The Isotope Distribution Program

Isotopes Branch, U. S. Atomic Energy Commission

On June 14, 1946, HEADQUARTERS OF the Manhattan Project first announced in *Science* a program for production and distribution of pile-produced radioactive isotopes for use in the Nation's scientific, technical, and medical investigations. On August 2 the first shipments of radioisotopes were made. On January 1, 1947, this program, with a fine record of five months of successful operation, was taken over, along with other operations of the Manhattan District, Corps of Engineers, by the U. S. Atomic Energy Commission.

With the passing of the one-year mark of isotope distribution it is appropriate that this journal, the official publication of the American Association for the Advancement of Science, should be the medium through which a report on the program is made. Numerous published technical articles have appeared on work achieved with distributed isotopes. A number of announcements on additional isotope distribution service have been published in the scientific journals, and popular releases on the uses of isotopes have appeared in the press and magazines. It has, however, been called to our attention by scientific and medical advisory groups that an occasional summary report of the over-all developments and accomplishments of the program should be published for the information of the Nation's scientific and technical personnel.

The Commission is indeed aware that it exercises a virtual monopoly in the distribution of many isotopes and that this distribution is now essential to a wide range of investigations and applications. The scientific importance of isotope distribution is evidenced by the report which follows. It is the intention of the Commission to press the program forward, within the provisions of the Atomic Energy Act of 1946, with a view to increasing benefit to scientific advance and human welfare.

Distribution of Radioisotopes

During the first year of distribution, pile-produced radioisotopes were shipped to over 160 institutions and organizations, representing more than 240 departments and 500 groups located in 31 states and in the Territory of Hawaii. Users in four states (California, Massachusetts, New York, and Pennsylvania) account for nearly half the shipments (Table 1). In the first 12 months of the program over 1,100 shipments had been made.

If the recipients are divided into four main categories, the number of institutions in each is approximately as follows: medical institutions and hospitals (including medical schools), for use in therapy, diagnosis, and research, 60; educational institutions (mainly universities), for use in research, 50; industrial and profit organizations, for use in both fundamental and applied research, 35; public and private nonprofit research institutions (other than educational), for use in fundamental and applied research, 20.

TABLE 1

Distribution of Radiomaterials by Location

(First 12 Months—to July 31, 1947)

State	No. of institutions	No. of shipments
New York	26	153
California	16	104
Pennsylvania	15	66
Massachusetts	13	169
27 other states and Hawaii	90	609
Total	160	1,101

About 60 different radioisotopes were shipped—a major portion of available kinds. In Table 2 are shown data on the total number of shipments in each of several major categories of available isotopes. Fission products have been grouped as one entry, as have most of those radiomaterials furnished without chemical processing (*i.e.* in "irradiated units" of the target material). P^{32} and

TABLE 2

Distribution of Radiomaterials by Isotopes

(First 12 Months—to July 31, 1947)

Radiomaterial	No. of shipments
C^{14} (separated)	99
P^{32} (separated)	261
P^{32} {unseparated in sulfur}	1
P^{32} (in phosphate)	52
I^{131} {unseparated separated}	313
I^{131} (in tellurium)	9
S^{35} (separated)	12
S^{35} {unseparated in chloride}	22
10 isotopes of fission products (separated)	17
40 isotopes in irradiated units (unseparated from target materials)	307
Service irradiations	8
Total shipments	1,101

I^{131}, used chiefly in medical diagnosis and therapy, constitute the largest number of shipments of chemically separated radioisotopes. These two also account for the largest total activity shipped in the form of separated isotopes (over 10,000 millicuries each). It is particularly noteworthy that the first year's distribution included over 90 shipments of C^{14}, with a total activity of about

130 millicuries. This quantity of the extremely important isotope, C^{14}, is millions of times greater than that heretofore available for investigations.

Uses of Distributed Radioisotopes

Hundreds of different uses are being made of distributed radioisotopes. The number of individual phases of investigation being undertaken is difficult to estimate but is certainly over 1,000.

The types of investigational problems in progress with the distributed radioisotopes are as varied as the interests and imaginations of the investigators. Most of the studies could not be approached satisfactorily, if at all, in any other way. It is not appropriate here to attempt to list or discuss the many types of uses. A general discussion and a few specific cases will, however, be enlightening.

From a functional standpoint, uses of radioisotopes may be classed as follows: tracer investigations (including medical diagnosis), medical therapy, sources of radiation for physical applications (radiography, etc.), and studies of nuclear properties and phenomena. The first two types of uses far outweigh the others in number and importance. As noted above, a fairly large number of medical institutions are using radioisotopes for medical therapy, diagnosis, and research. Tracer investigations, of course, promise a vast extension of knowledge in many fields, and their ultimate value to human welfare may far exceed that of the other applications of isotopes.

From the standpoint of fields of investigation, the uses of radioisotopes can be classified roughly into 9 groups, although most of the work has been done in the fields of medical therapy and physiology (animal and human). Agriculture, plant physiology, industrial research, chemistry, and physics account for most of the remainder, with lesser amounts of work being done in microbiology (bacteriology) and metallurgy. Many specialized phases related to the above fields are represented, such as animal husbandry, biochemistry, dentistry, entomology, industrial hygiene, petroleum engineering, pharmacology, radiology, soil science, surgery, toxicology, veterinary medicine, and zoology.

An appreciation for the scope of radioisotopes as tracers in biological and medical research can be gained from the following list of some of the biological materials that are being labeled and traced: alcohols, amino acids, antigens, bacteria, bile acids, blood cells, carbohydrates, carcinogens, enzymes, fats, fatty acids, hormones, insulin, nucleic acids, penicillin, pharmaceutical agents, proteins, starches, sulfa drugs, tissue fluids and salts, viruses, and vitamins. The synthesis, utilization, and excretion of such labeled materials are studied in the organs and tissues of a wide variety or organisms (plants, animals, and man).

Therapy of hyperthyroidism and certain thyroid cancers with I^{131} has been employed rather extensively as has that with P^{32} in the treatment of polycythemia vera and other blood dyscrasias. One laboratory has extensively tested the therapeutic value of colloidal radiogold (Au^{198}) in cases of lymphoid malignancy. Several others are testing the efficacy of certain radioisotopes in beta-ray applicators and in colloids for treatment of local lesions.

I^{131} has been used in studies of the fundamental metabolism of the thyroid gland. A considerable number of workers are attempting to elucidate the mechanism of both carbohydrate and protein metabolism by use of compounds labeled with C^{14}. A variety of problems, including those of bone and tooth formation, have been attacked by using radiocalcium and radiophosphorus. Radioiron is being used in studies of blood function, and radiosodium has been employed in the study of water balance and blood flow.

Of all the studies in plant physiology the most dramatic is probably the effort to learn the mechanism of photosynthesis by use of C^{14}, but others have initiated studies to increase our knowledge of the absorption by plants and animals of phosphorus, calcium, iron, potassium, and some trace elements by using the appropriate radioisotope in each case.

Many other studies related to agriculture are in progress, including storage in soil and uptake by crop plants of fertilizers and other soil additives; action of insecticides, fungicides, and weed killers on insects, plants, and animals; effects of industrial vapors and wastes on plants and animals; deficiency diseases and utilization of foods and essential minerals in crops and livestock.

In chemistry the principal emphasis has been on the use of labeled molecules in the study of reaction and exchange mechanisms. A similar effort is being made in certain industrial research work, notably in the field of catalysis in hydrocarbon reactions.

Physicists have used a goodly number of radioisotopes in their effort to arrive at more exact measurements of disintegration patterns.

A unique approach to the industrial hygiene problem of removal of air-borne toxic and infectious materials has been made possible by studying the capacity of filters and exhaust systems to remove finely atomized radioactive materials of short half-life.

Increasing applications are being made in industrial problems. These include investigations on friction, lubrication, diffusion, aging and oxidation of metals, kinetics of reactions in solid alloys, control of impurities in metal melts, petroleum cracking, oil field logging, and chemical process efficiencies.

Improvements in Availability of Radioisotopes

The initial announcement on the availability of pile-produced radioisotopes listed 80 procurable radioisotopes. It was emphasized in the announcement that none of the radioisotopes was yet in routine production. For a few isotopes only, production processes were under technical development. For most isotopes, processes were largely in the research or then untried stages.

During the elapsed year, Clinton Laboratories, Oak Ridge, Tennessee, the supplier, has achieved much progress in routine production of many items and has made significant improvement in the form and availability of those materials not yet in routine production. Production of the majority of items is now adequate to meet the legitimate demands of all users who can handle the materials effectively and safely. In addition, it has been possible to add 16 procurable radioisotopes to the list originally released to *Science*.

Investigators may also now secure service irradiations of their own materials when necessary. Special chemicals and other materials (suitable for exposure in the Clinton pile) may be subjected to pile irradiation. This enables qualified personnel to study the effect of pile irradiation on crystals, organic chemicals, seeds, intact metal parts, and numerous other materials of special interest. The Argonne National Laboratory, Chicago, Illinois, has also recently undertaken to perform certain service irradiations for qualified investigators by means of the Argonne heavy-water pile.

Improved and large-scale methods of producing C^{14} have permitted a significant reduction in the cost of this important item from $367 to $50 per millicurie.

Chemically separated S^{35} of high specific activity has been made available in the form of labeled H_2SO_4 and Na_2S. Increased yield in extraction of S^{35} (from irradiated chlorine compound) has also made possible lower prices on these items.

Improvements in the processes of extraction of P^{32} and I^{131} (from irradiated sulfur and tellurium, respectively) now enable the supplier to meet more rigid specifications on the chemically separated forms of these isotopes. This is important, since the materials are being extensively used in medical investigations on human beings, both in diagnosis and therapy.

Small quantities of chemically separated Ca^{45} of high specific activity have just become available. This isotope is produced by transmutation reaction in scandium. When extraction procedures have been developed further, the material should become routinely available.

Some of the important tracer radioisotopes, such as radioiron, radiocalcium, and radiochlorine, originally available only with low specific activity, are now being made available with much higher specific activity.

C^{14}-labeled compounds (other than $BaCO_3$) are being prepared by several Commission laboratories for their research programs. However, excess quantities of certain compounds can be synthesized for use by laboratories outside the Commission. C^{14}-labeled methanol (C^*H_3OH) is currently available, and C^{14}-labeled barium carbide and sodium formate should be available soon. Additional C^{14}-labeled compounds, useful largely as intermediates, are expected to become available also.

Availability, Distribution, and Use of Stable Isotopes

During the 7 months that the distribution program has been under the control of the Atomic Energy Commission, enriched forms of three stable isotopes have been made available. Heavy hydrogen is available as deuterium gas and heavy water, in which the ratio of the hydrogen isotopes is 99.8 deuterium to 0.2 protium. Boron is available in calcium fluoride-boron fluoride complex containing B^{10} concentrated to 96 per cent of the boron content (or about 5-fold enrichment of B^{10}). O^{18}, with a concentration about 7 times that in nature, is available in water in which the deuterium is not enriched.

Since the May 1, 1947, announcement of deuterium distribution, over 75 research groups in all parts of this country have been allocated an equivalent of about 28,000 grams of deuterium oxide. Lower price and greater availability of the material are permitting extensive and new uses of deuterium. Studies that were previously unfeasible are now being made in humans.

The deuterium or deuterium oxide is being used to supply bombarding deuterons for cyclotrons and other nuclear accelerating devices at 18 research institutions. Other applications in physics include: absorption spectra of deuterium-substituted inorganic and organic compounds; piezoelectric property of deuterium-containing crystals; photodisintegration of deuterons; filler for high-pressure cloud chambers; calibration of mass spectrometers; and molecular moment studies.

In chemistry deuterium is being employed to synthesize substituted compounds such as deuterium-labeled benzene, aliphatic hydrocarbons, and halogenated fatty acids, which are studied for their physical and chemical properties. The mechanisms of certain chemical reactions are very easily investigated with heavy hydrogen.

Deuterium is also serving as a tool in many biological and medical investigations. Biosynthesized tyrosine being labeled with deuterium will be used to study the metabolic aspect of this material. Studies of total body water and extracellular fluids in various physiological conditions of the human body are being made with heavy water, as are metabolism studies involving amino acids, bile acids, fatty acids, tryptophane, glycogen, nicotinic acid, etc.

Eleven leading institutions conducting nuclear research have received allocations of the complex containing B^{10}. Although B^{10} is being used chiefly in the preparation of ionization chambers and counters for neutron detection, some investigators indicate that studies of nuclear reactions of B^{10} will be made.

Since distribution of O^{18} has only recently been announced, no report is made on this item. Because of the relatively low enrichment of the material, it will in most cases be enriched further before use by several groups who have set up equipment suitable for the purpose.

Health Protection

Radioisotopes will perhaps find their greatest application when employed in small quantities as tracer substances rather than in large quantities as therapeutic or industrial agents. However, because of the radioactivity involved, any application requires certain fundamental knowledge for effective and safe use of radioisotopes.

Information on health protection is one of the most frequent requests received in connection with the program. Several circulars on health protection are available, and further informational circulars on medical and health protection measures are being prepared for distribution to radioisotope applicants and users.

For practical purposes, health protection may be considered as presenting two individual but related problems. The first, which is largely medical, consists of determining experimentally the biological effects of radiations and radioactive materials and of checking for possible radiation effects in the body. This is essential for the safeguarding of personnel using radioactive materials. Experiments are being conducted, and the results being made known, on the toxicity and radiation effects which may be produced by a wide variety of radioisotopes. Although we now have certain indices which are of value, improved methods of detecting possible radiation effects are continually being sought.

The second problem is largely physical and bears a causal relationship to the first. It is known as "health-physics." By this term we connote all those precautionary measures of routine monitoring, adequate shielding, handling techniques, decontamination, etc. which serve to avert any excess exposure to radioactivity. Research and development is under way to improve such measures.

Advisory Field Service

In view of the general need for health protection assistance in the use of radioisotopes, the Atomic Energy Commission has established, in conjunction with the distribution program, an Advisory Field Service. When a specific need for this service is indicated, it is provided to isotope users without charge. Its prime objective is to render assistance, information, and consultation on all matters of health protection. When feasible, it will attempt to advise and make available information on new techniques of measurement and application.

The service, which functions through the Isotopes Branch, now has a physician and health-physicist available for consultation. Although the service is at present limited to those in most need of it, it may be expanded as deemed necessary.

Instrumentation

During the war, manufacturers of radiation-measuring instruments diverted their entire production to wartime needs. The Manhattan Project was the largest single customer. The Atomic Energy Commission still requires a large number of the produced instruments to continue its work most effectively. Instrument-manufacturing companies, which now include many new firms, are, however, becoming increasingly able to meet demands from the open market.

Most types of radiation instruments developed on the Manhattan Project have been declassified and are already, or soon will be, commercially available. The Commission is continuing with vigor the policy of licensing for commercial production and sale those radiation instruments developed within its facilities. Commercial firms have also undertaken considerable development in instrumentation. Increasing availability of many types of improved radiation-detection instruments is therefore expected. The Isotopes Branch, upon request, will furnish lists of manufacturers and offer assistance concerning types of radiation instruments which will facilitate an investigator's work.

Declassification of Pertinent Information

Of the many Commission research reports written in connection with the development of atomic energy, three types—those on medical, health-physics, and instrumentation matters—are of special interest to the users of radioactive isotopes. Authors of reports falling in these categories are being encouraged to submit them for declassification, and to date more than 125 such documents have been declassified. A large number of these reports are available to the public through publication in widely circulated scientific journals. Copies may also be obtained through the Office of Technical Services of the U. S. Department of Commerce.

Procurement

The situation is good for procurement of most isotopes offered by the Commission. The stocks of stable isotopes are adequate for most uses. (C^{13} and N^{15} are not procurable from Commission facilities, but are obtainable in good supply from commercial firms.) Many of the chemically separated radioisotopes are produced regularly to keep supplies currently available. Other radioisotopes are separated in batches as demands arise. Radiomaterials furnished without processing are usually produced only after receipt of a purchase order by the supplier. A week to several months is then required, depending on the isotope desired. Details concerning availability and procurement of isotopes and related information and services may be obtained by writing the Isotopes Branch, Atomic Energy Commission, P. O. Box E, Oak Ridge, Tennessee.

The Isotopes Branch serves as an information and allocation agency, while production and distribution are accomplished by organizations under contract with the Commission. Submission of purchase orders and arrangements with the supplier concerning specifications and shipments of materials are made only after allocation. Allocations can be obtained in one to three weeks after submission of properly completed request forms, the time depending on action that may be necessary by advisory allocation groups.

Although it is not possible in this limited space to give due credit to all individuals who have contributed to the success of this program, it is possible to designate certain organizations and groups which have made enormous contributions.

The Clinton Laboratories pile has been chiefly responsible for the production of radioisotopes, although piles of other areas have been used to some extent. The preparation of chemically separated radioisotopes has been accomplished through the cooperative activities of the Chemical, Technical, and Production Divisions at Clinton Laboratories, operated for the Government by the Monsanto Chemical Company.

The Chemical Division at Clinton Laboratories and various groups at the Argonne National Laboratory and Radiation Laboratory of the University of California have made numerous contributions to basic radiochemical and physical techniques which aided the development of presently employed processes.

Matters pertaining to scheduling, shipping, and billing have been efficiently handled by the management and other groups at Clinton Laboratories. The Health-Physics Department there has given expert supervision to the safety and health protection phases of packaging and shipment.

Production of deuterium gas from deuterium oxide as well as the shipping and billing for the produced gas and deuterium oxide are being managed by Stuart Oxygen Company, San Francisco, California. The deuterium oxide was produced by facilities contracted for by the Manhattan Project.

Allocations by the Atomic Energy Commission have been made by the Isotopes Branch with the assistance of advisory committees composed of personnel outside the Commission staffs. Each request has been reviewed and rated on its individual merits by subcommittees on allocation and on human applications. These advisers are as listed in the original announcement in *Science*. Their continuing service, which is voluntary, is indeed keenly appreciated.

The success attained in the isotope distribution program has been the result of cooperation of a number of organizations and hundreds of interested persons. The Commission appreciates the fact that it can rely on the continued cooperation and efforts of these individuals, as well as on further participation by others. Increasing success of the program is therefore guaranteed.

Suggested Principles of "Social Physics"

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A NEW DEMOGRAPHIC INDEX, CALLED "potential of population," was found in 1940 (*1*). Studies have been resumed, and it is now established that, when averages are considered, principles resembling some of those of physics apply not only in demography but in related aspects of economics.

When celestial mechanics was being developed, in the 16th and 17th Centuries, the order of advance was: (1) the collection of quantitative observations (Tycho Brahe); (2) their condensation into empirical mathematical regularities (Kepler); and (3) theoretical interpretation of the latter (Newton). If there is to be a social physics, its beginnings must follow the same standard pattern. During recent years, social statisticians have published amazing amounts of numerical observations. That stage is well advanced. Several pioneers (especially G. K. Zipf and A. J. Lotka) have described significant empirical regularities. A great deal more attention must, however, be given to the third stage by numerous investigators before it is fully achieved.

Mathematical rules in demography are described in a current report (*2*) which contains numerous references to previous work. Intensive further studies have been carried on with the cooperation of the School of Economics and Politics of the Institute for Advanced Study. Only a partial and condensed description of these can be given below.

An important empirical relation is found between the population and the average area of cities in the U. S. Census of 1940, namely,

$$A = \frac{P^{\frac{3}{4}}}{350},$$

the area, A, being in square miles. This is the land area of the "political" city, within the official city limits. The rule holds statistically for cities above the rural limit of 2,500, including the largest ones. Examination of less inclusive data published by the Bureau of the Census for 1890 shows that the same formula applied, except that the numerical constant was 400 instead of 350. That is to