

# HUMAN HEALTH HUMAN HEALTH

## PROGRAMME OBJECTIVE

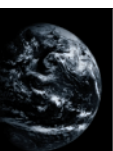
To enhance the capabilities of developing Member States to address important health problems through the development and application of nuclear and related techniques in areas where they confer advantage in comparison with conventional techniques or by themselves constitute the conventional technique.

## OVERVIEW

The main thrust of the programme continued to be cancer control and combating infection and malnutrition through preventive measures. In nuclear medicine, emphasis was placed on cost efficacy studies of inexpensive radiopharmaceuticals and the application of isotopes in molecular biology and new radioimmunoassay related procedures. In radiation therapy and radiobiology, development of quality assurance was the main topic and included the development of patient immobilization devices and protocols for cancer patients with HIV infection. In October, the Agency was invited to sign the 'Mutual Recognition Arrangement' for metrology institutes with the Comité International des Poids et Mesures (CIPM). The main benefits are expected to be improved intercomparison and quality audits organized by the Agency for Secondary Standard Dosimetry Laboratories (SSDLs). In the area of health related environmental studies, new strategies for nutrition intervention schemes were identified and the global network of analytical laboratories was strengthened.

## NUCLEAR MEDICINE

Efforts continued in 1999 on enhancing the awareness and capabilities of Member States in the efficient and cost effective use of in vitro and in vivo nuclear medicine technology for managing their critical health problems, and for undertaking basic and clinical research in relevant subjects. For example, special emphasis was placed on: the development of in vivo and in vitro



diagnostic methods, and treatment procedures with open sources of radioactivity; optimization of the cost effectiveness of health care using nuclear medicine procedures, development of multimedia and Internet based teaching aids; and transfer of technology to developing Member States on the management of a number of clinical problems, including viral hepatitis, genetic disorders, coronary artery disease, infection, cancer and paediatric disorders.

A new radiopharmaceutical using a bacterially binding radiolabelled antibiotic was evaluated in a CRP as a bacterial specific imaging agent (technetium-99m–Infecton, a Ciprofloxacin derivative which binds to DNA gyrase of living bacteria for the detection of active infection). The multi-centre study, which was concluded in 1999, yielded a sensitivity of 85% and specificity of 83% for detecting bacterial infections.

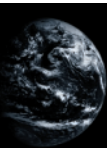
A regional CRP entitled 'Standardization of Iodine-131 Treatment for Hyperthyroidism with an Intent to Optimize Radiation Dose and Treatment Response' was concluded. In a prospective randomized therapeutic trial based on the absorbed dose concept, 900 patients suffering from hyperthyroidism were treated with iodine-131 (90 or 60 Gy). The best results were obtained in the high dose (90 Gy) group. It was also observed that a significant reduction in the administered activity of iodine-131 is possible with adjuvant lithium intervention.

An earlier CRP assisted some Member States in developing their own capability to produce samarium-153 from indigenously available reactors. The sequel to this was a new clinical CRP to evaluate the efficacy and toxicity of samarium-153 EDTMP in the palliation of painful skeletal metastases. Analyses of data from 417 patients who were treated and followed up for 16 weeks revealed significant pain palliation in 73% of the patients ('responders'), with only minimal or mild haematological effects and no systemic toxicity. In addition, for 82% of the responders, post-therapy analgesic intake was substantially reduced or stopped completely, which is considered highly cost effective in the management of such patients.

Nuclear medicine technology transferred to developing Member States through technical co-operation projects included:

- The use of radioisotope labelled DNA probes and primers to identify families with fragile x syndrome and myotonic dystrophy in Costa Rica. Seventeen families with this syndrome were identified, from which 73 individuals participated in the diagnostic tests, while 18 families with myotonic dystrophy were identified out of which 72 individuals were tested. The affected individuals were counselled about their risk of having a child with these complications.
- Transfer of PS2 IRMA and oestrogen receptor methodologies, developed within a CRP on tissue diagnosis of breast cancer, to participants from ten countries in an East Asian regional training course.
- Transfer of a new, low cost, synthetic peptide-based, anti-hepatitis C virus screening method, developed indigenously in Costa Rica, to seven countries in the Latin America region.
- Development of a new protection free version of the Portable Image Processing software. This software is used in more than 300 nuclear medicine centres for various clinical applications, in projects on upgrading gamma cameras with standard PCs and in training on image acquisition and processing in nuclear medicine.
- Production of a video tape on single head scintillation camera quality control, which was used in various training activities. This complements an Agency technical document on the quality control of nuclear medicine instruments (IAEA-TECDOC-602).
- Extension of the distant assisted training programme for nuclear medicine technologists to the African and Latin American regions.

With a view to integrating nuclear medicine services into health care systems, and to promote uniformity and standardization with respect to infrastructure development, teaching, training, patient care and research, an Advisory Group meeting was organized to prepare a resource manual in nuclear



medicine on the basis of the Agency's Safety Standards publications.

## **APPLIED RADIATION BIOLOGY AND RADIOTHERAPY**

Attention continued to be focused on developing country needs by: assisting them in identifying and acquiring techniques for curative and palliative cancer treatment with radiation; promoting clinical quality assurance in all aspects of patient management; and continually upgrading the Agency's available

***“A handbook was produced to illustrate the use of cost effective patient immobilization devices that were developed and distributed by the Agency.”***

information on current techniques in radiation oncology to identify those with the potential for wider dissemination. All of these activities were fully integrated into the Agency's technical co-operation programme, primarily through regional projects.

A handbook was produced to illustrate the use of cost effective patient immobilization devices that were developed and distributed by the Agency in 1998. The handbook was also distributed through related technical co-operation projects. In addition, an interregional workshop was held in Tunisia on the proper use of this equipment.

An Advisory Group meeting was held in Vienna in October on the role of radiotherapy in AIDS patients. This is a subject of great importance in sub-Saharan Africa, where HIV positivity can exceed 25% in some population groups. The disease is accompanied by a greater than five fold increase in many cancers, including Kaposi's sarcoma, non-Hodgkin's lymphoma, squamous cancer of the conjunctiva and Hodgkin's disease. Decision making (including the option of not administering any treatment at all) in the radiother-

apy management of patients infected with HIV who have limited life expectancy attributable to AIDS alone was addressed and a document prepared for clinical guidance. This work was facilitated by the provision of epidemiological data on the cancer increases by WHO/IARC.

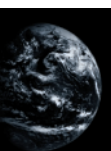
Work on clinical protocols specifically for developing countries in the radiotherapeutic management of advanced cervical cancer, disseminated bone metastases and advanced oesophagus cancer made progress. The last method won a prize as the best innovative protocol at the European Society Congress of Brachytherapy. The selection of patients has now ended and the preliminary results appear to be satisfactory. Final analysis and publication of the results is expected in 2000.

An Advisory Group meeting, held in Vienna in April, on a microsource high dose rate after-loading system examined the advantages of these very small source brachytherapy devices. The main result was the significant change that was seen in both developed and developing countries in the use of these machines in preference to low dose rate (LDR) machines. This is because brachytherapy treatment can be given on an outpatient basis using these machines, instead of the usual two to three day hospital stay required for LDR.

In high technology radiation therapy, a Technical Committee meeting was held to evaluate the present status of boron neutron capture therapy. The meeting examined the current status after 50 years of efforts to use reactor neutron interaction with boron for the treatment of brain and other malignant tumours. The conclusion was that notwithstanding improvements in delivery techniques of the neutron beam, the results to date have not demonstrated any clinical benefit to justify elevating this technique to more than investigational level.

## **DOSIMETRY AND MEDICAL RADIATION PHYSICS**

Following an invitation by the CIPM, the Agency signed the 'Mutual Recognition of



National Measurement Standards and of the Calibration and Measurement Certificates Issued by National Metrology Institutes' (the 'Mutual Recognition Arrangement', or MRA) for the IAEA/WHO Network of SSDLs. The signing of the MRA places the metrology of ionizing radiation in those developing countries having a laboratory that is a member of the SSDL Network at a level of international recognition that has no precedent in the past, allowing for the worldwide recognition of their standards and calibration certificates. This, naturally, imposes strict demands on the performance of the SSDLs, and will require a tightening of the conditions of acceptability of results of the intercomparisons and quality audits organized by the Agency for the SSDLs.

The IAEA/WHO SSDL Network currently includes 70 laboratory members and 6 SSDL national organizations in 59 Member States; the Network also includes 15 affiliated Primary Standard Dosimeter Laboratories (PSDLs), and five collaborating international organizations. An SSDL in Viet Nam was established under the framework of a technical co-operation project and admitted as a new member of the SSDL Network.

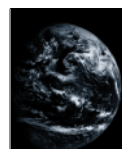
A total of 70 national standards and reference ionization chambers were calibrated at the Agency for Member States: about 80% were radiotherapy level calibrations and 20% were for radiation protection. The establishment of measurement standards at the Agency for diagnostic radiology beams used in mammography was also completed. The Agency reference standard was calibrated at PTB, the German standards laboratory, and calibration services of measuring instruments for mammography were made available to Member States.

Dose quality audits and intercomparisons were organized for SSDLs in order to check the traceability of their measurements and to monitor their performance. Nine SSDLs participated in the intercomparisons of radiotherapy ionization chamber calibration factors and 25 in the thermoluminescent dosimeter (TLD) audit for radiation protection level dosimetry; 123 radiation beams from cobalt-60 units and clinical accelerators at laboratories,

or supervised by SSDLs, were reviewed in the TLD audit for radiotherapy. Procedures for the intercomparison of calibration factors at therapy and diagnostic radiology (mammography) levels, within a project of the European Organization for Metrology in 2000, were developed jointly with German and Austrian PSDLs.

A survey was carried out of the activities of members of the SSDL Network. The results indicated that about 70% of laboratories are involved in quality assurance programmes for radiotherapy through postal TLD services or site visits to hospitals. Also, about 30% of the SSDLs have started to calibrate brachytherapy sources and equipment, and an additional 20% will soon start this activity. In the field of X ray dosimetry, 40% of the SSDLs are calibrating instruments for diagnostic radiology.

The IAEA/WHO TLD postal dose assurance service for monitoring the calibration of radiotherapy beams at hospitals worldwide audited 377 beams, of which 228 were cobalt-60 and 149 were high energy X rays from clinical accelerators. The percentage of the deviations within the  $\pm 5\%$  acceptance limits has increased from approximately 65% in the past (81% in 1998) to 87%. For results outside the  $\pm 5\%$  limits, the Agency had established a regular follow-up programme, contacting the hospitals either directly or through WHO (PAHO) for tracing the reasons for the discrepancy and performing repetitive TLD irradiations. Analysis of this follow-up programme has shown that 39% of the hospitals have improved their results in the follow-up irradiation, but 18% of the discrepancies still persisted. As a result, the Agency is in the process of establishing a mechanism to investigate and resolve these persistent TLD deviations and determine why some follow-up TLDs have not been returned for the analysis. The analysis also revealed the limitations for hospitals that do not participate regularly in external audits: 102 radiotherapy facilities in 92 hospitals, mainly from Eastern Europe and Asia, which had never been audited before were included in the IAEA/WHO TLD programme, with the finding that only 65% of the results of a first participation are within the  $\pm 5\%$  limits.



Following positive feedback on Agency assistance in setting up national TLD programmes for quality assurance in radiotherapy at the national level, five new countries were helped in starting national programmes within the framework of a CRP. And as part of a technical co-operation project in Central American and Caribbean countries, a network for reciprocal on-site quality audit visits was established where physicists from the different radiotherapy institutions of the region can carry out quality control measurements in other hospitals and countries.

Seventy-three cobalt-60 and three electron beam checks were performed for industrial facilities and research institutes in Member States through the International Dose Assurance Service.

A regional technical co-operation project for establishing a common Master's degree in medical physics in Latin America was initiated. The course will run consecutively in several national universities and has just been started in Venezuela after a written examination for regional candidates. Agency supported Fellows from the region will participate in the courses, which will be taught by an international panel of professors using a common syllabus.

## NUTRITIONAL AND HEALTH RELATED ENVIRONMENTAL STUDIES

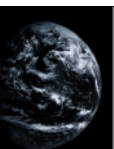
Nuclear and isotopic techniques were used to improve nutrition monitoring techniques and

to identify effective strategies in nutrition intervention schemes, particularly among vulnerable groups, in developing regions around the world. In this connection, a draft thematic plan entitled 'Isotopic Evaluations to Add Value to Nutritional Interventions' was developed as a template for new regional technical co-operation projects in the Latin America and East Asia and Pacific regions. The project in Latin America focuses on the use of isotopes for evaluating nutrition intervention programmes. The East Asia and Pacific project has as its major goal the measurement of the effectiveness of multinutrient supplementation using stable isotopic techniques.

An assessment of vitamin A body stores and the bioavailability of pro-vitamin A was performed using in vivo kinetics and the 2H-retinol method in developing countries. The results provided a more accurate picture of whole body retinol stores and vitamin A status in mothers and children. This isotopic technique can be used to monitor vitamin A status when measuring the effectiveness of vitamin A supplementation programmes. In addition, a CRP on the development and application of isotopic techniques in studies of vitamin A nutrition was completed. The main conclusion was that under conditions of vitamin A supplementation for food fortification and dietary improvement, the isotope dilution technique using deuterated vitamin A proved to be a less invasive technique than earlier traditional approaches used to assess body stores, such as direct measurement of vitamin A in liver biopsies. Along with other conventional methods, namely serum retinol determination and conjunctival impression cytology, this technique

### Lichens and Mosses — A Biomonitor for Environmental Pollution

Lichens and some lower plants have no roots and absorb their nutrients directly from the air. If the material absorbed is not metabolized, which is the case for many heavy metals (radioactive or stable), they accumulate in these organs over time. A CRP was conducted to evaluate the suitability of various organisms as biomonitors for trace element atmospheric deposition. As a result, several types of mosses, lichens and lower plants have been identified in different climate regions as appropriate organisms for monitoring long term air pollution status in the areas under investigation. Nuclear and related analytical techniques were used to demonstrate the presence of non-radioactive environmental pollutants. In support of the required analytical quality control, an interlaboratory comparison study on lichen samples was also carried out. ■



provides a more accurate assessment of vitamin A status, particularly in vulnerable groups such as children, and pregnant and lactating women.

The deuterium kinetics technique was established for measuring breast milk intake and body composition using both infrared spectroscopy and isotope ratio mass spectrometry. A technical co-operation Model Project in Senegal has successfully introduced this technique in the field and has been providing assistance to other African countries. In addition, as a result of a CRP on the isotopic evaluations of maternal and child nutrition to help prevent stunting, this technique has been extensively used in Latin American countries and in Pakistan, and is also being used in a new CRP on isotopic evaluations in infant growth monitoring, in collaboration with the WHO Growth Monitoring Programme.

Reports by WHO and other international organizations indicate that chronic diseases associated with ageing are becoming a serious problem in many developing countries, especially those undergoing nutritional and demographic change. In order to identify the mechanisms of disease development so as to define better methods of prevention, a CRP was initiated on the application of nuclear techniques in degenerative diseases in ageing. The first Research Co-ordination meeting was held in Vienna in May, where a protocol on the standardization of nuclear and isotopic techniques, including homeostatic model assessment to measure insulin sensitivity and methodologies for assessing body composition, substrate and energy metabolism, was developed.

An Advisory Group meeting on nutrition that included scientists from developed and developing countries, WHO and the Trace Element Institute for UNESCO took place in November. The purpose was to review the status of the Agency's work in nutrition, and to develop specific recommendations on expanding the application of isotopic techniques in human health areas for future projects and activities.

A global network of monitoring stations for determining elemental content in the PM<sub>10</sub>

and PM<sub>2.5</sub> fractions of airborne particulate matter was established through two CRPs. Health related epidemiological studies were carried out in these projects with the aim of linking results of chemical analyses with pulmonary and other diseases found in exposed general populations or exposed workers.

In support of analytical quality control efforts, an interlaboratory comparison for the determination of minor and trace elements in urban dusts (namely Vienna Dust and Prague

*“In a CRP on the application of nuclear techniques in degenerative diseases in ageing, a protocol on the standardization of nuclear and isotopic techniques was developed.”*

Dust), artificially loaded on air filters (for evaluation of heterogeneity) was carried out using a range of analytical techniques. A large number of loaded filters was prepared and characterized for use in future proficiency testing for the participating laboratories.

The Analytical Laboratories for the Measurement of Environmental Radioactivity (ALMERA) network was placed on a more formal footing by the issuance of letters of invitation to Member States to nominate one or more laboratories. More than 40 countries responded, nominating a total of 74 laboratories for the network. The first proficiency test involving the analysis of plutonium, americium, strontium-90 and gamma emitting radionuclides was initiated.

In support of analytical quality assurance for environmental studies, two lichen materials, IAEA-336 and IAEA-338, were characterized for their element content using various analytical techniques. Analyses for various trace elements for certification of a Japanese Diet Reference Material were carried out in support of the CRP on Reference Asian Man.

