPO Positron	RDS-111 MC-17 MGC-20	3

Non-OECD Asia & the Middle East (total 12 in 3 countries)

Country	Operator	Type	Number of units
China	Boshnan Zibo BNU/IAC Guangdong Prov Hospital Hong Kong Sana Hospital INR Pekin Union Hospital PLA General Hospital Shangai Huashan Hospital Xuanwu Hospital	PETTRACE TCC CS-22 RDS-111 RDS-111 8 MeV RDS-111 RDS-111 RDS-111 RDS-111	9
Chinese Taipei	Chung Shan Hospital VET's General Hopital	RDS-111 MC-17	2
Israel	Hadassah University	CYCLONE 18/9	1

Non-OECD Africa & South America (total 1 in 1 country)

Country	Operator	Type	Number of units
Argentina	CNEA	RDS-112	1

NON DEDICATED ACCELERATORS (total 29 in 17 countries)

OECD Europe (total 15 in 9 countries)

Country	Operator	Type	Number of units
Belgium	Louvain (UCL) Brussels University (VUB) Gent University (RUG)	CYCLONE AVR-560 CGR-520	3
Finland	Jyvaskyla University ABO AKADEMY	K-130 MGC-20	2
Germany	FZ Jülich FZ Rossendorf IMSS	TCC CV-28 U-120 TCC CV-28	3
Hungary	ATOMKI	MGC-20E	1
Italy	JRC-AMI	MC-40	1
Netherlands	Eindhoven University Tech.	PHILIPS AVF	1
Norway	Oslo University	MC-35	1
Switzerland	PSI	SIN	1
United Kingdom	Douglas Cyclotron Unit University Birmingham	MC-62 60″ Nuffield	2

OECD North America (total 4 in 2 countries)

Country	Operator	Type	Number of units
Canada	TRIUMF	TRIUMF	1
United States	DOE/BNL DOE/LANL University Washington	BLIP LAMPF MC-50	3

OECD Pacific (total 2 in 1 country)

Country	Operator	Type	Number of units
Japan	NIRS CYRIC	CGR-930 AVF-680	2

Non-OECD Eastern Europe & Former Soviet Union (total 5 in 2 countries)

Country	Operator	Type	Number of units
Kazakhstan	INP	KVEIC	1
Russia	Cyclotron Cyclotron KNPI Moscow Biophysics Inst.	U-150-1 RIC-14 PHASOTRON LUE-25	4

Non-OECD Asia & the Middle East (total 1 in 1 country)

Country	Operator	Type	Number of units
India	VECC	SSC	1

Non-OECD Africa & South America (total 2 in 2 countries)

Country	Operator	Type	Number of units
Brazil	IEN	CV-28	1
South Africa	NAC-FRD	SSC	1

Annex 8

QUESTIONNAIRES

EXPLANATORY NOTE

BACKGROUND

Besides nuclear electricity generation, atomic energy has found a large number of beneficial peaceful applications through the use of isotopes in medicine, industry, agriculture and research. However, there is no comprehensive assessment of the activities related to isotope production and uses world-wide. Therefore, the Nuclear Development Committee (NDC) of the NEA has included in its programme of work an activity on beneficial uses and production of isotopes. A first study on the subject matter, carried out in co-operation with the International Atomic Energy Agency (IAEA), led to the publication of an OECD report by the end of 1998.

Within the 1999-2000 programme of work, a group of experts on beneficial uses and production of isotopes was established. A list of the members of the expert group is given in Annex 1; you may contact the representative(s) of your country in that group for more information in the framework, objectives and scope of the study. During its first meeting on 5-6 May 1999, the group recommended that the Secretariat should collect information from NEA and non-NEA Member countries on isotope production through a questionnaire.

The attached questionnaire was prepared by the Secretariat following the guidance of the group of experts. Responses from NEA Member countries and IAEA Member States will be compiled by the Secretariat and a draft report based upon the information provided will be prepared for review by the group of experts. The outcomes will be published in paper and electronic format for distribution to NEA Member countries and IAEA Member States. It is expected that the information will be updated every 2-3 years.

OBJECTIVES AND SCOPE OF THE SURVEY

The main objectives of the survey are:

- To provide an overview on the status of isotope production facilities in the world.
- To identify the main isotopes currently produced for beneficial applications in medicine, industry, agriculture and research.
- To outline the role of governments in the sector of isotope production.
- To point out key issues to be addressed by governments in order to ensure adequate supply of isotopes for beneficial uses.

It should be stressed that, in line with the statute and mandate of NEA and IAEA the overall objective of the study is to provide comprehensive information relevant to governments. Therefore, commercial aspects related to marketing isotopes are excluded from the survey. In particular, recognising that, while governments have been and remain largely involved in the construction and operation of large capital-intensive facilities (reactors and accelerators) required for producing most isotopes, processing and selling isotopes in elaborated forms for end users are mainly under the responsibility of private companies, the survey focuses on the production of raw materials. Moreover, commercial aspects related to costs and prices of isotopes are not covered in the survey.

The survey aims towards identifying: the present level of involvement of governments in isotope production, the feasibility of establishing a fully commercial isotope production sector (drawing from the experience acquired in some NEA Member countries), and the role that governments should continue to play, if any, in order to maintain an adequate level of supply of isotopes for beneficial uses, at acceptable costs.

In particular, the study will address issues such as whether governments need to maintain, enhance or reduce support to the operation of existing facilities and/or invest in new facilities in order to ensure the production of isotopes for beneficial uses, in particular for research purposes. Furthermore, the study will investigate the potential role of international co-operation for optimising the production capability of existing facilities, reducing the need for further investments and ensuring security of supply.

1. HEAVY STABLE ISOTOPE PRODUCTION FACILITY

RESPONDENT

Name : ....
Title : ....
Institute/Organisation : ....
Mailing address : ....
Telephone : ....
Facsimile : ....
E-mail address : ....
WEB site : ....

FACILITY

- Type
  Centrifuge ☐ EM Separation (calutron, etc. ...) ☐ Other [*please specify*] ☐

- List of isotopes capable of being produced
  All elements ☐ Limited suite ☐ [*please provide a list*]

- List of isotopes available for sale [*please complete the following table and/or provide a catalogue*]

Isotope	**Enrichment level**

- Major isotopes sold in 1998
  [*please provide the list of top 5, in term of value*]

- Isotopes planned for future production (1-3 years)
  [*please provide a list*]

- Operation status:

In operation	☐ Yes	☐ No
Operable	☐ Yes	☐ No
Planned expansion (1-5 years)	☐ Yes	☐ No
Planned retirement (1-5 years)	☐ Yes	☐ No

Associated chemical and/or physical conversion facilities available
☐ No ☐ Yes (specify)

2. RESEARCH REACTOR

RESPONDENT

Name : ....
Title : ....
Institute/Organisation : ....
Mailing address : ....
Telephone : ....
Facsimile : ....
E-mail address : ....
WEB site : ....

REACTOR CHARACTERISTICS

Name of the reactor : ....
Date of first criticality : ....
Power : ....MW
Maximum thermal neutron flux : .... n/cm^2.s
Maximum epithermal neutron flux : .... n/cm^2.s
Maximum fast (> 1 MeV) neutron flux : .... n/cm^2.s

Loading/unloading during operation available	☐ Yes	☐ No
Storage capacity available	☐ Yes	☐ No
Hot cells available	☐ Yes	☐ No
Owned by private company(ies)	☐ Yes	☐ No
Operated by private company(ies)	☐ Yes	☐ No

REACTOR USES

☐ Radioisotope production
Share of isotope production .... % (time) .... % (budget)

☐ Others (specify)

REACTOR OPERATION

Number of operating days 1996 .... 1997 .... 1998................

Planned upgrading (1-5 years) ☐ Yes (date: ......) ☐ No

Planned retirement (1-5 years) ☐ Yes (date: ......) ☐ No

Planned replacement ☐ Yes (date: ....) ☐ No

ISOTOPE PRODUCTION IN 1998

Isotope	Activity[1] Ci or Bq (specify)	Mean neutron flux 10^{14} n/cm^{2}.s	Use of produced isotopes[3]			% of total capacity[2]	Production trends[4]
			Internal	External			
				Research	Commercial		
^{99}Mo							
^{60}Co							
^{192}Ir							
^{131}I							
^{32}P							
^{125}I							
^{89}Sr							
..........[5]							

1) Total activity at the end of irradiation.
2) Share of the capacity used for producing each isotope.
3) Put a cross in the relevant cell.
4) Specify =, ↗ or ↘.
5) Specify additional major isotope produced

PROCESSING FACILITY

RESPONDENT

Name : ....
Title : ....
Institute/Organisation : ....
Mailing address : ....
Telephone : ....
Facsimile : ....
E-mail address : ....
WEB site : ....

FACILITY(IES)

Isotope	Maximum limiting capacity	Hot cell primary processing	Hot cell product finishing	Waste management	Storage	Packaging

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PRINTED IN FRANCE
(66 2000 20 1 p 1) ISBN 9266461841761 – No. 51625 2000