research on this method. It is also actively engaged in a study of the bed load transport in a tributary of the Mekong River in South East Asia.

All of the foregoing has concerned the use of radioisotopes in hydrology. It may also be possible to use stable isotopes in hydrological research. For example, oxygen-18 and deuterium seem to be promising in the identification of waters, as the proportions of various isotopes contained in rain vary with the altitude at which the rain hits the ground. Consequently, these two isotopes are being analyzed in the world-wide survey of precipitation mentioned earlier.

RESEARCH APPLICATIONS OF CALCIUM-47

Calcium, one of the most common elements on earth, is also one of the main components of human bone. Nevertheless, we still know very little about calcium metabolism; we know little about the accretion of calcium into and release from healthy bones; we know that the dynamics of calcium metabolism are affected by a variety of bone diseases such as rickets, osteomalacia and Paget's disease as well as by a number of endocrinological disorders such as hyper- and hypothyroidism and hyperparathyroidism, but we have insufficient knowledge of these pathological processes. A more detailed insight in the dynamics of calcium metabolism as affected by disease would allow a better understanding of the underlying disturbance and perhaps a more accurate diagnosis at earlier stages of its development. Furthermore, one of the effects of certain bone lesions such as fractures or malignant tumours is an increased accumulation of calcium in the lesion; in the case of tumours the early detection of such accumulation would render therapeutic measures possible at a stage when they are likely to be more effective.

Finally, because of the similarity of the bone-seeking qualities of both calcium and strontium, and in particular of the radioactive isotope strontium-90, a dangerous fission product, a better understanding of calcium metabolism is an essential prerequisite for further improvements of health and safety measures against radiation hazards.

A radioactive isotope that would enable us to widen our knowledge of the rates of calcium absorption from the gut, its distribution within the body, and its accretion into and release from bone and ultimate excretion seemed an ideal tool for these different lines of research.

Such a radioisotope, calcium-45, has in fact been in use for a number of years in animal experiments. It is, however, less suitable for human studies because of its long half-life of about 150 days resulting in a radiation dose which may exceed that generally thought permissible in man.

At the Third International Symposium on Radioisotopes in Clinical Medicine and Research held in Bad Gastein, Austria, in January 1958, the possibility of using the isotope calcium-47 for this type of investigation was discussed. It seemed particularly suited for this purpose since it has a half-life of only 4.7 days; it is, moreover, a strong gamma-emitter which permits easy detection of very small quantities from outside the body. It was, however, produced on an experimental basis only and at a price of US $1400 per mC* which was beyond the financial possibilities of almost any medical research institution or hospital. In view of IAEA's mandate to promote isotope research in the fields of radiobiology and medicine the participants asked the Agency to carry out a programme of encouraging research that might lead to cheaper methods of producing this isotope and of assisting in its practical applications in diagnosis and clinical research. The Agency took up this suggestion and the way it has pursued the project might be considered characteristic of its methods of dealing with such problems on an international scale.

As a first step, a small group of consultants convened by the Agency met in Vienna in December 1958 to discuss methods of calcium-47 production. Of the various processes reviewed (irradiation of calcium-46, calcium-48 or titanium-50) neutron irradiation of enriched calcium-46 in a nuclear reactor was considered to be the most promising method. But since the almost prohibitive cost of enriching calcium-46 constituted the main obstacle to obtaining this product at a reasonable price, the consultants recommended that research should first be directed towards finding improved production methods of calcium-46. Electro-migration was thought to be the most promising approach. An additional question was whether potential producers could be convinced that the demand for this isotope would be sufficient to justify the considerable investment required for a regular production.

To clarify this point, the Agency began by sending a circular letter to all its Member States asking them to indicate those institutions which might be interested in using calcium-47 in their research projects. Answers were received from sixteen Member

* mC = *Millicurie, a thousandth of a curie.*

Curie = the unit of radioactivity = 3.7 × 10^{10} disintegrations per second.

States giving the names of 66 institutions. Requests were then addressed to these institutes for further details regarding their research programmes, their previous experience, the amounts of calcium-47 required, specifications as to desired specific activities, permissible contamination of calcium-47 with calcium-45, etc. Nineteen institutions in ten Member States provided this information. At about the same time, a research contract was awarded by the Agency to the Department of Physical Chemistry of the French Atomic Energy Establishment at Saclay for developing a laboratory method of enriching calcium - 46 by electro-migration.

This contract was financed from funds put at the Agency's disposal by the United States Atomic Energy Commission under a special agreement. Work is still continuing and the progress reports received by the Agency have shown encouraging results.

The next step for the Agency was to convene a second meeting of consultants, in December 1959, to review the progress made during the preceding year. The various possible production methods of calcium-47 were again discussed in the light of specifications drawn up by the Agency on the basis of the answers received to its inquiry. Electro-magnetic separation of calcium-46 had proved technically feasible and it could be shown that calcium-47, produced by irradiation with pile neutrons of enriched calcium-46, would be reasonably priced and only moderately contaminated with calcium-45. To induce producers to commence regular production of calcium - 47, the consultants recommended that the Agency should promote the utilization of this isotope by awarding research contracts to institutes capable of employing this radioisotope in medical and biological research.

Acting on this recommendation, the Agency in 1960 awarded contracts for medical research with calcium-47 to ten hospitals or institutes in Austria, Belgium, Denmark, France, Poland, South Africa, Sweden and the United Kingdom. The problems to be investigated included calcium metabolism in normal human beings and in patients with rickets, osteomalacia, Paget's disease and hyperparathyroidism, the effects of vitamin D and parathyroid hormone on calcium metabolism and the use of calcium-47 for the early detection of bone tumours. In contrast to its usual research contract policy, however, the Agency defrays in these cases only the cost of the calcium-47 because the institutes concerned are all situated in well-advanced countries and can be expected to pay for the required additional staff and equipment out of their own resources.

The Agency did not content itself with promoting this kind of research. It considered it not less important to act as a kind of co-ordinator by organizing an exchange of information between all those involved in the project. To this end the Agency convened, at the end of 1961, a meeting of all those persons principally engaged on its calcium-47 research contracts. In addition, the Agency enabled a number of scientists, who had either had previous experience with calcium-47 or intended to use it in the near future, to participate in the meeting.

The three days' discussions of the results so far achieved and of the different techniques employed indicated rather promising lines for further investigations, for example for methods that might lead to an early detection of bone cancer. They also provided guidance for further Agency action.

Since it appeared that inaccuracies existed in the chemical determination of stable, that is to say non-radioactive calcium, particularly in urine, it was decided that the Agency should organize a comparison of the results obtained by different institutes for the purpose of establishing unified and accurate methods of calcium analysis.

All but one of the ten institutes engaged on the Agency research contracts were asked to carry on with their projects and an additional contract was awarded to an institute in Argentina. In spring 1962 the records of the discussions held by the panel of experts will be published, and a similar meeting of experts is planned for 1963 when the great majority of contracts will have continued for three years, so that a comprehensive review of the results obtained could be made.

But even today, it can be safely stated that the Agency's calcium-47 project has largely achieved its goal. Calcium-47 is in regular production by two suppliers and at a price which is no longer beyond the reach of the average hospital or medical research institution: it has been brought down from $1400 to $200 per mC. A number of institutes are at present using the isotope for practical purposes such as the diagnosis and study of various bone diseases and for collecting data on calcium metabolism in the normal human being. Such data will, in addition, help to gain better understanding of the hazards arising from the possible release of certain bone-seeking fission products during peaceful atomic energy operations. Finally, it is expected that during 1963 the Agency will be able to withdraw gradually its financial support of the calcium-47 programme and to start similar programmes to promote the application of other rare isotopes and labelled compounds. Plans for these new projects are already under discussion.