# **BENEFICIAL USE OF ISOTOPES**

Evelyne Bertel, Geoffrey H. Stevens

OECD Nuclear Energy Agency, France

#### ABSTRACT

The paper gives an outlook on the main isotopes currently used for beneficial applications, provides an overview on geographic distribution of isotope production capabilities and identifies the main suppliers world-wide. It analyses trends in different countries and regions, including the refurbishment and/or replacement of ageing facilities and the implementation of new capabilities. Issues related to adequate supply of isotopes and potential under or over capacity of production for some key products are discussed. The evolution of the isotope production sector is analysed. Issues such as lowering of governmental support to production facilities, emergence of international co-operation and agreements on production capabilities, and developments in non-OECD/NEA countries are addressed. The paper offers some concluding remarks on the importance of maintaining and enhancing beneficial uses of isotopes, the role of government policies, the need for co-operation between countries and between the private and public sectors. The paper addresses the role of international cooperation in making efficient use of existing isotope production capacity and investigates ways for reducing the need for investment in additional capacity.

#### INTRODUCTION

Isotopes are widely used in many sectors including medicine, industry, agriculture and research. In many applications isotopes have no substitute and in most others they are more effective and cheaper than alternative techniques or processes. In contrast to nuclear power, which is now in place in some thirty countries, isotopes are used in practically all countries and around fifty countries are operating isotope production or separation facilities. At the world level, and in some countries, the sector of isotope production is a significant component of economic activities. However, owing to the wide geographic spread of the sector and to its relatively small size in many countries, there is no comprehensive information, country by country and at the world level, on the status and trends in isotope production and use. In particular, a comprehensive analysis of isotope supply/demand balance at the regional and world level has never been undertaken.

The isotope production sector, like many others, is affected by the global trend to market liberalisation and privatization of industries. Since in the past a large number of isotope production facilities have been built and operated by government owned entities, the transition to a competitive market based framework raises some new issues and may lead to concerns about security of supply.

In this context, the study carried out by the Nuclear Energy Agency (NEA) of the Organization for Economic Co-operation and Development (OECD), in co-operation with the International Atomic Energy Agency (IAEA), aimed at: collecting and compiling information on isotope production and uses; analysing the status and trends in the sector; and identifying key issues of relevance for governments with regard to ensuring security of isotope supply for beneficial uses.

The paper describes briefly the method used for collecting information, summarizes the main isotope applications in different sectors, provides an overview of isotope production capabilities by type and by region, and discusses isotope supply/demand balance. It offers some concluding remarks on the importance

of maintaining adequate isotope production capabilities and on the role of governments and international organizations in this regard.

### **METHODOLOGY**

The starting point of the study was an inquiry carried out through a questionnaire sent to some eighty countries producing and/or using isotopes. The inquiry was completed by a review of national statistical data published in some countries on isotope production and uses, and a survey of international literature on nuclear industries. Results from this preliminary work allowed the selection of fifty countries that have a significant role in the field of isotope production. Those countries were selected in the light of their overall economic activity and because they operate one or more isotope production facilities of significance by their size and/or the type of isotopes they produce. In a second step, the study focused on completing and analysing quantitative information on isotope production capacities in those countries and analysing trends in the sector including plans for shut down and/or implementation of new facilities.

Information on isotope applications was compiled through literature surveys and contacts with users and regulatory bodies in charge of issuing licenses to isotope users. The integration of this information with production capacity data served as a basis for characterising the isotope market status, trends, opportunities and supply/demand imbalance world-wide.

The data and analyses presented below result from the study carried out in 1996 and 1997. They are thought to be representative of the world situation, but are by no means exhaustive. NEA work in this field is continuing in order to complement by further research the information already collected and to enhance the analysis of trends in the sector.

## **USES OF ISOTOPES**

Medical uses are among the best known isotope applications and represent the largest volume of activities in the field of beneficial uses of isotopes. Industrial uses cover a very wide and diverse range of applications in various sectors including mining, process control and food irradiation for sterilisation. Isotopes are used in scientific research mainly in the fields of biology, materials and earth sciences. Other applications include pollution monitoring and abatement, and security systems.

#### Medical applications

Isotopes are used in medicine for imaging, diagnosis and therapy. Other applications include sterilization of medical products, drug testing and biomedical research.

Nuclear imaging is mainly based upon the use of gamma cameras and positron emission tomography (PET) cameras to detect radiation from radiopharmaceuticals administered to patients. The use of isotopes for measuring bone density, which is done in a number of radiological centres, is gradually being substituted by other techniques; only the existing equipment continues to be used but is not likely to be replaced shortly.

Gamma imaging of a number of organs, e.g., lung, thyroid, kidneys and brain, is used for diagnosis purposes. A total of some twenty thousand gamma cameras are in service in some five thousand nuclear medicine departments of hospitals. The use of gamma cameras is growing world-wide at a rate of around 5 per cent per year and new applications are being developed. The main isotopes used for gamma imaging are technetium-99m (60 per cent of the market), thallium-201 (20 per cent of the market) and to a lesser extent iodine-131, xenon-133, indium-111 and gallium-67. Also, cobalt-57, cesium-137 and barium-133 are used for calibration.

Positron emission tomography is used increasingly for diagnosis of brain and heart diseases in particular. The number of PET centres in operation is growing rapidly, at a rate of around 15 per cent per year world-wide. At present, there are around two hundred centres in service operating some three hundred cameras. About two thirds of the PET centres are producing the isotopes that they need on site, mainly fluorine-18 (90 per cent of the market) and to a lesser extent carbon-11, nitrogen-13 and oxygen-15. For calibration of PET cameras, the same isotopes are used as for gamma cameras, plus gallium-68.

Radioimmunoassay tests are done in medical laboratories for in vitro diagnostic purposes. Isotopes are used for marking tumours or hormones and the analysis of blood or body fluids taken from patients allows the detection of diseases. The main isotope tracers used are iodine-125 and to a lesser extent tritium and cobalt-57.

Radiotherapy methods include metabolic radiotherapy, remotely controlled cobalt therapy and brachytherapy. Metabolic radiotherapy, used mainly for treating hyperthyroidism and cancers, is an expanding market. Cobalt therapy is practised in some eighteen hundred centres and, at present, around one hundred new cobalt therapy units are installed each year. However, the use of cobalt-60 to destroy cancer cells is expected to be substituted progressively by more selective techniques. On the other side there are some five thousand brachytherapy units, which also are used for cancer treatment, and this number is expanding at a rate of around 10 per cent per year. The isotopes used for brachytherapy are mainly iridium-192, cesium-137, iodine-125 and gold-198.

#### Industrial applications

Practically all industrial sectors use isotopes for many purposes including: process control and optimisation; measurement and automation; quality control; and testing. In most applications, isotopes could not be substituted readily by alternative techniques and are, at present, the cheapest option available. Globally, the market for industrial uses of isotopes is stable in most sectors but some applications, such as on-line analysis in the mining industries, are expanding. The following examples illustrate various applications of isotopes in some sectors of the industry.

In the field of process control, gauges of density, level and weight (incorporating sources of americium-241, cesium-137 and cobalt-60) are used in most industries for performing on-line non-destructive testing. Gauges of thickness and specific weight (incorporating sources of americium-241, cesium-137, krypton-85, promethium-147 and strontium-90) are used mainly in steel making, plastics and paper industries. For those two types of applications, isotopes are in competition with radar and X-ray techniques.

In the field of on-site inspection, isotopes are relied upon in a number of techniques, including gamma radiography, X-ray fluorescence analysis, and humidity and density sensors. Those techniques are used in particular in automobile and aircraft manufacturing, steel making, metallurgy and construction industries.

Isotopes are used in oil exploration, oil well logging and for monitoring the efficiency of enhanced oil recovery methods by acid treatment of oil-bearing strata. In the last case, radioactive tracers allow acid flows to be followed.

In the field of process development and optimisation, isotope tracers such as xenon-127, technetium-99m, krypton-85, mercury-203, bromine-82 and iodine-131 are used for measuring fluid flows and detecting leakage.

A number of industries, including paper making, automobile, paint and magnetic tape production, use polonium-210 to prevent the accumulation of static electricity that creates a hazard to personnel and reduces process quality and efficiency.

## Application in agriculture and food industries

In agriculture, isotopes provide efficient means to improve quality and productivity. Radiation induced mutations have led to new species more resistant to diseases and/or better adapted to local conditions, thereby increasing crop yields and improving the quality of food products. Isotopes are used to monitor and optimise intakes of fertilisers and pesticides by plants. The sterile insect technique, based upon sterilisation of insects by gamma radiation, has been successfully applied for eradicating crop damaging species, such as the med-fly, without side impacts on human health or the environment. With regard to animal production, isotopes are commonly used for monitoring and improving the health of cattle.

Irradiation is an efficient means for food preservation. However, owing to restrictive regulation, the technique is applied in only a limited number of countries, mainly Belgium, Japan, the Netherlands, Russia and South Africa.

## Scientific applications

Isotope labelled nucleic acids and proteins are used in biomedical research to study plants, animals and humans. The isotopes involved are mainly phosphorus-32 and 33, iodine-125, sulphur-35 (for nucleic acids), carbon-14 and tritium (for amino acids). Isotope labelled atoms play an important role also in genetic research.

Isotope markers are used to trace water streams from their origin to oceans for example. Tritium measurements are used in geology.

Labelled molecules are widely used in chemistry where they provide more sensitive analysis methods than alternative techniques. Mossbauer spectroscopy, done with various isotopes such as cobalt-57 and cesium-137, is used in materials research.

#### Others

The use of isotopes in pollution monitoring is increasing. Isotopes play an important role in measuring carbon dioxide emissions from factories and investigating greenhouse gas pathways and their assimilation by plants, thereby enhancing our understanding of their impacts on the environment. Other atmospheric emissions, such as sulphur and nitrogen oxides, can be monitored by on-stream analysers using isotopes. Radioactive tracers can be used for measuring pollution of water reservoirs and contamination of soils by pesticides or oil pipeline leakage for example. Gamma emitting isotopes are used in the treatment of toxic waste.

In the field of security, californium-252 sources are widely used in airports and railway stations for checking luggage to detect explosives and drugs. Smoke detectors using americium-241 are installed in many types of buildings.

Isotopes are necessary in the nuclear energy field for power plant start up, process control and calibration of instrumentation.

## **ISOTOPE PRODUCTION**

Table 1 gives an overview of the main isotope production facilities in operation today. Isotopes are produced mainly in research reactors and dedicated cyclotrons; however, production facilities include nuclear power plants, isotopic separation units and other accelerators. There are nearly 300 isotope production facilities distributed in a large number of countries. Significant isotope production capacities are operated in some fifty countries. A large share of the production facilities are located in OECD countries. Outside the OECD, the main isotope producing countries are China, India, Russia and South Africa.

Type of facility	Number of units
Research reactors	94
Conventional	86
High flux	6
Fast neutron	2
Accelerators	186
Dedicated to radiopharmaceuticals	49
Dedicated to PET	125
Non dedicated	12
Separation facilities	21

Table 1. Main isotope production facilities in the world

## Reactors

Among the three hundred research reactors in operation in the world, nearly one hundred are used for isotope production during 5 per cent or more of their operation time. Those include six high flux reactors producing mainly cobalt-60 and californium-252 and two fast neutron reactors, operated in Russia, producing strontium-89. The main isotopes produced by research reactors, other than high flux and fast neutron reactors, are molybdenum-98m, cobalt-60, iridium-192 and iodine-121. The geographic distribution of research reactors by capacity range is shown in Table 2.

Isotope producing research reactors are in operation in all regions of the world. Around one quarter of those reactors are located in Asia and the Middle East; each of the three other regions of the world (Western Europe, Eastern Europe and the Former Soviet Union, and North America) operate twenty per cent or more of the isotope producing research reactors; only some 10 per cent are operated in the rest of the world.

Trends differ from region to region. In Asia, new research reactors are being built or planned to be installed and isotope production capability is expected to increase rather rapidly in the region. On the other side, in Europe and North America, existing reactors are ageing and, often, there is no plan to replace them by new units once they are shut down.

Region	Number of reactors			
	< 5 MW	5 to 30 MW	> 30 MW	Total
Western Europe	11	6	5	22
Eastern Europe & FSU*	2	12	4	18
of which Russia	0	7	3	10
North America	12	5	3	20
of which United States	12	3	2	17
Asia & Middle East	11	6	6	23
of which Japan	3	1	1	5
Rest of the World	5	5	0	10
Total	41	34	18	93

Table 2. Geographical distribution of isotope producing research reactors

\* FSU: Former Soviet Union

Only a few nuclear power plants, pressurised heavy water reactors in Canada and Argentina and RBMKs in Russia, are producing cobalt-60. In some countries, including France, Russia and the United States, research reactors produce tritium for civilian uses.

## Isotope separation facilities

Isotope separation facilities include plants, workshops and hot cells where isotopes are extracted from fission products and radioactive waste. Four industrial size facilities, operated in Belgium, Canada, the Netherlands and South Africa, and several smaller workshops, operated in Argentina, Australia, Norway and Russia, are extracting molybdenum-99m from fission products. Other facilities, including hot cells, are producing cesium-137 and krypton-85 extracted from radioactive waste. Most of those facilities are operated in India, Russia and the United States. Some ten hot cells, using more sophisticated processes for separating transuranium elements and alpha emitters from radioactive waste, are in operation in France, Germany, Russia, the United Kingdom and the United States.

#### Accelerators

Around one hundred and eighty accelerators are producing isotopes in the world. Most of those accelerators are cyclotrons dedicated to production of radiopharmaceuticals or to positron emission tomography. About a dozen general purpose accelerators, including four machines rated at 500 keV or above, are used partly for isotope production.

Nearly fifty cyclotrons dedicated to production of radiopharmaceuticals are in service at present and around two to three new machines are being installed yearly. About 50 per cent of the cyclotrons dedicated to radiopharmaceuticals are operated by private companies and some 40 per cent are located in North America (see Table 3). The main isotopes produced by those cyclotrons are thallium-201 and to a lesser extent iodine-123, gallium-67 and indium-111.

There are some one hundred and twenty five cyclotrons dedicated to positron emission tomography in operation at present (see Table 4). As this application is expanding, some twenty-five machines are built annually in the world. More than 90 per cent of the PET cyclotrons are operated in North America,

Western Europe and Asia (mainly Japan). The main isotopes produced by PET cyclotrons are fluorine-18, carbon-11, nitrogen-13 and oxygen-15.

Region (country)	Number of units		
	Private	Public	Total
Western Europe	10	2	12
Eastern Europe & FSU (Russia)	2	0	2
North America	21	0	21
of which United States	17	0	17
Asia & Middle East	6	8	14
of which Japan	6	4	2
Rest of the World	0	1	1
Total	37	12	49

Table 3. Geographical distribution of cyclotrons dedicated to radiopharmaceuticals

Region (country)	Number of units
Western Europe	41
of which Belgium	5
of which Germany	12
of which Italy	5
of which United Kingdom	6
Eastern Europe & FSU (Russia)	2
North America	52
of which United States	47
of which Canada	5
Asia & Middle East	28
of which Japan	21
Rest of the World	2
Total	125

 Table 4. Geographical distribution of PET cyclotrons

The geographic distribution of other, non-dedicated, accelerators producing isotopes is shown in Table 5.

Region (Country)	Number of accelerators		
	30 to 130 MeV	> 500 MeV	Total
Western Europe	5	1	6
Eastern Europe & FSU (Russia)	1	0	1
North America	0	3	3
Asia and Middle East	2	0	2
Rest of the World (South Africa)	1	0	1
Total	9	4	13

Table 5. Geographical distribution of non-dedicated accelerators producing isotopes

## **ISOTOPE SUPPLY AND DEMAND**

Most regions and countries in the world have some isotope production facilities but some isotopes, requiring specific equipment, are produced only in a few countries. Short lifetime isotopes, such as those used for PET cameras, have to be produced and used on the same site. Isotopes are used in practically all countries of the world.

The evolution of production capacities varies from region to region. While, at present, most of the isotope production facilities are operated in OECD countries, those countries are not planning to replace all the ageing plants that are being retired. In developing countries, on the other side, some new isotope production facilities are being built.

A large number of isotope production facilities are state-owned and operated. Public entities own most research reactors and cyclotrons dedicated to PET and one quarter of the cyclotrons dedicated to radiopharmaceuticals. Although, especially in OECD countries, the private sector is increasingly involved in isotope production, the viability of the sector in a purely market economy framework might be questionable.

On the demand side, trends vary from isotope to isotope and from sector to sector. Globally, the market for beneficial uses of isotopes is expanding as isotopes remain non-substitutable in many traditional applications and as new applications are being developed. In the medical field, the use of isotopes is growing steadily in particular for metabolic radiotherapy, brachytherapy and PET imaging. In the other areas, the demand is generally stable but is growing significantly in some specific sectors such as on-line analysis of mining products, security and environmental pollution monitoring.

#### **CONCLUDING REMARKS**

Owing to the wide range of isotope applications and to the geographic distribution of production and uses, it is difficult to assess the overall economic impact of the sector at the world level. However, the survey carried out by NEA shows that production and beneficial uses of isotopes represent a significant volume of activities in a large number of countries where they generate revenues and jobs.

Most of the applications of isotopes have been developed because substitutes were not readily available and/or were more expensive and less efficient. Technological progress in the field of isotope production and uses, as well as in other areas, leads on the one side to the development of new applications and on the other side to the development of cost effective substitutes. The evolution of demand creates a challenge for

the isotope production sector that has limited flexibility owing to the lead times for building production facilities (three to eight years depending on the type of facility).

Governmental bodies play an important role in the field of isotope production and uses. Governments are responsible for establishing health and environmental norms and standards applied to isotope production and use, licensing isotope users and controlling that they comply with regulations in place. Governmental agencies own and operate a significant share of production facilities, although private investors are progressively increasing their participation in the sector.

Privately owned isotope production facilities operating on a full cost recovery basis, would likely charge higher prices and might not be competitive with alternative technologies when they are available. In some sectors of uses, such as medicine, where isotopes generally have no substitute, prices based upon full cost recovery might require an adaptation of the health care support systems.

International exchanges are necessary today for ensuring isotope supply as practically no country is self sufficient for all the isotopes that it uses. The liberalization in the production sector as well as the evolution in demand, are calling for enhanced international co-operation aiming at optimising production capabilities at the regional and global level and ensuring adequate supply of isotopes, in particular for uses where they are not substitutable.

International organisations offer a forum for world-wide exchange of information and experience sharing. Thereby, they may assist in strengthening co-operation and enhancing the efficiency of investments in isotope production facilities as well as security of supply of isotopes for beneficial uses.