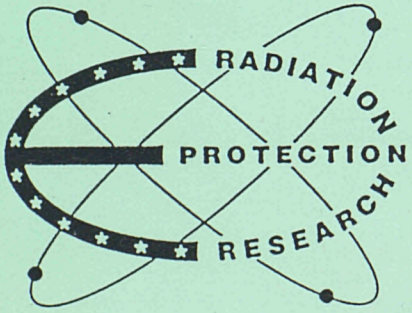
Commission of the European Communities

RADIATION PROTECTION RESEARCH AND TRAINING PROGRAMME

Review
Radiation protection programme 1960-89
Synopsis of results 1985-89



Report

EUR 13200 EN

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Directorate-General
Science, Research and Development

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Published by the
COMMISSION OF THE EUROPEAN COMMUNITIES
Directorate-General
Telecommunications, Information Industries and Innovation
L-2920 Luxembourg

LEGAL NOTICE

Cataloguing data can be found at the end of this publication

Luxembourg: Office for Official Publications of the European Communities, 1990

ISBN 92-826-1940-0 Catalogue number: CD-NA-13200-EN-C

Printed in France

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Preface

This document aims to:

- trace the evolution of the CEC Radiation Protection Programme over its 30 years of existence.
  During this time, research carried out in the framework of the Community Programme has made major contributions to the scientific understanding of the action of ionising radiation and the protection of man and his environment. This information was crucial for developing better radiation protection management for existing and new technologies and for providing the scientific basis for the regulatory activities of the Commission. One important feature of the Programme was the success of bringing together scientists from different Member States to co-operate in the various fields of radiation protection and to integrate different areas of radiation protection research into a coherent approach. The structures thus developed within the Programme have enabled research in radiation protection to be conducted in a cost effective manner on behalf of Member States.

- give a synopsis of the most important results of the 1985-1989 Radiation Protection Programme.
  This period was characterised by two challenges, the integration of two Member States into Community research and the impact of the Chernobyl accident. The Programme has, in spite of reduced funding, continued to provide a high degree of expertise for the Community in the context of the needs in radiation protection. This has been explicitly acknowledged in the evaluation of the Programmes 1980-1989 carried out by an independent panel.

This synopsis of the results of the 1985-1989 research Programme has been written with the help of the members and experts from the Management and Coordination Advisory Committee (CGC) "Radiation Protection" (see list, Annex I). Their dedication to the cause of the Community Radiation Protection Programme has been a major contributor to the success of the Programme in general, and to this document in particular, and is gratefully acknowledged.

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Executive Summary

The present "Review of the Radiation Protection Research Programme 1960-1989 and Synopsis of Results of the 1985-1989 Programme" traces the evolution of the CEC Radiation Protection Research and Training Programme over its 30 years of existence and summarises the most important results of the 1985-1989 Programme.

The Commission's radiation protection research activities are based on the Euratom Treaty which conferred on the Community the responsibility for "establishing uniform safety standards to protect the health of workers and of the general public and ensure that they are applied" (Article 2 b, see also Articles 30-39) and for "studying the harmful effects of radiation on living organisms" (Annex I, VI). The Treaty thereby establised a close link between regulation and research in radiation protection.

The Commission's radiation protection research activities, initially called "Biology - Health Protection", started with some preparatory actions in 1958/59 and took a concrete form in 1961. This was, therefore, the first Community (EURATOM) Programme that supported cost-shared actions and actively promoted co-operation between European scientists. Initially, in addition to radiation protection, the Programme included some research into applications of ionising radiation in agriculture and nuclear medicine. These topics were later abandoned for budgetary and political reasons or because they were more appropriately integrated into other Community Programmes.

The Programme was implemented along the following lines:

- research contracts were placed on a cost-sharing basis with institutes of Member States to carry out research in those areas given priority in the Programme and to initiate and promote co-operation between scientists in the Community;
- a radiobiology research group was constituted at the Joint Research Centre in Ispra to form a nucleus for research, development and training and also to deal with problems arising in the context of other activities of EURATOM. Following a period of rapid expansion, political support for the group waned and the group was finally dissolved in 1987, liberating means for cost-shared research contracts;
- Commission staff were detached to foremost scientific institutions in different Member States in order to establish permanent links between these institutions and the Commission and to act as a stimulating influence in their host institutions. The policy of the Programme with respect to the detachment of staff is now not to replace such staff when they retire;

- information exchange between scientists was promoted by study group meetings between contractors as well as by workshops, seminars and symposia attended by the international scientific community. Increasingly, these workshops, seminars and symposia were co-organised with contractors and/or other institutions such as the US Department of Energy, Atomic Energy of Canada Ltd....;
- training activities were initially focused on subjects which were of critical importance for European science i.e. in addition to radiation protection, molecular biology, application of radiation in agriculture. For a substantial number (about 300) of young scientists, they also involved preparing a thesis or learning new methods and establishing personal relations between institutes in different Member States. Today, training activities concentrate on radiation protection to maintain the expertise needed in this area.

The Community Radiation Protection Research and Training Programme started at a time when the introduction of nuclear power and the fears generated by nuclear war brought about a surge of interest and a rapid growth in new research in this area. This allowed the Programme to play a significant role both in national programmes and in developing co-operation among European scientists in a way unequalled in most other areas of research.

Principles, practices and challenges in radiation protection, and the corresponding research needs have evolved considerably during the 30-year period for which the Programme has been in existence. The Programme has not only mirrored these developments but has been actively involved in their instigation. The Programme identified many problem areas well in advance of the prevailing mainstream of research, and promoted them strongly on a Community scale. Indeed, the history of the Programme reflects the progressive integration of research in different disciplines and the influx of ideas from other areas of science. Over the lifetime of the Programme, there has been a gradual evolution and shift of emphasis from the short-term health effects of radiation exposure to its long term consequences and, more recently, towards a comprehensive risk approach.

The development of some important areas of research in the Programme is outlined in the main text including some of the transient activities of the Programme such as agricultural research, nuclear medicine and pest control. Some specific achievements of the Programme in radiation research, co-operation and training are also outlined, particularly with respect to the treatment of victims of radiation over-exposure, epidemiology of radium and thorotrast exposure, microdosimetry and biophysical models, repair of genetic damage, environmental behaviour and risks of

tritium and technetium, radon in homes, assessment and risks, dose reduction in medical diagnostic radiology, management of nuclear emergencies.

In addition, the Community Radiation Protection Research and Training Programme has lent crucial scientific support to the regulatory obligations of the Commission, providing basic data, co-operating in committees or specific task groups of ICRP and participating in the Group of Experts according to Article 31 of the Euratom Treaty and its subgroups. Among the more recent activities of the Programme, where regulation and research complement each other, are the elaboration of the revised EC Basic Safety Standards, the definition of the maximum permitted levels for radioactive contamination in human food and in animal feedingstuffs, the recent recommendations for intervention levels for radon in existing and planned dwellings, and the implementation of the Directives laying down the basic measures for the radiation protection of persons undergoing medical examinations or treatment.

The development of co-operation among scientists within the Community has been a particularly gratifying success of the Programme and was achieved by numerous study group meetings, by the creation of several large co-operative groups of scientists and, most recently, by the development of multinational contracts. Scientists have responded enthusiastically to these efforts. Needless to say, this co-operation initiated and sustained by the Community Programme has resulted in greater research efficiencies and substantial financial savings, avoiding duplication of research efforts and making optimal use of existing research facilities.

The Programme has progressively established links with international organisations and countries outside the Community. Memoranda of Understanding have been signed with the US Department of Energy, Office of Health and Environmental Research, and the Atomic Energy of Canada Ltd. The latter also involves the Canadian Atomic Energy Control Board and the Radiation Protection Bureau, Health and Welfare. Contacts, albeit not yet institutionalised, have been established with other EFTA countries and Japan, and scientists from these countries participate in meetings organised by the Programme.

The Programme supports the International Committee on Radiological Protection (ICRP) and the International Committee on Radiation Units and Measurements

(ICRU), and Commission staff participate in the Committee meetings of these organisations. Moreover, relations exist with the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the World Health Organisation (WHO), the Nuclear Energy Agency of the Organisation for Co-operation and Economic Development (NEA/OECD) and the Food and Agriculture Organisation (FAO). The International Atomic Energy Agency (IAEA) and the Community Programme have established co-ordinated research projects on radon and radiation doses in diagnostic radiology and methods for dose reduction.

The history of funding is revealing. Following a period of rapid expansion during the 1960s, funding became stationary and has declined progressively. Corrected for inflation and related to 100 million inhabitants to take account of the growth of the Community (Denmark, Ireland, the United Kingdom in 1973, Greece in 1981 and Spain and Portugal in 1986), funding of the Programme (excluding the supplementary activities) was of the order of 3.5-4 MEcu/100 million inhabitants during the 1960s and 1970s, then declined to 2.28 in 1985-1989 and, finally to 1.84 in 1990-1991. The number of contracts supported increased from 18 contracts in the period 1960-1962, 42 contracts 1963-1967, 34 contracts 1968-1970, 131 contracts 1971-1975, 185 contracts in 1976-1980, 266 contracts in 1981-1985 and 403 contracts, including the post-Chernobyl activities in 1985-1989. For the period 1990/1991, a total of 125, mostly multinational, contracts consisting of about 370 projects have been awarded so far. Obviously, the decline in budget while the number of contracts remained constant or even increased meant that individual contracts obtained less and less funding.

The structures for an efficient management of the Programme have gradually evolved during the 30 years. The initial "Advisory Committee on Biology" established in 1961 was replaced by an Advisory Committee on Programme Management Biology-Health Protection (ACMP) created by Council decision in 1974 was replaced by the present "Management and Coordination Advisory Committee, Radiation Protection" (CGC) in 1985. The development of the CEC Radiation Protection Programme would have been impossible without the scientific competence and the involvement of these Committees which not only gave advice on the

orientation and execution of the Programme but also helped to establish links between the different national programmes.

Following a call for proposals at the initiation of a new Radiation Protection Research and Training Programme, incoming proposals are evaluated by the Commission's services in co-operation with the CGC. Funding is either by cost-sharing, mainly with national institutes, or by marginal cost contracts, mainly with universities. The fraction of proposals accepted and funded by the Programme has decreased from about 80% during the early period of the Programme to about 50% in the 1980s and is now close to 30%.

The 1985-1989 Radiation Protection Programme was adopted by the Council of Ministers on 12 March 1985 with a budget of 58 MEcu (million Ecu). The period of this Programme was characterised by the accession to the Community of Portugal and Spain in 1986 and by the accident at Chernobyl on 26 April 1986. The Programme succeeded in rapidly incorporating the new Member States into its contracts and co-operative groups. The Chernobyl accident resulted in a stronger emphasis on research dealing with the assessment of accident consequences and with countermeasures. Moreover, a revision of the Programme with an additional budget of 10 MEcu was decided by the Council on 21 December 1987 as a response to research needs recognised after the accident. The results of the Programme revision will be reviewed in a separate publication to be issued late in 1990.

A total of 283 proposals consisting of 403 projects (without the post-Chernobyl actions) and involving a participation by the Commission of 48 MEcu were accepted for funding during 1985-1989. The research topics were classified in six sectors:

A) Radiation dosimetry and its interpretation
B) Behaviour and control of radionuclides in the environment
C) Non-stochastic effects of radiation
D) Radiation carcinogenesis
E) Genetic effects of ionising radiation
F) Evaluation of radiation risks and optimisation of protection.

Radiation dosimetry provides the concepts, procedures and methods for the determination of the amount of ionising radiation which is to be related to the biological effects induced. This involved the investigation of the fundamental

aspects of the interaction of radiation with matter, the relationship between physical quantities and biological effects, the practical development of dosimetric concepts and quantities as well as appropriate instrumentation, and the procedures for the establishment of limits and standards for the control of exposures.

Information on the **behaviour of radionuclides in the environment** represents an important input to the assessment of exposure from radionuclides released from the nuclear fuel cycle or from natural radioactivity enhanced by human activities. Particular attention was given to the transfer in terrestrial and aquatic environments, in particular to long-lived radionuclides, and the modifications in physico-chemical or biological properties during such transfer. This information represents a crucial input to the assessment and control of the transfer of radionuclides to man under normal situations and after accidental releases.

Non-stochastic radiation damage occurs only when, during an accident or for medical reasons, a certain threshold dose is exceeded. Effects on the developing organism have a lower threshold, especially with respect to brain damage after in utero exposure, or perhaps arise even at low doses. Investigations concerned the establishment of the threshold doses for damage, the elucidation of the pathogenetic mechanisms involved and the methods to recognise, prevent or treat non-stochastic damage. Particular attention was given to the haemopoietic-immune system, to skin and to the developing organism.

Radiation-induced cancer is of particular concern in radiation protection since such stochastic effects may arise at low doses without a threshold at full severity as a consequence of genetic alterations in a single cell. The progeny of such a transformed cell can then divide to form a tumour or, in the case of genetic damage in germ cells, be transmitted as hereditary disease to the child. Radiation exposure from natural, medical or industrial sources occurs mainly at low doses and at low dose rates; a quantitative definition of cancer risks from such exposure is, therefore, a primary problem for research. Since no direct evaluation of radiation-induced cancer is possible in the low dose range, the problem was approached by integrating biophysical, bio-molecular, cellular, animal and human studies.

Hereditary radiation damage with harmful consequences for future generations is, besides cancer, the most important risk after exposure to low doses. No information from man is available on such risks; therefore, the radiation-induced changes in the genetic apparatus of the cell and their repair were studied, including its variability among individuals. The induction of mutations and chromosome damage was also investigated in animal models.

Evaluation of radiation risks and optimisation of protection requires the integration information from all areas of radiation protection research. To this end, research evaluated human exposure from different sources, investigating, in particular, exposure and risks from radon and possible countermeasures as well as doses and their reduction by improved quality control and image criteria in medical diagnostic radiology. Research also aimed to put, as far as possible, radiation risks in perspective with other risks society encounters and to develop an integrated system of management for radiation protection. In this approach, normal as well as accidental situations were taken into account.

The document presents a synopsis of the most important results from the different sectors of the Programme; the original final reports, presented in 3 volumes, are available on request. The contracts of the 1985-1990 Programme, arranged according to sector or to country of origin are listed in Annexes II and III. In addition, the Programme continued to organise a substantial number of study groups, workshops, seminars and symposia. The proceedings of the most important ones are published in the open scientific literature; the reader will find a list in Annex IV.

A Radiation Protection Research and Training Programme for 1990-1991 was approved by the Council of Ministers on 22 June 1989 with a budget of 21.2 MEcu. The following structure of the new Programme, differing somewhat from earlier Programmes, has been introduced to emphasise the various goals of radiation research as well as their interdependence and the need for multi-disciplinary approaches for solving these problems:

A) Human Exposure to Radiation and Radioactivity
   A1 Measurement of Radiation Dose and its Interpretation
   A2 Transfer and Behaviour of Radionuclides in the Environment

B) Consequences of Radiation Exposure to Man; their Assessment, Prevention and Treatment
   B1 Stochastic Effects of Radiation
   B2 Non-stochastic Effects of Radiation
   B3 Radiation Effects on the Developing Organism

C) Risks and Management of Radiation Protection
   C1 Assessment of Human Exposure and Risks
   C2 Optimisation and Management of Radiation Protection.

Another important change in the 1990-1991 Programme is the new management structure of multinational contracts. These contracts, administered by one of the partners but co-ordinated with respect to scientific matters by the Commission's staff, will result in an even better integration of Community research. Moreover, training activity in the Programme will be substantially increased. In this way, it should be possible to maintain and expand Community expertise in radiation protection.

On reviewing the progress achieved during the 30 years of the Programme, and more specifically during the past 5 years, it is apparent that the Commission's Programme has been remarkably successful in establishing the scientific basis for the protection of man and his environment from exposure to ionising radiation. The effective co-operation and exchange between scientists in the EC, achieved largely through initiatives from within the Programme, has been a major contributor to their success.

Radiation protection will remain a topic of much public, political and scientific interest in the future. In order to provide an adequate response to the needs of these various interest groups, it is imperative that a substantive research programme is maintained in this area. The considerable success achieved during the past 30 years of the EC Programme augurs well for its future success. If the identified benefits from the use of radiation in the many spheres of industry and medicine are to continue to be obtained, it will be necessary to achieve an even better understanding of the effects of radiation on man and his environment.

Moreover, this understanding will need to be communicated more effectively to the public and/or its political representatives, an area which perhaps has received insufficient attention in the past. It is essential that public confidence in the system of protection is restored. The future Programmes, in addition to their more scientific objectives, will be directed towards this end.

I. Thirty years of Research within the European Community Radiation Protection Programme

A. Introduction and History

The Treaty establishing the European Atomic Energy Community (EAEC or EURATOM) was signed in Rome on 25 March 1957 and came into force on 1 January 1958. The European Atomic Energy Community was given the task of "contributing to the raising of the standard of living in the Member States and to the development of relations with other countries by creating the conditions necessary for the speedy establishment and growth of nuclear industries". The Treaty also envisaged the protection of the public from such developments by conferring on the Community responsibility for:

- "establishing uniform safety standards to protect the health of workers and of the general public and ensure that they are applied" (Article 2 b, see also Articles 30-39)
- "studying the harmful effects of radiation on living organisms" (Annexes I, VI)

thereby closely linking the two activities of regulation and research in radiation protection. The role of the Community in establishing uniform standards for the protection of its citizens and a co-operative approach to supportive research has taken on an increasing importance as European unity is realised in a greater number of areas.

The Treaty also endowed the Commission with two instruments for research:

- a Joint Nuclear Research Centre (JRC) (Article 8),
- research and training Programmes (Article 7) carried out by means of contracts with scientific institutions in Member States (Article 10).

Ten years after the establishment of the EURATOM Treaty, the European Economic Community, the European Community for Coal and Steel and the European Atomic Energy Community were fused in 1967. This brought a re-thinking of the role of Community research and an extension of the competence of the JRC to non-nuclear fields. Greater flexibility in the preparation and implementation of EURATOM research and training programmes was emphasised, and Council decisions after 1971

defined individual programmes rather than the entire EURATOM training and research programme. This, subsequently, opened the way for the development of Community research in other areas. More recently, the Single European Act and the ensuing Framework Programme of Community activities in the field of research and technical development (1987-1991) gave the research activities of the Commission a new unified structure in which the Radiation Protection Programme was incorporated under the heading "Quality of Life: Radiation Protection". The third Framework Programme 1990-1994 has developed the concept of "rolling programmes" and includes the Community action "Radiation Protection: Research and Training" in the Specific Programme "Nuclear Fission Safety". Notwithstanding its inclusion within the "Nuclear Fission Safety" Programme, research will continue on all sources of radiation encompassing natural, medical and industrial sources, and not just those associated with nuclear fission.

The Commission's radiation protection research activities, first called "Biology-Health Protection", started with some preparatory actions in 1958/59 and took a concrete form in 1961. This was the first Community (EURATOM) Programme that supported cost-shared actions and actively promoted co-operation. From its inception, the aims of the Programme went beyond filling gaps in ongoing research. On the contrary, they were oriented towards medium- and long-term goals, in particular focusing on activities which could encourage young scientists to pursue future promising areas of research and which could lead to increased and more effective co-operation between European scientists. Initially, the Programme included research not only in radiation protection but also into applications of ionising radiations in agriculture and nuclear medicine (see page 20). Several of the topics which were initially included in the Programme had later to be abandoned for budgetary and political reasons. A number of activities carried out within the Radiation Protection Programme have inspired the creation of independent Community research programmes, for example, the Programmes on Environment and on Biotechnology; indeed, these programmes have since overtaken the Radiation Protection Programme in size and importance.

The Programme has focused increasingly on radiation protection research and, in this area, has achieved a remarkable standard of scientific excellence made possible by the effective co-ordination of research and co-operation among scientists in the Community. In this way it has set a notable example of the benefits which a Community Research Programme can bring, in particular when it receives a consistent level of financial and political support over many years.

Initially, the Programme was to be implemented along several lines:

- contracts were placed, on a cost-sharing basis, with institutes of Member States to carry out research in those areas given priority in the Programme and to initiate and promote co-operation among scientists in the Community. This latter objective was also furthered through the creation, by the Commission, of co-operative groups of scientists such as the European Late Effects Project Group (EULEP) and the European Radiation Dosimetry Group (EURADOS);
- a radiobiology research group was constituted at the JRC (the Biology Group at Ispra). This group was independent of the JRC and was directly responsible to the former Directorate General for Research and Training. This group was to form a nucleus for research, development and training and also was to deal with problems arising in the context of other activities of EURATOM (page 21). Following a period of rapid expansion, political support for the group waned and, with a scientific staff varying between 10 and 20, it never quite reached the critical size to play the major role in radiation protection research within the Community that was initially planned for it. This group was finally dissolved in 1987 liberating means for cost-shared research contracts;
- Commission staff were seconded to some of the foremost scientific institutes in different Member States in order to establish close links between these institutes and the Commission and to act as a stimulating influence in their host institutions. These objectives were certainly met initially, and the detached Commission staff not only contributed substantially to the research in radiation protection, but were also influential in the elaboration of new Community research programmes in medicine and biotechnology. The policy of the Programme with respect to the detachment of staff has since changed and, in future, when detached staff retire, they will no longer be replaced. From an original number of about 30 seconded scientists, only 3 still remain involved with large contracts in Member States laboratories; they are, however, also charged with coordination and administrative tasks associated with the management of the Programme;
- information exchanges among scientists were to be promoted by study group meetings of contractors as well as by workshops, seminars and symposia attended by the international scientific community. Increasingly, these workshops, seminars and symposia have been co-organised with contractors and/or other institutions, such as the US Department of Energy, Atomic Energy of Canada Ltd...;
- training activities initially emphasised subjects which were of critical importance for European science during the sixties, i.e. in addition to radiation protection, molecular biology, application of radiation in agriculture. Fellowships given to a substantial number (about 300) of young scientists enabled them to prepare a thesis or to learn new methods; this helped to establish permanent links between institutes in different Member States. More recently, training activities have concentrated on radiation protection to maintain the expertise needed in this area.

Today, the cost-shared or full-cost contracts represent the backbone of the Programme, together with the support of co-operative groups and the various information and training activities.

B. The CEC Radiation Protection Programme, Element and Motor of Evolving Radiation Protection Research

1. General Trends and Implications

Efforts to protect workers and the public against industrial or natural noxious agents did not assume a prominent role until well into the 20th century. Indeed, it was the protection against the harmful effects of ionising radiation that became the principal starting point for which such considerations were first voiced and clearly defined, and for which appropriate regulatory actions were taken and supported by scientific research. It should not be forgotten that radiation protection had already generated quite a few of the required practices and regulations before nuclear energy developed. One motivation for radiation research was the need to base regulations and safe practices on a scientific understanding of the qualitative and quantitative aspects of the action of radiation on man. The other equally important motivation for research sprang from the passion to gain a better understanding of the basic mechanisms by which the physical agent, radiation, affects living matter at a molecular level, in particular the variety of physiological and pathological alterations including cancer and genetic damage. Both types of motivation have been influential in determining the nature and content of the research undertaken.

Occasionally, criticism is levelled at radiation protection research because it has still not entirely accomplished its pursuit for an exhaustive scientific foundation for a radiation protection; such criticism is, however, largely misplaced. While it must be accepted that a complete understanding of the effects of radiation on living organisms does not exist, this situation is neither unique nor surprising. However, it is pertinent to note that the quantitative understanding of the risks of radiation exposure, and thus the basis on which radiation protection standards are based, is more advanced than for any other carcinogenic agent. Radiation protection research, particularly that conducted in the last few decades, has been largely responsible for these achievements. Further efforts are, however, necessary in order to maintain and extend these achievements, to deal with new scientific or practical problems in radiation protection, to control new or expanding applications of

radiation and to restore public confidence. It is also noteworthy that several important and innovative scientific developments had their origin in, and were inspired by radiation research; notable examples include organ transplantation, immunology, cancer therapy, biotechnology; even modern molecular biology has some of its origin in radiation research.

Research into the effects of ionising radiation began during the last decade of the 19th century. It continued throughout the first half of the 20th century, mainly in the context of applications in medicine. After the second world war, the introduction of nuclear power and the fears generated by nuclear war brought about a surge of interest and a rapid growth in new research in this area. The Community Radiation Protection Research and Training Programme thus began at a fortunate time, and this allowed the Programme to play a significant role, both in national programmes and in developing co-operation among European scientists in a way unequalled in most other areas of research.

Principles, practices and challenges in radiation protection, and the corresponding research needs, have evolved considerably during the 30-year period during which the Programme has been in existence. The Programme has not only mirrored these developments but has been actively involved in their instigation. This can be readily seen from a perusal of the multiannual Programme Proposals and Progress Reports where many problem areas were identified well in advance of the prevailing mainstream of research. Indeed, the history of the Programme reflects the progressive integration of research in different disciplines and the influx of ideas from other areas of science. Over the lifetime of the Programme, there has been a gradual evolution and shift of emphasis from the acute health effects of radiation exposure to its long term consequences and, more recently, towards a comprehensive approach to risk.

The development of some important areas of research in the Programme is briefly described in the remainder of this section, including, at the end of this chapter, some of the transient activities of the Programme such as agricultural research, nuclear

medicine and pest control. A selection of specific achievements of the Programme in radiation research, co-operation and training are summarised in Section B2. (page 23).

Acute Effects of Radiation

For many years, the **acute effects of radiation**[1] were in the foreground of research interest, probably due to the immediate impact of the atomic bombs exploded over Japan. Many investigations dealt with physiological, biochemical and pathological changes after such exposure and the means to protect against them. The Programme has concentrated research on only a few topics in this area and these are:

- the treatment of individuals, exposed accidentally to high doses of radiation delivered to large parts of the body, emphasised research into bone marrow transplantation (choice and isolation of the transplant, avoidance of graft versus host disease) and, more recently, the use of haemopoietic growth factors. This subject is discussed in more detail in Section B2 (page 23);
- the mechanisms of damage to the haemopoietic and immune systems were investigated, with particular emphasis on gaining a quantitative understanding of the cell replacement systems involved and the cellular and humeral basis of early and late immune damage;
- an evaluation of the severity of biological damage after exposure of large parts of the body was made on the basis of cytogenetic (chromosome aberrations) and biochemical tests;
- the diagnosis and therapy of early and late radiation damage after local irradiation, particularly of the skin and underlying tissues, was improved by new scientific approaches. This subject is discussed further in Section B2 (page 25);
- the administration of chemical substances to protect against the consequences of radiation was found to be quite effective against acute but, somewhat less, against late radiation damage. When given in combination, these substances have enabled animals to survive exposures three times greater. However, the toxicity of these substances precludes, at least for the present, their practical application for man.

The study of the **cellular basis of radiation effects** began in the 1960s when new cell culture techniques and in vivo assays allowed the clonal survival of individual cells to be determined. Loss of cells and changes in cell function were found to be the

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[1] Two types of radiation effects must be distinguished: **non-stochastic or deterministic effects**, typified by acute and many late radiation syndromes, are due to the death or functional impairment of many cells and, therefore, arise only above a threshold dose. Since radiation standards are set well below these threshold doses, non-stochastic damage occurs only after accidental or therapeutic exposure. On the contrary, **stochastic or non-deterministic effects** to a single cell can be transmitted to the progeny of this cell either in the same organism, giving rise to cancer or, to future generations, causing hereditary alterations. Such changes may arise without a threshold.

factors responsible for nearly all acute and late syndromes observed after irradiation. At the same time, an understanding was gained of how the radiosensitive permanent stem cells must be able to replace, via intermediary cell stages, the functional cells of limited lifespan and low radiosensitivity, e.g. those in the blood or on the skin surface. This understanding allowed damage in relation to dose and time after exposure to be quantified not only for the acute haemopoietic, intestinal and skin syndromes but also for many late types of non-stochastic health effects. Scientists working in the Community Programme had a major influence on the development of these concepts, carrying out many of the underlying and decisive experiments and developing models to describe such behaviour. Indeed, the insights into cell replacement systems gained from radiobiological research was greatly influential in much clinical research in haematology and other disciplines.

Research in **immunology** has progressed markedly during the past thirty years with respect to the definition of the different cell types involved in the humeral and cellular immune response and the genetic and molecular basis of the formation of antibodies. Radio-immunology was formerly at the forefront of developments in immunology generally but subsequently was unable, until recently, to keep up with the very rapid development in this area. Nevertheless, Community-supported radio-immunological research maintained a key role in several areas; it led to the development of the immunology of bone marrow transplantation, including treatment with anti-lymphocytic sera, the understanding of the ageing of the immune system and the influence of radiation on it; the participation of different immune cell types in early radiation damage; and the development of rat monoclonal antibodies for such studies.

New methods in genetics and molecular biology enabled cultured cells to be used for the quantitative investigation of endpoints other than radiation-induced cell death, such as **chromosome aberrations, mutations and malignant transformations**, and to compare their respective radiosensitivities and the influence of different factors. Research on chromosomal aberrations has had, and continues to have, a prominent place in the Community Programme. The relation between chromosomal damage and cell death (and more recently cell transformation) for radiation of different

qualities was explored, thereby contributing to the establishment of the quality factor[2] for neutrons and other types of radiation. Chromosomal aberrations in circulating lymphocytes were used to develop a means of biological dosimetry for acute and chronic exposure. The form of the dose-effect relationship for chromosome aberrations at radiation doses of some tens of mSv has been investigated in a co-operative effort amongst Community scientists.

The study of **in vitro cell transformation** was lacking in the Programme until about 1984, and this was noted by an independent evaluation panel in 1984. However, once recognised, this deficiency was remedied and the topic is now being actively promoted within the Programme. Transformation studies in the Community have expanded considerably and now make a significant contribution internationally. These have also resulted in the development of several new cellular systems which are more relevant for studies of human carcinogenesis. Two recent workshops organised by the Commission on this subject indicate the progress and contribution made by the Commission's Programme (see Annex IV, page 235).

During the past thirty years, the **molecular target of radiation** in the cell has been better defined. It is now generally accepted that the more important effects, such as cell death, chromosomal aberrations, mutations and malignant transformation, come about as a result of radiation damage to DNA in the genetic apparatus of the cell. Radiation damage to DNA constituents has, therefore, been studied intensively and, over the years, the Programme has built up a very active multinational research group dealing with such "primary effects of radiation" on DNA and its constituents. This has resulted in European research becoming a leader in this field. However, in 1985, budgetary restrictions compelled the Programme to forgo research in this area because its contribution was considered to be only on a long- but not on a short-term basis to radiation protection. This led to a major decline in research into the primary effects of radiation in the Community, whereas such studies in the USA have continued to evolve towards research into radiation effects on higher

[2] The quality factor is an operational quantity used to take into account the differences in action of various types of radiation at dose levels of relevance for radiation protection. It must be distinguished from the Relative Biological Effectiveness (RBE) which represents the ratio of doses which give the same biological effect for a specific endpoint.

organisational levels of DNA. This can be considered an exemplary case of how critical support from the CEC Programme support can be in assuring continuity and cohesion to a given research area.

Non-stochastic (Deterministic) Late Effects of Radiation

During the thirty years under consideration, attention given by research and public concern shifted more and more from acute to late effects of radiation. Considerable knowledge has been obtained on **late non-stochastic radiation damage** from patients undergoing radiotherapy. This, however, is only partially relevant to accidental over-exposures where doses and conditions of exposure are generally uncertain. The Programme, therefore, concentrated on the general pathogenetic mechanisms of non-stochastic effects and, especially, in those tissues of relevance to practical radiation protection. A new hypothesis on the cellular and vascular pathogenesis of non-stochastic late effects was developed and tested in suitable experimental models (such as brain, heart, skin). This has helped in the prediction of the consequences of exposure and in the search for diagnostic tools and treatment modalities. Studies on the lung concentrated on the pathogenetic mechanisms of fibrosis and the role of macrophages with respect to radiosensitivity and removal of radioactive particles. The thyroid and the lens of the eye were other tissues studied, and an epidemiological study on patients given radiotherapy to the eye yielded data on the threshold doses for radiation-induced cataract.

Stochastic (Non-Deterministic) Late Effects of Radiation

The **carcinogenic action of radiation** in man was recognised a few years (1902) after the discovery of X-rays, and, in this context, it should be recalled that several pioneers in radiation research died from radiation-induced cancer. Quantitative information on the human risks of radiation-induced cancer, however, only became available during the late 1960s and even then only for exposures to high doses at high dose rates, mainly from the follow-up of the survivors of the atomic bomb explosions. Hereditary effects of radiation in plants were first observed in 1928, but quantification of these effects in animals was only made some thirty years later.

The assessment of the risks of radiation-induced cancer in man is based on the epidemiology of populations exposed generally at high doses and dose rates. For exposure at low doses and dose rates, these estimates must be supplemented by insights gained from animal experiments, cellular models, microdosimetry and biophysical models as discussed in more detail in Section B2 (page 27). The Community has made an important contribution in this area, particularly with respect to human carcinogenesis from radionuclides, integrating research undertaken in epidemiology, animal and fundamental radiation studies (see Section B2, page 26).

Community research in **animal radiation carcinogenesis** could never match the long-term studies with large animals undertaken in the USA because of the lack of facilities and funds. Nevertheless, Community studies have made a significant contribution to progress in this area. This has been achieved, using mainly rodents, by focusing on a careful analysis of the causes of death after irradiation, on different exposure situations and on the mechanisms of radiation-induced cancer. Extensive studies on specific radiation-induced tumours, such as mammary tumours, lung tumours, myeloid and lymphoid leukaemia, bone and liver tumours after internal exposure helped in the understanding of dose effect relationships and pathogenetic mechanisms. Other studies dealt with causes of death, in particular cancers, after neutron exposure, fractionated irradiation and on reduction of radiation-induced carcinogenesis by treatment with radio-protectors.

Several Community laboratories established effective collaboration with US laboratories enabling an exchange of knowledge and experience. Standardised pathological terminology and dosimetry were established with the help of EULEP (European Late Effects Project Group). More recently, research supported by the Programme has led to the development of new approaches for the statistical analysis and interpretation of long term animal studies These will be used to re-evaluate existing animal data and to plan effectively any future animal studies which may be needed to understand better the effects of exposure at low doses/dose rates.

Considerable resources have been devoted to elucidating **the molecular origin of carcinogenesis** in animals, and particular attention has been directed towards the role of retro-viruses. Emphasis was placed on thymic lymphoma and on bone and

mammary cancer. The retro-viruses were isolated and studies made of their molecular modifications, the activation of their transcription products and their relation to oncogenes. More recent investigations have examined changes in chromosomal structure in relation to radiation-induced cancer, and there is worldwide recognition of the eminent role of Community research in this area. This research has also provided a better understanding of carcinogenesis in general.

Quantitative estimates of genetic risks of radiation in man are currently based on extrapolation from animal data; no significant increase in genetic damage has been observed in irradiated human populations. During the 1960s, US scientists at Oak Ridge National Laboratories (ORNL) followed radiation-induced recessive mutations in several million mice, and these form the basis for the risk estimates in man. A major input into assessing genetic risks was, however, made by Community laboratories supported by the Programme during the 1970s and 1980s. This led to a determination of the risk of dominant mutations, the correction downwards of the risk estimates of ORNL using other recessive mutations, and an indication that the risk of non-disjunction (e.g. Down's syndrome in man) in mice is small. In addition to experimental genetic studies on animals, the Programme supported research into the repair of genetic damage in bacteria, the fruit fly and mammalian cells. This subject is discussed further in Section B2 (see page 30).

Dosimetry

Dosimetry has to provide a measure of the amount of radiation delivered to tissues and organs so that it can be correlated with any biological effect induced. It also has, for the purposes of radiation protection, to provide means for ensuring compliance with regulatory requirements and indicating the levels of risk associated with the exposure. The Programme, throughout its existence, has played a decisive role in stimulating and supporting research into:

- developing the concepts and quantities for determining tissue exposure from external and internal radiation, thus providing an input to the assessment of risks, the definition of regulatory limits and operational radiation practices;
- providing the scientific basis and the technical knowledge necessary for the development and improvement of procedures and instrumentation to determine doses reliably for external and internal exposure and for individual, area and environmental monitoring;

- investigating the microscopic pattern of deposition of energy by ionising radiation in relevant biological structures. This is a prerequisite for biophysical models to describe the quantitative action of radiation. This aspect is discussed in more detail in Section B2 on page 27.

In the last four decades international committees, such as ICRU and ICRP[3], have developed new and theoretically more sound and coherent dosimetric quantities and concepts. These developments have resulted in a more generally applicable and coherent basis for risk assessment and control of radiation exposure. Research had to provide the scientific background, the instrumentation, the operational practices and dosimetric calculation methods for the development and implementation of these new quantities. In 1977, ICRP introduced the quantity "effective dose equivalent" which takes account of the different radiosensitivities of individual tissues and provides a measure of the risks of radiation exposure regardless of its non-uniformity. The Programme co-operated closely with ICRU, hosting several of its meetings and placing contracts in order to facilitate and harmonise the implementation of the new quantities and concepts and to develop adequate calibration procedures and instruments in compliance with existing methods in radiation metrology. Computational dosimetry provided the quantitative relations between operational quantities and effective dose equivalents, and enables organ and tissue doses to be estimated for external exposure and from radionuclides incorporated into the body.

Research into the metabolism and dosimetry of radionuclides taken into the body has occupied an important place in the Programme. This information is essential for the establishment of standards for the control of internal exposure both in the workplace and from radionuclides in the environment. Initially, the research focused on workers but has since been extended to all groups of the general population, including adults of various ages, pregnant women, foeti in utero, infants and children. This information was an essential input into establishing maximum permitted levels for radionuclides in foodstuffs following the Chernobyl accident. Research concentrated on the metabolism of a range of radionuclides, with particular

[3] ICRP International Committee on Radiological Protection, ICRU International Commission on Radiation Units and Measurements.

emphasis on the actinides, where pulmonary and intestinal uptake were investigated together with metabolism in liver and bone. Models were developed and their parameters were obtained experimentally for deposition and clearance of inhaled particles in the lung of adults and children. These contributed to establishing more soundly based annual limits of intake for internal radiation exposure. In addition, they helped to improve knowledge of the pulmonary physiology and the behaviour of toxic aerosols and gases. Techniques were also developed to determine the body burden and organ contents of radionuclides based on monitoring of excreta and whole body or organ counting.

Thirty years ago, only X-ray and gamma ray dosimetry could be considered to be adequate. The need for reliable **neutron dosimetry** has increased during this period due to the developments of the nuclear industry, radiation therapy and other applications. This required the development of new and better detection methods as well as the elucidation of the basic physical phenomena and basic dosimetric quantities. New instrumentation and procedures to measure neutron dose have been developed in the Programme and are now in routine operation, e.g. tissue equivalent ionisation chambers, moderator type neutron dose equivalent meters ("rem-counters") for area monitoring, track-etch plastic film (CR-39 which is also used for radon monitoring). The success of these efforts is evident from the six International Symposia on Neutron Dosimetry and the several workshops and inter-comparisons organised by the Programme since 1972. Further research in neutron dosimetry, in particular in mixed radiation fields, remains, however, imperative to implement the change in quality factor now under consideration.

Although personnel dosimetry using film badges has been in use for a long time, **individual monitoring** needed substantial improvement and, for neutrons, had to be developed almost from scratch. Developments initiated by the Programme have increased the range of available instrumentation and the reliability of procedures. The film badge has been supplemented by small thermo-luminescence dosemeters (TLD) which can be read in automatic devices. Plastic film (CR-39) dosemeters, phosphate glasses and, more recently, solid state detectors for photons and neutrons developed within the Programme have complemented the arsenal available.

Moreover, micro-electronics will soon provide active dosemeters with real time display of exposure and alarm thresholds. Research has also improved the skin dosimetry of weakly penetrating radiation (beta rays, soft X-rays) and related it to the biological target. The need for accident dosimetry was recognised early, but the difficulties involved in measuring extremely high dose rates and defining the inhomogeneous dose distribution in the body at such accidents remain major challenges for future research.

To complement the new developments and to provide quality assurance of procedures, the Programme has organised several inter-comparisons of instrumentation and provided various guidance, e.g. editing a manual of dosimetry for radiobiological experiments through EULEP (European Late Effects Project Group). The consistent support by the Programme and efficient collaboration between research groups, partly within the EURADOS (European Radiation Dosimetry Group) working committees, has ensured continuous and effective progress in the field of dosimetry and maintained a high level of expertise. Neighbouring fields such as dosimetry of high LET radiation therapy and diagnostic radiology in medicine have benefited from the progress achieved.

Radioecology

Research in radioecology in the 1960s started out mainly as an observational science collecting data on fallout from nuclear weapons tests and studying a few well defined ecological pathways under experimental or field conditions. Progressively, attention was extended to entire ecosystems and to the overall behaviour of a radionuclide from its release into the environment to its transfer to man, and to the elucidation of the transfer processes themselves. In these ways, critical pathways in the food chain could be identified, and appropriate experimental studies could be undertaken. This has led to the progressive identification of the critical transfer processes and environments. Increasingly, attention has been drawn to the variability and uncertainty of transfer parameters of radionuclides under different situations and also of their dependence on their physico-chemical form and on any biological modifications that may occur in the environment. The results have provided the

means for obtaining a more complete assessment of the impact normal and accident releases can have on man and the environment. Nevertheless, not all problems have been solved and this was exemplified by the Chernobyl accident which drew attention to the role of natural and semi-natural ecosystems as sources for radioactive contamination and to special problems related to particles formed from nuclear fuel at high temperature.

Models have been developed to predict the transfer of radionuclides through the environment under normal and accident conditions. These models are based on a compilation of the diverse data obtained from research and measurement programmes and have provided a valuable means of identifying major areas of uncertainty where more research was needed. These developments required close co-operation between radioecologists and other disciplines and this was strongly promoted by the many workshops organised by the Programme. Research into the ecology of radioactive pollution has contributed significantly to the understanding of the ecology of other pollutants. Because of the relative ease with which radioactivity can be measured, radioecology has preceded and stimulated other applications of environmental research.

Marine radioecology in the Programme developed from an association with the CNEN (Centro Nazionale de Energia Nucleare) at Fiascherino (I). During the 1960s, the behaviour of stable elements as indicators for radioactive contamination, and their transfer through plankton and fish into the human food chain, were studied. This research gave the Community a firm basis in marine radioecology and enabled the development of methods for marine ecology in general. Following the expansion of the Community in 1973, 1981 and 1986, studies were initiated in other large national centres of marine research. These studies focused on the dispersion of radionuclides discharged into the marine environment, the exchange with sediments, the transfer to man via sea food, and the generation of wind-borne activity from ocean spray. The close co-operation formed between the different institutes for marine radioecology in the Member States enabled problems of marine contamination to be investigated on a Community scale. The models developed for the local and wide-range dispersion of discharged nuclides and their transfer to

sediments has provided a sound basis for the control of liquid effluents, both radioactive and other pollutants.

Freshwater radioecology was initially studied by the Biology Group at Ispra. Investigations were made of contamination through plankton, mollusca and fish in Lake Maggiore, near the Ispra Joint Research Centre, in relation to the life cycle and behaviour of these organisms. The Programme also supported research in other freshwater systems, in particular in the Meuse and Rhône rivers, as part of a co-operative project on two waterways into which several nuclear reactors and other industries discharge effluents. Binding to sediments was identified as having an important role as a sink and source of radionuclides, and radionuclides accumulated in some organisms can be used as biological indicators to assess average contamination over a period of time. These studies have also helped to develop the basis for regulatory control of radioactive and other effluents into fresh water systems.

Radioecological research into the **soil plant pathway** was developed in the association with ITAL (Instituut voor Toepassing van Atoomenergie in de Landbouw), Wageningen, NL, where the transport of radionuclides in undisturbed soil columns and plant uptake were studied. The Biology Group at Ispra and several other laboratories also investigated the **uptake of radionuclides in plants**. These laboratory studies were subsequently extended to the field and an extensive data base now exists on soil-plant transfer. Further investigations are, however, required to enhance the reliability of the data, especially for radionuclides in physico-chemical forms or in environments which differ radically from those for which the data have been acquired.

Community research benefited from unique facilities which enabled the **long-term behaviour of radionuclides in crops and in domestic animals** to be studied. A wide variety of radionuclides, including technetium, tritium, carbon and different heavy metals have been investigated, with respect to the uptake from contaminated soil, and the transfer from feedingstuffs to meat, milk and offspring. The information obtained from this research was important for establishing, by the Commission, intervention levels for radionuclides in food and feeding stuffs following the

Chernobyl accident. It also provided a better understanding of the physiology of animal nutrition.

The physico-chemical forms of radionuclides released into the environment, and any changes which subsequently occur, can greatly influence their behaviour and transfer. These influences, often designated under the term **speciation**, have been studied extensively in the Programme, e.g. binding to sediments or plankton, binding and absorption to soil constituents, influence of soil bacteria, modifications in the gastro-intestinal tract; particular attention has been given in this respect to actinides and heavy metals as well as to tritium and carbon-14. The studies dealing with the behaviour of tritium and technetium and to the problems of speciation are discussed further in Section B2 (see page 32).

Radiation Risks and Management of Radiation Protection

Quantitative risk management in radiation protection only became possible when sufficiently reliable **data on exposure and risk** became available. Much progress has been achieved in this area during the past thirty years and has been aided by close co-operation between the research and regulatory activities of the Commission. Thus, it became possible to develop radiation protection philosophy not only on the observation of limits but also on the implementation of the optimisation principle to keep radiation exposure As Low As Reasonably Achievable (ALARA), economic and social factors taken into account. The new ICRP recommendations will continue to place a major emphasis on this principle, thus further improving radiation protection for the public and workers.

In the course of these developments, it became apparent that certain sources of exposure, such as exposure from natural sources, in particular from indoor exposure to radon daughters, and exposure during medical diagnostic procedures, had not received the attention they deserved as the main contributors to the exposure of the population. Starting in the 1970s, the Programme made a major effort to quantify these exposures and identify how they could be reduced. Exposure from natural radiation and medical radiology are discussed in more detail in Section B2, pages 34 and 36 respectively. Several investigations were also made of occupational exposure

in the nuclear industry, including mining and waste disposal, and in medical radiology. The compilation of comprehensive and reliable **statistics of human exposure from all sources** is an important and continuing need in order to provide input to the optimisation of radiological protection.

The **risks** arising from radiation exposure are **quantified** mainly on the basis of epidemiology, supplemented by insights gained from animal, cellular and microdosimetry studies. In addition to the studies mentioned above, the Programme has also supported and stimulated epidemiological investigations of radiation workers. In order to consider radiation risks in the context of the overall risks encountered by man, several investigations have aimed at developing an index of harm. This is intended to provide a basis for comparing such different effects as immediate accidental death, late cancer risks, increased morbidity, etc, and to enable an objective comparison to be made between between risks from different sources and not only from radiation.

Moreover, in order to perform risk-benefit analyses, the social economic consequences of normal and emergency situations need to be better defined. Several studies have been undertaken in these areas, but more needs to be done to achieve a social consensus on risk management. In the future, risks must be quantified more accurately and more reliably, not only those from radiation but also from other sources in order to develop an optimal strategy of risk management. The socio-political dimensions of risks, as well as of the difficulties involved in communicating risks in a way which is not misunderstood or misinterpreted, must also be addressed.

Management of radiological protection received a strong impetus by the emphasis given to optimisation by ICRP in its Publication No. 26 and its reflection in Community Basic Safety Standards. The goal of optimisation can often be achieved in different ways. The Programme has, therefore, stimulated research into the theoretical basis of optimisation analyses and has supported case studies in various areas, e.g. effluent discharges, such as planned release of radioactivity, decontamination, maintenance etc. This research is an important input to a more uniform application of radiation protection principles in the Community. Research

into the management of nuclear emergencies had a prominent place in the Programme well before the Chernobyl accident, and this is treated in more detail in the Section B2 (page 38).

The large number of study group meetings, workshops, symposia and seminars dealing with assessment of exposure and risks, and with the optimisation and management of radiation protection, attests to the influence the Programme has had on a Community and international scale to bring about the effective introduction of the more recent advances in radiation protection principles and practices.

Supplementary Studies "Applications of Nuclear Techniques in Agriculture and Medicine"

A provision of the EURATOM Treaty also charged the Commission with the investigation of "Applications of Radionuclides in Agriculture and Biology", and this became a task for the CEC Programme "Biology - Health Protection" from its inception until 1975, i.e. during the period when this Programme essentially represented the only Community research carried out by means of associations and cost-shared contracts. This area was intensively pursued until 1970 when such applications appeared to be of less interest to some Member States. In 1970, only three, and, in 1973, five countries, after new Member States had joined the Community, showed an interest in this "Supplementary" Programme "Application of Nuclear Techniques to Agricultural and Medical Research". From 1976, new Community research programmes took over some of this research. Nevertheless, this research has been instrumental in developing competence in the Community, training young scientists, stimulating co-operation and opening up several new avenues of research. With respect to nuclear applications in medical research, an association between the Universities of Brussels and Pisa, together with some other cost-shared contracts, developed and improved methods of nuclear medicine to study blood circulation, lung functions, thyroid physiology and contributed to the understanding of protein metabolism.

Research into the application of nuclear technology in agriculture was carried out to a large extent in an association EURATOM-ITAL (Wageningen NL), supplemented by a few other contracts. This research included:

- crop plant improvement using, among other methods, seed irradiation to introduce mutation, contributed to a better understanding of mutational processes and selection procedures for useful mutants; improved durum wheat barley; and produced an "easy peeling" tomato;
- the investigation of the preservation of food by ionising radiation to define the optimal radiation doses which removed microbial contamination, while preserving food value and flavour and the search for possible deleterious effects of such irradiated food in animals;
- the study of the eradication of insect pests, in particular of the olive fly, in co-operation with the Biology Group at Ispra, using the sterile male technique.

The Community Programme was also instrumental in the development of other major European collaborative efforts. The expansion of the European Organisation for Research on Treatment of Cancer (EORTC) was encouraged and supported for several years by the Programme, allowing this organisation to reach the critical size from which it could then develop on its own. Moreover, a former head of the Programme was instrumental in founding the European Institute of Molecular Biology (EMBO).

The Biology Group at Ispra

The Biology Group at Ispra integrated itself in Community research in radiation protection and also oriented itself towards the specific needs of the Joint Research Centre at Ispra. The Biology Group at Ispra not only supplemented Community research in different areas but also represented an important asset for the Commission in being able to carry out urgent independent studies and to help in managing the Programme and evaluating its results. It studied, in particular, the transfer of radionuclides in the environment, genetic biochemistry, basic radiobiology, dosimetry and toxicology of organic reactor fuel. The work on basic radiobiology was abandoned during the 1960s when some key staff departed. The toxicological investigations were terminated when the organically cooled reactor did not materialise and were replaced, for some time, by other toxicological research. Research in dosimetry, mainly microdosimetry, was pursued until the 1970s whereas radioecological and genetic biochemistry research continued until the Group was dissolved in the late 1980s.

2. Selected Scientific Achievements

Treatment of Victims of Radiation Over-exposure

Radiation accidents requiring medical intervention can be of three types:

1) exposure of the whole or large parts of the body causing a loss of haemopoietic function and a suppression of immune response. Death can ensue when haemopoietic stem cells are reduced to levels insufficient to maintain life, i.e. after an acute exposure to more than 4 Sv to the entire body and to correspondingly higher doses accumulated at a low dose rate. Still higher doses cause damage to the intestinal tract and the central nervous system. This type of accident is exceedingly rare but, because of the serious consequences, treatment is necessary;

2) local exposure provoking acute or late damage that can impair tissue function and life quality. This type of accident, although rare, occurs more frequently than those involving the whole body. The skin and underlying tissues are most commonly affected;

3) radioactive substances incorporated into the body by way of inhalation, ingestion or absorption via wounds can cause whole body irradiation or local symptoms, or can cause damage after transfer into specific organs. Radionuclides of particular interest in this respect are actinides from the nuclear fuel cycle, various isotopes used in nuclear medicine, iodine and caesium after a nuclear accident, etc. Situations requiring direct medical intervention are, however, rare.

If an accidental exposure causes the **haemopoietic radiation syndrome**, it is vital to create optimal conditions for the recovery of the haemopoietic tissue or, if this is unlikely, to replace it with bone marrow from a healthy donor. The choice of the course of action to be followed can be very difficult, especially if the exposure has been inhomogeneous, since as little as 0.1% of surviving bone marrow stem cells can assure survival. Some indication of the level of exposure and its homogeneity are essential. Physical accident dosimetry is often not rapid or exact enough, although several new approaches such as thermo-luminescence of clothes or other artefacts carried on the body have been investigated. Consequently, biological parameters of radiation damage have been widely studied in the Programme. Biochemical tests did not confirm their initial promise in that, although being easy to carry out, they were not sufficiently specific for the radiation insult nor were they practical in cases of inhomogeneous exposure. However, cytogenetic tests, such as the determination of chromosome aberrations in cultured blood lymphocytes, although requiring special skills, seem to be sensitive and, as long as the exposure is not too inhomogeneous, the most reliable method. Chromosome aberrations also allow a determination of the long-term, low-level exposure to mutagenic substances, including radiation, in

a working environment. The Programme has made a considerable contribution to the international efforts bringing cytogenetic measurements to the present high level of performance. The integral management of such accidents must rely not only on dosimetry but also on a scientific understanding of the pathophysiology of the haemopoietic system and on an intimate knowledge of the evolution of symptoms of past accidents. Expert systems, using information from all the different sources, will probably be the best answer to the difficult problem of selecting and managing the treatment of such accident victims.

Research to develop the **transplantation of the bone marrow** started in the 1960s with studies on the immunology of transplantation and on the conditions under which host vs graft and graft vs host (secondary disease) reactions can develop. The ensuing improved understanding helped to define the protocols under which immunologically well-matched transplantations were possible. However, the need to work with poorly matched donors, with the risk of secondary disease, required the development of compounds and treatment modalities to suppress the undesirable immune reactions. Considerable progress in the development of such immunosuppressive compounds was made by the Programme. Another approach to remove those immune T-lymphocytes from the transplant that cause the secondary disease was pursued by means of physically separating the transplant cells, treating the transplant with anti T-cell monoclonal antibodies and using cells isolated from circulating blood or foetal liver. Most recently, attempts have been made to obtain an amplification of the stem cells to be used as grafts. Nevertheless, the transplantation of bone marrow remains a treatment fraught with risks and requiring great expertise in the techniques of transplantation and radiation haematology. It should be considered only as a last resort and used only when other conservative treatments would be expected to fail. The research on bone marrow transplantation carried out in the Programme has, however, been a major contributor to making bone marrow transplantation, combined with whole body irradiation, an effective treatment for leukaemia. By creating a solid scientific basis for the immunology of transplantation, it has also greatly benefited all areas of tissue transplantation in medicine.

Methods to treat radiation accidents **in a conservative way** have also been developed in the Programme. Originally they relied on the complete prevention of infection during the critical phase of low blood cell activity and low immune reaction response and on a carefully monitored replacement of blood cells (mainly leucocytes and thrombocytes) until spontaneous recovery set in. Quite recently, research in the Programme using molecular-biological techniques has characterised and produced several haemopoietic growth factors which, when applied in vivo, promise to speed up spontaneous recovery of the bone marrow.

Accidents involving **local exposure** also confront the physician with serious problems of patient management. The degree of radiation effects in the deeper tissue structure and, in particular, of vascular damage determines primarily whether there will be uncomplicated healing after the acute effect phase has passed or whether the patient will need surgery to avoid serious and unnecessary suffering. Moreover, as the accident at Chernobyl has illustrated, there might be situations where radiation damage to skin is combined with thermal or chemical damage or where, in addition to skin damage, a substantial whole-body irradiation has occurred. In such situations, the physicians responsible can face extremely difficult problems for patient management. New diagnostic methods to determine damage have, therefore, been widely explored in the Programme and have been found to be of value in other cases of skin and underlying tissue damage. Among the techniques thus developed or improved, vascular angiography, tele-thermometry, microwave imaging and capillaroscopy may be mentioned.

Treatment with skin flaps and more recently treatment with individual cells or sheets of cells to cover the damaged surface has also been investigated and improved in the Programme. In addition, studies have dealt with the definition of radiation protection criteria for skin, for example, under conditions where the radiation is of different penetrating ability, where local sensitivity factors play a role, and where the area exposed varies. Exposure from highly radioactive small particles deposited on skin has also been investigated.

Internal contamination at the workplace can occur from a variety of radionuclides, but contamination with actinides appears to be particularly important in some parts

of the nuclear fuel cycle. Investigations in the Programme have been concerned with decorporation techniques and have investigated how chelating substances bind to radionuclides, what their optimal configurations are and which are the most efficient treatments for different situations. New compounds have been developed and tested. Some investigations have also dealt with the use of non-radioactive iodide to prevent thyroid damage by radioactive iodine, for example, after an accidental release of radioactivity. The risk from irradiation in comparison with from stable iodine medication has been investigated, and basic information on thyroid radiobiology and physiology has been obtained. These studies have benefited not only radiation protection but also clinical medicine.

Epidemiology of Radium and Thorotrast Exposure

Only a few human data are available on the risks to man from radiation in general and incorporated radionuclides in particular. Some of the most crucial and reliable epidemiological studies in this respect have been carried out in the Community and have been stimulated and supported by the Radiation Protection Programme for more than twenty years. The two important groups being studied are:

- patients who received the short-lived radioisotope Ra-224 for the treatment of ankylosing spondylitis and, formerly, other diseases such as tuberculosis. Among these patients, there are two main groups, one given high doses consisting of 682 adults and 218 juveniles and one, added later, specifically to study low doses consisting of about 1500 patients. The number of patients alive is still considerably more than 1/3 in the first and about 2/3 in the second group. Thus, the study will need to continue for several more years;
- patients who, for angiography, were injected with a roentgen-opaque material consisting of a gel of radioactive thorium dioxide (thorotrast). One group in Germany of almost 900 patients has been studied now for more than twenty years and another Danish group has recently been added to this study. There are now fewer than 100 survivors in the first study, so that final results will be available in about 2-3 years.

The patients who received high doses of Ra-224 have shown a substantial increase in the number of bone cancers, some increase in breast cancer, and perhaps in leukaemia, liver and kidney cancer. In addition, cataract and changes in bone (tooth breakage, abnormal bone growth and growth retardation) have been observed. The increase in skeletal and bone marrow tumours in the low dose group is not yet quite significant. Supplementary animal experiments, carried out in several Community and US institutes, yielded information which enables the information available on

man to be extrapolated to other radionuclides and other exposure situations. A substantial study on the consequences of the long-lived Ra-226 isotope is also being carried out, especially in the USA. In contrast to the short-lived Ra-224, where most of the dose is delivered to the surface of the bone in a short period of time, Ra-226 delivers its radiation over a longer period and to the entire bone volume.

The people given thorotrast have shown a markedly increased incidence in liver cancer and liver cirrhosis. In addition, an excess of leukaemia has been found, and quite recently it has been observed that the lifespan of these people is shortened due to non-specific diseases. Obviously, these investigations require a careful follow-up, not only of the clinical status of the patients, but also of the level of thorium contamination which can be determined by measuring the exhalation of radioactive thoron gas, a daughter product of the thorium in the body. Parallel animal experiments have demonstrated that the increased risk is due to radiation and not, as might have been supposed, to the physical presence of thorotrast particles. In conjunction with other thorotrast investigations, notably those in Denmark, Portugal and, especially, in Japan, it has been recognised that dietary and ethnic factors also influence the level of liver damage caused by thorotrast

The information on the risks and metabolism of radionuclides which are deposited in bone (actinides, alkaline earths) or liver (actinides), provided by these studies, has formed the basis for establishing limits for intake of such radionuclides and has added to the understanding of the pathophysiology of bone and liver diseases. These studies were only possible thanks to the persistent support by the CEC Programme. It is also worth noting that the evaluation of these data has been performed in close co-operation with US colleagues.

Microdosimetry and Biophysical Models

Microdosimetry started from the observation that, for a given absorbed dose, there are large variations in the yield of biological effects depending on the type and energy ("radiation quality") of the ionising radiation. Ionising radiation traversing a cell causes random energy deposition interactions with matter along the haphazard tracks of the particles and alters a small percentage of biologically important

molecules. The spatial distribution of these interactions in cells as well as the energy deposited locally in such interactions depends on radiation quality, and it was recognised that the differences in energy deposition in microscopic volumes were related to the biological effectiveness of the different types of radiation. Microdosimetry relates the physical data of energy deposition in small volumes with biological effects, thereby aiming to interpret radiation mechanisms and quantify effects in living cells. Quantitative methods only became available in the mid 1950s, and the Community Programme has supported the development and application of such methods from its inception because of their relevance for the understanding of the effects of low dose, low dose rate and radiation quality. Research work focused on:

- the development and improvement of measurement and calculational methods to determine microscopic distributions of energy deposition, a topic which relies mainly on physics;
- the development of biophysical models of radiation action based on microdosimetric data, a topic which relies on interdisciplinary research in physics, chemistry and biology;
- the translation and application of the results in radiation protection practice.

The early work in microdosimetric methods concentrated on the use and improvement of tissue-equivalent low pressure proportional counters ("Rossi-Counters") for the determination of energy deposition spectra in volumes of tissue-like material with linear dimensions of 1 μm. The method enabled measurements to be made for penetrating radiation such as neutrons and photons and was therefore of immediate practical relevance. However, the method is restricted to interactions in gases and does not allow the simulated tissue site diameter to be reduced to dimensions of relevance for biological molecules such as DNA. With the availability, from 1970, of powerful computers, Community laboratories developed numerical methods based on Monte Carlo techniques to determine detailed track structures for energetic charged particles from basic physical interaction data. These complex methods are being continually improved from gaseous to liquid and solid material, and more and more complex target structures and extended with regard to type and energy of the particles. First attempts to include radiochemical processes in the calculations have recently been successfully made.

The physical information on spatial and temporal distributions, provided either in terms of experimentally determined energy deposition spectra or in terms of calculated track structures, has been used in comparisons with observed biological effects in order to develop biophysical hypotheses and models for radiation action. It has also been used to identify the nature of relevant chemical and biological damage and repair processes at the molecular and cellular level. The results of these investigations have provided useful information and constraints for various biophysical models developed as part of the Programme and have served to stimulate new dedicated radiobiological experiments to test the different predictions and interpretations. For example, the relevance of energy concentration over microscopic distances as small as a few nanometres has been demonstrated, and the special role of DNA damage, in particular DNA double strand breaks, has been identified. The progress achieved in this important field is impressive, as documented in the series of ten CEC International Symposia on Microdosimetry since 1967.

However, the final goal of understanding mechanisms, and thus enabling reliable predictions to be made for effects at low doses and low dose rates, still requires a great effort. In order to analyse the present state of knowledge and to further stimulate critical radiobiological experiments, the Programme has recently organised, together with the US Department of Energy, a workshop to identify radiobiological data suitable for use in the comparison of different biophysical models and to test the validity of the assumptions made in the models.

The methods and techniques developed in microdosimetry have also been applied for practical purposes and in neighbouring fields. The tissue-equivalent proportional counter has been used to develop dose equivalent meters for area monitoring which provide information on radiation quality (effective quality factor) and other properties of the radiation field. Exposure conditions which result in highly non-uniform dose distributions have been successfully investigated with methods developed in microdosimetry. They include radionuclide deposition in tissue macro-molecules in bone, lung and liver, the dosimetry of short-range particles (e.g. alpha-particles from radon), and dosimetry for tissue interfaces (e.g. bone/muscle or

fat/muscle). Microdosimetry has also contributed to the solution of the problem of radiation quality in medical applications of ionising radiation, in particular tumour therapy with high LET radiation such as fast neutrons.

Repair of Genetic Damage

Living organisms have always been exposed to natural ionising radiation and UV in sunlight, suffering damage to the DNA in the nucleus of their cells. In order to preserve the genetic integrity of the DNA, a cellular machinery has been developed to repair radiation-induced and other damage and thus reduce or eliminate the effect. Following early pilot observations, repair has been intensively studied during the past thirty years, and the CEC Programme has made a substantial contribution to the worldwide efforts in this area. The understanding of how DNA can be modified in the genome also led to the development of biotechnology and to a better appreciation of several diseases. Initially, observations concentrated on bacteria and yeast because these systems were more amenable to manipulation and because mutants showing abnormal repair could be readily isolated and characterised. Research in the Programme using bacteria and yeast has revealed several novel repair pathways, for example, the so-called SOS repair which is induced as a result of DNA damage.

Gradually, experimental models became available for the study of repair in higher organisms, first in the fruit fly, drosophila, and later in mammalian and human cells, and emphasis shifted to organisms and cells more relevant for radiation effects in man. In the 1960s, much work was done on repair pathways in germ cells of the fruit fly, and this permitted several repair-deficient mutants to be defined. It was then also recognised that certain hereditary diseases, such as Xeroderma pigmentosum (XP) which is characterised by an extreme sensitivity of the skin to sunlight and a propensity to skin cancer, are related to deficiencies of repair. Thus, XP cells were found to be unable to repair the pyrimidine dimers induced by UV in cellular DNA. The study of XP cells revealed nine different complementation groups indicating a complicated series of steps in the repair pathway of UV-induced DNA damage. Using modern molecular biological techniques, it has been possible to

transfect normal human DNA into a UV-sensitive Chinese hamster cell and thereby to obviate the UV sensitivity. This first human repair gene to be identified (ERCC1) was shown to have a length of 15 kilobases and to be situated on chromosome 10. The finding that this ERCC1 gene and the yeast repair gene RAD10 are closely homologous with respect to their amino acid structure indicated that DNA repair genes have been well conserved during the evolution of life. Two other human repair genes have now also been identified from studies on UV-sensitive mammalian cells.

Other human disorders showing sensitivity to DNA-damaging agents related to specific defects in the ability to repair DNA were also discovered, the ones most interesting for research in radiation protection being ataxia telangiectasia (AT) which shows an extreme sensitivity to ionising radiation and the Fanconi syndrome. Work on AT cells revealed that the sensitivity to ionising radiation is associated with a defect in the ability of these cells to repair DNA double strand breaks faithfully to the original situation. The gene responsible has recently been localised on chromosome 11 and identified in co-operation with US research teams. It is expressed as a recessive genetic phenotype, and calculations indicate that as many as 3% of the population can be carriers of the unexpressed gene. These people might, nevertheless, show some increase in radiation sensitivity, and the question of whether some apparently normal people suffer from a repair defect associated with increased radiosensitivity, and perhaps cancer proneness, is now being studied intensively.

Tremendous progress has been made in the understanding of the genetics and biochemistry of repair of radiation-induced damage in mammalian cells during the past thirty years, much of it due to the efforts of the CEC Programme. With the introduction of yet more refined techniques in molecular biology and cytogenetics, one can anticipate that this area will continue to yield striking advances not only for radiation protection but also for cancer research and biotechnology.

Environmental Behaviour and Risks of Tritium and Technetium

Tritium and technetium are two radionuclides which were considered of particular concern for radiation protection. Tritium is produced as a fission and activation product in nuclear reactors and is released into the environment at various stages in the fuel cycle, and will become even more important in nuclear fission. Technetium, in various isotopic forms, is produced in nuclear fission and is present in effluents from nuclear installations. In the form of ^{99m}Tc, it is now much used in nuclear medicine. Both radionuclides, although of relatively low toxicity, move readily through the environment and can undergo multiple conversions which profoundly alter their behaviour in the environment. Tritium released as tritium water or tritium gas can be converted to the manifold compounds of organically bound tritium (OBT), technetium to different valency states which can be bound to a variety of materials. In this context, the long-lived carbon-14 should also be mentioned as it is released from nuclear plants and remains available for uptake in the biosphere for tens of thousands of years. It resembles tritium in that it can be incorporated into all bio-molecules and has a similar metabolic behaviour in the organism.

Previous Community programmes studied these radionuclides intensively, largely in co-operation with different Community institutions allowing the relevant information to be obtained in a much shorter time and in a cost-effective manner. Most of the important data have now been obtained, and little additional research is required in this area, e.g. with respect to the behaviour and conversion of tritium gas. These investigations have provided important insights into environmental transfer and the influence of speciation which are of more general relevance.

Tritium, although primarily present in the environment as tritiated water or tritium gas, can also be converted into organically bound tritium (OBT). Tritiated water is usually diluted rapidly in the environment and can be readily traced. Critical transfer pathways involve organically bound and gaseous tritium which were investigated in order to determine their possible contribution to human exposure. The formation of OBT was studied in a wide range of systems including soil bacteria, micro-organisms in the cooling water of nuclear installations, plants and

animals. OBT is in equilibrium with tritium in water under most circumstances, although problems can arise when OBT is formed very near the release site thus entering the food chain in a relatively non-diluted form, or when OBT is formed during the development of an organism and then retained during much of its adult life. Studies in the Programme have been able to show that the additional risks from such situations compared to tritiated water are not very important. Conversion of tritium gas to a form usable by the human organism has been investigated more recently. This conversion was found to occur mainly via soil bacteria. This has been confirmed by field studies carried out in the Community and Canada. Some studies have also been carried out on carbon-14 indicating that, after some modification, tritium data can be used to describe the metabolism of radioactive carbon in the mammalian organism.

No large-scale studies of tritium toxicology have been carried out in the Community, but macro- and micro-dosimetric calculations and measurements undertaken to determine possible differences in the action of the soft beta rays from tritium compared to X-rays indicated quality factors for tritium in agreement with experimental data of the order of 1 to 2. The most urgent problems of tritium behaviour appear to have been solved and only a few questions remain with regard to the behaviour of tritium gas. It should be pointed out that the studies carried out on tritium and carbon have given information which is relevant not only for radiation protection but also for the transfer of organic material in soil, plant and animals and the atmosphere, as well as for animal and human nutrition.

Technetium can occur in different physico-chemical forms and valency states in the environment and the organism. Studies in plants have demonstrated that the pertechnetate anion is the form taken up and that the large differences in transfer seen under different conditions are mainly due to the presence of technetium in states other than pertechnetate. This finding now allows reliable predictions to be made for the soil-plant pathways. Differences in intestinal absorption of technetium seem to be due to the chemical state of technetium and other food present. Thus, polygastric animals absorb technetium much less readily than monogastric animals due to the reducing conditions in the gastro-intestinal tract of ruminants.

Technetium in the body was found to be highly concentrated in the thyroid with some radioactivity in other tissues. The long-term behaviour of Tc in adult and developing animals has also been determined. Long-term feeding experiments with technetium at concentrations many orders of magnitude higher than those which could normally occur in the environment, even under extreme situations, have indicated that significant effects on thyroid physiology and carcinogenesis or on fertility or the intra- and extra-uterine development would not occur. Thus, the risks of technetium to man now have been adequately determined, and these risks seem to be quite small.

Radon in Homes: Assessment and Risks

The risk of lung cancer from working in uranium mines has been known for a long time and has been related to radon exposure. In the past, measurements have also been made of ambient gamma radiation, of radionuclides in the body and of radon and radon daughters in spas and elsewhere. Nevertheless, radon has only recently been perceived as an important radiation risk to the public. This might be explained by the fact that radon was used for medical treatment for all sorts of diseases and perhaps also to some irrational notion that what is natural cannot be bad for man. Measurements of radon and radon daughters in dwellings drew attention to the occasional high levels which can be encountered in some areas, and the Radiation Protection Programme started to develop an approach to the problem of radon in dwellings in the 1970s. In doing this it had to:

- develop reliable and standardised methods of measurement and establish the statistical distribution of radon exposure in homes;
- evaluate the parameters which influence radon exposure indoors;
- assess the risks of radon and radon daughters with respect to the causation of lung cancer;
- develop an approach for effective, durable and affordable remedial actions.

The problem of **measuring radon in dwellings** was attacked first, and the Programme sponsored surveys of radon concentrations in dwellings in several European regions or Member States. Mean indoor radon concentrations in Member States were found to vary between 25 and 50 Bq/m^3, but in some places values of some thousands of Bq/m^3 were encountered, resulting in doses which would even

exceed legal dose limits for workers. Simultaneously, measurement devices were improved and an inter-calibration programme for radon measurements was set up with several inter-comparison exercises, the results of which reflected the progressive approach to reliable radon measurements in the Community. Today, surveys are mainly conducted by Member States themselves, but the Programme continues its inter-comparison efforts.

The radioactive noble gas, radon, is generated from radium in the soil, construction material or water. Studies supported by the Programme have investigated the different pathways of radon entry into dwellings and recognised that much of it diffuses through cracks in basement slabs, and that the crawl space under houses can act as an accumulator of radon. These findings are now being used in the elaboration of quantitative models to predict radon concentrations in typical buildings.

The radon gas decays in turn to radioactive daughters of the elements Bi, Po, Pb which can become attached to aerosol particles and which, after inhalation, can be deposited in respiratory tissues. The mechanisms and degree of this attachment under different conditions, the physico-chemical characteristics of these aerosols and their deposition in lung have been intensively studied in the Programme. Lung models have been developed which allow the calculation of the dose to different lung structures, and the currently accepted conversion factor of 1 Bq/m^3 per year corresponding to an annual dose of 50 μSv has been derived by research in the Programme.

The risk of radon exposure in dwellings has also been the subject of much theoretical and experimental research in the Programme. Epidemiological information on uranium miners from different parts of the world is already available for radon exposures at levels very close to the upper values encountered in some dwellings. However, the conditions of exposure between mines and dwellings differ, and this has to be taken into account in the evaluation of risks. One basic question is whether radon-induced lung cancer is simply added to spontaneous or smoking-induced cancer, or whether there exists an interaction which would make radon much more effective in the presence of smoking. This problem is not fully resolved,

but several studies, including those carried out in the Community, suggest the latter. Epidemiology in areas of elevated natural radioactivity have so far not yielded positive results. Investigations are continuing and the Programme has recently initiated a multinational Community programme on radon epidemiology which is being co-ordinated with similar investigations in the USA.

In view of the potentially important health impact of radon in dwellings, remedial actions for existing buildings or preventive actions for new buildings are a most effective way to reduce radiation exposure. Such actions, together with the characterisation of the exposure situation, doses and risks, have now become a major concern of the CEC Programme.

Dose Reduction in Medical Diagnostic Radiology

Medical diagnostic radiology and some radiotherapeutic treatments were the first applications of radiation for which some form of radiation protection was felt desirable. Precautions to limit the dose to the physician became urgent during the early part of the century, but the risk arising from the dose delivered to the patient was considered negligible compared to the benefit. As more and more diagnostic examinations were performed, as routine screening for tuberculosis or breast cancer became commonplace and, especially, as the risk of carcinogenesis from small doses of radiation was recognised, dose reduction to the patient became of increasing concern. Indeed, each person in the Community is, on average, now examined once a year with X-rays or radionuclides. Diagnostic procedures contribute an effective dose equivalent of 0.3 to 1.5 mSv per year, depending on the country, to the average annual exposure of the public. A few individuals, subject to repeated examinations, can, however, receive effective dose equivalents of the order of Sv.

Research on medical applications of nuclear energy formed part of the early Programme "Biology-Health-Protection" with emphasis on the development of methods for nuclear medicine. During the 1970s, the Programme concentrated on medical diagnostic radiology considering, in particular, the following aspects:

- evaluation of the dose to the patient from different procedures, as well as to the public at large;
- standardisation and optimisation of the parameters by which the diagnostic procedure is carried out;
- control and optimisation of the radiographic image quality to obtain the maximum information at a reasonably low exposure of the patient and, as far as possible, at a reasonable cost;
- development of benefit-risk considerations firstly for routine screening examinations for which no individual medical indication for an examination exists, then for examinations which are frequently performed or employ new techniques, and finally for procedures for which a choice could be made between ionising radiation and other diagnostic techniques.

The Programme supported research to determine the optimal X-ray spectra for different diagnostic procedures so that the conditions giving the best image resolution at the lowest dose could be chosen. This work was extended over the years to cover other instrumental and image producing and processing parameters. A seminar in Udine in 1984 and a workshop in Brussels in 1988 demonstrated not only the great interest of those efforts for practical radiology, but also increasing interest of industrial companies making X-ray equipment in joining these efforts.

Research, supported by the Programme, also determined the doses from individual radiographic procedures. Since the dose from an X-ray examination and the tissues exposed vary widely, dosimetric methods and models were developed for different conditions of exposure. In addition, it became necessary to define the exposure considered significant for cancer and genetic effects for different diagnostic procedures. These developments were paralleled by the newly defined quantities of dose equivalent. In addition, the Programme stimulated surveys of the frequency and procedures of different radiological practices in various regions of Member States such as Southern Germany, the UK, Ireland, France, North-East Italy, Spain and Portugal. The results revealed substantial differences between Member States in diagnostic practices and patient exposure. The CEC Directive "laying down basic measures for the radiation protection of persons undergoing medical examinations or treatment" reflected the increasing concerns arising as a result of such surveys.

It became clear that the image quality is a critical step in dose reduction and that, to this end, appropriate criteria must be established. This, incidentally, will not only reduce patient dose but also bring about economic savings. The first steps to

establish these criteria were taken in the late 1980s, and, following a workshop at Oxford in 1988, the various professional bodies concerned have co-operated to define quality criteria for several frequent, conventional examinations.

For the future, reducing the doses to patients will be one of the most cost-effective means for diminishing the total radiation exposure to the population. Therefore, the standardisation of parameters must continue, the doses, especially for new procedures, must be evaluated and quality criteria for the entire radio-diagnostic process must be further developed. In addition, in order to obtain the maximum benefit of this research, radiologists and radiographers must be informed of the role they can play in significantly reducing the dose to the public.

Management of Nuclear Emergencies

The assessment of the radiological consequences of potential accidents has been an important activity since nuclear energy was first used for commercial purposes. It is an integral part of safety assessments undertaken to ensure that nuclear installations meet the criteria set for them. It also plays a major role in both the development and application of off-site emergency arrangements for protecting the public in the event of an accident.

In order to estimate the radiological consequences of potential accidents, the transfer of released radioactive material through the environment to man by all significant pathways needs to be modelled and, subsequently, the biological effects of any resulting exposure assessed. Among the processes that must be modelled are atmospheric dispersion, behaviour of material deposited on a variety of surfaces, transfer through the terrestrial and aquatic environments to man, the metabolism of radioactive material taken into the body and the biological effects of the exposure of different organs and tissues. It is evident that a large part of the research undertaken within the Programme as a whole, in particular in the areas of radioecology, dosimetry and biological effects, is directly relevant to this task. The quality and extent of knowledge and understanding in these and related areas largely determines the reliability with which accident consequences can be estimated.

The accident that occurred at Windscale in 1957 acted as a major stimulus to the development of methods for predicting the radiological consequences of accidents. Inevitably, attention was focused on those nuclides that were of greatest radiological significance in that accident, in particular radio-isotopes of iodine. The widespread fallout of radioactive material dispersed during the atmospheric testing of atomic bombs in the late 1950s and early 1960s also provided an opportunity to investigate the environmental transfer of a wide range of radionuclides. The results obtained from investigations of this fallout continue to provide one of the major sources of information for predicting the environmental transfer of radionuclides both in normal and accident conditions. The role of the Programme in this context has already been described in the section on radioecology.

Initially, the assessment of the radiological consequences of accidents was confined to the estimation of doses to people. In general, the doses were estimated assuming the release to occur in adverse meteorological conditions and for those groups which, because of their habits or place of residence, were likely to be typical of the most exposed. At that time, these limitations were largely adequate, as most safety criteria for nuclear installations were then expressed in these terms.

However, radical changes occurred in this area in the early 1970s consequent upon the major advances made in the ability to quantify both the frequency and magnitude of postulated accidents in nuclear installations and the stochastic effects of radiation exposure. These advances made possible the comprehensive "Reactor Safety Study" of the risks presented by the operation of commercial nuclear power reactors in the USA undertaken by Rasmussen. These same techniques, albeit updated and improved with time, have now achieved widespread use as inputs to the regulatory process, to judgments on risk acceptability, to the identification of safety improvements, and to developments in emergency planning.

These changes had major implications for the methods then used for accident consequence assessment, both in terms of their reliability and their comprehensiveness. In order to estimate risk it was no longer sufficient to estimate the impact of a postulated accident occurring in one particular set of adverse meteorological conditions; account had to be taken of the release occurring in all possible conditions

with due allowance made for the probability of each. Moreover, much greater demands were placed on the reliability of the estimates, particularly when they were being used in the contexts of regulation and risk acceptability.

In order to respond to the developing needs in this area, a major activity was launched within the Programme at the beginning of the 1980s. The activity was entitled MARIA - Methods for Assessing the Radiological Impact of Accidents. The main objectives of this work were to develop a probabilistic accident consequence code that was modular, that incorporated the best features of those models then in use, that was broadly applicable and capable of finding wide usage in the EC, and that could be readily modified to take account of new data and/or model developments. Additional objectives were to quantify the uncertainties in the model predictions and to identify how, if necessary, these might be reduced. A significant programme of experimental work was also undertaken in parallel with the code development in those areas where improved data were essential to improve the overall reliability of the model predictions.

This activity is now largely complete and the code system that has been developed (COSYMA - COde SYstem MARIA) will be distributed to interested users later this year. The availability of this code will be of considerable benefit to many Member States at a time when increasing attention and importance, within both the regulatory and political processes, are being given to the quantification of risk from major industrial activities. Future research in this area will be directed towards refining those models which remain weak, and gaining a better appreciation of the uncertainties associated with their predictions. Further details of the research carried out in this area and its achievements are contained in the final report of the 1985-89 research programme.

The models described above are for use in estimating the radiological consequences of postulated accidents as an input to risk evaluation, etc. An equally important role, however, is the estimation of consequences when an accidental release is actually threatened or occurring. In this case the approach is very different in the sense that the assessment has to be carried out in real time and for the particular meteorological and environmental conditions then prevailing. Such assessments are

necessary if timely and effective decisions are to be taken on the introduction of countermeasures to protect the public.

Procedures for the rapid assessment of the radiological consequences of an accidental release have been an important feature of emergency planning since the introduction of nuclear energy for electricity production. There have, however, been major improvements in the ability to make such assessments in the intervening period, in particular during the past decade. Several factors have contributed to these improvements, not least the very substantial increases in available computing power, better meteorological forecasting and predictions of dispersion in the atmosphere and improvements in the monitoring of radioactive material in the environment. The two accidents at Three Mile Island and Chernobyl were also influential in the sense that they resulted in increased resources being allocated to this area in many countries.

This topic has featured prominently in the Programme throughout the past decade with a major increase in the resources devoted to it following the Chernobyl accident. Many of the models developed within the MARIA programme can also be used for real time predictions of consequences for use for emergency response purposes, albeit with some modification to reflect the different applications. The major achievements of the Programme in this area have largely been accomplished in the more recent years and these are described in more detail in the final report for the 1985-89 period. Briefly, however, much of the work has been directed towards the development of better methods for integrating model predictions with measurements made of radioactive material in the environment, thus making best use of all of the information available in predicting the likely situation elsewhere. This is a complex and difficult problem and the work being undertaken is at the forefront of international developments in this area. The development of atmospheric dispersion models that represent the best compromise between the conflicting objectives of reliability and speed of prediction is another area that has received significant attention. It has to be recognised, however, that, with the ever increasing computational power available, this point of balance is subject to continuing change.

3. Support for Regulatory Obligations of the Commission

The Radiation Protection Research Programme was conceived as a companion to the regulatory obligations of the Commission. Research carried out in the framework of the Programme provides not only the general foundation for an understanding of radiation exposure, effects and risks on which all regulatory activities are being built but also contributes to specific regulatory tasks. The "Basic Safety Standards for the Health Protection of the General Public and of Workers against Dangers from Ionising Radiation" first issued in 1959 and updated in 1976, 1980 and 1984, mainly follow recommendations issued by ICRP. In addition, several Community directives and recommendations have been issued which had to answer specific demands, for example, with respect to nuclear emergencies and applications of radiation in medicine.

Several examples of the relation between Community research and regulatory activities have been mentioned earlier. They range from providing the scientific data to co-operation in committees or specific task groups of ICRP or ICRU and to the participation in the Group of Experts according to Article 31 of the Euratom Treaty and its subgroups. Only a few recent activities of the Programme are cited as illustrative examples where research and regulation have complemented each other:

- the elaboration of the revised EC Basic Safety Standards require an assessment of risks on the basis of complete scientific information as has been obtained in the Programme;
- the definition of the maximum permitted level for radioactive contamination in human food and in feeding stuffs was based on metabolic data obtained in, and discussed at a workshop organised by the Programme;
- the recommendations recently made for intervention levels for radon in existing and planned dwellings required the development of methods to measure radon and its daughters and the techniques for countermeasures derived in the Programme;
- the implementation of the Directives laying down the basic measures for the radiation protection of persons undergoing medical examination or treatment require the development of the quality criteria for the entire radio-diagnostic process, as well as the standardisation of appropriate dosimetry.

4. Development of Co-operation

A Community research programme, in addition to providing relevant scientific information, also has the equally important task of developing co-operation among

scientists in the Community and of creating a European network of research. In order to appreciate what has been achieved, it is necessary to recall the situation in the early 1960s when, not too long after the second world war, links between European scientists were not yet established. It could be claimed that creating a Community climate of research in radiation protection was an achievement of the Programme as important as the scientific results obtained.

In fact, once the instruments and structures for co-operation had been set up by the Commission, scientists responded enthusiastically to the opportunity for co-operation. They rapidly learned that they could gain by being informed about new developments in other laboratories and became more open from their side, communicating not only results but also their plans for future research. They became aware that, by co-operating with other institutes, they could acquire samples or techniques and even use instruments which were not available in their own institutes. Collaboration developed from this to planning truly common research projects covering the definition of the problem, the planning and the execution of the experiments, the analysis of the results and their publication. Surprisingly, the somewhat natural suspicion that collaborators might deprive them of their ideas and work seemed much less prevalent when scientists from different Member States co-operated than when scientists came from the same institute. Needless to say, this co-operation, initiated and sustained by the Community Programme, has resulted in greater research efficiency and substantial savings, not only by avoiding duplication of research effort.

Several instruments were effective in promoting co-operation. The Radiation Protection Programme was the first to develop associations between different institutes, for example, between the Universities of Brussels and Pisa with respect to nuclear medicine, and between the CEN/SCK, Mol, and ENEA, Casaccia, with respect to animal radiation research. The Commission's services also organised regular study group meetings between contractors working in specific areas. Some of these groups, for example those dealing with the MARIA project (see page 40), have become a regular feature of the Programme. The recently introduced multinational contracts will certainly further increase the cohesiveness of the Programme in all areas.

The Commission has also initiated and supported co-operative groups of scientists to promote collaboration on a more technical level. The European Late Effects Project Group (EULEP) was the first to be formed in 1970 and now consists of 23 voting member institutions, 38 corresponding members and a total of 124 associated member scientists. EULEP is managed by a Council and is organised in task groups (15 of them at the present time). In addition, standardisation committees on external and internal dosimetry, on pathology and on cell and molecular pathology advise the co-operative ventures. Each year, EULEP organises 1-3 international meetings with proceedings being published together with the Commission, edits 1-2 issues of the pathology atlas and holds 20-30 task group workshops.

The European Dosimetry Group (EURADOS) has a similar structure to that of EULEP and presently consists of 6 task groups, concentrating on co-operation in all areas of dosimetry. Increasing co-operation between EULEP and EURADOS enables optimal advice on the execution of the different tasks to be obtained, for example with respect to dosimetry and risks from incorporated radionuclides. With respect to radioecology, the Programme has made use of the International Union of Radioecologists (IUR) in order to facilitate co-operation with countries outside the Community. At present, the IUR consists of 4 working groups which, in addition to co-ordinating research on a technical level, also promote the training of scientists and short-term exchanges of scientists between institutes for the execution of certain research projects.

The Programme has also established links with international organisations and countries outside the Community. Memoranda of understanding have been signed with the US Department of Energy, Office of Health and Environmental Research and the Atomic Energy of Canada Ltd; the latter also implements co-operation with the Canadian Atomic Energy Control Board and the Radiation Protection Bureau of Health and Welfare. In the new 1990-1991 Programme, Sweden now fully participates. Contacts, albeit not yet institutionalised, have been established with other EFTA countries and Japan, and scientists from these countries participate in meetings organised by the Programme.

Support by the Programme has been given to ICRP and ICRU, and Commission staff participate in Committee meetings organised by these organisations. Moreover, relations exist with the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the World Health Organisation (WHO), the Nuclear Energy Agency of the Organisation for Co-operation and Economic Development (NEA/OECD) and the Food and Agriculture Organisation (FAO). The International Atomic Energy Agency (IAEA) and the Community Radiation Protection Research and Training Programme have now established co-ordinated research projects on "Radon" and "Radiation Doses in Diagnostic Radiology and Methods for Dose Reduction".

5. Training in Radiation Protection

Development and maintenance of radiation protection expertise has always been an important aim of the Radiation Protection Research and Training Programme. This training has been carried out by several means, in particular, by training courses, grants for doctorates or postgraduate training, and, in a more informal way, by the different coordinating activities of the Programme (study group meetings, co-operative groups, etc).

During the period up to about 1975, the Programme supported 12 training courses in which more than 230 scientists participated. These courses dealt not only with radiation protection but also with molecular biology, genetics, and applications of radiation and radionuclides. Later, as the Programme concentrated on radiation protection research, some of these training activities were taken up by other Community Programmes and by the co-operative groups (EULEP, EURADOS and IUR). However, a major effort is now being made to develop new Community training courses in radiation protection (see page 57).

The Programme provided 234 fellowships and grants from 1960 to 1975, 15 from 1976 to 1980, 26 from 1980 to 1984 and 6 from 1985 to 1989. Until about 1975, many of the fellowships and grants dealt, in addition to radiation protection, with genetics, molecular biology and medical or agricultural applications of radiation. Special funds were foreseen for such fellowships during the early period but later

had to come from the budget of the Programme. Moreover, other new Community programmes, most recently the ERASMUS Programme, could take over some of these tasks, and the Radiation Protection Programme concentrated on radiation protection proper. Consequently, support for research for a PhD degree was no longer possible, and the Programme supported only postgraduate research in radiation protection where scientists from an institute in one Member State worked for a period of up to 6 months in an institute in another Member State.

For many years, there was no need to develop more specific training courses since a sufficient number of scientists were working at universities and national institutes. More recently, the impending retirement of many of the senior staff and the discontinuation of many university chairs and departments dealing with radiation protection, radiobiology or biophysics, make it necessary to restore and re-emphasise training activities in radiation protection at the undergraduate and post-graduate level. These are discussed on page 57.

C. Structure and Management of the Programme

1. History of Funding

The following table displays the funding of the different Radiation Protection Programmes up to the present 1990-1991 programme.

Table 1: Budget Appropriations for CEC Radiation Protection Programmes 1958-1991.

Year			Total	Adjusted/Year [d]
1958-1962	Initial phase of the Programme		3.100 M.u.a.[a]	
1963-1967	Joint Programme		15.900 M.u.a.	4.32
1968	Interim Programme (maintenance of staff)		0.800 M.u.a.	
1969	Joint Programme	3.000		
	Supplementary Programme	0.600		
	Total		3.600 M.u.a.	4.12 (3.64)[e]
1970	Joint Programme	3.200		
	Supplementary Programme	0.640		
	Total		3.840 M.u.a.	4.44 (3.33)
1971-1975	Joint Programme	18.886		
	Supplementary Programme	5.879		
	Total		24.765 M.u.a.	
1976-1980	Joint Programme		39.050 MEUA[b]	5.15 (3.92)
1980-1984	Joint Programme (1980 overlapping)		59.000 MEcu[c]	3.54
1985-1989		58.000		
	Revision (1988)	10.000		
	Total		68.000 MEcu	2.68 (2.28)[f]
1990-1991			21.200 MEcu	1.84

a) M.u.a. million units of account (u.a.=1 US$)

b) The u.a. unit was changed to the EUA (European unit of account), equivalent to a basket of national currencies, on 1 January 1978. In order to make allowances for this change, the budget of the Programme was adjusted to 39.05 MEUA (million European units of account)

c) At the beginning of 1980, 10 MEUA were carried over to the 1980-1984 Programme, since the two Programmes overlapped in 1980. At this time also, the EUA was changed to ECU (European Currency Unit)

d) The budget adjusted/year/100 million inhabitants has been calculated on the basis of the inflation rate based on 1 for the year 1980 and the population size of the Community at the middle of the running programme. New Member States have been taken into account from the date they joined the Community

e) Value in parenthesis excluding supplementary programme

f) Value in parenthesis excluding post-Chernobyl revision.

In judging these values in real terms, one should remember the progressive enlargement of the Community (Denmark, Ireland, the United Kingdom in 1973, Greece in 1981 and Spain and Portugal in 1986) as well as the inflationary trend. From this, the stagnation in the 1970s and the accelerating decline in the real value of the funding of the Programme in the late 1980s can be clearly discerned.

The number of contracts supported is also informative although a comparison is somewhat difficult because a few contracts were renewed during a multiannual Programme, and several contracts contained more than one project. There were 18 contracts in the period 1960-1962, 42 contracts 1963-1967, 34 contracts 1968-1970, 131 contracts 1971-1975, 185 contracts 1976-1980, 266 contracts 1981-1985 and 403 contracts, including the post-Chernobyl activities 1985-1989. It will be clear that the real value of the individual contracts decreased during the 1980s.

2. Personnel

In judging the development of personnel, one must bear in mind that the Radiation Protection Programme started out with staff who were to be used for:

- co-ordination and management at headquarters;
- detachment for research activities in Member State institutions;
- research in the Biology Group at Ispra.

Originally, it was envisaged that the Biology Group at Ispra should become a centre of radiation research activities in Europe serving as a stimulus for new lines of research and developing co-operation by short-term hosting and training for Community scientists and bringing expertise in radiation protection to the Joint Research Centre. However, due to restrictions in funding, the Biology Group at Ispra did not reach a size where it could fully develop this role. Therefore, a decision was made in 1970 not to develop the group further and the work of the group was terminated in 1988. The remaining staff were incorporated into other activities of the Joint Research Centre.

Staff seconded for research in Member State institutes increased rapidly, reaching a maximum during the 1970s. Some staff were recalled to headquarters to participate in the scientific management of the Programme, others retired for age

or health reasons. In 1989 only 7 seconded staff members remained. Total staff decreased from 97 in 1973 to 69 staff plus 10 local agents in 1976, 64 staff members in 1980, 60 staff in 1985, 28 staff in 1990, and 23 staff are foreseen in 1992.

3. Management and Advisory Structures

Following the proposal of the Scientific and Technical Committee (STC), a "Comité consultatif de biologie" was created in 1961 to assist the Commission. In 1969, the Advisory Committee on Programme Management (ACMP) was created by Council decision and this was replaced, by Council decision, by the present "Management and Coordination Advisory Committee" (CGC) (for list of present members see Annex I, page 208) which started its work in 1985. The development of the CEC Radiation Protection Programme would have been impossible without the scientific competence and involvement of these Committees which not only give advice on the orientation and execution of the Programme but also help to establish the links with and between the different national programmes.

Following a call for proposals at the initiation of a new Radiation Protection Research Programme, incoming proposals are evaluated by the Commission's services in co-operation with the advisory committee and a priority is assigned to each project depending on its scientific merits and the relevance of the proposal for radiation protection. Funding is either by cost-sharing, mainly with national institutes, or by marginal cost contracts, mainly with universities. The amount of funding is decided according to rules established to give comparable support to similar research in different institutes. The reduction of the Programme's budget and the desire to develop new relevant lines of research has, however, led to a reduction in funding of individual projects. Notwithstanding this, the rate of acceptance of a project has also decreased from about 80% during the early period of the Programme to about 50% in the 1980s and has now fallen to below 40%.

The structures for an effective and flexible management of the Programme have evolved gradually over the years. The Commission's services, together with the members of the advisory committee, monitor the scientific progress of each project. Progress reports are submitted, evaluated and published annually, and regular

contacts are maintained by means of study group meetings, by on-site visits and via the co-operative groups (EULEP, EURADOS, etc). The Commission's services intervene whenever supplementary co-operation has to be implemented or the project has to be re-orientated. At the end of a Programme period, a final report of each project is published, and the main results of the Programme are summarised in a synopsis prepared by the advisory committee in collaboration with the Commission's services.

II. The 1985-1989 Radiation Protection Programme: Synopsis of the results

A. Introduction

1. Adoption and Execution of the 1985-1989 Programme

The Council adopted the sixth Radiation Protection Research and Training Programme for the period 1985-1989 on 12 March 1985 allocating it a budget of 58 MEcu. This budget represented a substantial reduction from the amount originally proposed and also with respect to the budget 1980-1984 (59 MEcu) when allowing for inflation (see page 47). As a consequence of the reduction in funding, several areas of research originally proposed could not be pursued, in particular research into the primary effects of radiation and the collection of basic physical data on dosimetry. Other research also had to be curtailed. As an independent evaluation of the Programme noted in 1989 (EUR 12145 EN), this reduction in basic research could have adverse effects in the long term.

Research proposals were received and, after consultation with the Management and Coordination Advisory Committee (CGC) "Radiation Protection" (for list of members during 1985-1989, see Annex I, page 208). Some 200 contracts were accepted for funding in 1985. Later, an additional 80 proposals were funded so that the total (values in parenthesis including the post-Chernobyl actions) consisted of 283 (339) contracts with 339 (460) projects with a total participation by the Commission in contracts of approximately 55 MEcu. A reasonable balance between the sectors of the Programme was achieved in accordance with the Council Decision, as shown in Figure 1. The list of contracts, classified according to the Programme sectors and the regional distribution, is presented in

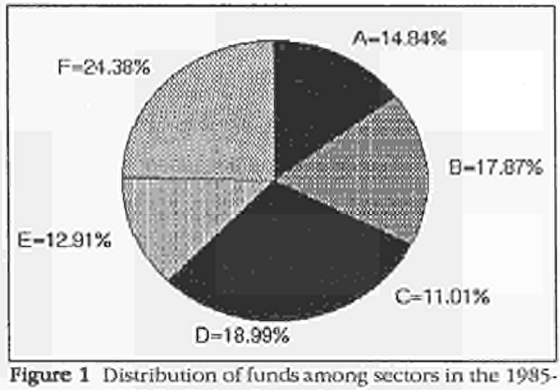

Figure 1 Distribution of funds among sectors in the 1985-1989 Radiation Protection Programme

Annexes II and III (pages 211 and 231).

Two major events markedly influenced the execution of the Programme during the 1985-1989 period:

- the accession of two Member States, Portugal and Spain, in 1986;
- the accident at the nuclear reactor at Chernobyl on 26 April 1986.

Research proposals from the two new Member States were submitted immediately after they joined the Community. By the end of the Programme a substantial number of contracts had been made with institutes in these countries and their integration into co-operative groups within the Community is now well established.

The accident at Chernobyl on 26 April 1986 represented a major challenge to the radiation protection community. Nevertheless, it is not true, as has sometimes been stated, that scientists working in radiation protection had been ill-prepared for such a situation and had reacted poorly to it. The scientific basis for a proper response to nuclear emergencies was broadly in place prior to the accident. The difficulties that arose were largely a consequence of the inadequate attention that had been given to proper communication to the public of the problems involved in a large scale accident with widespread dispersion of radioactivity. For example, the basic scientific information was already available with respect to the definition of maximum permitted levels of radioactive contamination of foodstuffs to be marketed or traded. It was difficult, however, to adapt this information readily to the partially contradictory exigencies of agriculture, trade, public opinion and radiation protection.

The Radiation Protection Research and Training Programme immediately took an active part in Community initiatives after the Chernobyl accident. Community scientists started at once to collect information and carried out an assessment within days which showed that significant health consequences were not to be expected in the European Community. About four weeks after the accident, the Programme, together with the US Department of Energy, organised a meeting in Brussels during which the data on dispersion of radioactive material were discussed and evaluated. Several other meetings on transfer in the food chain and possible health effects followed soon after. This assessment work was performed in close co-operation

inside the CEC with DG XI (Directorate General, Environment, Consumer Protection and Nuclear Safety) {formerly DG V, Employment, Social Affairs and Education}, and, externally, with WHO, IAEA and other international agencies.

In order to evaluate the situation created by the accident, and to improve preparedness for possible future accidents, the Programme re-orientated existing contracts and awarded many new ones. The staff of the Programme, with the help of the CGC, developed a series of 10 "Post-Chernobyl" research actions. These were submitted to the Council of Ministers with a request for a revision of the ongoing Programme. Due to the late acceptance of the Framework Programme, this revision, endowed with an additional budget of 10 MEcu, was only accepted at the end of 1987, with the work beginning during the early months of 1988. The final reports of this research will be available in 1990. They will be accompanied by a synopsis of the results of the overall post-Chernobyl programme and an evaluation of future needs in this area.

The 1985-1989 Programme, in addition to the research described in more detail in the following sections, also continued to direct resources to the development of co-operation within the Community via study group meetings, and provided support for the co-operative groups of scientists EULEP, EURADOS and IUR (see page 44).

Memoranda of Understanding were signed with the US Department of Energy, Office of Health and Environmental Research, and the Atomic Energy of Canada Ltd, the latter also involving the Atomic Energy Control Board and the Radiation Protection Bureau, Health and Welfare. These memoranda are being implemented by meetings of staff from both institutions to discuss priorities of, and approaches to, research by co-organising workshops, short-term visits of scientists and collaboration on selected research programmes, e.g. radon in homes.

The Programme continued its efforts on the dissemination of scientific knowledge in radiation protection. It organised a total of 258 meetings, 129 of them with participation from outside the European Community, with a total of more than 8,000 participants. It published 74 proceedings or review papers. These are listed in Annex IV (page 235).

Co-operation with international organisations (see also page 44) was very active during the period 1985-1989. Members of the Commission's staff participated in the meetings of Committees 3 and 4 of ICRP, as well as in those of ICRU. Staff also participated in IAEA meetings, contributed to their expert groups and developed a co-ordinated research programme on radon. Contacts were also maintained with UNSCEAR and WHO.

2. The Continuing Need for Community Radiation Protection Research

The research and training activities of the Programme aim to maintain essential radiation protection expertise and co-operation in the Community. At present, they support, by shared-cost contracts, about 30% of all radiation protection research carried out in the Community. About 500 full-time scientists are working in this field and more than 80% of all Community research is integrated into various co-operative efforts of the Programme. The Programme aims to provide:

- the scientific basis for the continued updating of the "Basic Safety Standards for the Health Protection of the General Public and Workers against the Dangers of Ionising Radiation" and the scientific background for the continued evolution of radiation protection concepts and practices;
- the scientific knowledge to evaluate possible carcinogenic and genetic effects and risks from exposure to low doses and low dose rates of radiation of different qualities arising from natural radiation, medical diagnostic radiology, and nuclear and other industrial activities;
- the methodologies to assess risks from accidents as well as the rationales and techniques for the implementation of monitoring and countermeasures to prevent or reduce the consequences of such accidents to man and the environment;
- the scientific knowledge to enable the relevant authorities to evaluate the impact of long-term choices in energy policy on man and his environment, to manage normal operational and rare emergency situations, and to inform the public about the risks and benefits of radiation;
- the incentive and support for co-operation between scientists in Member States;
- the training of young scientists which is indispensable for maintaining radiation protection competence in the Community;
- the efficient use and dissemination of the scientific knowledge in radiation protection.

Radiation risks have recently been re-appraised based on new scientific information. Moreover, the public has become more aware and concerned about the risks from industrial activities, especially those from radiation. ICRP, in the forthcoming revision of its recommendations, may reduce dose limits for workers and may also revise or at least refine radiation protection principles with respect to natural,

medical and accidental exposures. The revision of the ICRP recommendations may eventually form the basis of the revised Community Basic Safety Standards. In view of these developments, the Scientific and Technical Committee (STC) recently voiced its concern about the extrapolation of available risk estimates obtained from epidemiology of human populations exposed at high dose and dose rates to low doses and low dose rates which are of interest in radiation protection.

Examples of areas in radiation protection in which further research is particularly urgent are as follows:

- Since human exposure mainly occurs at low doses/dose rates, increased emphasis must be put on research into the reliability of the extrapolations of risk estimates from high dose to low dose/dose rate exposure. A direct determination of human risks under such conditions does not appear feasible; thus, a concerted approach involving microdosimetric, molecular, cellular, animal and epidemiological investigations on induction of radiation-induced cancer, genetic damage and other possible effects is needed. In this context, new methods to study the interaction of radiation with cellular targets and their subsequent fate and influence on cell behaviour will need to be developed. More attention needs to be given to epidemiological studies in populations suitable for assessing the effect of low doses, including exposure in the workplace, radon, etc, in order to establish improved upper limits on risk estimates.
- Radon in dwellings represents the largest contributor to exposure of man. In view of the recommendations which are to be issued on its control and the remedial actions which will have to be taken, one must obtain a better understanding of the ways in which radon and its daughter nuclides enter the human environment and from there into the lung, and of their effects on radiosensitive pulmonary tissues. A co-operative approach is being taken in the Community, together with the USA, to undertake epidemiological studies on lung cancer after radon exposure.
- Medical diagnostic radiology is the largest man-made source of exposure of the population and should be reduced as far as reasonably practicable without deterioration of image quality and diagnostic information. Recent pilot studies on quality control and dose reduction revealed the potential of dose- and cost-saving measures which can be taken. Expert systems for quality and dose control need to be developed to enable benefits to scientific research to be obtained in everyday practice.
- Radiological protection in the workplace must be optimised, establishing management procedures and practices on improved scientific information. In this respect, comprehensive statistics of human exposure from different sources, including natural and medical, are needed. The monitoring of workers for external and internal exposure under realistic working conditions must be assured with respect to accuracy and sensitivity in order to implement the ALARA principle. New and improved instrumentation and procedures must be developed to implement fully anticipated revisions of radiation protection recommendations, and further research on the metabolism of radionuclides must be carried out to improve the detection of low levels of internal contamination.
- The studies carried out post Chernobyl on an integrated nuclear emergency response system need to be developed further. The different modules of accident consequence analysis must now be integrated with the monitoring systems, and real time emergency management systems must be further developed on a Community level (eventually also involving EFTA countries). To this end, the scientific basis for quality criteria and detection of environmental radioactivity should be improved. Moreover, the scientific development of countermeasures to treat accident victims or to deal with contamination in the near, intermediate and far field

of a nuclear accident must be continued in the co-operative groups of scientists from the Community. Such countermeasures must be based on a reliable assessment of the dynamic behaviour of radionuclides in the environment. Co-operation amongst the European countries, within and outside the Community, is needed to exploit fully the huge amount of potential information generated by the consequences of the Chernobyl accident. The participation of the Community in the proposed "Chernobyl Centre for International Research", supported in the context of international co-operation, will be important to achieve this aim.

3. The Radiation Protection Programme 1990-1991

A Radiation Protection Research and Training Programme for 1990-1991 was approved by the Council of Ministers on 22 June 1989 with a budget of 21.2 MEcu. The sector structure has been modified in order to emphasise the main goals of radiation research as well as their inter-dependence and the need for multi-disciplinary approaches for solving these problems. The new Programme is divided into three sectors as follows:

A) Human Exposure to Radiation and Radioactivity

- A1 Measurement of Radiation Dose and its Interpretation
- A2 Transfer and Behaviour of Radionuclides in the Environment

B) Consequences of Radiation Exposure to Man: their Assessment, Prevention and Treatment

- B1 Stochastic Effects of Radiation
- B2 Non-stochastic Effects of Radiation
- B3 Radiation Effects on the Developing Organism

C) Risks and Management of Radiation Protection

- C1 Assessment of Human Exposure and Risks
- C2 Optimisation and Management of Radiation Protection.

Another important change in the 1990-1991 Programme is the new management structure of multinational contracts. These contracts, administered by one of the partners but co-ordinated with respect to scientific matters by the Commission's services, will result in even better integration of Community research.

Calls for proposals have been issued and a total of 308 projects comprising 783 individual topics has been received requesting about 75 MEcu funding from the Commission. From these, a total of 125 projects comprising 333 individual topics

have already been selected with funding by the Commission of about 13.9 MEcu. Budgetary constraints made the selection of proposals for support difficult, and many worthwhile proposals had to be refused.

4. Training Needs in Radiation Protection

Training in radiation protection must now be actively pursued as there will be a significant loss of expertise within the next few years due to the pending retirement of many senior scientists who entered the profession during its rapid expansion in the 1950/60s.

Training in the 1990-1991 Programme will be enlarged and extended to several levels of knowledge and adapted to various target groups:

- undergraduate students in medicine and the sciences must be trained by providing correct and up-to-date teaching material to university professors who are often only marginally interested in radiation protection;
- young scientists must be encouraged to carry out their research in an optimal way, be integrated into co-operative activity with other institutes and stimulated to devote their efforts constructively to the problems of radiation protection;
- training is needed to apply optimally the specific principles of radiation protection in different areas, e.g. to optimise radiological image quality and patient exposure, to utilise the emergency management systems developed in the Programme, to treat radiation accident victims, to reclaim contaminated land, etc.;
- training must be provided for persons responsible for the general management of radiation protection and for the teaching of these principles so that all actions are based on up-to-date information and conform to Community standards.

These training activities will be organised by the Commission's staff in charge of the action "Radiation Protection", where appropriate, together with existing CEC-supported co-operative groups or other groups created for this purpose, and in co-operation with the services of DG XI and the Joint Research Centre.

B. Principal Scientific Results Obtained in the Six Programme Sectors

1. Radiation Dosimetry and its Interpretation

Radiation dosimetry has to provide the procedures and concepts for the determination of the amount of ionising radiation which then can be related to the induced biological effects. In radiation protection, dosimetry is thus concerned, on one side, with fundamental aspects of radiation interaction and the relationship between physical quantities and biological effects and, on the other side, with practical aspects of developing dosimetric concepts and quantities for the establishment of limits and standards for the control of exposure of workers and the general public. Physical dosimetry is therefore involved in all radiobiological research of relevance for radiation protection and provides the quantitative basis for risk assessments and related dose limits.

The Programme proposal 1985-1989 stated the following scientific priorities in this section:

- dosimetric problems arising in the implementation of protection standards and measures;
- research for the improvement of personal dosimetry and area monitoring;
- assessment of dose in case of accidental exposure;
- physical data and methods in radiation dosimetry;
- interpretation of dose-effect relationships with respect to radiation risk.

The work carried out in the contracts awarded by the Programme essentially corresponded to this proposal. However, there were considerable differences in the number of research proposals submitted with regard to the various topics. In particular, the subject improvement of instrumentation attracted a relatively large number of proposals whereas only few proposals were received for research in accident dosimetry. Because of this fact and, partly, because of restrictions in the available funds, there was a modification of the working programme as compared to the Programme proposal with a shift in emphasis towards activities in fields of practical relevance.

The sector comsisted of 35 contracts with a total of 59 projects including some projects not yet terminated. The main topics and their subdivisions are as follows (the number of projects in respective areas are given in brackets):

a) Dosimetric quantities and standards in radiation protection (7).

b) Radiation protection instruments and dosemeters
   - area monitors and survey instruments based on microdosimetric techniques (8),
   - specialised instrumentation for external radiation (7),
   - instruments for internal contamination (1),
   - individual dosimetry (6)

c) Experimental and calculational methods for dosimetry
   - neutron and photon spectrometry (5),
   - internal dosimetry (6),
   - computational dosimetry (5),
   - accident dosimetry (3),
   - basic physical data (3)

d) Microdosimetry and biophysical modelling (7).

a) Dosimetric quantities and standards for radiation protection

Since 1980, important progress has been made in the development of a consistent set of operational dose equivalent quantities for monitoring external irradiation. The International Commission on Radiation Units and Measurements (ICRU, 027 and 217) proposed operational quantities for area and individual monitoring to be used as estimators for effective dose equivalent, which is the basis for limiting exposures. Many contractors and the Commission's services discussed the selection of these operational quantities with ICRU in much detail during 1985 and 1988, the Programme and the Physikalisch-Technische Bundesanstalt (PTB), Braunschweig organised seminars on "Radiation Protection Quantities for External Exposure" (1985) and on "Implementation of Dose-Equivalent Operational Quantities into Radiation Practice" (1988) which were also sponsored by ICRU, ICRP (International Commission on Radiological Protection), EURADOS and the US Department of Energy. These conferences were of great importance for achieving broad acceptance of the new quantities and for accelerating their practical implementation. In particular, the applicability of the new quantities, the consequences for instrumental requirements and calibration procedures and operational methods were investigated. In general, there was consensus among scientists and health physicists on the acceptance of the quantity ambient dose equivalent for area monitoring, as defined

in the 30 cm diameter ICRU sphere. Some problems were encountered with the practical implementation of the operational dose equivalent quantities for individual monitoring, for example with regard to calibration procedures, in particular the choice of appropriate phantoms. In the meantime, practicable solutions have been developed and appear to be more acceptable.

ICRU (027, 217)has published two reports on the "Determination of Dose Equivalents from External Radiation" (ICRU Report No. 39, 1985 and No. 43, 1988) and is currently preparing a report on practical measurements of dose equivalent quantities. Several contractors have been and are involved in the preparation of these ICRU reports and have provided relevant basic data such as fluence-to-dose equivalent conversion factors.

The conceptual and practical problems of individual monitoring procedures for neutrons were addressed by PTB, Braunschweig (012). The problems are related to the geometry, composition and structure of individual human beings and the variation of exposure conditions in the radiation field, e.g. due to the movements of workers. Investigations into the influence of the shape of phantoms used in calibration and in actual irradiations led to a proposal for simplified calibration procedures and showed that, in most cases of practical relevance, a calibration of neutron individual monitors, for example by using a D_2O moderated ^{252}Cf source and a simple anterior-posterior irradiation on a slab phantom, will provide sufficiently safe monitoring results. Correction factors for different phantom shapes and materials were developed. This work will be of direct relevance to the forthcoming third ICRU report on dose equivalent measurements. A related investigation into the response of individual dosemeters for photons for different phantom materials and shapes was completed in 1987 (NRPB, Chilton, 015).

The availability of computational competence and expertise within the Community has contributed to, and is still very useful in, the implementation of the new quantities and concepts. The theoretical determination of fluence-to-dose conversion functions for relevant dosimetric quantities (PTB, Braunschweig, 012; GSF, Neuherberg, 172) is an example of this. GSF developed tools for realistic three-dimensional modelling of real man ("voxel phantom") and uses these models to

calculate conversion factors for anthropomorphic phantoms. They have also carried out a workplace radiation field analysis in reactor environments and concluded that ambient dose equivalent, H*(10) greatly overestimates effective dose equivalent. Furthermore, a study of quality factors for neutron exposure has been carried out in view of the forthcoming new formulation of the quality factor by ICRP. The work of this group has been used extensively by ICRP and ICRU in the preparation of their recommendations.

A comparison of organ doses, effective dose equivalents and the readings from personal dosemeter readings under different conditions of photon irradiation by NRPB, Chilton (016) revealed serious errors in the interpretation of dosemeter readings when the body partially shields the dosemeter. The same group used existing expertise to calculate organ doses from an infinite plane source of gamma ray emitters, e.g. ^{137}Cs. This work was initiated after the Chernobyl accident.

In the general context of phantoms for calibration, one project (NRPB, Chilton, 018) investigated the possibility of developing realistic skull and chest phantoms suitable for the calibration of detectors for the measurement of ^{241}Am, ^{210}Pb and ^{90}Sr in bone. However, legislation changed, and difficulties arose in obtaining human bones; finally, it was found that phantoms commercially available in the US were satisfactory for further work.

b) Radiation protection instruments and dosemeters

The probable changes by ICRP to risk factors, dose limits and quality factors will increase the demand for improved instrumentation and dosemeters. Furthermore, there are still some principal problems in radiation monitoring for external radiation such as the availability of personal dosemeters for low energy neutrons and skin dosimetry in the work place. The availability of some new detector materials and modern micro-electronics has injected new impetus into the activities in this field.

In relative terms, research into instrumentation has attracted most of the proposals, which reflects the continuing need for such instruments as well as the considerable Community expertise existing in this field. Most work in this area has been carried out in close collaboration with, and has often been co-ordinated by, working groups

of the EURADOS (European Radiation Dosimetry Group) (026). This collaboration and exchange of information has been supported by several symposia and workshops jointly organised by CEC and EURADOS.

Area monitors and survey instruments based on microdosimetric techniques

Probably the largest, single, concerted research action within the dosimetry sector was the development and implementation of mixed field area monitors based on low pressure Tissue-Equivalent Proportional Counters (TEPC) (KFA, Jülich, 007; Univ. Saarland, 010; PTB, Braunschweig, 012; EURADOS, 026). These groups (other institutes from countries inside and outside the EC participated within EURADOS working group I) developed prototype instruments, investigated practical and fundamental aspects of this method and carried out an intercomparison of TEPC area monitors which was organised by EURADOS and PTB.

The principal potential advantages of TEPC dose equivalent meters, compared to conventional moderator-type neutron dose equivalent meters ("rem-meters"), should be a flatter energy response to neutrons in terms of ambient dose equivalent; the capacity to measure, simultaneously, neutron and gamma-ray doses and to provide estimates of the effective quality factor (and for some instruments lineal energy spectra), and a substantial flexibility in adopting newly defined concepts and quantities such as modification of the quality factor definition.

The intercomparison of seven different prototype or commercial TEPC area monitors in monoenergetic neutrons (thermal neutrons to 15 MeV neutrons) and photon (^{60}Co) reference fields and in a D_2O moderated ^{252}Cf reference radiation field provided a comprehensive and detailed basis for judging the suitability of this method and for further development and optimisation. Measurement procedures for TEPC instruments and those for conventional dosemeters differ mainly in that the former, in addition to the frequency of detector pulses, also require the pulse height distribution (or their variance) to evaluate dose equivalents. The dynamic range of pulse heights is almost five orders of magnitude and, therefore, requires complex electronics. The development of prototypes included the design and construction of compact measurement electronics using modern microelectronic components (KFA,

Jülich; Univ. Saarland). The technical realisation, the detector design and the evaluation procedures differed for the various systems compared. The main results of the intercomparison were:

- all TEPC systems are able to measure ambient dose equivalent and mean quality factors in mixed radiation fields and should be useful for area dosimetry;
- the ambient dose equivalent response decreased in monoenergetic neutron fields with neutron energy, in particular below several 100 keV. There were differences in response between the systems up to a factor of 20. This was attributed to differences in detector wall thickness and "simulated" diameter;
- for the broad neutron energy spectrum of the ^{252}Cf (D_2O) source, all systems tallied well in the dose equivalent reading;
- the sensitivity of TEPC can be made to be comparable with conventional instruments if the detector size is sufficiently large (approx. 10 cm diameter).

The intercomparison recommended:

- the conventional calibration in terms of the quantity lineal energy should be replaced by a calibration directly in terms of ambient dose equivalent in a neutron reference radiation field in order to improve accuracy;
- improvement of the ambient dose equivalent response at low neutron energies could be achieved by giving attention to several parameter (simulated diameter, counter size and material, gas composition and evaluation algorithm);
- the potential application of the diagnostic information provided by the TEPC in practical radiation protection has to be investigated and developed further.

The results of the intercomparison and other investigations were discussed in 1988 at a workshop on "Implementation of Dose Equivalent Meters based on Microdosimetric Techniques in Radiation Protection" jointly organised by CEC, EURADOS and GSF, Neuherberg. At the workshop, reports were given on the practical applications of TEPC monitors in nuclear industries, the environment of medical and physical accelerators and manned space flights. It was pointed out that there is a need for field calibrations for neutron energy dependent personal dosemeters (e.g. albedo dosemeters).

The design of the "KFA-counter" (KFA, Jülich, 001) was based on neutron transport calculations aimed at optimisation of the dose equivalent response for neutrons. The chosen wall thickness of 15 mm (plastic) is considerably larger than that of other TEPC detectors. As predicted by the calculation, an increase in response is observed, at for example, 24 kev monoenergetic neutrons. However, the thicker wall leads to a decreased response above 100 keV neutron energy due to fluence

attenuation. The group is continuing to optimise the response by modifying the quality weighting function and has experimented with practical applications. The Univ. of Saarland (010) has developed a portable battery-powered TEPC area monitor and used it in nuclear installations and accelerators. The instrument meets most requirements of instruments in routine radiation protection dosimetry such as being of light weight, easy 4-push button operation and adequate ruggedness. The group carried out several basic investigations to contribute to the understanding of the dose equivalent response of TEPC and its improvements. For example, the combination of adding small amounts of ^{3}He to the counting gas and varying the wall thickness of the detector provides a powerful method of influencing the energy dependence of the response at low neutron energies.

PTB, Braunschweig (012) carried out investigations into improving the performance and accuracy of TEPC measurements and to extend their range of application. The aim of this work is to evaluate the feasibility of constructing a TEPC-based transfer instrument for ambient dose equivalent for neutrons. In collaboration with Univ. Saarland, the improvement of TEPC calibrations has been achieved and the combination of TEPC pulse height and time-of-flight measurements has been developed.

The joint work on TEPC instruments was complemented by other investigations into the application of experimental microdosimetric techniques in dosimetry. A renewed interest in extending the use of TEPCs to investigating the statistics of energy deposition in submicron dimensions was evident. INFN, Legnaro (193) concentrated on the development of proportional counters for very low pressures, and thus simulated diameters of much less than 1 μm. First investigations into the performance appear promising. Proportional counters operating correctly at simulated diameters of the order of about 10 nm would be of immediate relevance to fundamental microdosimetry but possibly also to practical radiation protection. The experimental work is complemented by computational investigations at the Univ. Toulouse (292). The aim of this work is to optimise the operation of low pressure proportional counters on the basis of fundamental physical data and processes.

The Univ. St. Andrews (024) developed a co-axial twin proportional counter to be used for neutrons of intermediate neutron energy. After initial technical difficulties with the construction, the detector has now been built and is being used. The main attraction of such counters is that they can distinguish, in principle, between "crossers" and "insiders" and thus may overcome one of the shortcomings of the conventional TEPC. CEA, Fontenay-aux-Roses (020) investigated some of the basic aspects of the operation of low pressure TEPC. In particular, new tissue-equivalent wall material has been developed and gas gain characteristics for different counter geometries, including a multi-anode version were studied.

The applicability of a microdosimetric detector based on a different principle, the variance-covariance technique, has been investigated at the Univ. Würzburg (013). This method can be used for the determination of dose equivalent in time-varying fields. Using two identical (twin) detectors, the variance and covariance of many repeated short-term dose measurements are used to evaluate absorbed doses and quality factors. The group developed a first operational system and obtained good results when compared with conventional microdosimetric methods.

Specialised instrumentation for external radiation

Small sized, high pressure ionisation chambers were investigated for use in radiation protection dosimetry and radiobiological experiments (TNO, Rijswijk, 002). Such chambers are very sensitive and can provide radiation quality information either by taking advantage of initial recombination effects or by varying the gas pressure. The investigation included the study of cavity size effects and found, among other things, that Mg-Ar ionisation chambers exhibit complex behaviour in varying operating conditions and should be used with great caution.

The dosimetry of radiations of low penetrating power was paid scant attention in the earlier years of dosimetry research and still requires urgent improvement. The assessment of hazards to the skin due to irradiation with beta particles or low energy photons requires adequate dosimetry. Within a EURADOS working group (026) several European groups including some without a CEC contract co-operated in this field. In 1985, the Commission and EURADOS jointly organised a workshop

on "Skin Dosimetry" in order to establish the actual state of the art and to identify research needs and priorities. The working group carried out theoretical and practical studies on beta-ray dosimetry and identified problem areas in occupational situations. They also organised an intercomparison of beta-ray sources amongst primary national laboratories in order to harmonise measurements standards. The co-operation of the working group with EULEP in evaluating data on biological effectiveness of low-penetrating radiation and depths of sensitive layers in the skin is of great practical relevance. These two types of work are of immediate relevance to the important questions of quality factors for low energy radiation and the appropriate depth for skin dose equivalent measurements. A review document on dose rate meters for skin dosimetry is to be published soon.

The experimental and instrumental difficulties of skin dosimetry are demonstrated, for example, by the work reported by CEA, Grenoble (005). It was established that an ionisation extrapolation chamber can, in principle, be made suitable, for calibration purposes in beta ray dosimetry. The practicability of this approach is, however, limited. While ultra-thin TLD disc dosemeters provided satisfactory results in terms of sensitivity, the thermally stimulated exo-electron dosimetry with BeO thin film dosemeters appeared unsuitable for radiation protection dosimetry. The introduction of laser heating for reading TL-dosemeters, which confines heating to the surface layer, could contribute to a better sensitivity and, thus, applicability in skin dosimetry (Univ. Montpellier, 231; Univ. Barcelona, 232). This method is still under investigation.

Two contracts (Univ. Giessen 022; CEA, Fontenay-aux-Roses, 020) studied and developed beta-ray dosemeters based on thermally stimulated exoelectron emission (TSEE) either individually or in combination with radio-thermoluminescence. The work involved the development of suitably robust, composite detector material and appropriate reading devices for the two types of signals. The lower detection limit of the exoelectron emission dosemeter to tritium beta-rays has been reported to be about 100 nGy. The method enables the mean electron energy to be assessed and appeared to the investigators to be mainly suitable for development into an operational beta dosimetry system. It appears, however, that further effort is required to optimise the designs for individual dosemeters and dose rate survey

instruments. The sensitivity of thin thermoluminescent detectors should be further increased and robustness improved to make them adequate for routine application. In addition, the suitability of TSEE techniques for routine dosimetry should be demonstrated since this technique still has some problems with respect to its reproducibility and the influence of environmental conditions. Also, specific problems, such as the computational dosimetry for highly active "hot" particles, require further attention.

Instruments for assessing internal contamination

The evaluation of effective dose equivalent and organ doses due to intakes of radioactive nuclides, in particular natural and man-made alpha particle emitters, requires precise information on the concentration of radioactivity. In order to be able to comply with regulatory requirements with regard to monitoring plutonium, alpha particle detectors of sufficient sensitivity must be developed. In one contract (ENEA, Bologna, 023) spark counting for large area cellulose nitrate detectors, as applied to chemically treated samples of urine, was shown to be potentially useful. This passive registration technique can integrate over sufficiently long exposure times. It can also be used for radon measurements.

In a project started more recently and not yet completed (Univ. Rome, 302), a large area multi-wire counter is being constructed to be used as a high sensitivity spectrometric alpha particle detector. If further developed successfully, this instrument may be able to detect low levels of activity of airborne man-made alpha particle emitters in the presence of radon.

Individual dosimetry

The new quantities proposed by ICRU for operational individual monitoring appear to find increasing acceptance by scientists and radiation protection officials, and this has largely been the result of the current development of substantial and practical procedures for their implementation, for example, the calibration of individual dosemeters on phantoms. Several contractors have been actively involved in this development by providing results and data, and contributing to the preparation of

the new ICRU reports. One important result of these investigations is that the introduction of the new quantities does not require the development of new instrumentation.

The fact that considerable effort was made on instrumentation for individual monitoring during 1985-1989 has to be attributed to the obvious inadequacies of existing instruments, in particular those for monitoring neutrons and beta-rays. The types of detectors investigated included photographic films (for neutron monitoring), TLD (for photon and beta-rays), TSEE (for beta-rays), track etch detectors CR39 (for neutrons) and, more recently, solid state electronic dosemeters (photons, neutrons).

CEA, Fontenay-aux-Roses (020) studied the suitability of individual dosemeters based on various nuclear emulsions combined with a hydrogenous converter and tested various methods to evaluate the silver content in the emulsion (neutron activation and X-ray fluorescence). The results show that these methods are only applicable at doses above the range of interest to radiation protection.

The application of Thermo Luminescence Dosimetry (TLD) techniques in routine individual (and environmental) dosimetry was the topic of a EURADOS working group which finalised its task in 1987 and published six reports individually in refereed papers and together as a bound volume as a EURADOS-CENDOS and CEC publication on "Aspects of Individual Monitoring". The original task of the group, i.e. to disseminate information on the effective and efficient use of the TLD technique for individual monitoring, was undertaken by organising a workshop on Application of Thermo-luminescence Dosimetry to Large Scale Individual Monitoring in 1985 and by presenting four reviews at the 8th International Conference on Solid State Dosimetry in 1986. While the work on TLD in monitoring for photons was focused on integrating this technique into routine dosimetry, research on monitoring weakly penetrating radiation had to solve more fundamental problems with regard to the competing requirements of low detector thicknesses and sufficient sensitivity. In one contract (NRPB, Chilton, 016) carbon-loaded TLD (LiF/PTFE) were used in order to confine the detection layer to the surface in the material. A satisfactory energy response was achieved; the sensitivity, however, was poor.

Efforts were directed towards an improved understanding of the response of thermoluminescence of lithium fluoride (UKAEA, Harwell, 019). By studying the fading properties of thermoluminescence and by modelling the TL processes theoretically, a contribution was made to improving the techniques for multiple reading of TLDs and re-evaluating doses after high exposures. Related work was carried out at NRPB, Chilton (016) on multiple dose re-assessment for the determination of high doses and in situations where the primary information had been lost.

The plastic material CR39 (poly-allyl-diglycole-carbonate, PADC) has been found to be of considerable interest for use in individual dosimetry of neutrons (and radon). Tracks produced by recoil protons and, at higher neutron energies, alpha particles, can be made visible by chemical etching. Optimisation of etching procedures allowed the lower limit of neutron energy detected to be increased well beyond that of nuclear emulsion films formerly used. Another advantage of CR39 is the flat energy response in terms of dose equivalent. A EURADOS working group carried out an inter-comparison of chemical and electrochemical etch procedures under operational situation and performed three irradiations jointly organised at PTB, GSF, Neuherberg and PSI (Paul Scherrer Institute, Switzerland) in monoenergetic neutron radiation fields ranging from 0.075 MeV to 27.8 MeV and with ^{252}Cf neutrons. These irradiations, in well calibrated neutron radiation fields over the large range of energies, allowed assessments to be made of individual systems and inter-comparisons of systems from Europe, the USA and Canada. In 1987, the working group, with CEC and UKAEA, organised a workshop on track etch detectors at which all relevant groups working on this technique in Europe and North America were represented. The technique has been accepted for individual neutron dosimetry in some countries. There are still, however, considerable problems with background and reproducibility. The EURADOS group carried out a joint study on the background characteristics of etch plastics from various sources. The conclusions and recommendations were published.

Some of the problems associated with CR39 were studied at ENEA, Rome (023). This group demonstrated the advantages of electrochemical etching processes and the extension of the use of CR39 by varying different parameters of the procedure.

The proper choice of parameters allows the energy response to neutrons to be modified, the background to be reduced, and the energy of recoils and time of track formation to be assessed. The same group was involved in the development of a CR39 neutron personal dosemeter for an important dosimetry service. Background readings could be reduced somewhat but not enough, and this remains the main obstacle to its introduction as a large-scale routine dosimetry system.

The Univ. Limoges (192) studied the possibility of extending the energy range of applicability of CR39 detectors by the use of a polyethylene (PE) converter doped with ^{10}B atoms. Fast neutrons are detected on the basis of recoil protons released in the PE whereas albedo neutrons are detected on the basis of the ^{10}B (n,p)^{7}Li reaction with thermal and intermediate neutrons. The response of such a detector has been calculated theoretically and compared to experimental results. Although agreement between calculated and measured values was satisfactory, the group concluded that the technique could be improved if the CR39 detector were replaced by a semiconductor detector. Work on this combination of converter and solid state detector has commenced. A multinational group of contractors (Univ. Aarhus 303; Univ. Strasbourg 304; PTB, Braunschweig, 305; Univ. Rome, 306; CERN, Geneva, 307) have recently started collaborating on the development of a universal individual dosemeter based on CdTe semiconductors.

c) Experimental and calculational methods for dosimetry

The need for developing instrumentation for radiation protection dosimetry mainly arises from the requirement for operational area and individual monitoring. However, there is also a need for basic research in dosimetric methods and their application in the general field of radiation protection as it maintains the general preparedness for optimal radiation protection practices and provides a sufficiently high level of research in the fields on which dosimetry is based. This more basic research is also very well suited to the training of young scientists entering the field of radiation protection.

Neutron and photon spectrometry

The operational quantities introduced by ICRU and the forthcoming changes in dose limits and quality factors, as well as the correct interpretation of individual dosemeters, require a better characterisation of radiation spectra in operational situations. Developments of neutron spectrometers with the aim of using them in field measurements were carried out at UKAEA, Harwell (019), at PTB, Braunschweig (012) at NPL, Teddington (003) and at CEA, Fontenay-aux-Roses (020). Neutron spectrometers must cover a wide dynamic energy range (thermal neutrons to some tens of MeV) and must have sufficient detection efficiency giving precise information at dose equivalent rates below 100 μSv/h and have adequate rejection of photon-induced pulses. The work on Bonner spheres (PTB) included the calibration of two sets of spheres in monoenergetic neutron fields, together with sets from NPL and GSF. In close co-operation with these two groups, fluence response matrices were established. Problems were encountered in the comparison of experimental results with results obtained by analytical neutron transport calculations. There are indications that more realistic Monte Carlo Codes will describe the experimental data better. However, modified analytical calculations fitted to the experimental data could be used to calculate the response matrix required for the energy spectrum unfolding. The unfolding of spectra using only few channel Bonner spheres exhibits substantial uncertainties and depends greatly on the a priori information required in some unfolding procedures. Integral data such as fluence and dose equivalent can, however, be determined with an acceptable uncertainty. A EURADOS working group on Numerical Dosimetry contributed to this work by carrying out a benchmark study on response functions for Bonner spheres.

At PTB, Braunschweig (012), the operational spectrometry system using a NE213 liquid scintillation counter and proton recoil proportional counters was tested in various known, partly known, or completely unknown, neutron fields, together with the Bonner spheres. The proton recoil spectrometers cover the energy range that is most important for dosimetry (energy above 10 keV). However, their detection efficiency is limited. The main drawback of the scintillation spectrometer is its sensitivity to photons. At CEA, Fontenay-aux-Roses (020) a combination of

spherical proton recoil proportional counters and a NE213 scintillator was also developed, and its basic properties were determined. The energy range covered is 20 keV to 20 MeV. Like PTB, CEA found that the overall neutron sensitivity is limited mainly by the spherical proportional counters.

The various systems developed by contractors in the past will be available for operational use. As mentioned above, the analysis of field characteristics in the workplace will be of importance in view of reduced dose limits and increased quality factors. This type of instrumentation, together with other types providing spectrometric information on radiation quality such as TEPC area monitors, will also contribute to improved individual monitoring by offering the possibility of field calibration of individual dosemeters, for example, albedo dosemeters, which mostly have a noticeable energy dependent response.

An analysis of photon fields at 26 workplaces in nuclear and other sites was carried out by NRPB, Chilton (015) by measurements with GM counters with various shieldings in order to assess the photon spectra. In only one of the workplaces a significant contribution from low energy photons was observed. Earlier doubts, whether the quality factor for low energy photons should be increased, are therefore probably of limited significance in practical situations.

Internal Dosimetry

The improvements required for the assessment of hazards due to the intake of radioactive nuclides, in particular actinides, do not only need improved instrumentation for monitoring but also improved knowledge on metabolic pathways and distribution of nuclides in various tissues. Several contractors addressed some of the many detailed problems in this field. At the Univ. Bristol (006) previously developed track etch detectors were used to carry out plastic autoradiography of human lung and human bone. Lung tissue was taken from autopsy cases and slices of tissue mounted against the nuclear track detectors. The main result is that most alpha-active particulates detected were found in the visceral pleura, and that many of those represented multiple point decays. The multiple activity appeared to emanate from small grains of uranium and thorium-bearing minerals. Radioactivity

measurements made on bone samples, taken from autopsy cases, were used to calculate the doses to red marrow and to the endosteal cells lining bone surfaces. The group also started a study on the foetal transfer of alpha radioactivity at natural exposure levels. In a third project, autopsy samples from cases of occupational exposure to plutonium were examined by plastic autoradiography, but results are not available for publication for legal reasons. A purpose-built tissue preparation laboratory has been constructed at Univ. Bristol.

The micro-distribution of ^{224}Ra, ^{239}Pu and ^{241}Am in the bones of beagles has been investigated by KFZ, Karlsruhe (029) applying autoradiographic techniques. A kinetic model for plutonium distribution and excretion was used to calculate dose factors for bone dose depositions, and the results were confirmed by the measurements on dogs.

The radiation doses due to the daughter products of radon deposited in the lung were calculated by applying improved data on aerosol parameters and on deposition and clearance mechanisms at the South Bank Polytechnic, London (025). The calculational model was improved taking into account physical effects and microdosimetric aspects. The model was then extended to include radiobiological data in order to attempt risk estimations.

During the contractual period, a EURADOS working group on the Assessment of Internal Dose was created. The general objective was to prepare guidance on the interpretation of monitoring data relating to internal exposure of radiation workers and the implementation of ICRP recommendations within Europe. The group has made rapid progress towards providing comprehensive European data bases for internal dosimetry, and is investigating whether European registries of internal dose assessment models, autopsy data and other biological data are feasible.

The group works in close co-operation with the corresponding EULEP group.

Computational Dosimetry

The availability of computational techniques and expertise was an important factor in the process of implementing new quantities and concepts and several laboratories have contributed the data required for the work of ICRU and ICRP committees.

NRPB, Chilton (016) and GSF, Neuherberg (172) co-operated in these activities and compared their results of, for example, calculations of effective dose equivalent for different irradiation geometries.

The use of computational techniques in dosimetric research is quite diversified and is often incorporated into projects dealing with specific aspects. A EURADOS working group on Numerical Dosimetry has been involved in several areas, mostly in close co-operation with other groups and institutes, thus providing the computational support requested for other research activities. The group carried out an intercomparison of unfolding codes for Bonner sphere measurements and a benchmark study on response functions for Bonner spheres. Work was performed to calculate radiation doses from Cs ground contamination. Finally, the group is involved in work for standardising phantoms for external and internal dosimetry. At the Univ. Toulouse (001) neutron transport calculations were made in order to evaluate neutron energy spectra from a moderated ^{238}U source to be used for calibration purposes.

In general, computational methods for solving the radiation transport problems of photon and neutron radiations are now well developed but the task of linking these methods to a comprehensive modular system of computer programmes for the majority of radiation dosimetry problems still needs to be addressed within the framework of the Programme. The calculations did reveal that improvement is still required with regard to the quality of basic atomic and nuclear data.

At the Univ. Würzburg (013), mathematical and numerical studies in microdosimetry have been carried out introducing mathematical methods developed in other fields. One of the problems studied was the reconstruction of the inchoate distribution from its proximity function. The similarity of problems in stochastic geometry and stereology suggests that the methods developed in these fields should be applied to numerical methods in microdosimetry.

Accident Dosimetry

In the case of accidental exposure, radiation doses and the homogeneity or inhomogeneity of the exposure must be rapidly assessed. In spite of many years' work, there is no entirely satisfactory solution available. At CEA, Fontenay-aux-

Roses (020), two projects were devoted to the development and study of accident dosimetry. The first concentrated on thermoluminescence of normal clothing tissue and of special textile tissue doped with a radio-thermoluminescent product. Only the doped material provided promising results. Loading textile fabrics with alumina of grain sizes of up to 44 μm gave acceptable results in terms of sensitivity (detection threshold a few tens of mGy) and met mechanical, tactile, optical, thermal and washing constraints. The readout is carried out by chemically extracting alumina and subsequent TLD and TSEE readings. If this method proves to be applicable on a large scale, it could provide all the information required in the case of accidental exposure, in particular with regard to the homogeneity of the exposure.

In the second project, electron spin resonance (ESR) induced in natural and synthetic fabrics was investigated for its suitability to assess doses. The study showed that only fabrics made of cotton or polypropylene are sufficiently sensitive for this method. Successful application, however, requires a complex procedure which may be envisaged in the rare cases of accidental exposure but not in routine personal dosimetry. If clothing covers the entire, or most, of the body, the information on the homogeneity of the irradiation would again be very useful for the decision on the medical treatment potentially required.

At Risø (028), ESR of alanine was investigated for suitability in accident dosimetry following photon, neutron and heavy ion exposure and observed that, in the dose range of 50 to 5000 Gy, a high accuracy can be achieved.

Basic Physical Data

Research in basic radiation physics continues to be an important tool for teaching and training. The evaluation of doses to different organs and tissues from measurements with detectors and dosemeters requires the knowledge of basic physical data for the quantitative understanding of the processes in the detectors and in biological tissue. For these reasons, some research in the dosimetry sector is devoted to basic radiation physics. The emphasis of the research activity has, however, shifted from fundamental to practical work if compared to previous Radiation Protection Programmes.

At Univ. Saarland (010) basic physical data for the dosimetry and microdosimetry of fast neutrons have been investigated using low pressure counters of different materials (mainly graphite and A-150 tissue equivalent plastic). Kerma factors for A-150 and carbon have been determined for neutrons with energies up to 60 MeV. The method of employing proportional counters simultaneously as cavity chambers and spectrometers continued to be developed by combining A-150 and graphite counter measurements and a combination of pulse height with time-of-flight techniques (jointly with PTB, Braunschweig (012)). For the evaluation of the data, new procedures to determine effective W-values and gas-to-wall absorbed dose conversion factors were developed. At lower neutron energies, data on W-values and on neutron transport processes were obtained. The low pressure proportional counter technique was also used to study the applicability of cavity chamber principles for metallic detectors exposed to photons.

At Univ. Würzburg (013), physical properties of heavy ion beams were investigated. Radial distributions of energy deposition in planes perpendicular to the trajectory of protons were measured for 4-11 MeV protons in nitrogen gas. The method used was the measurement of the intensity of the fluorescent light emitted from delta-ray interaction with nitrogen. The results were compared to computed data from Monte Carlo simulations. The results for lateral distributions of absorbed dose matched very well. This type of work is essential for the interpretation of radiobiological experiments carried out with heavy ions.

At Univ. Strasbourg (021), physical features of tracks of heavy charged particles were measured in ionographic detectors with emphasis on range determination, ionisation of molecules of radiobiological interest by protons and electrons, elastic scattering of low-energy electrons and methods of describing energy loss mechanisms by multi-dimensional graphical representations.

d) Microdosimetry and biophysical modelling

The fields of microdosimetry and biophysical modelling have been an important part of the Radiation Protection Programme of the CEC for a long time and are likely to continue to be so. Indeed, there is no alternative to theoretical models for fully

understanding radiobiological mechanisms, and these, in turn, must provide the basis for an interpretation of biological effects from different types of radiation at low doses and low dose rates. Microdosimetric research is, thus, fundamental for radiation protection in order to improve risk assessments for low doses and low dose rates. Although substantial progress has been achieved in several aspects of this field, it is, obviously, a long-term research activity which requires consistent support.

It is important to note that biophysical modelling requires both biological input data and physical data and some of the contractors are involved in obtaining both types of data. In order to increase the interaction between radiobiologists, physicists, chemists and model builders, a workshop on "Biophysical Modelling" was organised jointly with the US DOE in 1988. One of the objectives of this workshop was to prepare a comparison of biophysical models by identifying "benchmark" radiobiological data.

The calculation of track structure properties for ionising particles attracted considerable attention, and a total of six contractors carried out projects on various aspects of track structures. At GSF, Neuherberg (011), the energy range of particles, to which the formerly developed Monte Carlo programme is applicable, was extended to cover 1eV to 30 MeV for electrons and 1 kev to 1 GeV/u for heavy charged particles. Experiments and theories are still lacking to deal adequately with this problem; therefore, much effort was devoted to the evaluation and description of cross-sections for all interactions needed for the calculation of tracks. This time-consuming computer task can be done more rapidly and accurately once the parallel supercomputer is available in the very near future. Differential secondary electron ejection cross-sections for 15 different target materials, including DNA, for protons and alpha particles have been calculated. The computer code was further developed by including complex geometry routines. This will enable the simulation of realistic three-dimensional bodies like DNA coiled histones. Furthermore, the code was extended to enable the fate of chemical species in a biological cell to be simulated. This work showed that there are basic differences in the biological nature of primary relevant events in mammalian cells produced by high and low LET radiation. The group concluded that more than one quantity is needed to characterise charged particle tracks with regard to their biological effectiveness. There is evidence that

the combination of primary effects on three different structural levels determines this effectiveness.

The Univ. Toulouse (180) applied track structure calculations to obtain the spatial and temporal evolution of chemical species such as H, OH, OH^+, etc. induced by interactions (water radiolysis) with electrons of initial energies of 50 eV to 10 keV. These basic data are now available for applications in radiophysical, microdosimetric or radiobiological applications.

RIVM, Bilthoven (008) developed a track structure model in liquid water and applied it to the investigation of the linear or alpha component of biological effects. The quadratic or beta component was investigated by comparing the effects of gamma rays and UV radiation for cell killing. The group concluded that the quadratic term arises from the combination of two events which occur at different times and that the combined effect can be modified by repair. They recommend that future research in this field focuses on the determination of the sensitivity of track structure models to changes in parameters in the fitting of calculated data to experimental data.

One of two projects at MRC, Chilton (009) was directed towards the analysis of physical properties of different radiations in relation to their observed biological effectiveness. The group calculated and compared local energy depositions by radiations of different qualities in target structures of varying size and shape, including simple models of macromolecules such as DNA duplex and higher order DNA structures. The group experimentally investigated the radiobiological properties of "analytical" radiations (characteristic ultrasoft X-rays, cyclotron produced monoenergetic alpha particles of 30 and 35 MeV and protons of the corresponding LET and 24 keV filtered neutrons) with well defined track structures. The aim of the project is to seek the particular properties of radiation tracks which may be most relevant to the biological consequences and thereby to place constraints on possible mechanisms of action. The track structure calculations showed the very large stochastic variations of energy depositions by a given particle (for example, ranging from a few eV to several keV in a nucleosome sized target for alpha particles) and very large differences in distributions between different particle

energies and types. The calculation for ultrasoft X-rays revealed that low energy electrons deposit substantial amounts of energy in small targets. Calculations for Auger-electron emitting radionuclides showed that a decay of a ^{125}I within DNA is liable to be much more damaging than the passage of a slow alpha particle.

The data from MRC and those from other laboratories for ultrasoft X-rays showed that RBE values vary significantly and correlate with thickness of the cell but also (almost) with its radiosensitivity. In collaborative experiments involving four laboratories, the earlier finding of Belli was tested where protons with LET of 20-30 keV μm^{-1} have substantially greater biological effectiveness than alpha particles of the same LET. The analysis of the data has not been finalised but a qualitative confirmation of the results has been obtained for the inactivation of V79 cells. If further substantiated, these results have important implications for the mechanistic relevance of details in track structure. Analysis of the project has led to a set of working hypotheses which postulate that microscope damage from radiations can be classified in four broad types with respect to the relation of the target in or near DNA.

In a second project of MRC, Chilton (009), a variety of different experimental techniques and methods was developed for the radiobiological experiments conducted in the first project. This included the development of different sources for ultrasoft X-rays and ultrasoft X-ray dosimetry and the development of non-destructive methods to measure the dimensions of cells. The group also organised a first international workshop on "Ultrasoft X-ray Radiobiology" in 1987.

At KFA, Jülich (007) energy deposition spectra for Auger-electron emitting ^{125}I incorporated into DNA were calculated, and analytical functions were developed to describe energy deposition spectra for ions in sites ranging from 1 to 1000 nm. The group also used radiobiological data from the literature and microdosimetric distributions to derive biological response functions using unfolding procedures. This work is of potential relevance to radiation protection because it contributes to the determination of radiation quality for different radiations. Such an approach, if successfully completed, could contribute towards short-cutting the long-term research needed for the understanding of all basic mechanisms.

At GSF, Neuherberg (172), analytical calculations based on continuous slowing down models and Monte Carlo calculations of track structures were used to calculate energy deposition in sites of different sizes. Within the project the possibility of using imaging cytometry in biological monitoring was also investigated.

2. Behaviour and Control of Radionuclides in the Environment

Information on the behaviour of radionuclides in the environment represents an important input into the assessment of exposure and risks from radionuclides released from the nuclear fuel cycle or from natural radioactivity enhanced by human activities. This information is also needed to control the transfer of such radionuclides to man in normal situations and after accidental releases. The 1985-1990 Programme proposal aimed to investigate:

- the different source terms, i.e. the entire nuclear fuel cycle, the industrial and medical applications of radionuclides, the redistribution of natural radioisotopes;
- the improvements in the determination of very low quantities of long-lived radionuclides in the environment;
- the dispersion in the atmosphere, water and ground on a local, intermediate and global scale;
- the entry and behaviour in the biosphere of radionuclides and the interaction with the natural environment;
- the methods to counteract the spread of radionuclides and the procedures for decontamination.

A total of 45 contracts (66 projects) in this sector dealt with the following topics:

a) Terrestrial environment
   - the behaviour of actinides and other long-lived radionuclides (10),
   - the deposition of radionuclides on vegetation (2),
   - the behaviour of tritium and carbon-14 (6),
   - the behaviour of technetium in terrestrial environments (5),
   - the effect of countermeasures (3),
   - the behaviour of radionuclides in semi-natural environments (4);

b) Aquatic environment,
   - field studies (3),
   - the behaviour of long-lived radionuclides (13),
   - radioecology of continental waters (6),
   - modelling of river systems (2).

Compared to the previous Programmes, research activities were focused more on some critical problems of radioecology where special attention was paid to the long-term behaviour of long-lived radionuclides, in particular, actinides, technetium, caesium and strontium and the influence on transfer of chemical, physico-chemical or biological changes of radionuclides. The Chernobyl accident drew attention to some areas which until then had not been studied so thoroughly, in particular the behaviour of accidentally released radionuclides into semi-natural and natural

ecosystems, the transfer to feedingstuffs and the practical implementation of countermeasures.

a) Terrestrial Environment

The behaviour of actinides and other long-lived radionuclides

Dynamic models (RNL, Risø, 030) were used to simulate the behaviour of ^{131}I and ^{137}Cs in the Roskilde area of Denmark after the Chernobyl accident. Model predictions seemed to be out of phase with the observations made in food and milk indicating that the impact of deposition is inadequately simulated by the model. Considerable uncertainty exists with respect to the fraction or elementary and organic iodine. Thus, a higher level of elementary iodine could account for the higher radioactivity in grass seen during the initial period after the accident. The model predictions of ^{131}I in milk agree with the observations for animals kept under cover, but not with those left out to pasture. However, a model for the behaviour of caesium, adapted from a programme developed in another institute, predicted levels of caesium in grass, milk and beef less well, but, nevertheless, could be used to demonstrate the influence of the seasons following a release at different times of the year.

The behaviour of radionuclides in soils and sediments has been studied with particular respect to strontium and caesium. It is generally thought that the ability of micaceous clays to retain alkali ions of low hydration preferentially represents the most important factor governing radiocaesium retention in soils and sediments. The specific sites responsible for this process are localised at the interlayer-edge zones of the clay crystals, the so-called frayed edge sites (FES). The methods to study this retention were developed (KUL, Leuven, 035) and applied to agricultural soils, freshwater sediments, estuarine sediments and soils from upland pastures. Caesium competes strongly with potassium, and even more with ammonium, for these sites. Where high concentrations of Na exist, e.g. in estuaries, competition between K and Na plays a major role. Soil in upland areas contains very little clay and much organic matter; nevertheless, it is thought that the FES of clay particles could play a role in caesium retention in such soils. Mathematical equations to describe the different ionic interactions of caesium were developed, and these predict behaviour

in simple systems well. In contrast to the sorption of caesium, the sorption behaviour of strontium in soil and sediments is, in general, not determined by specific interactions but rather by reversible ion exchange processes. It is well known that alkaline earth cations only display small differences in binding to such complexes; one may assume, therefore, that the overall K_D value of the bivalent ions (Ca, Mg) in soil or sediment systems reflects the solid/liquid distribution coefficient of strontium quite well.

An investigation of radionuclide deposition on vegetation (CEA, Cadarache, 037 and UKAEA, Harwell, 046) provided a time-series of data on radiocaesium, radiostrontium and actinide levels close to, and at some distance from, nuclear sites in Great Britain and in France. The dependence on season, latitude and rainfall and the variability of the data were analysed. Inventories, especially after the Chernobyl accident, of deposition and removal of radionuclides in plants, together with information on radionuclide accumulation in soil, helped in understanding the relative importance of soil to plant transfer compared with direct deposition on foliage. At some plots near nuclear sites, interception and retention of plutonium and ^{241}Am by foliage represented the most important transfer pathway for radionuclide accumulation in plants.

The soil to plant transfer of ^{237}Np, ^{241}Am and ^{244}Cm is greatly influenced by soil type and soil amendment. Uptake of actinides by rye grass in acid brown earth, at an only slightly acid pH value (in water) of 5.8, is greater than in any other of the soil types studied; this observation suggests that a much higher transfer might be found in more acid soils with pH from 4.0 to 5.5. The influence on root uptake of actinides by microbial activity and the use of organic fertilisers requires further study, especially in view of the possible reduction such treatment may have on the soil to plant transfer of ^{237}Np and ^{244}Cm.

Investigations on the liquid phase of soil (NRPB, Chilton, 048) can give an insight into the mechanisms of transfer from soil to plants. However, analysis of bulk soil solution does not always provide sufficient information. In addition to a comprehensive chemical analysis of the soil solution, a detailed study of the speciation of the polyvalent radionuclides is needed. The ^{137}Cs-K interactions in soil

solution have been investigated with a view to using potassium addition as a countermeasure after accidental contamination of soil. However, before such a measure is contemplated on a larger scale, factors influencing the ^{137}Cs-K interactions must be better understood.

Small-scale laboratory experiments, under conditions of radionuclide equilibrium, can provide initial information for a practical evaluation of countermeasures on soil. The uptake of ^{239}Pu, ^{241}Am and ^{90}Sr to barley from three principal agricultural soil types (loam, peat and sand) decreases with time after contamination, but the uptake of ^{137}Cs can increase with time in predominantly peaty soils.

The long-term foodchain transfer of ^{129}I and its possible accumulation in the human thyroid gland was investigated (NIR, Hannover, 041). It was shown that ^{129}I can be mobilised from pasture soil by chemical conversion under temporary anaerobic soil conditions, and that this might occur when the pasture is flooded by a river. Differences in transfer were noted between stable iodine and radioactive iodine indicating that a physico-chemical equilibrium has not yet been attained in these experimental plots. However, the feed-to-milk transfer of radioiodine is the same regardless of whether the contamination originated from superficial deposition due to fallout or from root uptake by the plant.

The deposition of radionuclides on vegetation

Deposition coefficients of radionuclide particulates under turbulent conditions and at different heights over ground were determined (RWTH, Aachen, 033) both in the field and in a wind tunnel. The methods have been improved, for example, with respect to determining wind speed in grassland, ground covered by wheat, barley or maize, or in tree canopies, and a substantial amount of data has been collected. Models, together with appropriate computer programmes, have been developed to describe the deposition rate of aerosols on plants. The equations relating deposition rate to concentration of radionuclides in aerosols or in the gaseous phase also take account of wind speed and air flux and have been verified in wind tunnel experiments.

Other wind tunnel experiments (ICST, London, 032) yielded similar deposition velocities on two different crop species for caesium delivered as two aerosols of very different physico-chemical forms but of the same aerodynamic size (5μ). This indicates that size, but not physico-chemical form, determined deposition and interception of these aerosols from the atmosphere. For cabbage, the inner leaves were well protected from aerosol contamination; this might indicate that the dose, after removal of the outer leaves, would be not as large as otherwise expected.

Uptake and transfer of radionuclides in animals (except ^{99}Tc, ^{14}C and ^{3}H)

The speciation of radionuclides in plants and foodstuffs and its influence on gastrointestinal uptake were investigated (NRPB, Chilton, 048). It was observed that ^{239}Pu after injection into potatoes can be detected in potato juice as a complex of citrate and a still unidentified compound, and that no low molecular weight complexes are formed with lactoferrin or milk. The fraction of radionuclide absorbed by the intestine (f1 value) was determined for Pu, Am, Fe, Co and Nb under a variety of conditions and for several different animals, but absorption data often vary substantially due to factors which are difficult to control. It was concluded that an f1 value of about 2×10^{-4} would be appropriate for the ingestion of Np (V) and Cm (III) citrates from food by adults.

The behaviour of tritium and carbon-14

Deposition on soil and uptake into plants of tritiated hydrogen gas (HT) and tritiated water (HTO) depend on several critical factors, such as concentration in air, wind speed, time of day, rainfall, dew formation, accessibility of the soil surface, diffusion into the soil and, for HT, microbial conversion (NIR, Hannover, 041). Whereas tritiated water can be incorporated into plants from foliage as well as from roots, tritium gas is taken up by plants only after micro-biological reduction in the soil; direct uptake from foliage is minimal (CEA, Cadarache, 037). Diffusion into the soil depends on its pore volume and moisture content (NIR, Hannover, 041), and these factors are not only dependent on climate and soil characteristics but also on any disturbance of soil by agricultural practices. At a low moisture content, the

micro-biological activity responsible for the conversion of HT to HTO and to some Organically Bound Tritium (OBT) is reduced, and the deposition rate is small; while at a high moisture content, deposition is limited by the rate of diffusion of HT and O_2 into soil and not by the process of reduction of HT. The soil type also influences deposition velocity as revealed by in-field release tests in France and Canada where deposition in various soil types was measured. Microbial activity and rate of deposition are also reduced when the soil is disturbed, e.g. by agricultural practices. Tritiated hydrogen diffuses more readily into soil than tritiated water, reaches deeper soil layers, is more readily converted and, therefore, more readily available to plant roots. Soils which have homogeneous pore volumes and HT oxidising ability display an exponential decrease of HTO activity with depth. On the other hand, deposited HT that has been partially transformed into HTO can be re-emitted into the atmosphere. This reemission is influenced by vegetation cover, being higher from bare than from plant-covered soil. These processes would have to be considered in the assessment of the impact of accidental releases of tritium.

Other potential tritium sources, such as CH_3T or formaldehyde, were also investigated with respect to assimilation by plants (CEA, Cadarache, 037). Very little CH_3T is assimilated (deposition rate $< 10^{-6}$ m/s). Formaldehyde, labelled with ^{14}C, was incorporated into amino acids, membrane proteins and organic acids after a few hours of exposure. A method has been tested to measure tritiated formaldehyde released from nuclear installations.

The deposition rate of HT in peas, maize and sunflower kept in plots covered during exposure (CEN, Mol, 040; CEA, Cadarache, 037) was found to vary between 0.5 and 1.10^{-6} m/s. Studies in vitro indicate that the epidermis of potato tubers exposed to HT can apparently convert some HT to HTO which then diffuses into the tuber.

In order to estimate the risks of tritium to man, the metabolism and retention of HTO and OBT in monogastric and polygastric animals (pigs and rats; minigoats and cows) was investigated during pregancy, lactation and in adult animals (CEN, Mol, 040; Agricult. Univ. Wageningen, 051). While adequate data were available on the metabolism of tritiated water, doubts existed as to the long-term risks posed by OBT especially when OBT is incorporated into long-lived structures laid down during

pregnancy or infancy. In order to study these aspects, OBT contained in hay was fed to minigoats and OBT contained in milk powder and potatoes was fed to pigs during most of the pregnancy and/or during lactation. As may be expected, more OBT is found in the organism after feeding OBT than after giving tritiated water. The largest fraction of OBT is replaced about as rapidly as tritiated water, but some OBT is retained for very long periods of time, especially when it is laid down during lactation or pregnancy and, particularly, in tissues such as brain and connective tissues. Nevetherless, it is expected that these tissues are not at risk because much of the long-lived tritium would be present in extra-cellular sites. Studies on the distribution of tissue activity after feeding with a diet composed of different forms of OBT indicate that lipids undergo the smallest metabolic dilution of activity in the body, whereas amino acids, carbohydrates and their intermediate metabolic products are much more diluted. The results of these studies are not only of interest when assessing the risks of tritium but also help in understanding some aspects of animal nutrition and metabolism.

Large variations in specific activities of ^{14}C were observed in different crops and vegetation around nuclear installations (ANS, Epsom, 194). These could be attributable to differences in plant growth and development relative to the discontinuous patterns of ^{14}C discharges. Thus, a low specific activity was found in common grass, Poa commune (which obtains the majority of its nutrients from the atmosphere) compared to a reed, Juncus effusus, (which has a very well developed rhizome system and much arenchyma tissue). Experimental exposure of pasture grass, Lollium perenne, to ^{14}C bicarbonate solutions indicated that uptake occurs by the roots and, from there, activity is transferred into shoots.

The behaviour of technetium in terrestrial environments

Technetium was given much attention in the Programme because it represents a significant component of discharges to the environment during enrichment and fuel processing and was thought to be relatively readily transferred between various environmental compartments. There was also some concern that chemical toxicity would have to be taken into account. Investigations dealt with the behaviour of Tc in soil, plants and animals and the transfer between these compartments.

Technetium has the property that it is readily reduced from the pertechnetate, the form in which it is usually discharged into environment.

Redox processes, therefore, play a particularly important part in long-term Tc behaviour in soil since plants can only take up pertechnetate. However, after uptake, the pertechnetate can again be reduced in the plant. Reduction processes in soil occur mainly as a result of the intervention of soil micro-organisms. The general chemical aspects of these reactions are now rather well known but the mechanisms involved in microbiological actions and the binding to soil constituents are still insufficiently understood. Studies to characterise the different types of micro-organisms involved and to determine their presence in different soils and under different climatic or agricultural conditions have not yet met with much success.

Investigations in the laboratory (KUL, Leuven, 035) demonstrated that technetium, introduced as TcO_4^- into soils or sediments, becomes more and more insoluble when reducing conditions prevail. The principal results of this research showed that:

- the reductive immobilisation of Tc occurs rapidly within a few days provided redox conditions are adequate;
- micro-organisms act essentially in an indirect way generating the reducing environment (UCL, Louvain-la-Neuve, 042);
- most technetium gives complexes with humic acid;
- the reductive formation of complexes proceeds at a significantly higher rate than the re-oxidation process;
- technetium, once bound in a reduced form, is strongly immobilised and does not exchange readily with other immobilised technetium.

With regard to the long-term availability of technetium for transfer into plants it was found (RIVM, Bilthoven, 036) that:

- uptake, translocation and incorporation of TcO_4^- in plants proceeds via (pseudo) first-order kinetics dependent on the age of the contamination; uptake is reduced when nitrate concentrations are high. These observations in soil correspond to those made in simple nutrient solutions;
- TcO_4^- can be reduced in plants, most probably via the photosynthetic electron transport chain, resulting in complexes which depend on the species and state of growth of the plant.

Starting from these results, a mathematical model was developed describing transfer on the basis of measurable chemical characteristics of the soil and the physiology of the plant.

Forest trees accumulate Tc more readily from mineral than organic soil (UCL, Louvain-la-Neuve, 042), and this activity shows up first in young needles. It was also noted that technetium sprayed on leaves is retained in their waxy coating.

Uptake, metabolism and toxicity of technetium in animals were studied (CEN, Mol, 040). The redox potential and the possibility for technetium to bind to food differ among poly- and mono-gastric animals. Sheep and rats were fed either TcO_4^- or Tc incorporated into plants (labelled as ^{95m}Tc and in some cases ^{99}Tc). Mono-gastric rats showed a greater absorption of Tc than poly-gastric sheep, and pure pertechnetate was better absorbed than technetium incorporated into plants. These data also indicate that pertechnetate is the form of technetium which is absorbed by animals. Changes in organ content, with time, after injection of pertechnetate indicated that most technetium has a relatively short half-life in the body, and that the highest concentrations occur in the thyroid. Nevertheless, a significant amount of technetium can be retained for longer periods of time. Relatively high activities were also found in the hair of sheep suggesting that this material may be used as a readily available indicator for exposure. A comparison of the behaviour of injected and ingested technetium enabled quantitative estimates of technetium absorption to be made.

The same contract also investigated the toxicity of technetium in long-term feeding experiments with $^{99}TcO_4^-$ with respect to reproduction and effects on the thyroid.

Very high concentrations of ^{99}Tc (10 $\mu g/g$ food or even 50 $\mu g/g$ food) were required to reduce reproduction, cause intra-uterine death or result in changes in thyroid hormones or thyroid pathology of rats. Animals on a low iodine diet showed some, although not very striking, increases in toxicity of ^{99}Tc. A long-term feeding experiment in which the thyroid was stimulated with amino-aza triazol did not yield a significant increase in benign or malign tumours.

In conclusion, technetium does not seem to be very toxic to mammals, and its concentrations in the environment are unlikely ever to reach toxic levels. The transfer of Tc is governed by redox cycles in all compartments, and TcO_4^- is the compound transferred to plants or animals. These results are of interest not only

with respect to the behaviour of technetium but also to the behaviour of other similar radio-elements whose transfer behaviour is strongly influenced by their valency state.

The effect of countermeasures

Prior to the accident at Chernobyl, countermeasures to reduce radioactive contamination were mostly considered from laboratory and experimental aspects and less so from the point of view of their practical application. Various studies mentioned above on lysimeters or in small plots dealing with soil plant transfer provided the scientific basis for countermeasures, and several possible means to reduce soil contamination or impede uptake by plants were considered and tested with lysimeters under laboratory conditions. Attention was paid to soil amendment with fertiliser, the addition of potassium to reduce caesium uptake, the application of organic matter, and ploughing the activity below the root zone (RIVM, Bilthoven, 036; CEA, Cadarache, 037). Following the Chernobyl accident, countermeasures with respect to agricultural contamination in the near, intermediate and far field of an accident came to the forefront, and the RESSAC project (Rehabilitation des Sols et des Surfaces après un Accident) was initiated at Cadarache. This project, originally conceived for the near field only, is now being extended to a Community scale as EURO-RESSAC and to cover countermeasures in the intermediate and far field.

Some more specific topics studied by the CEA and RIVM groups indicating the problems that may be encountered are worth mentioning. When stable isotopes of caesium and cobalt were added to soil contaminated with ^{137}Cs and ^{60}Co, uptake of these elements by plants increased rather than decreased. A reduction in uptake was obtained when the contamination was ploughed into deeper soil strata or when organic matter was added to the soil. However, enormous amounts of organic matter were needed to obtain a significant effect. These results emphasise the need for caution in taking such measures and also the need for more research to ensure that such measures have the intended effect.

Countermeasures in the agricultural environment after an accident can have a substantial economic and social impact. Consequently, they must have a sound scientific basis supported by appropriate research and practical tests regarding their practical implementation and, where appropriate, the disposal of generated waste.

The behaviour of radionuclides in semi-natural environments

Semi-natural environments, i.e. those used only occasionally or partially for human food production, came under the spotlight when, as a consequence of the widespread contamination following the Chernobyl accident, certain areas being used only as pasture for sheep, etc, displayed a high level of transfer of radioactivity into the food chain. This stimulated several investigations into the transfer processes in these areas, particularly with respect to caesium but also for actinides since some semi-natural environment pastures exist in the vicinity of nuclear installations.

Long-lived radionuclides were studied in a Mediterranean region (NRCPS, Athens, 293), and transfer parameters of ^{137}Cs, ^{85}Sr and ^{141}Ce were obtained for six typical plant species and in several different types of soil, including loam and soils with different organic content and pH values ranging between 5.2 and 8.0. The data, roughly corresponding to information gathered from other areas, extend their applicability to areas not yet studied thoroughly.

Actinides were studied in soils of different organic content and found to be bound to soil particles and the humic and fulvic acid fractions. These humic and fulvic acid fractions were isolated and shown to have much higher specific activities than the soil in general (ITE, Merlewood, 023), e.g. 4 to 5 times greater for the activity per g of the humic acid fraction. Each of the humic or fulvic acid fractions was further separated into a high and low molecular weight fraction. Pu and Am are not distributed uniformly throughout these fractions; the plutonium content was highest in the high molecular fractions. The characterisation of the organic fractions and the associated activity require further study.

The ^{137}Cs deposited from the Chernobyl accident is retained and recycled in peat moorland ecosystems, (Univ. Aberdeen, 318) in the Scottish highlands and the Greek basin peats. It appears that the clay component of the mineral fraction of the Greek

peats is responsible for the retention profile. Ammonium, derived from animal excreta and from bio-degradation of organic matter caused by freezing and thawing, competes with caesium for binding sites, but the density of plant roots and soil microbial activity also influences the re-cycling rate of caesium.

Radioactivity in Irish soils, studied after the Chernobyl accident, (NEB, Dublin, 218) displays very slow migration in the soils of the areas investigated. The lower the pH value of the soil, the greater the transfer factors to agricultural produce. It was also found that caesium from the Chernobyl accident behaved in the same way as that already present from weapons-test fallout. The relatively rapid transfer of caesium in these soils can be attributed to the high organic content of the peat soil and/or to the absence of clay minerals binding the caesium.

Transfer of caesium in good quality, undisturbed agricultural soil is very slow (Univ. Dublin, 043), and the ratio of activity in crops to activity in soil is small. As mentioned above, the situation is different in upland areas with poor soil where caesium is readily available for transfer to heather and other plants and from these to grazing sheep. Significant caesium activities in sheep meat may thus be expected for several years.

b) Aquatic Environment

Field studies

Inventories have been compiled of radionuclides in large areas of the European seas and oceans. The movement of radioactivity has also been used to obtain important and unique oceanographic information on currents and transport in deeper waters and on the sedimentation of pollutants, e.g. from data obtained on technetium at Risø, Roskilde (030). Although technetium released from the reprocessing plants at La Hague and Sellafield is considerably diluted, it can still be detected in the English Channel, the Arctic Sea and the Baltic Sea indicating the corresponding movement of water currents. Routine samples were collected during 8 major cruises and the levels of ^{99}Tc, ^{137}Cs and ^{90}Sr determined. After the Chernobyl accident, ^{99}Tc proved to be the most useful indicator whereas caesium activities released from the reprocessing plants were confounded with those originating from the accident

fallout. These studies demonstrated that ^{90}Sr originated mainly from fallout of weapons-tests, ^{137}Cs was derived from fallout of both bomb tests and the Chernobyl accident, and ^{99}Tc came only from the reprocessing plants.

Plutonium distribution in sediments of coastal waters and in deep sea was investigated (ENEA, Santa Teresa (034). Deep-sea sediments were sampled during cruises in the context of other important international programmes investigating different sedimentary situations (abyssal hills, abyssal plains and fault areas). In this way, an inventory of plutonium content in sediment cores could be obtained. Plutonium is removed from seawater mainly by binding to the Fe and Mn coating of inorganic and organic suspended particles. There are few such particles in the open sea, most are faecal pellets from zooplankton, and these settle slowly: deep-water sediments, therefore, contain little plutonium. Conversely, shallow water contains many such particles, from land runoff among other things, and bottom sediments are readily resuspended due to currents and biological mobilisation. These factors result in a rapid removal of plutonium from coastal water into sediments.

The vertical distribution of $^{239+240}Pu$ in deep-sea sediments was used to describe the mixing phenomena at the sediment-water interface. In general, the concentration of these radionuclides is greatest near the surface of the sediment and decreases rapidly with depth. Radionuclides penetrate the deep sediment layers extremely slowly and by pore water diffusion only. Since plutonium was introduced into the atmosphere by weapons-tests, the time has been too short to cause significant sediment deposition; any activity in the lower strata of deep-sea sediments must, therefore, have been derived from the mixing of particles. Diffusion models have been used to calculate this mixing layer. Simultaneous determination of ^{14}C in the sediment strata confirmed that sedimentation rate in deep sea has been essentially uniform during the past ten thousand years.

Radionuclide measurements (NIOZ, Den Burg, 199) at and near a deep-sea dumping site for radioactive waste revealed that radionuclides in the bottom sediments were confined to the immediate neighbourhood of the site, probably due to ruptured waste containers. Rather high plutonium activities were found in the gut content of sea

cucumbers living on these sediments although only traces of plutonium could be detected in the sea water near the site.

The behaviour of long-lived radionuclides

The investigation of the estuarine and lagoon environments in the Friuli-Venezia Giulia region (ENEA, Rome, 034) represents part of a larger radioecological investigation which aims to improve the knowledge of the dynamics of radionuclides in natural environments. Particular attention was paid to the transport of radioactive material into the lagoon by rivers and also the influence of hydrological parameters and the role of benthic organisms on sediment deposition and redistribution. The radioactive contamination in the lagoon is present mainly in the form of suspended particles and is derived from material originating from the land either carried directly into the lagoon or transported into it by currents from the estuaries of the Tagliamento and Isonzo rivers which flow directly into the sea. In addition, detritus, carried by the Cormor river and the "litoranea veneta" channel, to which radioactive material can become attached also accumulates in the lagoon. These data enabled the different pathways of contamination of the lagoon to be better understood.

Neptunium in marine ecosystems is present mainly as Np (V) (CEA, Cadarache, 037), in contrast to americium which is present in the trivalent form. Plutonium can be detected as Pu (III, IV, V or VI) with Pu (V) being dominant. Neptunium is fixed to sediments, but with a lower distribution coefficient K_D than Pu and Am, and it also has a lower bioavailability. Its transfer into sea perch was also investigated.

The role of sediment surfaces, especially those coated with organic material (organoliths), and surfaces of marine animals (mussels) in binding actinides and thus providing a pathway to the human foodchain, was investigated (NERC, Plymouth, 038). K_D values were obtained for a wide variety of materials and for conditions relevant to open oceans and lakes. Uranium and polonium were studied in addition to actinides. A particularly surprising finding was that mussels, placed in water of low mineral content, accumulate radioactivity in the soft tissue because some of the radionuclides in the shell are rendered soluble under these conditions.

The benthic fauna, suspended particles and sedimentation rate were studied in the area of the Vera Gulf (CIEMAT, Madrid, 195) in order to provide parameters for predicting transfer of radioactivity to sediments. Shallow regions, due to their bio-geochemical characteristics, show the highest capacity to concentrate radionuclides in the sediments. Radionuclide concentrations (^{239}Pu, ^{241}Am, ^{137}Cs) decrease as the depth of the water increases; the concentrations were also found to increase towards the south of the estuary of the Almanzora river due to certain currents. However, the concentrations decrease in other areas along the coast as the radionuclides bound to the particulate matter are deposited in the sediments.

The formation of aerosols carrying radioactive material from the sea surface into the atmosphere was investigated (CEA, Cherbourg, 037). Monodisperse particles coated with a protein film were produced as aerosols, and studies on how radioactivity dispersed from bursting air/sea bubbles (artifical sea spray) becomes attached to these aerosols were conducted. During this process, the radionuclide concentration activity is enriched compared with that in the water, most markedly for americium and less so for cobalt. This difference is due to the fact that americium, because of its insolubility, is almost entirely absorbed into the particles whereas cobalt is more soluble.

The exchange of radioactive material between the sea and the atmosphere was also investigated (UKAEA, Harwell, 044) using a bubble-burst aerosol sampler in a wind tunnel. It was found that the concentration of sea spray depends mostly on wind speed, that aerosols are enriched with inorganic constituents of sea water and that an important fraction of the aerosols is represented by particles with an aerodynamic diameter greater than 50 μm. However, the aerosols become depleted of large particles with increasing distance from the source, and their concentration is about two orders of magnitude lower at a distance of 200 m than at a distance of 13 m. Seasonal variations exist with respect to the enrichment of Pu and Am in the aerosols, and this seems to be due, in part, to differences in the surfactant activity of the sea and the number of inorganic particles present in the surf zone. The transfer of such aerosols inland can contribute to actinide contamination of coastal areas.

The transfer of americium and curium in fresh and saline water crustacea (gammarus and artemia) and fish kept in aquaria and the influence of bacteria were investigated (SCK, Mol, 050). Sediments for the aquaria were taken from different areas containing different amounts of sand, clay and silt. Uptake of the actinides in crustacea is high and dependent on sediment composition and the presence of bacteria. Bacterial intervention is most effective when clay or silt sediments are present. Transfer also depends on the pore size through which the water was filtered. The data illustrate the difficulties encountered in obtaining reproducible quantitative data on transfer in aquatic environments which can be extrapolated to in-field conditions.

The uptake of technetium was investigated in marine organisms (brown algae and molluscs) occurring on the Belgian coast (IRSNB, Brussels, 009). Most Tc in aerated seawater is present as pertechnetate but this can be reduced and immobilised, mainly in sediments under the influence of chemical and biological processes. The situation thus resembles that encountered with respect to Tc in soil and plants. Most of the transfer, especially that in fish, occurs directly from water, with sediments playing only a minor role. However, the technetium taken up by the organisms then undergoes various reduction reactions followed by binding to polysaccharides and proteins. A substantial part of the effort of the contract was devoted to the characterisation of the products to which Tc is associated. Similar studies, with emphasis on lobster cell proteins, were carried out at the Univ. Nantes (047). These studies of characterising technetium have neglected to define more accurately the valency state of the Tc {(IV) or (V)} in the organism.

The in-field research on long-lived radionuclides (ENEA, Santa Teresa, 034) was supplemented by laboratory investigations focusing on the behaviour of Tc and Se in the marine environment. Both these elements display a high affinity to anoxic sediments, selenium even more so than technetium. Natural ligands containing sulpho-amino acids, play a major role in reducing and binding Tc in organisms. Polychaeta worms living in sediments can remobilise a substantial part of the Tc but a large population of worms would be needed to make this pathway significant in practice. Benthic fish could receive Tc from worms, but the most edible parts of the fish would remain uncontaminated.

Radioecology of continental waters

The investigations undertaken in this area dealt with in-field studies on the transport of radionuclides in rivers, the determination of transfer through trophic food chains, the characterisation of the physico-chemical behaviour in freshwater environments and different approaches to model the behaviour of radionuclides in rivers. Each river has unique properties with respect to physical, chemical and biological transport mechanisms which, furthermore, depend on the season. It is, therefore, difficult, if not impossible, to establish general rules and quantitative models valid for all situations. Nevertheless, by concentrating on certain rivers, particularly the Rhône, the Tejo and the Meuse, and by selecting some of the critical parameters, considerable progress has been made in the understanding of the different factors involved. Further studies must improve the definition of the degree of uncertainty of these parameters, and the models on which they are based, must be used to investigate in more detail some of the critical mechanisms of transport and evaluate the conditions under which information from one river ecosystem can be extrapolated to another.

On the basis of data from three measurement stations along the Tejo river, several important radioecological parameters where obtained (LNETI, Lisbon, 198), in particular, composition of sediments, ionic (potassium) content, and composition of phyto- and zoo-plankton (mainly bacillarophyraceae and cladocera) respectively.

Experimental studies were made of the transfer of man-made radionuclides in a fresh water trophic chain and sediments (CEA, Cadarache, 037). Transfer via water was found to be a more important pathway than transfer via food. Bio-accumulation in the trophic chain is avoided due to high excretion rates. K_D values seem to depend on sediment concentration, and this indicates the need for a more fundamental study.

Modelling of river systems

Hydrodynamic modelling of the Meuse and the Rhône rivers (CEN, Mol, 040; CEA, Cadarache, 037) has been undertaken to simulate river flow, velocity and water levels, and to correlate these parameters with radioactive and other releases.

Radioactive contamination of the Rhône basin originates from different sources, including atmospheric fallout, nuclear power plants, reprocessing and the Chernobyl accident. In addition, one must also consider the many releases of chemical or household waste which influence physico-chemical properties, fauna and the content of particulate material in these rivers. A model was elaborated consisting of four levels:

- a hydro-dynamic sub-model that represents and computes for any time and any location the flows, water heights, river cross-sections and bottom pressure;
- a sediment sub-model that calculates concentrations of solids suspended in the water column and deposited sediment;
- a radionuclide sub-model assessing transport and distribution in water, sediments and suspended matter;
- a radioecological sub-model describing the food chain transfer and computing the amounts of radionuclides incorporated into the various biological compartments as well as the fluxes between those compartments.

The research at the CEA, Cadarache (037) also dealt with measurements of radioactive material and some basic laboratory studies. For example, an increased concentration of radiocaesium as well as ^{110m}Ag, ^{103}Ru and ^{106}Ru was noticed near the discharge areas of nuclear power stations, and the concentration of the latter isotopes seemed to increase over the years. Observations on mussels showed that such organisms can act as filters for radionuclides and promote the transfer to bottom sediments. The transfer of ^{60}Co through algae and crustacea was also investigated, and another group from the CEA investigated the transfer of Ra from an old mining site to nearby aquatic ecosystems.

Conclusions

A wide variety of problems of relevance for the behaviour and transfer of radionuclides in the environment and for their control were investigated in this sector. All the important goals of radioecology were pursued, namely, to understand the basic mechanisms of transfer, to follow the movement of radionuclides in real environments, to provide models for prediction in normal and accident situations and to develop countermeasures after an accident. These approaches concerned aquatic and terrestrial environments. Certain problems have assumed greater prominence than in the past; these are the influence of chemical, physico-chemical

and biological conversion on the behaviour of the radionuclides in all environments and the importance of some specific environments on transfer to man, e.g. semi-natural and natural environments.

Radioecology remains an important subject for future research, on the one hand to solve problems in the environment related to radionuclides and, on the other hand, to serve as a basis for the study of other pollutants. In the future, the objective must continue to be the development of a quantitative description of the processes involved based on a better scientific understanding of the underlying mechanisms.

3. Non-stochastic Effects of Ionising Radiation

Non-stochastic radiation damage arises only when the dose exceeds a certain threshold level, and its severity increases with dose. Therefore, such damage would be expected to occur only after accidental over-exposure. Effects on the developing organism may be an exception because it is not yet known whether a threshold exists for damage to the developing brain.

The Programme proposal 1985-1989 stated as its aim to investigate:

- the pathogenesis of non-stochastic effects;
- the level of threshold doses, their dependence on exposure conditions and their individual variability;
- the influence and eventual interaction of different environmental factors;
- the scientific basis for diagnosis and treatment.

The substantial reduction in funding made it necessary to concentrate efforts. Thus research into the pathogenesis and treatment of damage to the haemopoietic-immune system and, particularly, of other tissues had to be reduced whereas research into radiation protection criteria for skin was slightly increased and that into developmental effects was substantially, although still insufficiently, increased compared to the 1980-1985 Programme.

Four main topics are considered in this sector which consists of 24 contracts consisting of 32 projects; the number of projects in each area given in parenthesis:

a) Acute and chronic effects on the haemopoietic system as a consequence of accidental exposure of large parts of the body,
   - treatment of radiation accidents and the underlying pathogenetic mechanisms (10),
   - damage to the adult immune system (2),
   - biological indicators of radiation damage (2).

b) Radiation damage to skin and underlying tissues,
   - diagnosis and treatment after accidental local exposure (2),
   - radiation protection criteria for skin (3).

c) Radiation effects in other tissues (lens, thyroid, lung) (3),

d) Effects of radiation on the developing organism,
   - the cultured embryo model (2),
   - brain and haemopoietic damage (4),
   - carcinogenesis in the developing organism (2).

a) Acute and chronic effects on the haemopoietic system as a consequence of accidental exposure of large parts of the body.

Treatment of radiation accidents and underlying pathogenetic mechanisms

Accidents involving irradiation of large parts of the body, although exceedingly rare, pose serious problems for clinical management. Bone marrow transplantation, extensively studied in the Programme, should only be used as a last resort when less than virtually all bone marrow cells have been destroyed, and, under such conditions, it can be life-saving. In order to evaluate the benefits and risks and treat the patients in an optimal way, one must understand the pathogenetic mechanisms, the role and radiosensitivity of the different constituents of the immuno-haemopoietic system, the regulatory controls and the evolution of haemopoietic damage. The studies carried out in the Programme dealt with problems related to bone marrow transplantation as well as the pathogenetic mechanisms involved in the regulation of bone marrow replacement and stromal cell support.

The diagnosis of haemopoietic damage and the different means of restoration of the haemopoietic system after acute and fractionated whole or partial body exposure has been investigated in monkeys and patients at the International Centre of Radiopathology (Fontenay-aux-Roses, 065). The data pertain to a large number of biochemical and pathological observations, not only in haemopoietic tissues, but also in lung, liver, salivary glands and other tissues. They also show that the usefulness of chromosomal aberrations as indicators after inhomogeneous exposure is limited, and that increases in amylase, cortisone and ACTH are characteristic for radiation exposure but may not give quantitative information on the damage except in very specific situations. In addition, transplantation of haemopoietic stem cells from umbilical blood and the application of haemopoietic growth factors to reconstitute bone marrow after secondary insufficiency were investigated.

Residual haemopoietic injury was investigated with respect to the different haemopoietic progenitor cells and stroma following acute and chronic radiation

exposure in mouse, dog and man (Patterson. Lab., Manchester, 062). The radiosensitivity of different haemopoietic progenitor cells was also determined for different growth factors used for stimulation. Although the type of stimulation influences radiosensitivity, dog progenitor cells are, in general, more radiosensitive than those of man or mouse. A comparison between stem cell loss and bone marrow failure, based on published data, indicates that larger species are less tolerant to the depletion of stem cells than smaller ones. The stromal fibroblast forming units (CFU-F), which are probably identical to the cells forming the ossicles, represent an important factor in the micro-environment of the bone marrow. Long-term recovery was investigated with respect to stromal cells and the different stem cells, in particular, with respect to the relation between haemopoietic and stromal recovery. From this it appears that stromal recovery occurs without persistent defects after doses up to 10 Gy.

At the TNO, Rijswijk (079), methods were developed to purify large amounts of monkey and human bone marrow cells rapidly by a combination of physical (centrifugation) and biological methods (specific removal of T cells by antibodies based on the expression of antigens). Difficulties were encountered when DR (MHC) antigens were used for selection because their expression is heterogeneous; ICH3 antibodies gave better results, and later data showed an enrichment of progenitor cells by a factor of 60 to 100 with a 100 to 1000 times reduction in T cells. This was achieved with rather large amounts of bone marrow. Another important result of this contract is the cloning of the gene encoding human interleukin 3 (IL3). Human IL3 was found to be less active on monkey than on human bone marrow cells. A comparison of the cloned rhesus IL3 showed 90% homology with human IL3 although its activity spectrum differed. The rapid biochemical and functional divergence of IL3 during evolutionary development is remarkable. Stem cell replication and differentiation in culture depends on a complicated interplay of different growth factors. As it would be desirable to maintain cultures at an undifferentiated state for further transplantation, restriction of differentiation with different growth factors was studied thoroughly, but the problem has not yet been fully solved. Another aspect of this contract dealt with the conditioning of the host prior to transplantation. This development was undertaken to avoid the large,

highly toxic radiation doses (>10 Gy) otherwise needed to make a host accept mismatched marrow. Monoclonal antibodies were tested in mouse models, but so far their immunosuppressive activity, when given as a single agent, was insufficient. Methods were therefore developed to produce and purify lymphokinine to suppress the lymphocytes that cause the graft vs host reaction. Preliminary results are promising, but greater amounts of lymphokinine are needed for further work.

At the Univ. Ulm (061), the response and tolerance of the canine haemopoietic system to partial body and inhomogeneous exposure was investigated on the basis of in vitro assays of the various progenitor cells. Following a survey of the distribution of haemopoietic stem cells in different marrow sites, regeneration was investigated under different conditions of exposure. An inhomogeneous exposure allows marrow from other sites to recolonise the irradiated areas. The response is in accordance with that predicted from the distribution of progenitor cells. Thus an exposure of 30% of the marrow did not greatly affect blood granulocytes and platelets, but depression of lymphocytes was much more serious than one would have expected from the exposed body volume. This would seem to indicate that lymphocytes are not suitable for monitoring the seriousness of an accident. The repopulation of irradiated bone marrow by immigration started on day 7. The data on whole body irradiation showed a large and surprisingly long-term depression of erythroid stem cells (BFU-E); this is, therefore, the most radiosensitive cell among all haemopoietic elements investigated in different species. The data obtained were also compared with those from different radiation accidents and will help to establish an expert system to aid the management of such accident victims.

The second project in (061) concentrated on the role of stroma in supporting the haemopoietic function and employed the fibroblast colony assay (CFU-F). The distribution of CFU-F cells in different marrow areas is closely related to their haemopoietic activity; these stromal cells are about 4 times more radio-resistant than haemopoietic progenitor cells and show good recovery after split doses. In dogs exposed to inhomogeneous radiation, little difference in stroma is seen between exposed and non-exposed areas one year later. Some damage, unrelated to CFU-F cells, seems to persist, however, as shown by the temporary appearance of local fibrosis.

A third project in the same contract investigated the pathogenetic mechanisms of myeloid leukaemia in dogs and mice comparing, among other things, the action of benzene with that of radiation.

When a bone marrow transplantation is required, it is crucial to assess the suitability of a donor rapidly (Univ. Dublin, 309). Thus, it would be useful to have available new sensitive methods for assessing rapidly and reliably whether graft cells are present in blood and marrow. Besides exploiting the presence of specific sex chromosomes by cytogenetics, a distinction between graft and host cells could be made, for example, by probes detecting differences in DNA either by measuring restriction fragment polymorphism or the variable length of tandem repeating blocks. Specific DNA regions were primed with oligonucleotides for subsequent copying with DNA polymerase and more especially to analyse sex mismatch by amplifying chromosome Y specific sequences or, for sex matched transplants, tandem repetitive blocks. The method has been assessed successfully in 20 patients.

As a general conclusion it can be stated: European research in the area of the pathogenesis of the haemopoietic syndrome after irradiation and its treatment has attained a very high degree of expertise. In the future, it will be crucial to maintain this expertise by providing opportunities and stimulation for further advanced research, by developing expert systems and by training young scientists and physicians. This is certainly an area where the spin-off from research from radiation protection to clinical medicine will remain substantial.

Damage to the adult immune system

The understanding of the complexity of the cellular and humeral immunological reactions as well as their interplay has made marked progress in recent years. This has largely benefited, and has even been promoted by, immunological studies on irradiated animals.

T helper (Th) cells play an important role in the modulation of the immune response because they express specific receptors and secrete lymphokinines activating antibody production in B cells. These helper cells are very radiosensitive (ENEA, Rome 059) and show significant defects and reduction in interleukin-2 production

6 months after exposure to 4 Gy. Synthetic alpha thymosine enhances IL2 production and IL2R expression by accelerating maturation of T cell precursors or by expanding the T cell population. Accordingly, thymosine and other thymic hormones might be useful in the treatment of immunodeficiency in irradiated animals and man. However, IL1 has inflammatory effects, and therefore, a synthetic nona-peptide fragment was produced and tested. This showed good immuno-restorative activity without the side effects mentioned. The marked changes in immune response during ageing are paralleled by a two to three fold increase in radiosensitivity of Th cells. This indicates the need for more extensive studies on radiation and immune response in the aged.

B lymphocytes are either re-circulating, situated in the follicular zones of the spleen, expressing IgM and IgD receptors and dependent on the thymus, or non-circulating, situated in the marginal zone of the spleen, expressing IgM only and independent of the thymus (UCL, Brussels, 187). A single acute exposure as well as chronic exposure caused a noticeable reduction of B cells, especially in the marginal zone of the spleen. On the other hand, the spleen displayed constant levels of IgM plasma cells accompanied by a marked increase in IgA plasma cells after exposure to 5 Gy, and this was accompanied by fluctuations in blood levels of IgM and IgG serum levels. When lymphocytes, which had been isolated from the spleen or mesenteric lymphnodes, were transplanted into 5 Gy irradiated rats, circulating follicular cells were rapidly restored, whereas the non-circulating marginal cells took longer, especially when the graft was taken from lymphnodes.

Biological indicators of radiation damage

In the case of accidental overexposure, the doses and their distribution in the body are usually not well known. Information on the degree of severity of the radiation insult is, however, indispensable as a guide to therapy and for making predictions as to the outcome. The determination of chromosome aberrations in cultured circulating lymphocytes appears to be the method of choice for this purpose if the dose distribution is not too inhomogeneous; it also enables low level chronic exposure to all clastogenic (chromosome-breaking agents), including radiation, to be detected. However, the technique is cumbersome and slow, requiring experienced

personnel. Therefore, the search for more rapid and specific indicators of radiation damage has continued.

Flow cytometry of the chromosomes might allow a large number of cells to be analysed rapidly and reliably (CEA, Fontenay-aux-Roses, 073). Flow cytometry was used to detect chromosomal changes either directly or after labelling of the centromeres with specific antibodies. In addition, membrane alterations were investigated by means of fluorescent lectin or antibody probes. It appears that direct detection would be suitable only for some specific chromosome abnormalities: thus a recurrent break point (t11;22) was mapped, and attempts were made to detect oncogenes by enzymatic amplification of sorted chromosomes. The use of anti-kinetochore antibodies from scleroderma patients suffering from the CREST syndrome indicated some staining of centromeres but the specificity so far was insufficient to make this method useful for the detection of dicentric aberrations. Studies on human and rat blood samples using labelling of the membranes with fluorescein isothiocyanate followed by flow cytometry were unsuccessful in detecting radiation-induced changes due to the high inter-individual variability.

A variety of potential indicators of radiation damage was investigated in the blood of radiotherapy patients (BGA, Neuherberg, 066). The binding capacity to lectins of human platelet, leucocytes and erythrocytes was increased after in vitro exposure to 0.5-5 Gy. Rather small doses had an effect, but increasing the dose further did not raise the binding capacity any more. The variability of the binding capacity was, moreover, substantial after in vivo exposure and no clear pattern emerged. An increase in serum amylase, released when salivary glands are irradiated, has been reported in the literature, and this was confirmed in the present study. However, the variability, even at the same dose, was such that only the fact that irradiation had taken place, but not its dose, could be ascertained. A similar variability was observed with respect to the increase in the electrophoretic mobility of erythrocytes after irradiation. Flow cytometry in conjunction with specific antibodies was used to investigate shifts among subpopulations of lymphocytes, and the results were compared with the rosette technique. Both correlated well, but data on irradiated blood is not yet available.

In conclusion, it may be stated that, while the need for reliable and sensitive indicators of radiation damage after exposure to large parts of the body remains urgent, no methods other than chromosomal aberrations seem at present more than a remote possibility.

b) Radiation damage to skin and underlying tissues

Diagnosis and treatment after accidental local exposure

Clinical symptoms after accidental over-exposure were classified according to information accumulated from patients over a period of 30 years (Centre International Radiopathology, Fontenay-aux-Roses, 065). The early pathological evolution largely determines the late consequences, and its appraisal is, therefore, crucial for an optimal management. Several physiological changes which precede other clinical symptoms, particularly blood flow, have been investigated in this contract with particular emphasis on the situation encountered after accidental exposure of the hand. Infrared thermography shows significant hyperthermia shortly after irradiation; the isothermal curves delineate the irradiated area well, and, together with the thermic gradient estimated from a comparison with the corresponding symmetrical non irradiated area, yield an indication of the seriousness of the exposure. Computerised dynamic and static scintigraphic imaging and capillaroscopy also supply useful information which can be evaluated by multi-parametric analysis. Conservative treatment adapted to the particular situation has been developed, and the indications and modalities of surgical interventions removing ulcerations and potential or actual necrotic tissues have been defined. Future work will have to concentrate on the elaboration of protocols which, based on a spectrum of objective clinical and paraclinical criteria, will depend less on the unique experience of the physician in charge of the patient than is the case at present.

As a complement to the investigations in patients, studies on pig skin (CEA, Jouy-en-Josas, 058) have concentrated on the analysis of different modern methods to assess physiology, cytogenetics and biochemistry of the irradiated skin. Microwave thermography (at 3 GHz) has enabled the early detection of profound lesions,

whereas X-ray computed tomography and nuclear magnetic resonance imaging has enabled oedema to be visualised before becoming clinically apparent. The early inflammatory reaction could be visualised by gamma scintigraphy following injection of a ^{201}TlCl or ^{99m}Tc labelled glyco-lipo-peptide. The latter test indicates the infiltration by macrophages into the necrotic tissue. Biochemical studies of serum proteins showed distinct differences between animals exposed to high or intermediate doses. The use of these methods should allow discrimination between ulcers and deep muscle damage which require surgery and those which do not. The threshold for muscle necrosis was found to be about 30-40 Gy and that for delayed fibrosis 10-20 Gy. Investigations of the pathogenesis of fibrosis suggest that degradation products of the cellular matrix could regulate the fibrotic process.

Overexposure of the skin and underlying tissues represents the most frequent radiation accident; it is important, therefore, that further efforts be made to develop diagnosis and treatment. This will not only benefit such accident victims but also patients who have undergone radiation therapy and will help to treat skin exposed to heat and caustic agents.

Radiation protection criteria for skin

Skin (and lens) are the only tissues for which radiation protection takes account of the non-stochastic rather than the stochastic effects but, in the case of skin, this also depends on the size of the exposed area and the penetration of the radiation. Three contracts (St. Bart's. Hosp. London, 057; Univ. Oxford, 063; BNL, Berkeley, 082) co-operated in a study of the non-stochastic and stochastic effects
following exposure from non-uniformly or uniformly distributed alpha and beta radiation sources of different sizes. The studies were carried out on mice and pigs.

At St. Bart's. Hospital London (057) **stochastic** skin cancer was studied after uniform and non-uniform (8 or 32 point) beta exposure of mouse skin (^{170}Th, 0.97 MeV). The dose effect relationship for uniform exposure in SAS-4 mice showed a nearly linear increase to approximately 65% tumours at 100 Gy and saturation at higher doses. When the same dose was concentrated on 32 points distributed over the same surface area, the carcinogenic response was somewhat less, with saturation

occurring at 150 Gy; exposure over 8 points showed only small carcinogenic potential. Differences in the behaviour of different mouse strains were also noted, with the CD1 strain having the highest incidence of radiation-induced skin tumours. In C57Bl/6 mice, a threshold for skin tumours seems to exist. Consequently, albino mouse strains appear to be more susceptible to skin cancer, a behaviour similar to that observed for human UV-induced melanoma. Alpha irradiation (^{244}Cm) which penetrates only about 30 μ into skin did not elicit any tumours. **Non-stochastic** effects (desquamation and ulceration) were investigated in SAS-4 mice after exposure to $^{90}Sr/^{90}Y$, ^{170}Th and ^{147}Pm with E max of 2.27, 0.97 and 0.23 MeV respectively. Moist desquamation showed a marked dependency on the exposed area and the beta energy. The Pm only caused moist desquamation at doses of 100 Gy and then without ulceration. The area effect was most pronounced with the more penetrating beta radiation with threshold doses ranging from 140 gy for 1 mm ^{90}Sr sources to 10 Gy for sources of 22.5 mm diameter. Alpha radiation did not cause any moist desquamation even at the highest doses and with the largest sources. The effects of area and energy are best explained by assuming that moist desquamative lesions heal by migration of cells and by division of basal cells situated either at the periphery, in the basal layer or in hair follicles of the irradiated field.

A detailed analysis of the reaction of pig skin to beta and alpha emitters was carried out at the Univ. Oxford (063). Following early transient erythema, the main erythematous reaction develops after 3-6 weeks with a time course and severity dependent on dose and area involved. It could be shown that the target population is the epidermal basal cells and that the appearance of damage and its repair can be readily explained on the basis of cell cycle and radiosensitivity parameters. An interesting observation is that regeneration can start from groups of basal cells associated with hair follicles, and this seems to be largely responsible for the different effects of non-uniform exposure. Late oedema, characterised by a mauve coloration, impaired lymph flow at 9-12 weeks after exposure and appears to be related to damage to deep dermal vessels. This localisation would also explain the relative efficiency of different penetrating beta rays. The pathogenesis of late skin atrophy remains uncertain; it may be associated with a degeneration of muscle cells and arterioles but seems unrelated to a loss of fibroblasts. Studies to simulate the

effects of "hot particles" with highly concentrated ^{90}Sr or ^{170}Th exposure yield acute ulceration within 2 weeks leaving a scar after healing.

The investigations carried out by BNL, Berkeley (082) contributed to the dosimetry of the sources employed and also led to a number of conclusions for radiation protection based on the experimental data. Thus, the lifetime chronic uniform dose to skin should not exceed 40 Gy if late detrimental cosmetic effects due to chronic dermal exposure are to be prevented. Present ICRP limits (20 Gy) would thus include a sufficient safety margin. This dose value is lower than that calculated for intolerable risks of skin cancer (100 Gy). The acute average dose over 1 cm^2 from hot particles should not be higher than 1 Sv delivered in a few hours. Dose measurements for stochastic and non-stochastic damage require measurements at two depths for dermal (300-500 μ) or epidermal (20-100 μ) damage.

Radiation protection criteria for skin need further study to follow other exposure situations and to take account of forthcoming recommendations by ICRP.

c) Radiation effects in other tissues (lens, thyroid, lung)

Only three studies were carried out on tissues other than bone marrow or skin, i.e. much fewer than in past programmes, and these concentrated on the lens, the thyroid and the lung.

An epidemiological study (Health Research Board, Dublin, 176) in 165 patients who had received radiation therapy to the eye revealed cataract in 23 patients about 20 years later and with a frequency approximately five times greater than in controls. A substantial number of people also showed various pathological changes in the eye. Whereas eye pathology appears to occur independently of the radiation dose and is thus related to the underlying disease, more cataracts were seen in patients who had received more than 10 Gy than in those who had received smaller doses.

Cultured cells from dog thyroid are a useful model to study cell proliferation and differentiation as well as the action of growth factors on these parameters (ULB, Brussels, 220). Three pathways control cell proliferation but only the one acting via TSH enhances differentiation. Thyroid tumours were induced in rats by ^{131}I followed by perchlorate treatment. Selenium deficiency decreases glutathione

peroxidase (an enzyme detoxifying oxygen), causes growth retardation and increases thyroid hormone levels, but has no influence on such ^{131}I-induced tumours. Based on the experience with canine thyroid, a human thyroid cell culture was developed which can pass through up to 10 divisions and responds to different growth factors. This system will be useful for further studies. The cell kinetics of human thyroid was investigated by autoradiography and in vivo. The results show that human thyroid cells only divide about 5 times during adulthood. Oncogenes were sought for human tumours but only one was found; a technique more recently introduced could be more promising. The epidemiological follow-up of thyroid tumours in irradiated patients continues slowly and the recall rate is unsatisfactory. Another study dealing with thyroid is discussed on page 131.

Alveolar macrophages (AM), harvested by lung lavage, were studied in CBA mice lung after inhalation of $^{239}Pu\ O_2$ (UKAEA, Harwell, 074). Total AM as well as those in S phase were reduced for 2 weeks after deposition of 400 Bq. In addition, the functional capacity of such AM was investigated after exposure. Fluorescent labelled polystyrene particles (FP) inhaled following Pu contamination were also taken up by AM. The results indicated that phagocytosis is not altered, and that cells with a high Pu load tend also to absorb many FP, either because these were cells with particular phagocytic activity or because these cells were situated near preferential deposition sites. AM from Pu treated lungs contain a substantial number of nuclear abnormalities such as micronuclei detectable even after relatively small doses (0.76 Bq). Large amounts of Pu deposition (500 Bq) also affect epithelial lung cells, increasing proliferation of type II cells and causing hyperplastic changes. These results draw attention to the crucial role of AM in the handling of Pu deposited in lung. Several studies dealing with lung carcinogenesis are mentioned on page 138.

d) Effects of radiation on the developing organism

The cultured embryo model

The development in utero can be divided into the periods of pre-implantation, organogenesis and foetal development. Recent progress made with respect to the in vitro culture of mouse embryos enabled the investigation of radiation damage during

the very early stages of gestation for which no human information is available. Moreover, such cultured embryos made it possible to investigate certain important general mechanisms of cellular damage and repair

Loss of embryos occurs not only near the time of implantation but also before the first cleavage (CEN, Mol 069). This "one cell block", i.e. failure or delay to cleave at the one cell stage, occurs preferentially when one-cell embryos of an age of 5-12 hours after fertilisation (maximal sensitivity at 8 hours) are exposed to radiation. The percentage of cells blocked increases linearly with dose to 90% after 2 Gy but the block is partially reversible since a substantial percentage of cells entered division with a delay of some 20 hours only to die soon thereafter. The block is strain-dependent; it occurs readily in BALB/c mice but requires much higher doses in CF1 mice. The block does not seem to be a consequence of chromosomal damage although it is associated with it. More likely, it is related to a defect in the synthesis of specific polypeptides needed for division. Surprisingly, caffeine treatment can overcome the delay, possibly via an action on protein phosphorylation, without, however, preventing ultimate death of the embryo.

Chromosomal aberrations, micronuclei, malformations and foetal death were studied during the later phases of the pre-implantation period after exposure to X-rays, neutrons, or beta rays from tritiated thymidine or arginine (Univ. Essen, 077). The relative biological efficiency (RBE) of neutrons is in the order of 5 to 7. ^{3}H thymidine displays a maximal effect during S phase.. ^{3}H arginine is more effective than thymidine, and its action does not depend on the cell cycle. A surprising and important observation is the induction of malformations after X-ray exposure during the preimplantation period. The frequency of gastrochisis and exencephaly is increased among surviving foeti irradiated at different times during preimplantation, the most sensitive phase being soon after conception without an indication of a threshold. The RBE for neutrons is from 2 to 3. These results have great relevance for radiation protection because they indicate that radiation can damage the pre-implantation embryo to give malformed neonates and not just kill it outright as has been assumed before.

Brain and haemopoietic damage

Observations of an increased incidence of mental deficiency and a decreased intelligence quotient in children born to mothers exposed especially during the 8th-15th week of pregnancy have raised the question of whether a threshold dose exists for this effect. It appears impossible to answer this question from human data only, unless one understands the pathogenesis of this type of damage. Although animal models are still far from modelling human intelligence, new approaches based on quantitative image analysis of morphological and biochemical alterations and more refined biochemical and physiological tests have made animal models increasingly more useful.

Rats were irradiated during the principal period of cerebral organogenesis on day 15 post conception (some animals also on day 10 and 12) (SCK/CEN, Mol, 071), and the brains were analysed at different ages. Atrophy (reduction in weight) was noted after doses as small as 0.05 Gy, and microcephaly after 0.10 Gy. The size of the cortex, particularly the cingulum, is significantly reduced. Cingulum size, being the most sensitive indicator, was used to determine the RBE of neutrons of energies of 600 keV and 2.5 MeV; values found were about 2.8 and 1.6 respectively. Glia changes which were prominent after high level exposure of the adult brain seem less significant after in utero exposure; the total number or the distribution in the brain of glia cells was little altered but the cells seemed to be smaller. Biochemical investigations of a variety of neurotransmitters and their receptors were also carried out in several brain areas. It was thought that mental changes would be reflected by the activity of such neurotransmitters, but the observations did not show marked alterations. Both, increases and decreases, were observed after irradiation in utero, and the changes occurred only after relatively high doses; most of them seemed to indicate that the brain attempts to maintain its total amount of neurotransmitters and receptors even in the presence of marked atrophy. Autoradiographic investigations on receptors in different brain areas also did not indicate a major shift in tissue distribution, but it must be pointed out that all these determinations are subject to some variability.

The question of whether in utero exposure delivered at a low dose rate also damages the developing brain is of considerable importance in radiation protection (CEA, Fontenay-aux-Roses, 310). Exposure of mice or rats to low dose rates at different times of pregnancy showed only a small reduction in foetal weight and a marked reduction of relative adult brain weight dependent on dose and dose rate. The effect was the same, regardless of whether exposure was delivered during the entire pregnancy or only during the last third. The dose rate effect was noticeable for an exposure of 1 Gy, particularly on day 15, at dose rates above 4.75 Gy/day. Malformations were observed only at this dose rate.

It was observed earlier that the maturation of the haemopoietic system in infant mice is associated with an increase in radiosensitivity of the respective stem cell. This can result in a greater biological effect after fractionating an exposure during infancy, a behaviour which is the opposite normally observed and which has been seen, for low LET radiation, for only a very few endpoints (SCK/CEN, Mol, 071). A test to determine whether bone marrow irradiated during infancy or adulthood can still respond to a stimulation of the erythropoiesis by hypoxia has been carried out. Adult mice show a decrease of the reticulocyte response soon after irradiation followed by repair. On the contrary, infant mice display a noticeable high reticulocyte response early after exposure which then decreases gradually. This observation could be explained as being the result of a preferential stimulation of erythropoiesis in irradiated neonate mice, or of damage to dividing stroma cells. After an acute exposure to 2 Gy in utero or after birth, no long term changes were noted in spleen histology, total number of B and T lymphocytes or levels of specific antibodies (UCL, Brussels, 187). The analysis of T cell populations with monoclonal antibodies suggested differences in the response of females and males.

Mice contaminated with ^{241}Am were investigated on the basis of long term bone marrow cultures (CEN, Mol, 081). Both haemopoietic and stromal cells are radiosensitive and potential target cells for early and late effects after in utero contamination, but stromal cells may play a more important role in the foetus. A large percentage of the contamination occurs during lactation. The distribution of ^{241}Am in the foetus differs from that in the adult. An in vitro bone-forming system

was developed in order to define more accurately the mechanism triggering osteogenesis.

Carcinogenesis in the developing organism

Carcinogenesis in general, and liver carcinogenesis in particular, was investigated at the SCK/CEN, Mol (071) in 14 or 21 day old infant mice (a total of 5020 mice) after treatment with diethylnitrosamine (DEN), DEN in combination with X-irradiation or neutrons, or after X-irradiation or neutron irradiation alone (mean energy of the neutrons 3.1 MeV). Data, particularly on late carcinogenesis, are not yet fully available. So far it has been shown that X-irradiation does not affect liver carcinogenesis due to DEN, irrespective of whether irradiation was given prior to or after DEN. Similar results were also obtained with respect to neutron exposure.

Glial tumours (60-70%) are induced in rat brain by treatment with ethylnitrosourea (ENU) during pregnancy, and this can be reduced by prenatal X-irradiation in a dose-dependent manner (GSF, Neuherberg, 068). Radiation exposure alone alters the cytoplasmic membranes of the neuroglioblasts as shown by the affinity to a lectin. Therefore, the role of lectins in controlling the growth of ENU-transformed glia cells in the brain and in vitro was studied. Wheatgerm agglutinin increased brain tumour response to ENU, probably because of its antagonistic action on the nerve growth factor. In vitro growth of glia cells was also repressed by concanavaline. Transplantations made from a glioma cell line did not take after prenatal X-irradiation whereas they grew rapidly and killed the animal within 6 days in controls, thus confirming the growth depression caused by radiation. From studies with opiate receptors it appears that a greater density of these receptors is correlated with the suppression of proliferation in perinatal brain.

Several recent reports in scientific journals and the media claiming increased cancer incidence in children following exposure of the fathers, or after exposure during intra-uterine development or in infancy emphasise the fact that radiation protection of the developing organism remains a high priority subject. Current animal models for brain damage and for cancer are only partially satisfactory, and it will only be

through a patient search for the mechanisms of action that answers to these urgent problems can be given.

4. Radiation Carcinogenesis

Causation of malignant tumours represents the problem of greatest concern in radiation protection of workers and the public since such stochastic effects may arise at low doses without a threshold at full severity as a consequence of genetic alterations in a single cell. The progeny of such transformed cells can then divide to form the tumour or, in the case of genetic damage in germ cells, be transmitted to the child. Radiation exposure from natural, medical or industrial sources occurs mainly at low doses and at low dose rates; the quantitative definition of the risks of cancer from such exposure is, therefore, a central problem in radiation protection.

The Programme proposal 1985-1989 stated as its aim to investigate:

- the molecular basis for the alterations in the structure of the cell;
- the mechanisms by which cells are transformed and tumour growth is promoted after irradiation;
- the dependence on dose and exposure conditions for radiation-induced cancer in animal models pertinent to the human situation;
- the relation between deposition of radionuclides in tissues and their action on biological target structures;
- the frequency and types of cancer in exposed human populations.

The substantial reduction in funding for the 1985-1989 Programme made it necessary to concentrate efforts. Thus research into the molecular basis of damage, the so called "primary effects of radiation", although highly interesting with regard to understanding the basic mechanisms of radiation action, had to be abandoned because it was considered to give practical results for radiation protection only on a long-term basis. On the other hand, research on radiation-induced cellular transformation, including cells relevant to human cancer, was expanded, thereby following the recommendation of the independent evaluation panel. Research into the role of oncogenes in radiation-induced cancer also increased compared to the 1980-1985 Programme concurrently with the important scientific developments in this area, while studies on the role of viruses in radiation-carcinogenesis remained at a constant level. Few large-scale studies involving externally exposed animals have been started, probably because scientists are reluctant to initiate such long-term efforts unless they are assured that they can be completed. The

epidemiological studies on ^{224}Ra were continued successfully; other epidemiological studies are mentioned in sector F on page 197.

No area of research on radiation-induced cancer, be it molecular biology, cellular investigations, animal study or epidemiology, can by itself provide a direct answer to the problem of risks of low doses of radiation delivered at low dose rates; rather, one must integrate the information obtained from these different approaches to allow extrapolation to dose levels for which a reliable detection of the carcinogenic effects is not possible any more because they occur so rarely.

Five main topics are considered in this sector comprising a total of 45 contracts with 63 projects; the number of projects in each area is given in parenthesis:

a) The role of oncogenes and viruses in radiation-induced cancer
   - leukaemia, thymic lymphoma and general problems (8),
   - osteosarcoma (3)

b) Cellular studies
   - cell death, chromosome aberrations and similar endpoints (2),
   - classical transformation systems (5),
   - novel transformation systems (5)

c) External irradiation of animals (7)

d) Metabolism and effects of radionuclides
   - transport of radionuclides and decorporation treatment (4),
   - metabolism, dosimetry and effects in the respiratory tract (8),
   - metabolism, dosimetry and effects of bone-seeking radionuclides (6)

e) Human investigations (epidemiology of ^{224}Ra)(2).

Introduction

The understanding of the molecular and cellular nature of cancer has made substantial progress in recent years. Today, it is generally accepted that cancer disease arises as a multi-stage process passing through several sequential steps: initially, a cell would become immortalised thus escaping the normal ageing process and becoming capable of dividing indefinitely; next the cell would be transformed to a malignant state possibly by the activation of an oncogene; finally, the transformed cell would be promoted and escape the surveillance of the defence of the organism to grow into a clinical cancer. Most of these reactions can be elicited or influenced by radiation, but the transformation event has been studied most thoroughly so far. Transformation might occur when radiation exposure activates oncogenes or

inactivates a "suppressor" or "anti-oncogene", and several mechanisms for this effect can be envisaged, e.g., induction of mutational damage, rearrangement of chromosomal material leading to an uncontrolled amplification of the oncogene, integration of a retrovirus into the genome or impairment of an oncogene suppressor gene. In the latter mechanism, one would expect that the genetic damage is of a recessive nature, whereas the others would act in a dominant manner. Studies on activation of oncogenes directly or by retrovirus integration have so far been given most attention. Many oncogenes and their transcription products have been characterised in recent years, and we are now beginnning to understand how these products could alter cellular functions. On the other hand, the subsequent steps which make a transformed cell grow into a clinical tumour present more difficult obstacles to experimental study, but they may be critical in order to advance our understanding of the risks of low doses delivered at low dose rates.

Co-operation in late effects research

Studies on the late effects of radiation are expensive, and it takes a long time to obtain results; therefore they require consistent financial support. Such studies must also be carefully prepared, executed in a reliable and standardised manner and interpreted in a way that reflects the consensus of the scientific community. Co-operation on a Community and international scale is therefore indispensable to obtain optimal results.

The European Late Effects Project Group (EULEP) (099), now in existence for 25 years, has continued to develop **scientific co-operation** on a technical level in all areas of radiation late effects. EULEP is organised around a proven structure of different committees. Standardisation committees for external radiation dosimetry, internal radiation dosimetry, pathology and cell/molecular biology provide an indispensable service for a reproducible and reliable execution of experiments, for example by carrying out dosimetric inter-comparison programmes, helping pathological diagnosis of animal experiments, and editing an atlas on pathology in which, in the future, US scientists will also participate. Research is currently arranged in 15 task groups dealing with such different subjects as the molecular and cellular basis of haemopoietic tumours and osteosarcoma, vascular effects in the

irradiated brain, damage to the developing and adult central nervous system, decorporation of radionuclides from the body, interspecies comparison of lung clearance, metabolism of bone-seeking radionuclides, fetal dosimetry. The EULEP sponsored research into an interspecies inter-comparison of standardised ^{57}Co particle deposition and retention can serve as one among several examples of the work of a task group and is mentioned again below. EULEP, together with the Commission, has also organised a large number of different meetings and workshops and has helped in the training of young scientists.

Co-operation has also been expanded outside the Community. For example, to improve and test biophysical models for the action of radiation on cells and organisms, the Radiation Protection Programme together with US Department of Energy is defining sets of data most suitable for modelling.

a) The role of oncogenes and viruses in radiation-induced cancer

Myeloid leukaemia, thymic lymphoma and general problems

Much basic information on the role of virus-related oncogenes has been obtained from studies on mouse thymic lymphoma. Several laboratories have attempted to elucidate the role of the radiation leukaemia virus (RadLV) and have also co-operated in a EULEP task group with other laboratories not directly supported by the Programme. The scientists at the SCK/CEN, Mol (090) cloned the RadLV/VL3 virus which includes thymotropic and leukaemogenic components. This virus was shown to consist of 8318 nucleotides and to resemble other murine leukaemia viruses with respect to its genes. The long terminal repeats (LTR) contain the typical promoters for RNA synthesis including an enhancer region which could exert a remote influence on the genome by means of "insertional mutational oncogenesis". No specific insertion points of the virus responsible for cancer were found. Retroviral insertion near the myc oncogene indeed causes modification in the myc but further studies showed that this insertion is not related to the leukaemia. These and other studies indicate that the virus may facilitate growth of the cells but is not prerequisite for the tumour. The ras oncogene showed mutations in the tumour

cells, but they were not of clonal origin. They indicated rather that leukaemic cells are hyper-mutable.

The properties of the ecotropic recombinant viruses isolated from radiation-induced thymic lymphoma were investigated at the Fond. Bergonié, Bordeaux (078). These recombinants were not highly leukaemogenic and, after an extensive search, only one replicating, infectious virus with an abnormally long LTR sequence could be found. This virus and another weakly leukaemogenic one were sequenced and characterised. Both viruses show repeats of enhancer sequences in the LTR region, but differences exist with respect to the binding of specific nuclear factors.

Bone marrow cells from ^{224}Ra or X-ray induced myeloid leukaemia commonly show changes in chromosome 2, either in the form of translocations, rearrangements or small deletions (MRC, Chilton, 064). No consistent loss of a single band could, however, be observed, and breakpoints were not restricted to a single chromosomal subregion. Although molecular studies cannot yet unambiguously identify a specific gene, it appears that many of the lesions are close to the interleukin-1ß gene. Molecular studies suggest that structural rearrangements in chromosome 2 may be associated with a deregulation of this gene, but considerable uncertainty still exists with respect to the mechanism of action. Cytogenetic studies in X-irradiated CBA/H embryo fibroblasts indicate that this strain is particularly sensitive to radiation-induced breaks, perhaps due to instability regions imprinted during gametogenesis. The high frequency of chromosome 2 rearrangements in irradiated haemopoietic cells may, however, reflect not an immediate transformation so that a second genetic event would be required to initiate leukaemogenesis.

Proto-oncogene activation was investigated in radiation-induced lymphoma, spontaneous mouse reticulum sarcoma and Friend leukaemia cells using transfection into NIH/3T3 cells and subsequent appearance of transformed foci to detect the oncogene (Ist. Super. di Sanità, Rome, 103). No oncogene was detected in the lymphoma whereas three reticulosarcoma contained an oncogene which seemed highly homologous to polyoma virus DNA. High levels of c-myc oncogene expression was observed in the Friend cells, but this was not modified by irradiation. K-ras or

H-ras were not expressed. A curious observation is that metastasising Friend cells express more H2 class I antigens on their surface than non-metastasising ones.

Attempts to introduce genes into bone marrow cells by means of retroviral vectors and thus cause leukaemia failed, and the expression of the insert soon declined after transfection (Univ. Leiden, 185). A new transgenic mouse strain, recently obtained and now tested, seems to be more promising for such experiments. Irradiation of cell cultures in which an activated oncogene had been introduced aimed at studying the influence of radiation on growth. Most cell lines proved unsuitable for this assay. Transgenic mice containing the pim-1 gene appear more suitable and are now being bred.

A morphological transformant (T-neo) was found in NIH/3T3 cells after they had been transfected with irradiated fragmented mouse DNA (TNO, Rijswijk, 072) and included several copies of the putative oncogene Sa9. This Sa9 contains the well known open reading frame of MMTV LTR which was detected in various tissues of several vertebrates. It is suggested that this LTR, characterised by MMTV-orv sequences, could be involved in oncogenic deregulation, and that the separation of the MMTV-orv sequences due to radiation could play a role in some cases of radiation-induced cancer.

Methylation of a gene and its lack of expression are correlated, and radiation might affect the degree of methylation (Univ. Rome, 106). Rat M9 myoblasts were grown either in a "growing" or a "fusion" medium (the latter causing differentiation of the cells) in the presence and absence of methylation inhibitors. Fusion was inhibited by radiation, regardless of whether or not fusion-promoting agents were added, but this no longer occurred once the cells were committed to fusion. Single strand breaks, studied by alkaline elution, reflected this sensitivity. Exposure of cells to drugs inhibiting methylation also caused an increase in sister chromatid exchanges. These did not return to normal after removal of the drug and restoration of methylation. Further studies in this contract dealt with the elucidation of the regulation of methylation, the development of a new methylation assay and the biochemistry of methylation in relation to the structure of DNA.

Fibroblasts transformed by radiation expressed more parvoviral transcripts than normal cells (ULB, Brussels, 178), and were killed to a substantial extent as a result of the lytic action of the virus. As these cells are not tumorigenic, it appears that sensitivity to parvoviruses may be used as a marker of the pre-neoplastic transformed state.

Transformation could involve the transposition of genes and this was studied using Ty-integration near promoter regions in haploid yeast (GSF, Neuherberg, 085). Exposure to mutagenic agents (EMS) causes a dose-dependent increase in transpositions similar to that of mutations. Gamma-radiation was less effective but an increase in Ty-specific mRNA was observed, especially in rad mutants. Inhibitors of protein or DNA synthesis interfere with such induced transposition. Transposition yield is much lower in diploid than in haploid yeast. The sites of DNA integration during transposition were investigated using recoverable plasmides and then sequencing them. No specificity for integration was detected.

Osteosarcoma

The injection of ^{224}Ra results in the activation of N-ecotropic XC+ and xenotropic C retroviruses in bone marrow, spleen and bone of BALB or C57/bl mice (GSF, Neuherberg, 080). The virus can be isolated from the tumour, and sufficient material for characterisation was obtained after expansion in syngeneic mice. A large percentage of the tumours had acquired ecotropic pro-viruses in the genome, and it may be assumed that radiation-induced osteosarcoma develop by clonal expansion of sub-populations of distinct tumour cells. The tumours frequently display amplification of c-myc and MLvi-1, and double-minutes containing these oncogenes could be demonstrated. Amplification and rearrangements in the myc region were presumably causing the increased c-myc gene expression observed in some tumours. LTR Sequences of retroviruses isolated from osteogenic tumours often display alterations in the enhancer region. These alterations affect the transcriptional activity of the viral promoters as demonstated by CAT-assays. Although these viruses are basically murine leukaemia viruses unable to transform mesenchymal cells in vitro, they have specific bone-pathogenic properties such as inducing osteopetrosis and osteoma, and the virus can be isolated from primary

skeletoblast cultures after inoculation of the mice. Cultured cells from the mandibular condyles, which can differentiate, were found to be a suitable target for the actions of the virus and most useful for transformation studies.

Research at the Univ. Aarhus (086) provided important complementary information to the investigation at the GSF. Different murine viruses associated with osteosarcoma and thymic lymphoma were characterised with respect to their biological properties and their LTR sequences. Among other things, a hypervariable zone in the region associated with transcriptional enhancement was identified and defined. Methods were developed to determine virus expression and its signal strength by means of vectors. A critical region in the repeat module was identified which binds Nuclear Factor I proteins. The study of tandem repeat sequences indicates that they not only increase expression levels but also make expression more independent of the flanking DNA. To identify the sites of integration of the provirus in the host genome, specific tagging methods were developed and several of these sites have been identified and analysed.

Studies at the SCK/CEN, Mol (090) indicate that radiation-induced osteosarcoma in Balb/c mice contain somatically acquired pro-viruses and sometimes show amplification of c-myc. No consistent pattern of expression of the oncogenes could be identified.

In conclusion, the progress made in the understanding of the role of oncogenes has been fully reflected in the research on radiation-induced cancer. While one might regret that, in some studies, radiation was not emphasised more, it should be obvious that only a close connection between basic and radiation research will assure its innovative nature and will enable the crucial answers as to the effect of low doses and the repairability of the lesions involved to be given. Research on the molecular nature of radiation-induced cancer thus remains one of the most promising and intriguing areas in research on radiation-induced cancer and, at the same time, is likely to have important spin-offs for the understanding, prevention and treatment of cancer in general.

b) Cellular studies

Cell death and chromosomal aberrations

The relationship between chromosome damage, reproductive death (inability to form a clone) and transformation in different cell lines and in dependence of dose and radiation quality was studied at the TNO Rijswijk (067). New methods of flow cytometry were developed for the rapid analysis of chromosome aberrations, and irradiated and transformed cells were investigated for chromosomal changes. Among many other results, it should be mentioned that no influence of fractionation (3 mGy/min vs 150 mGy/min) was seen on transformation induced by 1 MeV neutrons. On the basis of the different data obtained, it was postulated that lethal lesions induced by single tracks arise from 2 double strand breaks (DSB) located at a distance of less than 10 nm in a chromatin fibre (corresponding to an energy deposition of ~300 eV). Potentially lethal lesions could be associated with somewhat greater distances between 2 DSB produced by a single track. The different packing of DNA in the cell nucleus may account for differences between cell stages and cell lines. The induction of repairable sublethal damage (energy deposition 100-150 eV) is nearly independent of LET in the range of 5-25 keV/μm. The interaction between radiation of different LET can be explained on this basis.

The fascinating question whether very low doses have a stimulating (hormetic) effect was investigated in human fibroblasts (Univ. Toulouse, 201). Continuous exposure to 6.25 mGy/day caused a temporary reduction in the activity of some glycolytic enzymes on day 4 with a return to normal on day 7. No changes were noted in catalase or glutathione reductase and, in most experiments, in the protein pattern as studied by SDS electrophoresis. It thus appears that radiation exposure of human cells only causes transient changes but no important hormetic effects as had been found earlier in single cell organisms.

Classical cell transformation systems

Cell transformation of C3H10T½ fibroblasts, grown on mylar foils, was studied after single or fractionated exposure to 4.3 MeV alpha rays (Univ. Milano, 091). Whereas survival followed an exponential function with a Do of 0.61 Gy, dose effect relationships for transformation showed an apparently constant region of

transformation in the low dose range followed by a linear increase with dose. Dose rate between 0.005 and 0.11 Gy/min did not affect transformations due to alpha rays but a reduction of transformation of about 3 at high doses and 1.5 at low doses was observed after split exposure to 1.82 KeV protons. Growth kinetics of an irradiated population indicates that a surviving cell continues at normal division rates whereas a non-surviving one gradually slows down division rate before losing its ability to divide.

The RBE of mono-energetic electrons produced inside a cell by exposure to ultra-soft X-rays (generated by bombarding suitable targets with protons) was investigated in C3H10T½ fibroblasts (GSF, Frankfurt, 236). The initial data on Co gamma rays indicate a linear relationship at low doses and a cubic one at high doses with respective oxygen enhancement ratios (OER) of 2.9 and 1.5. Double strand breaks (DSB) studied in yeast exhibit similar OER and RBE characteristics, and it is concluded that DSB are involved in cell transformation.

Neutrons of intermediate energy (24 kEV) were used to study C3H10T½ fibroblasts, human Hela cells and blood lymphocytes (BNL, Berkeley, 095). Survival of the two lines had an RBE of 3.3 and 3.4. Induction of micronuclei in lymphocytes yielded an RBE of 21 and 7.5 for 24 keV neutrons and 23 keV alpha particles respectively. Only preliminary data are available on cell transformation suggesting an RBE of about 12 for the neutrons.

Transformation of C3H10T½ cells is reduced when gamma radiation is fractionated (GSF, Neuherberg, 085). Transformation frequency decreased by a factor of 2-3 at doses between 4 and 8 Gy when the dose rate was diminished from 1 Gy/min to 1 Gy/hr. A further protraction to 1 Gy/d gave a dose reduction factor of 5. No difference in transformation was found between 1 and 4 Gy/d.

The different steps involved in transformation were investigated in Syrian hamster embryo cells after exposure to X-rays or ENU (Univ. Leiden, 202). Immortalisation appeared to require at least 3 individual sequential steps (escape from senescence, increase in cloning efficiency and increase in growth rate) until rapid, indefinitely maintained, cell division was achieved. Step one occurs with the highest frequency, in the order of 10^{-4}, the others at about 10^{-8}. No spontaneous immortalisation was

observed in these experiments; its probability thus is below 10^{-10}. Induction could occur via indirect mechanisms and be unrelated to the appearance of cellular aneuploidy. Calculation of the risks in different species suggests that cellular lifespan could be the rate limiting factor in carcinogenesis.

New cell transformation systems

Primary cultures from explants of a variety of human tissues were investigated for their use as transformation systems (St Luke's Hospital, Dublin, 092). In such cultures, Co gamma irradiation induces, in a dose-dependent manner, responses akin to the properties of cancer cells: increased numbers of proliferating foci, accelerated growth rate, appearance of cytokeratins, nuclear abnormalities, decrease in mitochondrial number. Although these endpoints cannot be considered as truly reflecting transformation they could represent intermediate stages in this process.

Such in vitro systems were also utilised to investigate potential synergism between radiation and carcinogens such as a benz(a)pyrene, ß-propiolactone or nitrosoethanolamine (Trinity College, Dublin, 184). A low dose of carcinogen combined with a dose of less than 5 Gy of gamma-rays can stimulate the outgrowth of cells from human oesophageal and urothelial tissue explants and cause the proliferation of endothelial cells; responses differed somewhat among carcinogens. Proliferation of endothelial cells occurred only in tissues treated with both carcinogen and radiation. These results may suggest synergistic actions between radiation and carcinogens, but the experiments need to be interpreted with care because the development of cell foci is not equivalent to malignant transformation.

Human and sheep thyroid cells were investigated by an in vitro assay for cell survival and transformation (Fed. Dublin Hospitals, 093). Sheep thyroid cells were found to have a Do of 1.5-2 Gy for ^{60}Co gamma rays with an extrapolation number ranging from 5-20. Irradiation with ^{131}I have D_0 of 7-10 Gy. The D_0 for human cells was 0.5-2 Gy with an extrapolation number close to 1 for gamma rays and a D_0 of 6-9 Gy for ^{131}I. The Do for an increase in thyroid gland weight after goitrogen stimulation is substantially higher because only a few cell divisions are assayed under these conditions. The dose levels inducing hypothyroidism were calculated

at 25-50 and 250 Gy for acute gamma rays and ^{131}I respectively. The corrected transformation response (soft agar clones) shows a linear curve to about 10 Gy with an increase of about 1 order of magnitude for 2.5 Gy. No such transformation could be demonstrated with ^{131}I or with human cells. In addition, calculations were carried out for thyroid dosimetry dependent upon age, sex and iodine intake. (For related studies on thyroid cell radiosensitivity and transformation see page 113).

The ENEA, Rome (004) investigated the in-vivo and in-vitro transformation per surviving cell of epithelial tissue using Harderian gland cells transplanted into syngeneic hosts with respect to long-term dysplastic and neoplastic lesions. A similar method was also used for hepatocellular tumours. Dose effect relationships were obtained in both models suggesting a quadratic dose effect relationship for X-rays.

Primary human keratinocytes were used for transformation assays based on different growth characteristics in selective culture media allowing or not allowing terminal differentiation (ULB, Brussels, 178). Other studies in the same contract investigated AT (Ataxia telangiectasia) cells deficient in the enhanced reactivation response (ER), a process similar to the SOS response in bacteria. Another response investigated was enhanced mutagenesis. Results indicate that AT cells are deficient in an ER component of importance only for the rescue of single but not of double stranded DNA. Other investigations indicate that the accumulation of mRNA in irradiated cells treated with interferon alpha is related to the expression of genes acting on the stability of mRNA, and that this may allow vital cellular processes to continue during DNA repair.

In conclusion, radiobiological information on cellular models have provided many crucial data for the understanding of cell death and transformation. The relation between cell death on the one hand and chromosomal aberrations and double strand breaks is now well established, and a substantial amount of data is available on the influence of radiation quality. The radiobiology of cell transformation remains a more formidable task. The relevance of the classical fibroblast system for human cancer remains in doubt, although even a complete understanding of the radiobiological mechanisms would be a major advance, and epithelial cell

transformation systems, as promising as they seem, have not yet supplied good quantitative information. The role of promotion in radiation carcinogenesis remains perhaps the greatest challenge for future studies. Cellular models are probably the area where biophysical models show the greatest promise for making predictions about behaviour in the low dose/dose rate range. Efforts to develop benchmarks from cellular data for the testing of such models must therefore be continued in co-operation with the US Department of Energy.

c) Animal studies after external irradiation

Investigations into the late somatic consequences of external irradiation delivered to the whole or part of the body of experimental animals have yielded a substantial amount of information on the induction of a variety of tumours. Research in this area has declined in recent years because it is expensive and not very popular, but several critical questions remain unsolved such as what is the shape of dose effect relationships in the low dose range, how do the effects decrease when a low or a high LET radiation exposure is fractionated or protracted and how does biological efficiency relate to radiation quality, particularly at low doses and low dose rates? As these problems are not directly accessible to epidemiological investigations, and since it is uncertain to what extent animal models reflect the situation in man, future research must concentrate on the integration of all available information coming from animal experiments as well as from biophysical modelling, molecular carcinogenesis and epidemiology. An important task in this respect will be the evaluation of existing animal data in the light of novel statistical and modelling approaches.

A population of rhesus monkeys which were subjected to an acute X- or neutron exposure (average dose 6.7 Gy and 3.4 Gy respectively) is being studied for the development of cancer and other late effects (TNO, Rijswijk, 075). After a follow-up period of about 25 years, about 90% of the irradiated group has died compared to about 50% of the controls, and there was a marked increase in tumours in the exposed groups corresponding to risk factors of 63×10^{-4} for X-rays and 229×10^{-4} Gy^{-1} $year^{-1}$ for neutrons. When calculated for cumulative risks, the RBE neutrons to X-rays would be about 7. Taking into account the fact that rhesus monkeys have

about one third the lifespan of man, these risk values and the new risk estimates from the Japanese survivors correspond remarkably well.

Myeloid leukaemia in CBA mice has already been studied extensively by several research groups, in particular by the MRC, Chilton, and seems to be a suitable model for human leukaemia. Recent experiments, carried out at the Netherlands Energy Research Foundation, Petten (203), show that the incidence of leukaemia following exposure to 0.4 Gy of fission neutrons delivered at dose rates of 2, 10 or 100 mGy/min is independent of the dose rate. Survival time also does not vary with dose rate, but lymphosarcomas occur more frequently after the high dose rate.

The incidence of thyroid tumours in rats given external irradiation of 0.01, 0.1 and 1 Gy and stimulated by anti-thyroid treatment did not increase after low doses (Univ. Wales, 097). This is in contrast to earlier, preliminary reports by the same group. Observations on the rate of onset of different types of lesions suggest that focal hyperplasia can progress to adenomas. Lesions introduced by a 120 day goitrogenic treatment are still reversible, but not after a treatment of 200 days. Application of ^{131}I and goitrogenic stimulation produced a high incidence of focal hyperplasia and adenoma. After withdrawal of the goitrogene, focal hyperplasia and, less so, adenoma regressed indicating their continuing dependence on thyroid stimulating hormone. Histochemical studies indicate that all these lesions are of a monoclonal nature.

The nuclear DNA content of rat and human mammary tumours was studied by flow cytometry carried out on cells isolated from tissue sections, and the DNA content was assayed in single cells using renal tissue as internal standard (TNP, Rijswijk, 212). In addition to the degree of aneuploidy, the mitotic activity and cellular and nuclear polymorphism were assessed. Twenty percent of the benign rat tumours were hypoploid and only one hyperploid, in contrast to the situation in man where few aneuploid benign tumours are seen. Malignant tumours were more often aneuploid, especially hyperploid, in both rat and man, but whereas aneuploidy is associated with a poor prognosis in man, rat mammary tumours are in general non-invasive and metastasise rarely.

The biological effectiveness of low doses of 250 kVp X-rays and 1.5 MeV neutrons with respect to life shortening and tumour induction in female BC3F1 mice was studied at ENEA, Rome (004). Mean survival decreased linearly with dose, apparently without a threshold, and an RBE of 12.3 could be calculated. Tumour incidence displays more complicated patterns, for example, myeloid leukaemia increase with doses to maxima at about 1 and 2 Gy for neutrons and X-rays with a decline at higher doses. A study on fractionated exposure to X-rays and fission neutrons is still being evaluated.

SCK/CEN, Mol (071) investigated whether administration of C Cl_4 acts in a synergistic way with radiation. It was observed that radiation alone increases liver tumours in an approximately linear way up to a dose of 4 Gy. When the promoter C Cl_4 is given before or up to 3 months after large doses (6 Gy) of X-rays, the incidence of liver tumours increases further. Liver appears severely damaged after C Cl_4 treatment with many abnormal mitosis.

In the same contract, the earlier data from the extensive lifespan studies on mice irradiated in a single or repeated application of X-rays or 50 MeV neutrons have now been fully analysed. Survival time did not differ significantly for a same dose of acute gamma or neutron irradiation. Fractionated gamma exposure was, however, less efficient than a single one, and a a slight increase in life shortening was seen when neutrons were fractionated. However, cancers occurred more frequently after fractionation of gamma rays or neutrons whereas non-stochastic effects were much less prominent after fractionation. Consequently, while the RBE for lifetime shortening does not differ significantly from unity for the neutrons used, the RBE is between 1 and 3 for cancer induction.

The analysis of dose effect relationships for radiation-induced cancer in animals (Univ. Leiden, 219) has been developed taking account of new mathematical approaches, and these were adapted for use on a personal computer. The methods were employed to evaluate existing data on mammary carcinogenesis for which an RBE of 0.5 was found for ^{137}Cs gamma rays compared to X-rays.

In conclusion, animal studies have, in the past, (including the period under review) contributed critical information on cancer risks to man. Certain problems, such as

the influence on risks of fractionation and protraction of exposure or the influence of different endogeneous and exogeneous factors can only be elucidated on the basis of animal experiments. Nevertheless, due to budgetary reasons, the reluctance to start animal experiments and the declining expertise in animal radiation pathology, probably very few animal experiments will continue in the Community. It is all the more important, therefore, to assemble the available information on existing animal data, in co-operation with the US DOE, and re-evaluate them using modern statistical and, where possible, pathological approaches.

d) Metabolism and effects of radionuclides

Research in this area concentrated on tumours of the lung, the bone and bone marrow, the thyroid and the liver. Lung tumours could be a risk of exposure to actinides at the workplace but are, even more commonly, considered in relation to exposure to radon in homes or in mines, (a subject discussed in more detail on page 141).Research on bone tumours has spanned the entire range from molecular, cellular, animal and human studies and involves problems related to exposure to actinides and other bone-seeking radionuclides in the occupational and medical context. Liver tumours are discussed in the context of the epidemiology of thorotrast patients (page 200).

Transport of radionuclides and decorporation treatment

An understanding of the binding properties is indispensable for an effective removal of radionuclides from the body. Research in this area concentrated on actinides because of their importance in the workplace.

Actinides (and lanthanides) are transported in the body by means of transferrin, thus following a binding mechanism similar to that of iron (KfK, Karlsruhe, 091). The type, binding properties and stability of these complexes were studied in detail showing the importance of this transport and also possible ways to interfere with it. Uptake of these complexes by cells occurs via specific receptors and these bind actinides nearly as well as iron but keep the actinides mainly bound to the cell membrane (perhaps a sort of detoxication mechanism) whereas they allow iron to

pass into the cell. It is not yet clear whether the actinides remain irreversibly bound to the receptor or are transferred to other membrane sites. Studies on subcellular distribution of Pu in the liver reveal a small, mass-dependent percentage bound to the nucleus. Actinides taken up by the cell are rapidly bound to a protein and transferred to ferritin. Model studies on Pu speciation in the gastro-intestinal tract indicate that absorption is related to the small amount of electrically neutral species. In conclusion, in vitro studies, together with computer simulation, can thus usefully extend the limited data obtained on man or experimental animals.

Treatment with decorporating agents can reduce the burden of radionuclides in target organs and this should reduce risks of cancer or non-stochastic damage (SCK/CEN, Mol, 094). Weekly injections of Zn DTPA not only reduced bone burdens by about one half but also the risk of osteosarcoma and, to a lesser extent, tumours of the liver and the reticulo-endothelial system. Transplantation experiments indicate that the Zn-DTPA treatment protects against the Am effects by preventing radioactivity in the circulation to re-deposit on bone. Earlier, no protection against bone tumours has been found when ^{226}Ra contaminated mice were given alginate. In contrast to Am, the principal dose to bone surfaces from the ^{226}Ra occurs early after contamination, and this probably is related to the approximately 20 times higher toxicity of ^{241}Am compared to ^{226}Ra.

Decorporation of Pu and Am in rat lung by repeated injections of DTPA reduced concentrations to 1 and 2% respectively of untreated animals (NRPB, Chilton, 089). A new compound, Licam C, tested within the framework of a EULEP project proved to be inferior to DTPA. Other iron binding drugs related to desferrioxamine confirmed their potential usefulness, but currently DTPA remains the drug of choice. DTPA was, however, much less effective for removing thorium from the body, and no effective treatment seems to exist to remove soluble uranium compounds.

A two-year contract (GSF, Neuherberg, 087) investigated insoluble substances (BAC2) which can bind alkaline earths and thus interfere with the intestinal uptake of radiostrontium. While this product indeed reduced the absorption, its effectiveness was limited to a very short time after the intake of the radionuclide.

Metabolism, dosimetry and effects of radionuclides in the respiratory tract

Some information on human risks of lung tumours is available from miners with respect to radon and its daughter nucleides, and with respect to external irradiation from the survivors of Hiroshima and Nagasaki. However, only animal data exist for actinide exposure, and the extrapolation to the radiation protection of workers requires an understanding of the deposition pattern of radioactive particles and their subsequent fate, as well as of the dose to target tissues. Unfortunately, the question as to the identification of the target cells for human lung cancer and their distribution and anatomical sites in the airways is far from being solved. On the other hand, considerable progress has been made with respect to the deposition and clearance pattern of radioactive particles during the past years, and research has increasingly concentrated on situations and particles relevant to radiation protection in the workplace. Moreover, a EULEP co-operative inter-species comparison has provided a better base to compare animal data with the human situation.

A new inhalation facility, constructed at NRPB, Chilton (089), has been used to study the biokinetics of actinides and test decorporation by chelating agents. Work concentrated on ^{239}Pu and ^{241}Am containing particles encountered in the industrial environment. For several of these dusts, the ^{241}Am nuclides are transferred more rapidly than the ^{239}Pu nuclide, but this may be due to the fact that the two nuclides are in different chemical forms or that the former represents only a daughter of the original nuclide. Nevertheless, Am may often be used to trace the Pu contamination in man but, for other radioactive industrial contaminants, accompanying ^{144}Ce or ^{137}Cs may be more suitable. The studies on UO_3 and UF_4 confirm that these are D and W compounds respectively (compounds which are cleared at rates in the order of Days, Weeks or Years), and that chemical and not radiological toxicity limits intakes. Other U oxides with a longer half life can probably be attributed higher ALI (Annual Limits of Intake) than suggested by ICRP and might be detected by chest monitoring.

Another project in the same contract (089), dealing with translocation from the respiratory tract to the blood, was actively involved in the EULEP ^{57}Co experiment. It was found that, in rats, deposition increases with age, and that rates of

translocation were greater in young rather than in old rats and greater in rats rather than in hamsters or guinea pigs. Translocation was also more rapid for the "porous" than for the "dense" particles. Studies on in vitro dissolution by alveolar macrophages from different species showed marked differences between species although the pH of the lysosomes was quite similar.

NRPB Chilton, (089) is also investigating human volunteers after inhalation of inert ^{97}Ru (or ^{99m}Tc) labelled polystyrene or aluminosilicate particles with sizes from 0.5 to 50μ for deposition and clearance behaviour. However, only particles up to 15μ gave reproducible results. Long-term clearance in man was also studied with ^{88}Y particles (t=107 d), and the data show a two-term exponential function with most retained material being absorbed to bone surfaces. The results were supplemented by extensive studies on rats, and the entire investigation was carried out in close co-operation with other Community institutes.

Deposition and clearance of particles (1-3μ AMAD) were investigated in human volunteers, 29 adults and 41 children, as an important contribution to the development of lung models (CEA, Fontenay-aux-Roses, 101). Measurements were taken after nose and mouth breathing. In children, nasal resistance decreased with age, adult values being reached only at puberty. Nasal filtration is, however, less efficient in children. Children also had a higher deposition during mouth-breathing, especially during exercise, but total deposition does not differ much from that of adults because of the lower total ventilation of children. Patients with obstructive lung diseases also showed a higher deposition of particles

The determination of the lung burden of ^{239}Pu depends on the external measurement of soft x-rays emitted (UKAEA, Winfrith, 102). Often, the ^{239}Pu is contaminated with ^{241}Am and ^{241}Pu and this, together with the unknown distribution of activity in different areas of the lung, further complicates the application of the usual chest phantoms. Therefore, two software programes were developed taking into account individual parameters, and calibration factors for the chest phantom were developed and tested among others also in man who, within the framework of the EULEP project had inhaled ^{57}Co particles, as well as on some people who had accidentally inhaled actinides. These investigations, together with the development of better

detectors, have substantially reduced the uncertainty of determining actinide lung burdens although the sensitivity of detecting contamination with actinides remains a major concern especially in view of the impending reduction in ALI. The second project dealt with was the EULEP co-operative study in which two volunteers inhaled ^{57}Co particles of 0.8μ and two others of 1.7μ diameter. Excretion and lung content was followed up for almost 3 years and yielded short term clearance of about 1 day and a long term clearance of 200 days. In one subject, an intermediate clearance rate (44 days) was also seen. The last project followed solubility of U, Am, Pu O_2 dust particles in "mock lungs". Solubility followed a tri-exponential relationship and paralleled that of class Y compounds. Transferrin addition rendered U more soluble; the effect was doubtful for Pu and absent for Am.

The retention and translocation of labelled particles deposited either by inhalation, intra-tracheal instillation or directly injected into the lung tissue of rats were studied at the MRC, Chilton (076). Particles of ^{198}Au injected into subpleural alveoli are rapidly taken up by macrophages. After 15 months, about half of the activity was still in the body, more than 90% of it in the lung, most of it close to the injection site; only a small percentage was found in thoracic lymphnodes and liver. ^{133}Ba labelled particles instilled in the trachea were also removed very slowly. This laboratory also participated in the co-operative EULEP experiment investigating the interspecies behaviour of inhaled ^{57}Co particles. Other studies in this contract dealt with the long term behaviour and the effects of UO_2 in rats. The local deposition of particles in the human lung under working conditions is being followed on the basis of autopsy material from tin miners who are inhaling tourmaline particles.

The synergism between $^{239}PuO_2$ and smoking was studied in CBA/H mice (UKAEA, Harwell, 235). The data show that smoking inhibits clearance of Pu (14.2 Bq retained from 100 Bq inhaled with smoking compared to 3.3 Bq without smoking) but also reduces tumour incidence. The interpretation of these experiments is that either smoking has caused an increased radiosterilisation of target cells for lung tumours or that smoking actually protects from Pu exposure. The second project in this contract studied metabolic models of bone-seeking radionuclides, based on animal and human (with ^{133}Ba) experiments. Model validation showed that the Oak Ridge model, probably to be used for age-related dosimetry by ICRP, is somewhat

flawed, but also that the uncertainty of risk estimates is greater than that for dosimetric models. Autoradiographic studies on the distribution of radionuclides in contaminated human (^{241}Am, thorotrast), baboon (Pu) and rodent bone and bone marrow help to interpret the risks of osteosarcoma and leukaemia from these nuclides.

Studies on uranium toxicology in the industrial environment were carried out in the CEA-IPSN, Pierrelatte (088). Industrially used compounds were characterised with respect to their solubility under different conditions in vitro and a cell culture medium was found to be most suitable for this purpose. The addition of macrophages seemed to reduce solubility. The excretion of inhaled or intra-tracheally instilled compounds in rats gave results corresponding to the solubility observed in vitro. Monitoring of workers for uranium exposure was carried out according to a newly developed metabolic model and confirmed the in vivo and in vitro results. Particular attention was paid to UF_4 for which a component of rapid metabolism could be discerned.

The lung tumour risks from radon in combination with other toxic agents (acetaldehyde) was investigated at the TNO, Rijswijk (067). The construction of an exposure chamber which allowed reliable long term exposure presented considerable difficulties, and the rats were only recently exposed to 200 and 800 WLM giving an expected lung tumour incidence of 10% and 30% respectively.

Metabolism and effects of bone-seeking radionuclides

The epidemiology of long-lived ^{226}Ra delivering its radiation mainly to the entire bone volume and of the short-lived ^{224}Ra which decays while still being localised at the bone surface has provided an impressive body of information on the risks of alpha emitters. In order to extrapolate this information to beta emitters, such as strontium or to long-lived alpha emitters staying at the bone surface, such as Pu, an impressive amount of animal data has been obtained. It has become increasingly clear that the tumour spectrum caused by radionuclides deposited in bone depends on the dose. Thus, the risks of leukaemia, particularly in the growing organism, require further study.

The studies at the GSF, Neuherberg (080) not only continued the research on molecular/cellular models and on epidemiology, but also complemented it by investigations on osteosarcoma and lymphoma incidence in NMRI mice given various short-lived alpha or beta emitters concentrating on the effect of dose, fractionation, protraction, radiation quality and age of the animals. For example, low doses of alpha emitters seem to produce a tumour spectrum different from higher ones, and this agrees with the observations in man. The sensitivity to tumour induction varies with age, but this also depends on the dose. Tumour induction caused by beta irradiation appears to be partially repaired when the dose is fractionated but this is not the case with alpha radiation. Experiments where two alpha emitters of a different half life were given in combination suggest that there is a less than additive effect. Whereas ^{144}Ce can induce local osteosarcoma, due to the high energy ß rays of the daughter ^{144}Pr, only distant osteosarcoma were caused by the local injection of a ^{228}Th or ^{227}Th colloid gels which must have been due to the circulation of soluble radium daughters.

The relation between the induction of osteosarcoma and myeloid leukaemia in CBA mice after single or multiple injection of ^{224}Ra was investigated at the MRC, Chilton (064). Not all mice in the experiment have died, but more myeloid leukaemia than osteosarcoma have so far been observed although this may change since osteosarcoma tends to occur later. Nevertheless, it appears that, at low doses, myeloid leukaemia could be the more serious risk compared to osteosarcoma, and this may be true for man, although the sensitivity of CBA/H mice to radiation-induced myeloid leukaemia is greater than that of man.

Skeletal uptake and distribution of Ra, Th, U, Pu and Am were investigated at the NRPB, Chilton (089) mainly in rodents with some studies of pigs and baboons, the latter in co-operation with the CEA and UKAEA. Early deposition in various bones is thought to reflect mainly their blood supply but the variations among bones are much greater for Pu than for Ra, U or Am. The data were used to verify the ICRP dosimetric model (ICRP 30), which seems to be quite reliable for Pu in the bone and marrow cavities of the adult man. The comparison of doses delivered by ^{224}Ra and ^{226}Ra suggests that the approximately six times greater toxicity in rodents of the Pu is not only due to its preferential exposure of bone surfaces but also to its greater

deposition in trabecular bone. The comparative study of tissue retention and toxicity of ^{239}Pu, ^{241}Am and ^{233}U in mice has not been entirely completed; retention patterns have been obtained but a substantial number of animals is still alive.

e) Human studies (epidemiology of radium)

The epidemiology of patients treated with ^{224}Ra has been followed for many years by the GSF, Neuherberg (083), and these data, together with those on ^{226}Ra, have become the principal basis for estimating risks from bone-seeking radionuclides. The short-lived ^{224}Ra has the interesting property that it delivers its alpha radiation to the bone surface in a way similar to Pu, albeit at a higher dose rate. A high and a low dose group are being studied. The high dose group consists of 900 patients, 682 adults and 218 juveniles, of which 529 are deceased. The treatment, given after the second world war mainly for ankylosing spondylitis and bone tuberculosis, but also for a variety of other diseases, caused an average skeletal dose to adults of 4.16 Gy and much higher doses to juveniles. Osteosarcoma appeared from 3.5 years after the injections started, peaked after 8 years and then declined. The cumulative life time risk of bone sarcoma is about 0.8% per Gy at high doses and probably less at low doses. The data also suggest that injections spaced over a longer period of time are more effective in causing osteosarcoma than those given frequently at a higher dose rate. An excess of breast cancer in irradiated juveniles is at the borderline of significance. Six liver cancers (compared to 1.1.-1.2 expected), 6 kidney cancers (2.4-2.6 expected) and 6 leukaemias (2 expected) have also been noted in the treated patients. In addition to the non-stochastic bone and teeth changes observed earlier, cataracts have been found to be markedly increased in the Ra^{224} patients, and this was now investigated in more detail (GSF, Neuherberg, 221). The causation by radiation could be inferred by slit-lamp examinations of some immature cataracts which indicated that the respective lens fibres had been laid down around the time of exposure. Cataracts are diagnosed from 40 years after exposure and appear to arise according to a linear dose-effect relationship with a threshold or, alternatively, a quadratic dose effect relationship.

The low dose group consists of 1,579 ankylosing spondylitis patients who received repeated injections of the short-lived ^{224}Ra between 1948 and 1975 resulting in an

average alpha dose to the skeleton of 0.63 Gy; the control group, spondylitis patients not treated with radiation consists of 1461 patients. Until now 500 exposed and 636 non-exposed patients have died, and the causes of death have been ascertained in most of them. Three malignant tumours in the skeleton compared to one in the control group have so far been observed, none of them an osteosarcoma. The difference is not quite significant. However, a significant increase in chronic myeloid leukaemia was seen in the treated patient whereas acute lymphoblastic leukaemia occured more frequently in the controls perhaps as a result of the intake of pain-killing drugs. The interpretation of the ^{224}Ra data also required the development of new methods for statistical evaluation, and these methods also served for the evaluation of other studies, such as the recently updated follow-up of the survivors of Hiroshima and Nagasaki and the experiments on lung cancer in radon, neutron and X-ray exposed rats at the CEA.

5. Genetic Effects of Ionising Radiation

Radiation induces a wide variety of damage to DNA which may result in mutations, chromosomal aberrations and cell death. In somatic cells, this damage may lead to malignancy. In germ cells the damage may be transmitted to future generations as hereditary defects. Research in this sector concentrates on the molecular and cellular consequences of radiation damage to DNA in somatic and germ cells in an attempt to provide a better understanding of the mechanisms of radiation action in support of the assumptions made in estimating risks of low doses of radiation especially in view of the lack of human data on genetic effects. The Programme proposal 1985-1989 stated as its aim to investigate:

- the factors which govern the induction and repair of genetic damage;
- the induction of hereditary damage and its consequences for man;
- the risks from small doses of radiation by studying dose-effect relationships.

The stringent budget conditions and an initial preference for the more applied research at the start of the programme meant that priorities were concentrated on effects in eukaryotic cells to the cost of some previously supported research in prokaryotes. However, a well balanced, if somewhat restricted, choice of projects in the sector was achieved as the programme progressed.

The sector comprised 47 contracts with 65 projects; the number of projects in respective areas are given in parenthesis:

a) Repair of genetic damage and radiosensitivity (16)
   - repair in microorganisms and yeast,
   - characterisation of human repair deficient cells,
   - characterisation of rodent repair deficient cells,
   - isolation of repair genes,
   - DNA repair, recombination and mutagenesis,
   - induced effects associated with repair

b) Cytogenetics and cell radiobiology (23)
   - detection of DNA damage and its consequences,
   - repair and the induction of chromosomal aberrations,
   - low dose effects and chromosome damage

c) Radiation effects in germ cells (8)
   - mutations induced in the mouse,
   - reciprocal translocations induced in spermatogonia of the mouse and primates,
   - non-disjunction in the mouse,
   - effects in repair defective Drosophila.

The research carried out in this sector is relatively basic, but it is all aimed at providing a better understanding of the mechanisms of radiation action and experimental data on the shape of cellular dose-effect relationships in order that the assessment of risks at low doses may be based on the most probable extrapolation of epidemiological data in man at high doses. The most probable extrapolation relies on the interpretation of radiation action at the cellular level using biophysical models and extending the interpretation to animal and human data. An understanding of the mechanisms of radiation action at the molecular level and the generation of relevant cellular data are germane to the whole aim of radiation protection research.

a) Repair of genetic damage and radiosensitivity

The normal cell's natural ability to repair a wide variety of radiation induced DNA damage and, in so doing, reduce the severity of the radiation effect, is of direct relevance to the shape of dose-effect relationships and to a knowledge of the critical types of DNA damage. The study of the repair of DNA damage has continued through the previous programmes where attention originally focused on repair in prokaryotes and lower eukaryotes which were more amenable to study and where the genetic background of the repair deficiencies was well defined. In recent years, there has been a definite trend to mammalian and human cells because of their closer relevance to the problem of radiation risk assessment in man. Much work in the programme has been concerned with the isolation and characterisation of different human repair deficient cell lines and research with these cells continues unabated. Newer repair deficient rodent cell lines have been isolated having in some cases comparable repair deficiencies to the human strains. These rodent cell lines are used in parallel studies with the human strains especially in experiments where the molecular biological methods prove more successful in the rodent cells than in the human cells. The application of newer molecular biological techniques continues to provide more detailed information on repair genes in different species, DNA repair rates in different parts of the genome. Although progress in some areas using the new techniques has been less successful or slower than at first anticipated, the continued development of the arsenal of molecular biological investigative techniques

will certainly lead to crucial advances in our understanding of the molecular nature and cellular consequences of radiation damage and repair.

Repair in micro-organisms and yeast

When the replication fork is blocked by DNA lesions, a series of products is induced which are involved in repair, replication and cell division. This phenomenon has been called SOS repair and is studied in E.coli. The analysis of mutations induced by a variety of SOS-dependent mutagens showed a site-specific and mutation-specific spectrum characteristic for each treatment. The conversion of pre-mutagenic lesions into mutations is governed by several factors such as DNA configurations, DNA sequence, etc and the mutations are not randomly distributed along the DNA. When mutations are found in undamaged phage introduced into a damaged bacterial host, the mutations are classified as untargeted mutations. However, the origin and existence of untargeted mutations has not definitely been established (ULB, Brussels, 155). More untargeted mutations are produced in UV irradiated mismatch repair deficient host bacteria, so mismatch repair eliminates some untargeted mutations. Mismatch repair is a multi-enzyme system which corrects over 99% of replication errors in E.coli and evidence has now been found for mismatch repair in vertebrate cells. Discontinuous DNA synthesis in eukaryotes might provide the necessary signal for mismatch correction of replication errors (Monod Inst., Paris, 154). Two types of mismatch repair have been identified. Long patch mismatch repair which appears to abort strand exchange between non-identical, partially homologous DNA and thus conserves genetic information in replication and recombination stabilising chromosome structure in general. Very short patch mismatch repair appears much more specialised causing diversity of genetic information in recombination. It has been shown that in the absence of long patch mismatch repair, two different genera, E.coli and salmonella, can be mated and recombined over one million times more efficiently than in wild type strains (Monod Inst., Paris, 154). It is suggested that long patch mismatch repair prevents recombination between interspersed, repetitive sequences and thus prevents an excess of chromosomal rearrangements.

In a study of the repair of mitochondrial DNA in yeast, three mutants at the pif1 locus have been isolated which affect recombination between rho^+ and rho^- genomes, although general recombination between other alleles is normal (UCL, Louvain-la-Neuve, 160). Work on recombination and the PIF1 product also indicates an important role for DNA topology in recombination. In pif1 mutants, a defect has been found in the recovery of intact DNA molecules after mutagen treatment suggesting that the PIF1 gene product controls repair via recombination. Indeed PIF1 protein appears to have an essential DNA stabilising function and it is plausible that PIF1 is either a DNA helicase or is associated with a DNA helicase complex.

In an investigation of mutations in the RecA gene of E.coli, some mutations were found showing a split phenotype, each mutant supporting one function of the RecA protein. One other mutation totally prevents mutagenesis. Thus, it appears that RecA protein has an essential role in mutagenesis and it is suggested that RecA protein acts at the replication fork to block a mutator protein or it cleaves a third protein that is involved in the bypass of the lesion by the replisome (CNRS, Gif-sur-Yvette, 145). Two proteins, KIN2 and KIN17, appear to have some homology with parts of the RecA protein and it is suggested that the KIN polypeptide may lead to the basis of SOS functions in mammalian cells. In another study of proteins from yeast showing immune cross-reactivity with RecA protein from E.coli, a single nuclear protein was detected which was induced by UV and X-ray exposure. Although this protein had several properties associated with recombinase, it had no effect on recombination and was shown not to be homologous to RecA protein (Univ. Milan, 204). The Holliday junction is a key intermediate in genetic recombination and is a cruciform structure formed by two interacting duplex DNA molecules. A new class of DNA binding protein which binds to such a cruciform structure was purified from rat liver proteins.

Another set of enzymes which play an important role in recombination and repair are the topoisomerases I and II. Investigations of topoisomerase I and II reveal two classes of potential eukaryotic cleavage sequences, master sites and slave sites. The master sites of topo I act as a substrate for catalytic activity of the topoisomerase I (Univ. Aarhus, 170). The slave sites appear to have common structural features

rather than any sequence homology. The master sites of topo II provide a substrate for both cleavage and catalytic activity and it has been shown that topoisomerase II-mediated, double-strand DNA cleavage has DNA strand specificity. Topoisomerase poisons are currently being investigated as potential cancer chemotherapy agents, indicating the important role of topoisomerases in the maintenance and repair of the DNA in the cell.

Characterisation of human repair deficient cells

Fibroblast cultures were established from skin biopsies taken from patients with disease associated with mutagen hypersensitivity. These are Xeroderma pigmentosum (XP) (UV sensitivity), Ataxia Telangiectasia (AT) (ionising radiation sensitivity), Nijmegen breakage syndrome (NBS) (ionising radiation sensitivity), Fanconi's anaemia (FA) (DNA crosslinking sensitivity) and trichothiodystrophy. In co-operation with American groups, cells sensitive to ionising radiation were characterised into four AT complementation groups and two with NBS. The AT gene for complementation groups AB was ascribed to the human chromosome 11q22-23, the first chromosomal assignment of a radiation sensitive human disorder (Erasmus Univ., Rotterdam, 141). The XP syndrome is associated with a hypersensitivity to sunlight and UV and a high incidence of skin cancers and provides a good example of the relation between unrepaired DNA lesions and tumour induction. Three activated oncogenes have been found among 12 XP tumours all involving the ras oncogene and showing typical base substitution mutations found in activated ras oncogenes. The mutations occurred at a position in the DNA where a UV induced lesion would be expected to occur, confirming the association between DNA lesions and oncogenesis (CNRS, Villejuif, 163). In FA, two complementation groups A and B have been identified and although cells from both groups are able to incise the cross links induced in DNA the incision process is slower and the number of cross links incised is lower than in normal cells. Use has been made of illumination of cells containing trimethylpsoralen (TMP) with different wavelengths of light to induce differing proportions of cross links and monoadducts. This showed that the presence of monoadducts in normal cells interferes with the removal of cross links but that this interference is more severe in FA cells. Using

the same techniques, the response of the FA cells to the TMP monoadducts has been examined. The FA cells have been found to be much less efficient at incising the monoadducts than normal cells even though FA cells show an almost normal sensitivity to UV and several other monofunctional compounds. The answer to this seems to be that the FA cells are sensitive to the amount of modification of the DNA helical structure caused by the presence of the monoadducts rather than to the monoadducts themselves (Inst. Curie, Paris, 151). It has also been found that FA cells show a lower frequency of induced mutations after psoralen and light exposure to produce cross links than do normal cells.

It has been estimated that up to 5% of the population might be heterozygote for the AT gene and it is possible that AT heterozygotes might be more sensitive to radiation than the normal population. Claims have been made that AT heterozygotes are at an increased risk for cancer, especially early breast cancer. Radiation sensitivity of fibroblast cell cultures and of T-lymphocytes separated from whole blood have been examined for a large number of samples taken from AT patients, obligatory AT heterozygotes and normals to assess the reproducibility of the radiation sensitivity assay and to try to distinguish between the three different classes. Cell survival studies in both fibroblast and T-lymphocyte cells revealed a clear distinction between AT and the rest and suggested that AT heterozygotes were a little more sensitive than normals, but the difference in sensitivity was not sufficient to be able to provide a method to distinguish AT heterozygotes in a normal population. The results from one interesting, recently developed method suggest that the heterozygotes are defective in the repair of potentially clastogenic damage (MRC, Brighton, 142).

Trichothiodystrophy is a new genetic disorder found to exhibit some photosensitivity. In a study of seven patients, three categories have been found: cells with a normal UV response, cells deficient in the repair of UV induced damage being indistinguishable from XP cells and cells showing a normal response to killing and mutagenic effects of UV but having a defect in the ability to remove 6-4 photoproducts from DNA. These cells are able to excise cyclobutane dimers normally (MRC, Brighton, 142).

Characterisation of rodent repair deficient cells

Human cells have some disadvantages such as difficulty of long-term culture and more importantly being refractory to DNA transfection, so that some effort has been devoted to the isolation and characterisation of rodent repair deficient cells. Of thirteen repair deficient mutants isolated using ENU treatment (Univ. Leiden, 166), three were UV sensitive, four X-ray sensitive, four mitomycin-C (MMC) sensitive and two methylmethanesulphonate (MMS) sensitive. Cells sensitive to X-rays showed the least cross-sensitivity to other agents. The four X-ray sensitive mutants fall into two complementation groups. In a comparison with previously isolated cells one UV sensitive cell line was found to be very sensitive, have no repair of pyrimidine dimers but 60% repair of 6-4 photoproducts, revertants of this cell line showing almost normal UV sensitivity still could not repair dimers, but 6-4 repair was normal. This could be interpreted to suggest that 6-4 products are the main cytotoxic and mutagenic lesions. The three X-ray sensitive cell lines have normal induction and repair of single and double strand breaks but do have a lower inhibition of DNA synthesis than normal cells. This group of cells has a similarity to AT cells. In these cells the induction of aberrations was higher than normal cells and in all three cell lines both chromatid and chromosome aberrations were found in the same cell, a phenomenon typical of AT cells. It was concluded that DNA dsb are the most important lesion leading to chromosomal aberrations in normal cells, but in repair deficient cells other lesions may also lead to chromosomal aberrations (Univ. Leiden, 166).

Three mutant cell lines, irs 1-3, were isolated from V79 Chinese hamster cells (MRC, Chilton, 144) which appeared to be in a different complementation group to most of the other rodent repair deficient cell lines. DNA single and double strand break repair was normal in these cell lines but differences in the effect of radiation on DNA synthesis were found. Mutation frequency measurements in irs 2 and 3 showed no increased sensitivity to mutation by X-rays. In irs 1, however, an enhanced mutability was detected. In a study of the ability of the irs mutants to repair DNA damage faithfully, it was found that while irs 2 and 3 appear to repair DNA dsb as faithfully as normal cells, in irs 1 cells there was a reduction in the fidelity of the repair, similar to that found in one AT cell line. The lack of fidelity

of repair has been confirmed in several different types of experiment including one developed to use cell free extracts and examine the repair of dsb in vitro. In another study the repair of dsb induced in a recombinant vector by X-rays and enzymes and introduced into hamster cells suggested that the dsb induced either by X-rays or enzymes were the major inactivating lesion.

Isolation of repair genes

Considerable difficulties have been encountered in trying to transfect human cells with DNA to isolate repair genes and attention has consequently moved to transfection experiments with rodent repair deficient cells and other methods of isolating repair genes. ERCC1 (Excision Repair Cross Complementing rodent repair deficiency) gene has been isolated using transfection. It corrects excision deficient CHO cells of complementation group 1 for sensitivity to DNA damaging agents, incision of damaged DNA, lesion removal, repair synthesis, damage induced mutagenesis and chromosomal aberrations and preferential repair of active genes. It appears not to be a mutated gene in either the XP or the CS (Cockayne's syndrome) diseases and its expression does not seem to be stimulated by UV exposure. The ERCC1 amino acid sequence shows homology with the yeast repair protein RAD 10 and in some parts also homology with E.coli repair proteins (Erasmus Univ., Rotterdam, 141). That the ERCC1 gene does have a function in repair has been demonstrated by cloning the gene in an antisense orientation into a high copy vector pECVG25 which was then introduced into repair proficient human cells. Transfectants were found to be sensitive to mitomycin C indicating that the ERCC1 gene is probably involved in cross link repair (Univ. Leiden, 167). The ERCC3 gene has also been isolated and characterised (Univ. Leiden, 169). It corrects the excision repair defect in rodent mutants of complementation group 3, is located on chromosome 2q2.1 but has no homology with known repair genes from yeast or E.coli. The gene was found to correct unscheduled DNA synthesis in one XP complementation group and thus indicates an overlap between rodent and human excision deficient mutants. ERCC6 gene has also been isolated by DNA transfection.

Working on the assumption, triggered by the analysis of the ERCC1 gene, that a number of repair genes have been strongly conserved in evolution, a new method of isolating human repair genes has been developed. The method relies on looking for homology between known repair genes from lower organisms and DNA fragments from other species. In this way a yeast homologue of ERCC3 was isolated. By working in the opposite direction, from yeast to man, the human RAD 6 DNA has been cloned. The yeast RAD 6 protein appears to be involved in chromatin remodelling needed for repair and recombination. The yeast RAD6 has been used to identify drosophila RAD6 and eventually the human RAD6. RAD6 yeast mutants are highly sensitive to a variety of DNA damaging agents and are impaired in post-replication repair thought to be defective in XP variant patients (Erasmus Univ., Rotterdam, 141).

The abnormal response of FA cells to DNA cross-linking agents has been corrected by transfection with normal human DNA. Since the transfected DNA could not be distinguished from the host DNA, the FA defect was corrected with mouse DNA (Inst. Curie, Paris, 151). Mouse DNA from an established cell line was unable to correct the repair defect in FA group A cells although DNA from total mouse embryos did give partial correction and it seems difficult, using mouse DNA, to transfect the proper sequences suitably expressed to correct the FA defect. The sensitivity of FA cells to diepoxybutane has been corrected using DNA from Chinese hamster lung cells. Two groups of mouse cells have been isolated showing sensitivity to cross-linking agents and being apparently equivalent to the two complementation groups in FA. Experiments are being carried out to use human DNA to correct the mouse cell deficiencies. Co-cultivation experiments suggest that a diffusible agent released by normal human and mouse cells and by FA group B and mouse group II cells can correct in part the chromosomal defect in FA (A) and mouse (I) cells.

DNA repair, recombination and mutagenesis

The processes of replication and transcription have been shown to be associated with the nuclear matrix and experiments have been carried out to see if repair of UV induced damage is confined to the points of attachment of the DNA at the nuclear

matrix or not. In confluent human fibroblasts, repair sites were distributed throughout the DNA and not preferentially at the nuclear matrix after a relatively high UV exposure. It was also shown that the repair events were not randomly distributed but appeared to be clustered in DNA loops. After low UV exposure, early repair occurred preferentially at the nuclear matrix but at later times repair was distributed throughout the DNA. It is clear that certain parts of the DNA associated with the nuclear matrix and comprising transcriptionally active DNA are more rapidly repaired than the rest of the DNA. It seems likely that the preferential repair of the DNA associated with the matrix is associated with the repair of 6-4 photo products. These findings suggest two independently acting repair pathways directed towards repair of pyrimidine dimers in active or inactive chromatin. XP-C cells have lost the ability to repair inactive chromatin but have retained the ability to repair active chromatin. In growing cells UV resistance is apparently provided by preferential repair of pyrimidine dimers from active genes and efficient removal of 6-4 photo products throughout the genome which is interpreted to indicate a strong cytotoxic effect of 6-4 photo products (Univ. Leiden, 166).

In work using specific genes carried on viruses or shuttle vectors as probes for mutagenesis, several problems have been encountered and the research has been less fruitful than originally anticipated (MRC, Chilton, 144; CNRS, Villejuif, 163; MRC, Brighton, 142). Using SV40 to study UV induced mutation spectra, it was found that the spectra were sensitive to the mode of DNA transfer into the host cell, although the lethal nature of pyrimidine dimers and the mutagenic nature of both dimers and 6-4 photo products were demonstrated. Using a 2 gene vector, one transformant revealed that X-rays induced both point mutations and deletions/rearrangements in contrast to the results with a single gene vector, when only large deletions were found. These results suggest that the main action of radiation is to induce large genetic changes unless the genetic region targeted does not allow these to survive, in which case smaller changes may be found. In an analysis of 41 UV induced and 18 EMS induced inactivation of the bacterial gpt gene stably integrated in a human fibroblast cell line, it was found that many cases of gene inactivation occurred by alterations of gene expression through methylation or "phenotypic switching" and very few gpt inactivations arose from point mutations.

The advent of the technique using the polymerase chain reaction (PCR) should enable mutations of endogenous mammalian genes to be analysed relatively easily and probably makes shuttle vectors obsolete.

An analysis of 163 mutations at the hgprt locus in mammalian cells induced by a variety of DNA damaging agents has confirmed the initial results showing that radiation induces a large genetic effect in comparison with EMS. Little difference was found between the spectrum of mutations induced by gamma-rays and alpha particles although the resolution of the hgprt system may be too low to detect real differences in the mutagenic effects of different types of ionising radiation (MRC, Chilton, 144). The frequency of spontaneous hgprt mutants in T-lymphocytes from normal donors, XP and AT patients as well as for XP and AT heterozygotes has revealed an approximate 10-fold increase in mutation frequency in the first 20 years of life, followed by a slower increase during adult life. Heterozygotes are comparable in mutation frequency with normals but both XP and AT patients exhibited a clear increase in mutation frequency above the normals. In an analysis of the nature of the mutations, very few deletions were found and a sequence analysis using the PCR technique has revealed a wide variety of alterations in the hgprt gene. Out of 41 mutants analysed, 17 had no detectable alteration which suggests alterations in a different gene might also lead to thioguanine resistance. The hgprt mutations, spontaneous and UV induced, have also been examined in normal and XP human fibroblasts. The results suggest that the nature of the UV mutations in normal and XP cells might be different (MRC, Brighton, 142).

Induced effects associated with repair

Exposure of bacteria to DNA damaging agents causes a transient activation of a number of phenomena, so-called SOS functions. Similar sorts of phenomena have also been observed in eukaryotic cells after UV treatment and their significance has been investigated. UV irradiated Herpes Simplex virus (HSV-1) is introduced into UV exposed human skin fibroblast cells and its survival and mutagenesis is measured. An enhancement of survival (enhanced reactivation, ER) and an enhanced mutagenesis (EM) of the virus is found to be maximum about 24 hours after exposure of the host human cells. In some cases, dependent on the host cell,

EM was observed without ER and it was noted that the XP cells giving EM without ER were from patients free of tumours. In trichothiodystrophy (TTD) cells which are photosensitive but the patients do not exhibit increased cancer incidence EM was found but without ER. In cells from cancer-prone patients of several diseases very much higher levels of ER were found than in normal cells, thus confirming the previous impression that ER is associated with the process of cancer induction. These experiments also revealed that cells from some patients with Wilm's tumour and some with dysplastic naevus syndrome were especially sensitive to UV cell killing suggesting that they might be defective in repair (Univ. Leiden, 169).

It has been found that UV exposure of human keratinocytes increases the synthesis of a number of proteins. A special group of proteins classified as small proline rich proteins (spr 1, 2 and 3) have been studied. UV induction of spr mRNAs were followed after UV exposure and it was found that while spr 2 and spr 3 are induced by UV exposure, the amount of spr 1 remains constant. Tumour promoters are also known to modulate gene expression and the effect of TPA exposure on spr gene expression was investigated. In this case, spr 1 and spr 2 are increased whereas spr 3 remains constant. It has also been shown that spr 1 protein increases as the cells go through terminal differentiation (Univ. Leiden, 167).

The introduction of pR plasmid in bacterial cells has caused an increased resistance to UV and 4NQO, thought to be associated with an inducible response to the DNA damaging agent. The pR plasmid has consequently been introduced into mammalian cells and the effect of different agents has been examined. pR transformed cells exhibit increased resistance to UV and 4NQO but are significantly more sensitive to agents such as bleomycin which cause DNA double strand breaks (Univ. Rome, 205).

The enzyme poly(ADP-ribose) polymerase (pADPRP) plays a central role in the modulation of cellular response to DNA damage. In human lymphocytes, the activity of pADPRP increased 24 hours after stimulation reaching a maximum at 3 days. When lymphocytes were treated with DNA damaging agents the activity of pADPRP was stimulated but at high doses of the DNA damaging agents, the enzyme activity tends to disappear. The activation of pADPRP appears to be related to the

appearance of newly formed single strand breaks in DNA (Univ. Pavia, 158). The activity of pADPRP does not appear to be different in FA cells compared to normal cells suggesting that pADPRP activity is not associated with the defect in repair in FA cells. DNA ligase, another enzyme involved in repair, has been classified into two groups, ligase I and ligase II. However, it has been found that DNA ligase is very heterogeneous and the results do not support the idea that ligase I and II are coded by different genes. In Bloom's syndrome (BS) cells but in BS cells it appeared that the structure of ligase I was altered, which may be associated with the defective response of BS cells (CNRS, Villejuif, 163; Univ. Pavia, 158).

b) Cytogenetics and cell radiobiology

The induction of chromosomal aberrations by ionising radiation is the most visual indication of DNA damage in the nucleus of the cell. The formation of aberrations is associated with DNA repair, mutagenesis and malignancy. The process of aberration induction after radiation has been studied to provide information on dose-effect relationships and the basic mechanisms involved in aberration formation. It is generally accepted that in normal cells, double strand breaks induced in the DNA backbone of the chromosomes are the lesions which lead to aberration formation, but the actual mechanisms by which the various aberration configurations arise has not yet been elucidated. Work in the programme has concentrated on understanding the mechanisms involved in aberration formation dealing with the detection of different types of DNA damage, the use of new techniques to follow the induction and disappearance of chromosome breaks, the effect of repair inhibitors and the application of aberration measurements to biological dosimetry.

Detection of DNA damage and its consequences

The detection of frank DNA strand breakage can be achieved using several centrifugal or elution techniques, although the sensitivity of the techniques is not always sufficient to compare the measurements with biological effects. The detection and identification of a variety of other alterations induced in DNA by radiation, such as base damage, requires a different approach. The development of immunochemical methods using antibodies against radiation induced lesions has therefore been

continued. Small pieces of DNA are synthesised carrying the DNA damage to be sought. Thymine glycol and thymine dimer are two such lesions. The modified DNA is used to generate antibodies specifically directed against the modification. Attempts to produce antibodies against thymine glycols yielded some fractions of polyclonal antisera which could detect the glycols in cells exposed to 20 Gy of gamma-rays. An immunochemical assay to detect radiation induced single strandedness has been developed which permits the detection of damage after 1 Gy of radiation. This assay has been used to detect the induction and repair of this type of damage in germ cells where initial rapid repair followed by a slower repair was seen in all stages except in elongated spermatids where no repair was seen (MBL-TNO, Rijswijk, 148). Using the technique of alkaline elution coupled to fluorometric quantitation of DNA, both single strand breaks and after endonuclease treatment, general base damage could be detected at doses down to 1 Gy. Following UV exposure, dimers can be detected as UV-endonuclease sensitive sites and it was shown that repair of dimers was much poorer in rodent cells than in humans. In a Chinese hamster mutant defective in the repair of dimers the introduction of the ERCC1 gene completely restored the repair of the dimers. In an investigation using the immunochemical techniques the photoreactivation effect in humans was studied. No photoreactivation removal of dimers was found after single exposures to UV-B but when a fractionated regime of UV-B and photoreactivating light was continued with 2.5 hour intervals, some enhanced removal of dimers was observed. Photoreactivation only occurs under very special circumstances in humans.

Using neutral sucrose gradient sedimentation to detect DNA double strand breaks in yeast the relative efficiency of ultra soft X-rays was compared with gamma radiation. The ultra soft X-rays were found to be considerably more efficient in inducing dsb than gamma-rays and the relative biological efficiencies (RBE) dsb's are comparable with RBE values found for inactivation, mutation and chromosome aberrations in different mammalian cells. The induction of dsb was found to be linear with dose indicating the induction by a single particle track and it is concluded that the induction of DNA dsb by sparsely ionising radiation occurs predominantly by the slow electrons with energies of a few hundred electron volts (GSF, Frankfurt, 159). In a study to compare the effects of low energy protons on

the induction of dsb, cell killing and aberration induction, the neutral elution technique was used for the measurement of dsb. Survival curves for gamma-rays and 7.4 MeV and 3.0 MeV protons were analysed using the linear-quadratic dose relationship to obtain limiting RBE value of 2 for 7.4 MeV and 3.4 for 3.0 MeV protons in general agreement with other published values. The RBE values calculated for chromosome aberrations did not agree with these values and the results were interpreted to indicate that for low energy protons the frequency of aberrations does not necessarily correspond with survival, although it was pointed out that this was not in agreement with other published work (NRCPS, Athens, 224).

In a study of cell progression and aberration induction after heavy ion exposure, several factors were elucidated which can confuse a direct comparison between heavy ion exposure and gamma-ray exposure. Studying the progression of cells to mitosis after heavy ion exposure, it was found that only a small proportion of cells continued to mitosis within 48 hours of exposure. The other cells were seriously delayed and it was concluded that any cell hit by at least one particle would be blocked in the S and G2 phases of the cell cycle for at least 48 hours. Using synchronised cells, the radiation sensitivity in the cell cycle to heavy ion exposure was investigated. It was found that radiation resistance is higher in G1 phase and decreases to a minimum at the S-G2 border and it was suggested that this variation in cell cycle was directly related to the size of the nucleus and the probability that a cell would be hit by a particle. Chromosome aberration measurements showed that heavy ion exposure effects differ from sparsely ionising radiation in that the appearance of aberrant cells is delayed compared to X-rays and the distribution of aberration types is different (GSI, Darmstadt, 197).

One controversial result published previously has concerned an inverse dose rate effect on cell transformation after neutron exposure. In an investigation to examine whether this effect was more general for densely ionising radiation, the induction of mutations at the HGPRT locus and the induction of cell transformation has been quantified for different dose rates of neutrons and alpha particles. The results of the mutation analysis clearly indicated no inverse dose rate effect for either neutrons or alpha particles in stationary cell cultures and a small indication of an

inverse dose rate effect for neutron exposure of dividing cell cultures could be explained by variations in radiosensitivity during the cell cycle. In the case of cell transformation after different dose rates of alpha particle irradiation, no effect of dose rate was observed in agreement with other published results. However, the absolute frequency of cell transformation was dependent on the plating density of the cells (UKAEA, Harwell, 190).

Repair and the induction of chromosomal aberrations

A study of repair kinetics in relation to aberration formation measurements using human lymphocytes post treated with repair inhibitor (ara C) indicated that repair of radiation induced damage and reduction in yield of aberrations occurred in the first 30 minutes post-irradiation. This was confirmed in parallel studies of prematurely condensed chromosomes (PCC) formed by fusing the lymphocytes with mitotic CHO cells. When yield of breaks was determined in cells fused immediately post irradiation or after 60 minutes, it was found that about 50% of the breaks disappeared. The PCC technique was also used to study the rejoining of chromosome breaks and the formation of dicentrics. Frequencies of breaks observed immediately after irradiation were 10-fold higher than the number found at metaphase. The frequency of breaks decreased with time whereas dicentrics were formed very rapidly and the frequency remained the same. It was concluded that early repairing lesions lead to chromosomal aberrations, especially exchange type aberrations (Univ. Leiden, 166). The induction of DNA double strand breaks by restriction enzymes has contributed to the identification of dsb as an important lesion leading to aberration formation. The repair inhibitor (ara C) was found to enhance the frequency of restriction enzyme induced chromosome aberrations in the same way as it affects X-ray induced aberrations.

In human fibroblasts irradiated with X-rays and treated after irradiation with the repair inhibitors (ara C), it was found that the frequency of G2 chromatid breaks increased with time in the presence of the drug in comparison with untreated cells which showed a decrease in breaks. This was interpreted to indicate an interaction between a lesion induced by ara C with an X-ray induced lesion and was contrary to results with ara A which had given a constant level of breaks with time.

Contrasting behaviour in fibroblasts and lymphocytes was found when ara A treatment was given after X-irradiation. The results are interpreted to suggest differing modes of action for ara A and ara C and that while the disappearance of breaks with time represents the repair of a lesion such as dsb, the mechanism of exchange aberrations is independent of that involved in the rejoining of dsb. In a comparison of the rate of disappearance of chromatid breaks in normal and X-ray sensitive CHO cells at 37° and 33° C, no differences could be found. The results indicated a four-fold higher conversion of DNA damage into visible chromatid breaks in the sensitive cell line (Univ. St. Andrews, 294).

Low dose effects and chromosome damage

Stimulated lymphocyte cultures treated with a low dose of radiation (.01 Gy) and challenged later with a larger dose, show a lower number of aberrations scored than would normally be induced by the challenging dose alone and this process is called adaptation. The priming dose appears to make the lymphocytes more tolerant to the challenging dose. This process has been investigated in three laboratories (Univ. Rome, 186; Univ. Leiden, 166; Univ. Seville, 311). Using a combination of male and female cells, it was shown that selective killing of a radiosensitive population of cells by the priming dose did not occur and could not explain the adaptive effect. Similarly, it was shown that the adaptive response was restricted to the primed cells and was not due to any diffusible factor. Results with an inhibitor of poly (ADP-ribose) polymerase showed that inhibition of pADPRP after irradiation reverses adaptation (Univ. Rome, 186). In an examination of the variability in the adaptation response in different normal healthy donors, it was found that 4 out of 18 donors did not show adaptation when first tested but in later tests some of the four adaptation negative donors did show an adaptive effect. The adaptive effect seems to depend on the metabolic state of the cells. In another examination of the "adaptive" effect in different donors the magnitude of the adaptive effect varied between donors and between different blood samples from the same donor and in some cases no adaptive response was found (Univ. Leiden, 166). In an investigation of the induction of the adaptive response using a priming dose of hydrogen peroxide, it was found that the adaptive response could be induced by a single pulse of H_2O_2

but when 3 pulses of H_2O_2 were given at 6h intervals, the adaptive response disappeared (Univ. Seville, 311).

In a collaboration effort between five contractor laboratories (NRPB, Chilton, 225; Univ. Leiden, 166; Univ. Essen, 223; Univ. Rome, 171; SCK/CEN, Mol, 146) and one non-contractor (BNFL, Sellafield) the shape of the dose-effect relationship for aberrations induced in human blood at low doses of X-rays was examined. A previous publication of a study coordinated by the IAEA had revealed an apparent threshold dose at 50 mGy in contradiction to the expected linear relationship through the origin. The aim of the study was to investigate whether the threshold was real or not. In a first experiment, blood from four healthy male donors was irradiated at 37°C to 8 doses, zero, 3.13, 5.8, 9.65, 19.3, 28.7, 47.7 and 290 mGy. Slides were coded and distributed to the different laboratories. At these low doses a very large number of mitotic cells has to be scored for aberrations, dicentrics, rings and acentric fragments in order to achieve reliable results, and this accounts for the collaboration. Yields at three doses indicated that one of the donors might be more sensitive than the others and a second experiment was carried out using 18 donors to try to avoid the problem of donor variability. This second experiment used four doses: zero, 4.82, 28.5 and 280 mGy. In the second experiment, no indication of donor variability was found. In spite of some inter-laboratory and marginal inter-donor variations, the data could be pooled for analysis. Fits of the data from expt. 1 have been made to a linear-quadratic dose relationship for all the data and a linear dose-relationship for doses up to 50 mGy. The fits appear to be good but at doses up to 9.65 mGy the yield of dicentrics lie below the zero dose control, although they are not inconsistent with a linear extrapolation to the origin. Experiment 2 reveals data which show the yield of dicentrics at 4.82 mGy to be less than the zero dose control. At 4.82 mGy two laboratories scored low and these laboratories will rescore the data at this dose level. The comment is made that it is surprising that in three different experiments the yield of dicentrics has been found to be lower than the zero dose control showing, albeit non-significantly, a low dose plateau at less than 10 mGy. This effect is not found for acentric fragments, however, and there is no reduction in aberration yield at low doses when all aberrations are combined.

Previous studies have shown that radiation induced aberrations may not be random and a study of peri- and paracentric inversions induced by gamma-rays shows a preponderance of the same inversions found as recurrent in the human population. This could imply that after breakage the number of reassociations leading to inversion within a given chromosome is limited. An analysis of some 1600 break-points enabled the identification of both hot spots and cold spots in chromosome regions where breakage is too frequent or too infrequent. In the spider monkey, which has very large and small chromosomes, the large chromosomes were under-affected. It was noted that the spider monkey chromosome 10, equivalent to human chromosome 11, was too frequently affected as is the human 11 (CEA-IPSN, Fontenay-aux-Roses, 149). Using a newly developed technique, it was possible to measure the frequency of various rearrangements and their association at each cell division.

In a study of spontaneous chromosome anomalies as a control for dose-effect relationships, it was found that the level of chromatid type lesions was related to age and that the breaks were not distributed at random. All controls had fragile sites, e.g. 3p14 and 16q23 and fra(X)(q27). Chromatid exchanges are rare and indicate recent exposure to mutagens. Chromosome rearrangements are differently distributed in neonates and adults with many 7 and 14 rearrangements in neonates. Other rearrangements are rare in newborns but increase with age and this age dependence is important for low dose studies. In this study, no effect of doses up to 200 mGy could be demonstrated in old adults whereas in newborns an effect could be found at 50 mGy. These studies reveal the difficulties of doing chromosomal dosimetry at low doses (Inst. Curie, Paris, 147).

Three techniques offer the possibility of increasing the sensitivity of aberration detection, the micronucleus test, prematurely condensed chromosomes and flow cytometry. The micronucleus measurement is much simpler than the detection of aberrations and is amenable to automatic scoring. The method has been improved by the use of cytochalasin B, to prevent cytokinesis which leads to the presence of two nuclei in each cell that has gone through mitosis, thus identifying the fraction of cells that has divided. However, it was found that following stimulation the proliferation of lymphocytes varies considerably from individual to individual so that

the continuous monitoring of proliferation is required in order to add cytochalasin and harvest the cells at the optimum time (Univ. Essen, 312).

The use of prematurely condensed chromosomes (PCC) from lymphocytes would allow a new, early assessment of radiation injury as this technique permits the direct observation of chromososome damage without having to culture the lymphocytes for 2-3 days as is now the case for chromosome aberration techniques of biological dosimetry. Preliminary results suggest that the technique will be useful when standard dose-effect relationships have been established (NRCPS, Athens, 206). The PCC technique has also been used in plateau phase cells to compare the effect of repair on chromosome damage and survival using the repair inhibitor (ara A). After irradiation, a rapid repair of chromosome damage was measured with a half-life of one hour, comparable with that obtained for the repair of potentially lethal damage in cell survival measurements. It was also noted that the concentration of ara A that caused a total inhibition of repair at the chromosome level also caused complete expression of the ara A sensitive portion of potentially lethal damage.

Flow cytometry offers the possibility of scanning automatically individual chromosomes at a very rapid rate. Using slit-scanning of chromosomes stained with DNA specific dyes, it has been possible to identify dips in the fluorescence signal as the chromosomes pass through the laser beam which are associated with the centromeres. By using culture conditions to give elongated chromosomes, a better resolution of the fluorescent signal can be achieved. Developments up to now have made it possible to apply an automated detection of aberrations and derive dose-effect relationships (Univ. Amsterdam, 330).

A technique has been developed which allows the position of a cell in the DNA replication phase to be identified very precisely. This means that in the scoring of aberrations, the position of a cell in the cell cycle at the time of irradiation can be precisely defined and improved reliability of quantification should result. In normal cells, the DNA synthesis takes 6-7 hours and it proceeds discontinuously in bands in the different chromosomes, but the overall programme is very precise so that four or five key patterns can be defined which permit the exact location of the cells in S phase. In this way, cohorts of cells can be collected at mitosis which were all

irradiated at the same part of the S phase, independent of any delay in the progression of the cells. Using this technique, it has been shown that the methotrexate block used to synchronise cell cultures by accumulating them at the G1/S phase border actually halts the cells in S phase and on release they continue unchanged. It has also been used to investigate the nature of inherited fragile sites especially. This event was shown to be S dependent occurring early in the S phase. The commonly held idea that sulphur mustard causes aberrations late in S phase only was shown to be an artefact caused by the selective interphase death of early S phase cells (MRC, Chilton, 164).

In an investigation of Wilm's tumour, an inherited propensity to kidney tumours in childhood in which a deletion in chromosome 11 has been associated with the disease, the nature of the deletion has been examined. Lymphoblastoid cell lines were established from a number of patients and their parents. Cells from the patients exhibited the typical deletion involving chromosome 11p13. Cytogenetic analysis of the parents has shown that the parents are karyotypically normal and are not carriers of the 11p13 deletion so that the deletion or translocation most probably originates in a parental germ cell. The parental origin of the mutated chromosomes has been examined and in agreement with others, it has been found that the mutation occurs preferentially in the paternal chromosome and that the corresponding sequences lost in those cells that emerge as kidney tumour are maternal sequences. Cells carrying a single copy of the deleted 11p13 were selected in different ways and probes were developed to map the 11p chromosome arm. In this way, seven discrete but overlapping intervals have been defined spanning the 11p13 band. It has been shown that the translocation breakpoint cluster at 11p13 known to be associated with human T cell acute lymphocytic leukaemia is located near to, but outside, the Wilm's tumour locus. The work has shown that the 11p13 region of the human chromosomes which is frequently involved in spontaneous and mutagen induced chromosome breakage contains a number of important genes (MRC, Edinburgh, 157).

c) Radiation Effects in Germ Cells

Although no indication of hereditary effects in the atomic bomb survivors has yet been confirmed, the data from the survivors permit an upper limit on the risk to be defined. Experiments on insects, plants and animals have long indicated the potential of radiation to induce hereditary effects and there are thus good reasons to continue to gain more information on the nature and dose-effect relationships for these effects in animals to provide an improving background for estimating the genetic risk of radiation in man.

Mutations induced in the mouse

In a study of the induction of both dominant cataract mutations and recessive specific locus mutations in male germ cells, linear dose-effect relationships were fitted to data for 3 dose points and it was found that 24 times as many recessive mutations were induced than dominant mutations. This is interpreted to be in agreement with the idea that radiation mainly induces deletions and a recessive mutation would arise from the loss of a functional gene product. Dominant mutations are expected to arise from point mutations rather than deletions. Using the data, the doubling dose for recessive mutations is calculated to be 0.7 Gy whereas that for dominant cataract mutations is 2.4 Gy. Previously, it has been assumed that the doubling dose derived for recessive specific locus mutations was the same for all types of mutation. In addition, a study comparing the doubling dose for recessive mutations in the mouse with that for dominant mutations in man suggests that such a comparison cannot be made although the doubling dose for dominant cataract mutations in the mouse is comparable to that calculated for dominant mutations in man (GSF, Neuherberg, 156).

In a comparison of the sensitivity of four mouse strains to induction of recessive specific locus mutations and dominant cataract mutations in spermatogonia using a 3 + 3 Gy fractionated irradiation, it was found that three strains gave very similar results for the recessive mutations with one strain much lower - the first indication that mutation rate to specific locus mutations depends on the genotype of the male irradiated. For the dominant mutations, again three strains were similar with one high, but the low result for recessive mutations was not in the same strain as the high result for dominants. It is concluded that these results are not clear cut

enough to assume an effect of genotype on sensitivity. To examine the validity of the extrapolation between species, the induction of dominant cataract mutations in the golden hamster was compared with the mouse. It was found that a 3 + 3 Gy treatment resulted in 90% sterility in the hamster and experiments were made with 2 + 2 Gy treatment. The first results indicated no difference between the two species (GSF, Neuherberg, 156).

In a study of the induction of recessive specific locus mutations and dominant cataract mutations in female germ cells, oocytes, of mice, it was found that when the interval between irradiation and fertilisation was greater than one week the cell killing effect of the radiation led to a very small number of offspring. In the interval to one week, results were obtained showing radiation was effective in inducing both types of mutation and the mutation rates appeared to be comparable to those found after irradiation of spermatogonia (GSF, Neuherberg, 156). In an attempt to avoid the disadvantages involved in the detection of specific locus mutations, a method of detecting enzyme activity mutations used the erythrocytes of offspring. However, very few mutants were found in all the irradiation treatments used and no dose-effect relationship was derived. Examinations of the nature of the mutations found indicated that they were large deletions.

Reciprocal translocations induced in spermatogonia of the mouse and primates

Translocations induced in spermatogonia of mice are readily detectable cytologically and have provided much information on the shape of the dose-effect relationship for genetic effects and on how the shape of this dose-effect curve is dependent on the biology of spermatogenesis. In a comparison of two different strains of mouse, a similar humped dose-effect curve was found in both strains but in the strain more sensitive to cell killing, the peak yield occurred at lower doses. Using a model analysis it was calculated that the difference between the two strains could be explained if either one strain was allocated a higher proportion of sensitive cells in the spermatogonia or by a higher intrinsic sensitivity of the cells. The fractionated irradiation results, which did not show differences between strains, suggested that the higher proportion of sensitive cells provides the explanation. This is supported by the finding that dominant lethal induction is the same in both strains - no

difference in repair capacity was noted, spermatocytes were no more sensitive to cell killing and a 1 + 5 Gy at 24 hour fractionation gave the same response (MRC, Chilton, 143). By using a combination of chemical treatments with radiation, it was found that the stem cells in G1 in the spermatogonia are the most sensitive to X-ray induced mutation. Indeed, one combination gave the highest mutation rates per unit X-ray dose recorded. Other stages of the cell cycle must therefore be much more resistant. In a comparison of mutation frequencies and translocation yields, a parallel was found between the two end-points for different treatments suggesting that the cells most sensitive to mutation induction are also most sensitive to translocation induction.

A comparable study has also been carried out but using some different combinations of chemicals and radiation (Univ. Leiden, 166). In a combination of hydroxyurea and radiation, a clear correlation was obtained between cell killing and translocation induction and it was concluded that the probability that a radiation induced DNA lesion gives rise to cell killing is about 10 times greater than that it gives a translocation. Evidence was also obtained showing that cells carrying a translocation spend longer in the meiotic prophase than normal cells and this may explain why the transmission of translocations to the next generation is only half that expected from the measurement of multi-valent configurations at diakinesis - metaphase I of meiosis.

Translocations have also been measured in spermatogonial cells from primates and compared with the mouse. The induction in stump-tailed macaques was significantly lower at 1 Gy than that found in the rhesus monkey. Data in the rhesus monkey indicate that a reduction in dose rate does lead to a reduction in translocation yield but the reduction is less than that found in the mouse. An RBE of 2.1 was found for neutrons compared with 4 for the mouse. It is suggested that in species showing a high sensitivity to cell killing by X-rays such as the rhesus monkey and man, smaller effects of dose rate on the reduction of translocation yield will be found (Univ. Leiden, 166).

Non-disjunction in the mouse

Various tester stock mice strains carrying marker Robertsonian translocations have been developed to study radiation induced non-disjunction. The results of several experiments were frustrated either by the high incidence of new mutations or by the rarity of non-disjunctional events. However, in a test using a single Robertsonian translocation, but with markers on both arms of the chromosome, non-disjunction was detected at a level of +/- 20% at 4 Gy. Although each of the test systems proved effective for detecting non-disjunction, some more effective than others, two other problems were encountered. The frequency of radiation induced loss events varied from chromosome to chromosome indicating that chromosomes may differ in their sensitivity to radiation damage that leads to chromosome loss. But more importantly, the effect of chromosome imprinting has been detected in some tests. Imprinting is revealed when it is found that a complete set of chromosomes is not in itself adequate for normal foetal development but the parental origin of the chromosome is important. Thus, if two maternal or two paternal copies are present, in place of one each, abnormality or embryonic lethality may occur. Chromosome imprinting is proving important for the understanding of many abnormality syndromes in man including the occurrence of certain sporadic cancers and it is suggested that the finding of imprinting effects in these results is an important and significant result (MRC, Chilton, 143).

A study was made of chromosomal abnormalities in embryos deriving from irradiation of mouse oocytes. Embryos were screened for numerical and structural chromosome anomalies. In all cases a significant increase in anomalies was found for all the stages of oogenesis and embryonal development examined. Although previous results had indicated the induction of trisomy in 1 cell embryos from mice given 4 Gy of X-rays 1-2 weeks prior to ovulation, the more recent results have failed to confirm this result and it is concluded that the lack of trisomic post-implantation embryos suggests that embryos with radiation induced chromosome gains do not survive to the early post-implantation stage of development. Hyperploidy was found to be significantly increased by 1 Gy of X-rays but the incidence in morulae blastocysts was lower than in 1 cell embryos as was the case for other anomalies and it was suggested that there is a progressive loss of embryos

carrying genetic damage as gestation proceeds. The results suggest that although hyperploidy is induced by irradiation of mouse oocytes the resultant embryos appear incapable of progression to even early stages of post-implantation development (MRC, Harwell 173).

Effects in repair defective Drosophila

Two excision repair defective lines mei-9 and mus-201 have been studied and compared with a normal line of Drosophila. In a study of repair proficiency in cells from the different Drosophila stock, it has been found that both mei-9 and mus-201 are deficient in the incision step of the excision process after UV but the repair of X-ray induced breaks appears to be normal. Evidence has been provided, from other experiments, for a preferential repair of UV damage in active genes. In a study using the repair proficient cell lines, the repair kinetics in one active and two inactive genes were studied after UV exposure, no difference in repair kinetics was found and, moreover, the rate of repair appeared to be independent of dose. In a study of the molecular nature of X-ray mutations from irradiated spermatozoa in the different Drosophila stocks including one deficient in post replication repair (mei-41), it has been found that the defect in excision repair backgrounds (mus-201) leads to relatively more intragenic and less multi-locus deletions than in the repair proficient background, whereas the reverse was found in mei-41 post-replication repair deficient background. The molecular analysis of a series of white mutations arising from each background indicates a predominance of deletions and few base changes, although the spectrum of mutations in the excision repair defective background might differ from that found in a repair proficient background (Univ. Leiden, 166).

Studies in humans

An assessment of the effect of radiation on meiotic chromosomes depends on a knowledge of the normal progression of meiosis. This has been studied using light and electron microscopy techniques in various organisms including man. The various events such as the recognition of homologous chromosomes, formation of the synaptonemal complex, bivalent formation and the formation and resolution of

interlocking of chromosomes has been found to be a common feature of meiosis in many organisms including man. The enigma of why so few interlocked chromosomes are seen at metaphase I when a high probability of interlocking is expected to occur at synapsis has been solved by examining complete reconstructions of chromosome complements at zygotene. Reconstruction of human and silk worm (Bombyx) spermatocytes confirmed that chromosomes frequently interlock during synapsis and also showed that the interlocked chromosomes are released by breakage and rejoining of one or more of the involved chromosomes prior to the completion of pairing at pachytene. These breakage and reunion events are regular and frequent events of chromosome pairing. Short-term effects of radiation on Bombyx spermatocytes were studied and revealed that the immediate response to radiation is a temporary arrest of meiosis but after a few days meiosis proceeds repopulating the testis with meiotic prophase cells in similar stages to control group. Even after a dose of 10 Gy the gonads have the capacity of restoring morphologically almost normal meiotic prophase within 13-15 days (Carlsberg Lab., Copenhagen, 168).

An attempt was made to develop a technique to visualise human sperm chromosomes and to investigate the effects of radiation in sperm from patients treated with radiotherapy for testicular cancer. Sperm from patients treated up to 5 years prior to examination were still seriously disturbed, reducing the possibility of obtaining data by the standard sperm chromosome technique. Recovery to oligospermic status could occur if the total tumour doses were less than 40 Gy and unilateral scrotal shielding was used. At doses above 50 Gy, even with shielding, patients were totally azoospermic. The success rate for producing analysable sperm metaphases using the normal technique varied from 2-60% for untreated samples and 0-3% for radiotherapy patients. Therefore an alternative procedure for sperm chromosome analysis was developed and assessed but it was not sufficiently effective to permit routine sperm chromosome analysis (Univ. Galway, 162).

The genetic risk of radiation is based, in one form of assessment, on the estimated dose needed to double the spontaneous incidence of hereditary defects which affect about 10% of all live-born children. Recently it has become clear that many other chronic diseases have at least a partial genetic base and a study has been made of

the prevalence and severity of these common, multifactorial diseases. The diseases have been divided into three groups: I. severe, including schizophrenia, multiple sclerosis, acute myocardial infarction, etc; II. less severe, including diabetes, gout, glaucoma, asthma, psoriasis, etc; and III. least severe, including varicose veins, allergic rhinitis, etc. The prevalence of group I is $500/10^4$, group II $3000/10^4$ and group III $2800/10^4$. Heritability estimates range from 0.3 for diabetes mellitus to 0.9 for systemic lupus erythematosus. The common, multifactorial diseases are not generally associated with mortality in the first 20 years of life but are the leading causes of death between 20 and 70. Overall, about 16% of all deaths in Hungary can be attributed to these diseases. The mean number of years of life lost is substantial for only five diseases, 30 years for epilepsy, 20 years for multiple sclerosis, systemic lupus erythematosus and affective psychoses and 13 years for schizophrenia. In comparison with mendelian diseases as a whole the multifactorial diseases are associated with a much greater detriment (Univ. Leiden, 226).

Conclusions

Satisfactory progress has been maintained in general over the whole area of research covered in this sector with outstanding progress being made in some areas. The wider application of modern molecular biological techniques has opened new possibilities for more detailed analysis of damage to DNA and its repair even at the DNA sequence level. Further exciting developments can be anticipated.

New cytological techniques are being developed and perfected which will allow more sensitive detection of low doses of radiation and offer good perspectives for biological dosimetry. These techniques, coupled with new methods for detecting DNA damage, should permit a better investigation of the way initial damage at the molecular level is converted to cytological effects on chromosomes and mutations. All these factors have to be understood if a rational choice is to be made of the appropriate methods of extrapolating effects at high doses and high dose rates to low doses and dose rates in order to estimate the low dose risk of radiation.

Several specific recommendations can be made:

- repair studies in mammalian cells should concentrate on ionising radiation and should aim to identify the nature of the critical molecular lesions leading to the biological effects;
- studies are needed to correlate repair processes with the effects of repair at the cellular level, especially with a view to understanding the dose rate effect;
- studies on the effect of low doses of neutrons on the induction of aberrations in lymphocytes will provide direct information on the low dose relative effectiveness of neutrons compared with X-rays;
- more work is needed on the influence of the biology of spermatogenesis on the induction of mutations and translocations in the mouse and other species to facilitate an understanding of the effect in man;
- a better understanding of the mechanisms involved in the formation of radiation induced chromosomal aberrations is needed both for sparsely and densely ionising radiation.

6. Evaluation of Radiation Risks and Optimisation of Protection

An integrated approach was taken to evaluate the risks to man of the utilisation or presence of ionising radiation, and an attempt was made to develop a consistent framework to place radiation in perspective with other risks. Consequently, the Programme proposal 1985-1989 stated as its aims to:

- assess individual and collective doses in order to establish an overview of population exposure and its temporal and regional distribution;
- assess the detriment of ionizing radiation by developing mathematical and conceptual models and by using epidemiological data from suitably exposed populations;
- evaluate the social and economic implications of the use of ionizing radiation and alternative procedures with the aim of optimising the protection of man and his environment;
- develop methods to analyze accidents at the critical steps of the nuclear fuel cycle with respect to public health, economic consequences and appropriate countermeasures;
- assess risk in a comparative way by quantifying risks and the factors determining them;
- reduce exposure from medical diagnostic procedures.

In absolute terms, research on risk assessment did not fully attain the level foreseen in the Programme proposal; compared to the other sectors, however, this research increased substantially. The Chernobyl accident stimulated interest in several areas considered in this sector and intensified the development of improved procedures for the assessment of the radiological consequences of accidents and the optimisation of countermeasures. With respect to the reduction of patient exposure, research on quality assurance increased, while that on the diagnostic efficiency of various procedures remained very limited.

Six main topics are considered in this sector which comprised 75 contracts consisting of 104 projects. The number of projects in each area is given in parenthesis:

a) Risks from exposure to natural radioactivity
- physico-chemical properties of radon daughters (4),
- improvement of lung dosimetry and assessment of health effects (6),
- processes underlying the ingress of radon and development of models (7),
- development of effective remedial actions (4),
- natural radioactivity in the environment (3).

b) Risks from industrial uses of radioactivity
- probabilistic accident consequence assessment including socio-economic consequences and countermeasures (22),
- real-time accident assessment (6).

c) Comparative risk assessment
- methodological approaches (2),
- regional case studies (2).

d) Optimisation of radiological protection
- occupational exposure (5),
- guidance for the implementation of the ALARA principle (4).

e) Risk assessment from epidemiological data
- exposure for medical reasons (2),
- childhood cancer (1).

f) Reduction of patient exposure to radiation from medical diagnostic procedures
- evaluation of radiological practices in Member States (4),
- methods and models for dose calculation and measurement (5),
- assessment of risk related to organ and tissue doses from routine and special radiological examinations (4),
- determination of dose-increasing and dose-reducing factors (6),
- establishment of quality criteria of radiographic techniques, radiographic images and patient exposure (4).

a) Risks from exposure to natural radioactivity

During the past ten years, the Programme has stimulated and supported research dealing with the modalities and consequences of exposure to radon and its daughter products. From 1980 to 1984, efforts concentrated on the assessment of the extent and the distribution of exposure to radon within Member States through national and regional surveys. These have yielded reliable data on the average exposure of the European population and the distribution at regional and national levels. They have also indicated those regions where exposure is above average. During the 1985-1989 Programme, emphasis was given to the study of those parameters and processes that are influential in determining the levels of exposure to radon, aiming to increase the understanding of the physical and biological processes and to develop practical and cost-effective remedial actions. Some surveys of indoor exposure to radon continued in the more recent Member States of the EC, and regular intercomparison and intercalibration exercises were carried out to ensure the quality of the radon measurements. In 1987, an ad hoc working party of the group of experts set up in accordance with Article 31 of the EURATOM Treaty published a report outlining the present situation within the Community.

Physico-chemical properties of radon daughters

The size distribution of the aerosol particles, the percentage of the unattached fraction of radon daughters and the equilibrium factor are important parameters for developing models to estimate radiation exposure to lung.

Indoor activity size distributions were measured in different rooms with radon levels ranging from 200 to 1,700 Bq m^{-3} (Univ. Göttingen, 130). All rooms were slightly or moderately ventilated and without additional aerosol sources; concentrations of aerosol particles were between 2,000 and 16,000 cm^{-3}. Activity size distributions for ^{218}Po can be approximated by bimodal log-normal distributions (activity median diameters (AMD) of 1.2 and 181 nm), whereas the size distributions for ^{214}Bi and ^{214}Po are almost unimodal log-normal (AMD 197 nm). Depending on aerosol particle concentrations, one fifth to one half of the ^{218}Po activity was unattached, and the activity median diameter (AMD) ranged from 0.5 to 2.0 nm with quite high geometric standard deviations; this indicates that radon daughter products attract molecules of various atmopsheric gases)H_2, NO_x, SO_x and grow by cluster formation before becoming attached. When additional aerosol sources are present, a third type of aerosol, those in the nuclei mode with sizes of less than 100 nm, were sometimes found beside the unattached and aerosol-attached activities. In the presence of cigarette smoke or aerosol particles from a tiled stove, AMDs of about 300 nm were observed.

Outdoors, about 90 percent of the activity is associated with aerosol particles with median diameters of 300 to 400 nm. Outdoor aerosol sources or special meteorological conditions can sometimes result in radioactivity being present in the nuclei mode size range (<100 nm) or coarse mode size range (>2,000 nm). Aerosol particle concentrations in the outdoor atmosphere are higher than those indoors; consequently, a mean value for the unattached fraction (fp) of 0.02 and for the equilibrium factor (F) of 0.67 was found (Univ. Göttingen, 130).

Measurements in rooms under realistic conditions without additional aerosol sources (e.g. bedrooms) were compared with predictions from room models. Under these conditions, radon decay products have mean plateout rates of 54 h^{-1} for the unattached fraction, 0.21 h^{-1} for the attached fraction and a mean attachment coefficient of 5.10^{-3} cm^3h^{-1}). With increased aerosol concentration, the unattached

fraction decreased and the equilibrium factor increased. A mean **equilibrium factor** and a mean unattached faction were defined for a mean aged aerosol concentration (6,100 cm^{-3}): fp = 0.096 and F = 0.3 (Univ. Göttingen, 130).

In the presence of aerosol sources, the behaviour of the radon decay products depends markedly on the sizes of the aerosols produced. For example, if the aerosol sources produce small particles in the nuclei mode size range (some tens ofnm , the unattached fraction of the radon daughters is only slightly less than in a closed room since the attachment rate to particles of these dimensions is relatively small. Other aerosol sources, such as cigarette smoke, wood burned in a tiled stove or soot particles from burning candles, mostly produce particles in the larger size ranges, e.g. the accumulation or even the coarse mode, and these greater particle sizes result in an increased attachment rate with unattached fractions below 0.005 and an equilibrium factor up to 0.8.

The numerical code AERO1A (Univ. Gent, 112) was used to describe the size distributions of three relevant short-lived decay products of radon (^{218}Po, ^{214}Pb and ^{214}Po). Most of the relevant processes were taken into account, physical (ventilation, attachment, deposition of the attached and unattached fraction and recoil) as well as physico-chemical (clustering, growth and neutralisation of the free radioactive ions). The model, applied to some selected conditions, showed that the active size distributions and the amount of airborne radioactivity are largely affected not only by the aerosol loading of the atmosphere but also by its chemical composition and the dielectric/conductive characteristics of the surfaces in the room. The large spread found in values for deposition rates of the unattached fraction reported in the literature is suggested to be partly due to the fact that a steady state situation has been assumed, whereas any disturbances (e.g. closing a door or a window) can influence this deposition rate over long time periods (some hours).

The effect of the behaviour of radon decay products on the effective dose equivalent

Measurements of the unattached fraction show that calculations of natural exposure of the public are mostly based on incorrect values for the unattached fraction of short-lived radon decay products. Under normal conditions, the mean fp value of

0.095 is three times greater than that proposed in the literature (fp=0.03). Such a low, or an even smaller, value for the unattached fraction would be found only in rooms with additional aerosol sources (cigarette smoke, aerosols from cooking, etc) and in the outdoor environment. Measured radon daughter concentrations were fitted to a room model using average deposition rates of the unattached daughters, and the parameters important in dosimetric models were assessed. This enabled the effective dose equivalent to be computed by means of the Jacobi-Eisfeld or the James-Birchall model, and yielded a conversion factor per unit of radon gas concentration of 50 μSv annual effective dose equivalent for 1 Bq.m^{-3} radon concentration (Univ. Gent, 112; NRPB, Chilton, 116).

Improvement of lung dosimetry and assessment of health effects

Aerosol transport and deposition in the respiratory tract, with special attention paid to the upper airways, was investigated using a hollow anatomical cast and two nasal casts obtained from cadavers, and monodisperse aerosol particles in a range of 6 to 150 nm (NRPB, Chilton, 116). Very few particles with diameters greater than 20 nm are deposited in the nasal airways, most entering the lung. Smaller aerosols are deposited in the upper respiratory tract, especially if the particle sizes are smaller than 10 nm. It was suggested that half of the unattached fraction (size from 0.5 to 3 nm) is deposited in the nose. Penetration through the oral cavity of the cast was similar to that through the nasal casts; thus, the lung dose from unattached radon daughters would be about the same when breathing by either the nose or the mouth.

Radon ingress and development of models

In order to develop measures to reduce radon concentrations in dwellings, the mechanisms responsible for the **infiltration of radon from the soil**, i.e. the static or diffusive flow and the pressure driven flow, must be understood. Measurements in a test dwelling showed radon concentrations in crawl spaces and living rooms to be larger than when calculated from measured static source strengths (Univ. Groningen, 120). The changes with time of radon concentrations when pressure was

applied indicate that pressure driven flow through the soil accounts for the difference between measured and predicted radon concentration the crawl spaces and living rooms. It can, therefore, be a predominant pathway of radon infiltration into dwellings.

Exhalation rates from soil or construction material are usually measured using small samples, generally in "closed can set-up". Since these laboratory conditions are very different from exhalation from walls, three-dimensional steady-state radon diffusion was modelled by defining an equivalent sample geometry with a reduced thickness and applying a pure one-dimensional model to the reshaped sample (Univ. Gent, 112). In this way, exhalation from small samples could be compared with the one-dimensional exhalation from walls.

Development of effective remedial actions

The effectiveness of dose reduction by **treating the indoor air** by means of conventional filtration, electro-filtration and electrostatic plate-out was assessed (Univ. Lingby, 113). Simple filtration only gave a modest reduction in exposure. In most dwellings, radon originates mainly from soil gas, and the preferred remedial measures would be barriers preventing radon entry, but many presently available barrier techniques have not yet been evaluated with respect to their effectiveness and long term reliability. Even where an effective barrier technique is properly installed, the settling of a house could create new entry points after a few years. Indeed, under conditions favourable for radon entry (i.e. high soil permeability, an underpressure across the house foundation slab, etc.), small entry points suffice for significant radon flux into a house.

Ventilation can reduce the potential alpha energy concentration (PAEC) and the dose to about 20% of the unventilated level, but may conflict with household comfort and energy budgeting and, if incorrectly applied, may cause an increase in indoor radon when it depressurises the soil.

Removal by filtration and electrostatic plate-out is nearly as effective as ventilation. Each of these procedures reduces exposure to 30-40% and dose to about 40-60%, depending on the type of device and the size of the room (Univ. Lingby, 113); when

both procedures are used together, the effectiveness increases further. A combination of filtration and electrostatic plate-out appears an optimal, easy-to-install and cost-effective solution and reduces not only radon levels but also air pollution. Most tests on filtration and field-enhanced plate-out were laboratory experiments, but some were also carried out under conditions closely resembling normal living and working environments (Univ. Dublin, 117).

In order to investigate **radon barrier techniques**, two structures were erected on a soil with high radium concentrations, one with a concrete slab floor, used as a reference, the other with a ring-beam foundation, used as a test structure able to be fitted sequentially with a variety of floor types (NRPB, Chilton, 118). The maximum indoor radon concentration in the test structure was about 60,000 Bq m^{-3}, and the radon entry could be varied from a diffusion to a pressure-driven ingress. Significant radon entry can occur when the soil covers the wall-to-floor joints of the building. A monolithic floor structure with walls built off the floor resulted in little radon entry, provided service openings were adequately sealed. At a ventilation rate below 0.2 h^{-1} in the test structure, radon ingress was predominantly caused by diffusion from the sand. With low underpressure inside the structure (5 Pa), pressure-driven flow of radon from the sand into the structure was four times greater than that from diffusion alone.

A suspended timber floor of tongue-and-groove construction with gaps at the edges and with three air-bricks in each of the front and rear walls was then installed to provide natural ventilation of the underfloor space. The radon concentration under the floor was, on average, nearly two orders of magnitude lower with wide variations caused by wind speed and direction. These results suggest that adequate ventilation of underfloor spaces can reduce radon concentrations substantially.

Natural radioactivity in the environment

Substantial concentrations of **radon** occur **in some water** sources, and these have been used, and are still being used, for health care purposes. In Greece, several dozen radon treatment centres exist with a total of about 1 million visitors per year. The concentration of ^{222}Rn in these Spa water is among the highest in the world (up

to 10^7 Bq m^{-3}). Conservative estimates of annual effective dose equivalents of personnel for current operational practices may be over 100 mSv y^{-1} and, typically, from 3 to 30 mSv y^{-1}. Conservative estimates for the patients do not exceed 3 mSv y^{-1}.

In the same regions of Greece, e.g. in Attiki, well waters with elevated ^{222}Rn concentrations (0.15 to 13 kBq m^{-3}) are distributed to significant population groups for domestic use (NRCPS, Athens, 114). The consumer-weighted distribution has a maximum of about 4,000 Bq.m^{-3} resulting, under normal conditions of domestic use, in an additional annual effective dose equivalent of less than 50 μSv y^{-1} for the highest concentrations observed.

Technologically enhanced natural radiation arises, among other things, from phosphogypsum derived from uraniferous phosphate rock with ^{238}U activities of about 1500 Bq Kg^{-1} which is a by-product in the manufacture of phosphoric acid. About 2 million tonnes of waste phosphogypsum are disposed of in the United Kingdom each year, mostly to estuaries and coastal waters but some is also dumped on land (NRPB, Chilton, 118). Annual effective doses to individuals from exposure to the waste are unlikely to exceed 100 μSv, and the annual collective effective dose from the current discharges to UK coastal waters is of the order of 1 man Sv. This latter value can be compared with an annual collective effective dose in the UK of more than 50,000 man Sv due to radon daughter exposure.

In the Netherlands, the regional distribution of ^{210}Po, ^{210}Pb and ^{226}Ra in estuaries was investigated in order to determine the radiological impact of releases from non-nuclear industries in estuaries of large European rivers (NIOZ, Texel, 328).

Surveys of indoor exposure to radon in the recent EC Member States

In Portugal (LNETI, Lisbon, 208), radon in houses in the vicinity of the uranium tailings at Urgeiriça and an old radium salts factory at Barraçao, as well as in some villages from the granitic region of Beira Alta and other granitic regions, were compared with radon in houses in other regions of the country in order to complete the European Atlas on natural radiation. The results reveal three different concentration ranges according the region studied:

- high concentrations are due to waste from the old radium salts factory and from the uranium tailings (mean indoor value of 800 Bq m^{-3});
- medium concentrations in the granitic region (mean indoor value of 108 Bq m^{-3});
- low concentrations in the non-granitic region (mean indoor value of 41 Bq.m^{-3}).

More than 2,300 measurements of radon levels in Spanish houses (Univ. Santander, 314) yielded a geometric mean value of 41 Bq.m^{-3} following a log normal distribution. Houses largely exceeding this mean are located in Castilla, Extramadura, Galicia and the vicinity of Madrid where 10-15% of the houses have indoor radon concentrations exceeding 300 Bq.m^{-3}.

Radon metrology

Most surveys are carried out using time-integrating alpha-track dosemeters with CR-39 plastics, though the geometry and etching procedures may differ. Intercomparison and intercalibration exercises for active and passive measuring devices were organised in 1982, 1984 and 1987. These intercomparisons enabled participants to identify conditions that might cause measurement problems, e.g. at low radon concentrations or when a high unattached fraction of radon decay products is encountered. The sensitivity and reliability of passive alpha track detectors may be affected by environmental conditions such as extreme temperatures, humidity levels, organic vapours, or high concentrations of dust or smoke particles. A pilot field intercomparison was carried out in 1988 with the participation of a French, an Irish and an Italian laboratory in order to evaluate the feasibility and appropriate design of a large multinational field intercomparison.

Conclusions

The Programme period under consideration has been characterised by rapid progress in the determination of the parameters responsible for radon exposure and the understanding of the basic mechanisms involved. Among the most important achievements are the definition of a conversion factor of 50 μSv per Bq m^{-3} radon gas concentration, the elaboration of means to determine radon exposure in a reproducible way and the development of cost-effective countermeasures. Indoor radon exposure, being the most important single contributor to the exposure of the

population, requires not only regulatory initiatives, the elaboration of building codes etc., but also remains an important challenge for Community research and an area for continuing effective co-operation with the United States and Canada.

b) Risks from industrial uses of radioactivity

Efforts in this area were directed towards the development of methods to evaluate the risks presented by nuclear installations in normal operational and accident conditions. Particular emphasis was placed on the development of a comprehensive methodology for assessing accident risks as an input to decisions on risk acceptability, siting, emergency planning and choices between alternative design options. Significant resources were also directed towards the development of systems to aid the off-site management of accidents. These are intended to provide timely and well considered advice which is a prerequisite of effective intervention in an accident.

Probabilistic accident consequence assessment

A project entitled "Methods for Assessing the Radiological Impact of Accidents" (MARIA) began during the last 2 years of the 1980-84 Programme and continued, in a substantially enlarged form, during 1985-89. KfK, Karlsruhe (128) and NRPB, Chilton (127) were the principal contractors for this second phase which, overall, involved some 18 different contractors from 12 organisations in 28 separate projects. Five additional projects, supported in the framework of the Programme's post-Chernobyl actions, contributed, at least partially, to progress within the MARIA project. The second MARIA project aimed primarily to:

- develop a probabilistic ACA code that was modular, that incorporated the best features of those models currently in use in the EC, and that could be readily modified to take account of new data and/or model developments in the future;
- develop a code that would be broadly applicable and capable of finding wide usage within the EC;
- issue the code to interested users and provide guidance on its application;
- acquire a better understanding of the limitations of current models and develop more rigorous and complex approaches for application where current methods are neither valid nor sufficiently reliable;
- quantify uncertainties in the model predictions with a view to identifying their origins and how, if necessary, they might be reduced.

The project has led to the development of a new probabilistic accident consequence code, COSYMA (COde SYstem MAria), which will be made generally available to interested users in mid-1990. The development of this code is based on a wide range of research dealing in particular with:

- atmospheric dispersion and deposition;
- assessment of human exposure from airborne and deposited radionuclides;
- health effects models;
- countermeasures models and economic impact;
- uncertainty analysis.

Atmospheric dispersion and deposition

Considerable progress has been made in the modelling of trajectories, the modelling of non-uniform releases of moderately long duration, the more realistic modelling of the spatial and temporal deposition of material by rainfall, the description of deposition phenomena and how they might be better modelled in the future and dispersion in complex terrain.

Dry deposition phenomena, particularly in the context of deposition in urban areas were investigated by SRD, Culcheth (131). Several difficulties have yet to be overcome, however, before a sufficiently reliable model can be developed to predict the spatial distribution of deposited material on to various urban surfaces. The dispersion of particles with appreciable settling velocities, and dispersion and deposition occurring in foggy conditions, were also investigated.

The influence of precipitation on accident consequences was carefully evaluated (ICSTM, London, 108) and a new model developed for predicting wet deposition with the aid of radar measurements of precipitation.

Atmospheric dispersion in complex terrain, in particular dispersion around mountains, was investigated in a variety of atmospheric stability conditions (NRCPS, Athens, 114) and also in the presence of sea breezes. The methods used are too complex and demanding in terms of computer time for use in general probabilistic Accident Consequence Assessment (ACA) codes. However, the results provide general guidance on how, and under what circumstances, predictions of simpler models can be modified to approximate dispersion in complex terrain.

KfK, Karlsruhe (128) and NRPB, Chilton (127) investigated and compared in a comprehensive manner the predictions of several models which are potentially suitable for use in ACA codes. Trajectory models provided more realistic predictions than straight-line Gaussian models without any undue increases in computer time. Both types of model, along with other options, are included in COSYMA, with the choice of approach for any particular application being left to the user. A new model has also been developed to predict the consequences of releases in excess of several hours and ranging up to days and weeks.

Short distance atmospheric dispersion models were validated (Risø, Roskilde, 296). The results of these experiments are being used to establish data sets of instantaneous cross-wind concentration profiles both for assessing uncertainties in near-in atmospheric dispersion model predictions and also, in future, as a basis for testing the performance of real-time models in emergency response systems.

Assessment of human exposure from airborne and deposited radionuclides

One of the main objectives of the work in this area was to gain a better understanding of the behaviour of deposited material following an accident and to develop improved models to describe this behaviour in so far as it influences the exposure of people. Particular attention was paid to external exposure from material deposited on the ground and building surfaces and to exposure from ingestion of contaminated foodstuffs. Models were also developed for resuspension of deposited material and for predicting the deposition of radionuclides on skin and clothing (NRPB, Chilton, 127; KfK, Karlsruhe, 128).

The integrated air concentration of aerosols inside and outside a house with closed windows and doors was measured following the Chernobyl accident (Risø, Roskilde, 107). The indoor concentration of caesium was about one quarter of that outdoors. A model was also developed (ICSTM, London, 108, 228) to predict the reduction in indoor exposure, compared with that outdoors, taking account of filtration effects on air entering houses, air exchange rates and deposition on indoor surfaces. Deposition on to indoor surfaces was identified as an important contributor to the reduction of indoor air concentrations.

The deposition of Chernobyl fallout, weapons' fallout and simulated material was measured on a wide range of surfaces in various orientations (Risø, Roskilde, 107; GSF, Neuherberg, 111), and recommendations were made for dry deposition velocities for a range of nuclides on a wide range of surfaces commonly found in urban and rural environments. The subsequent behaviour of deposited material has been investigated by measuring run-off and wash-off of caesium from a variety of roof materials with different slopes, and a useful data base was compiled to obtain parameters for modelling. The measured removal rates are, in general, low. The rates of deposition of airborne material to the interior surfaces of both furnished and unfurnished rooms were also measured (ICSTM, London, 228; Risø, Roskilde, 107), and methods were developed for non-invasive measurements of the ingress and re-distribution of deposited material within dwellings.

Two major models, FARMLAND and ECOSYS, to describe transfer through food chains have been developed within the EC by NRPB and GSF respectively. Data libraries generated by both models for the transfer of radionuclides to a wide range of foodstuffs, as function of the time following unit deposit of nuclides of potential importance, are incorporated into the COSYMA code. Several improvements and modifications have progressively been made to FARMLAND (NRPB, Chilton, 128) including a better model for the translocation of deposited material from plant surfaces to the edible portions of root crops. Comparisons between the model predictions of FARMLAND and ECOSYS, as well as with measurements collected within the EC of the transfer of Chernobyl fallout to foodstuffs, are continuing. Particular consideration is being given to the influence of agricultural practice and soil characteristics on the magnitude and time dependence of transfer. The reduction of radioactive contamination during food preparation and processing, both domestic and commercial, and the influence of food distribution practices on resulting exposure, were also investigated.

External radiation from deposited material is an important exposure pathway. Its evaluation was a major feature of the research programme prior to the Chernobyl accident, but it was allocated even greater resources after the accident because of the opportunities provided for model validation. An improved and more realistic model, EXPURT (EXPosure from Urban Radionuclide Transfer), has been developed

(NRPB, Chilton, 127). Deposition and subsequent removal of material is modelled on to a variety of surfaces, including walls, roofs and paved areas, with account being taken of fixation of material, run-off and migration through permeable surfaces. Based on the predicted temporal and spatial distributions of deposited material, dose estimates are made taking due account of the effects of shielding by buildings, etc. However, significant uncertainties remain, especially with regard to predicting the levels of deposition to, and the subsequent behaviour on, the wide range of surfaces in an urban environment. There are also indications that material deposited on trees can make an important contribution to external exposure and, therefore, may need to be modelled explicitly in future.

Models of varying complexity were developed for calculating the shielding provided by buildings against gamma radiation from a passing radioactive cloud and from deposited material (Risø, Roskilde, 175; GSF, Neuherberg, 111; CEA, Fontenay-aux-Roses, 119; NRCPS, Athens, 114). The models were compared with respect to their respective performance, validated against experimental data in some cases, and applied to evaluate the effectiveness of shielding in a number of specific environments. Comprehensive data bases of external doses from deposited radionuclides were compiled (GSF, Neuherberg, 111) and can now provide the basis for rapidly estimating doses in a wide range of locations, subject to the specification of the levels of deposition on potentially relevant surfaces. The methods used to calculate doses from unit concentration of airborne and deposited material are now broadly adequate for use in probabilistic ACA codes. Major uncertainties remain, however, in the prediction of the external doses due to uncertainties in predicting the spatial and temporal distribution of deposited material.

Skin beta exposures from radionuclides deposited on the skin and clothing were improved, and the data bases in COSYMA for internal dosimetry are continuously updated to reflect international developments in this area.

The existing data bases on EC population and agricultural production were improved, updated and extended to include the more recent Member States of the Community (CEA -CEC Assoc., Fontenay-aux-Roses, 122). Other useful data bases are now also being compiled, including housing, land use and/or other measures of

economic activity. Continuing effort will be required to improve these data bases and to ensure that they remain up to date.

Health effects models

Effort in this area, like that on internal dosimetry, has been limited to remaining abreast of new developments, of which there have been several in recent years, and to ensuring that the models included in COSYMA are consistent with the latest recommendations of national/international bodies. Considerable flexibility is, however, being maintained in the modelling of health effects in the COSYMA code consequent upon the continuing debate over the most appropriate choice of risk coefficients and dose and dose rate effectiveness factors.

Countermeasure models and economic impact

The modelling of countermeasures has been improved (NRPB, Chilton, 127; KfK, Karlsruhe, 128), in so far as was practicable within the constraints imposed by the requirements of an ACA code, and the approach was made as flexible as possible. This will enable the code to be broadly applicable and accommodate readily the detailed differences in emergency planning between countries and various types of nuclear installation. The following countermeasures have been modelled: evacuation, sheltering, issue of stable iodine, relocation, resettlement, food restrictions and decontamination of various types. Flexibility is maintained over the timing and spatial extent of these measures and over the criteria on which their introduction is based.

Socio-economic impact

Two new improved models (COCO - Cost of Consequences Off-site, and MECA - Model for assessing the Economic Consequences of Accidents) were developed (NRPB, Chilton, 127; UPM, Madrid, 227) to estimate the off-site economic consequences of accidents in the context of the UK and Spanish economies, respectively. They are, however, generally applicable in the EC subject to the input of the relevant economic data. The costs of the following countermeasures can be

estimated: sheltering, evacuation, food restrictions and decontamination and, in addition, the costs of health effects in the exposed population. An intercomparison of the predictions of the two codes, MECA and COCO, will be undertaken in due course.

Uncertainty analysis

A package of statistical techniques (GRS, Garching, 125) that can be used to estimate sensitivity and uncertainty has been developed. In parallel, a wide range of investigations (NRPB, Chilton, 127; KfK, Karlsruhe, 128; CEGB, Berkeley, 209) has been made of the uncertainty in the predictions of particular modules or sub-models of ACA codes and of the codes overall. These have been undertaken for various purposes including investigations of the relative merits of alternative uncertainty analysis techniques; identification of the major sources of uncertainty as an input to directing further research effort; and, most importantly, as an input to assessing the overall uncertainty that is typically associated with predictions of ACA codes.

Improvements are still needed in the methods used to communicate the meaning and significance of uncertainty estimates to a wider audience, both lay and scientific. Greater attention also needs to be given to how the uncertainty distributions in the many model parameters of ACA codes are generated; expert judgement elicitation and evaluation are likely to be used for this in future.

Conclusions

Considerable progress has been made in the second phase of the MARIA project and its main objectives have been met. Improvements have been made in several modelling areas and greater understanding has been gained of the limitations of the approaches commonly adopted and where alternative and generally more complex methods are necessary. A comprehensive and new probabilistic accident consequence assessment code, COSYMA, has been developed and this will be made available to interested users in mid-1990. Its modular form provides a sound basis for the incorporation of future developments.

A third, more limited phase of the MARIA project will be undertaken within the 1990-1991 research programme. Resources will be directed towards consolidation of what has been achieved, providing continuing support for the code when it is issued and upgrading particular models where practicable and necessary. The analysis and communication of uncertainty will continue to receive major attention.

Real-time accident consequence assessment

Many of the models developed within the probabilistic framework are equally applicable for use in real-time computer-aided emergency response systems. Research in this area increased steadily in the Programme during the past decade and then considerably after the Chernobyl accident. Prior to the Chernobyl accident the research was directed towards specific topics, such as the use of monitoring data to update predictions, development of expert systems for decision support in the event of an emergency and the development of the systems for use in training (SCK/CEN, Mol, 106).

Following the Chernobyl accident, four institutes collaborated on the development of some of the basic modules of a real-time system for use in emergencies. Three of the modules developed are concerned with the prediction of atmospheric dispersion over short, medium and long distances; the fourth module is concerned with the assessment of the radiological impact of a release based on the predictions of these dispersion models and/or environmental monitoring information. Procedures for the feedback of monitoring data in order to update the predictions of the dispersion models are included. A software package containing the various modules is being made available to other interested groups (ICSTM, London, 256; ENEA, Rome, 254; CEA, Fontenay-aux-Roses, 253; GSF, Neuherberg, 255).

c) Comparative risk assessment

Risk assessments of industrial facilities have become increasingly commonplace over the past decade as it has been recognised that economic as well as safety benefits result from the risk assessment process. Moreover, they have become a regulatory requirement in many areas following several major industrial and transportation

accidents. The assessment of the risks of nuclear installations, both in normal operation and in accidents, has been at the forefront of developments in this area. Methodological improvements are, however, no longer confined to the nuclear sphere. Consequently there are benefits to be gained from remaining abreast of developments elsewhere, with a view to achieving cross-fertilisation of ideas and facilitate the transfer of methods, where appropriate, between the various disciplines. These considerations have been the major motivation behind the research being carried out in this area. The other major consideration has been to put the risks of radiation exposure into perspective with other carcinogenic and mutagenic agents.

Methodological approaches and regional case control studies

Methodologies for risk management in the nuclear and non-nuclear fields were compared (CEPN, Fontenay-aux-Roses, 207) with the aim of identifying methodological convergence and exploring the extent to which the ALARA concept was being, or could be, applied in non-nuclear areas. These matters were elucidated by means of case studies performed in two main areas: firstly, the management of carcinogenic risks in industry, where the nature of the risk and its management are similar to those encountered in radiation protection; and, secondly, the management of the transportation of hazardous substances.

A methodological framework was established comprising five steps, namely risk identification, analysis of the system, risk management issues (e.g. constraints and options for risk reduction, criteria, etc), risk evaluation and the use of formal decision making aids, and development work on methodologies was undertaken in each of these areas. The case studies comprised analyses of nickel compounds, benzene, PCB transformers, chromium compounds, acrylonitrile and of transportation of hazardous materials in Lyon and Grenoble. Significant differences were evident in the application of ALARA in the nuclear and non-nuclear fields. The costs of human life that could be implied from risk reduction measures taken in non-nuclear industries were found, in general, to be broadly comparable with those in the nuclear field, although the range of variation was considerable (from less than 0.1 to more than 100 MEcu).

In the previous Programme a comparative assessment was initiated on the chemical and radiological hazards to which the population of southeast France (Greater Rhône Delta) was exposed. The purpose of the analysis was to determine the relative importance of the various sources of pollution, including natural, domestic and industrial sources, and to provide inputs to decisions on their management. This assessment was continued in the present research programme (CEDHYS, Fontenay-aux-Roses, 121) and consideration given to emissions in normal operation and to accidents. The emission sources assessed included electricity generation (coal, oil and nuclear); use of energy for heating in residential and tertiary industry sectors; specific industries, to the extent that relevant data were available; medical radiological diagnosis; exposure to natural radiation; and exposure to pollutants in the home. A generic methodology has been developed to estimate the impact of any emission to the atmosphere and to the aquatic environment.

Estimates have also been made of the concentration distributions in the region of six major pollutants (sulphur dioxide, particulate, nitrogen oxides, volatile organic compounds, carbon dioxide and carbon monoxide) released in the use of energy for domestic heating and the use of tertiary heating in industry. For identical fuel consumptions, residential heating in general results in greater concentrations of each of the six pollutants than tertiary industrial heating or power generation. A data bank has been compiled of the emissions from a wide range of household products and of the frequency and type of usage. The significance of these emissions has been compared with that of indoor radon exposure.

An investigation has been made of the release of radioactive materials from coal fired power plants (approximately 3 GW installed capacity) and their environmental impact in the Valley of Ptolemais in northern Greece (Univ. Thessaloniki, 104). Extensive measurements have been made at various locations of external dose rates both indoors and outdoors, of radon concentrations indoors, of concentrations of radioactive materials in air, on the ground and in grass and tree leaves. High indoor external dose rates (about twice the average values) were measured in the vicinity of the fly ash tips and also in a village where workers in the plants reside.

Conclusions

Comparative risk assessment is a complex topic and the work being undertaken in the Radiation Protection Research Programme is but a small part of overall work being undertaken in this field. The research so far carried out has, however, made a useful contribution to the development of more consistent and complete methodologies for assessing the impact of diverse pollutants released into the environment and to putting each in better perspective. It must be recognised that this work can never be exhaustive given the vast number of potentially significant pollutants released to the environment. Consequently, the research effort has mainly been directed towards the development of methods that can find generic application, irrespective of the nature of the pollutant. This same approach will be followed in any future research carried out in this area within the programme.

d) Optimisation of radiological protection

Radiation protection is founded on three basic principles. These are, that any exposure is justified, that is, there is a positive net benefit from the introduction of the practice, that it is optimised, i.e. the exposure is reduced to As Low As Reasonably Achievable, social and economic factors taken into account (ALARA), and that dose limits are observed. In practice, compliance with the optimisation principle has the greatest influence in determining exposure.

Optimisation is central to the development of standards and day-to-day radiological protection. The importance given to it in the current recommendations of ICRP, and carried into the EC Basic Safety Standards, is likely to be reinforced in the forthcoming revision of the IRCP recommendations. Given its importance, the Programme has devoted significant efforts to this topic at both the conceptual and practical levels.

Occupational exposure

Occupational exposure was assessed and analysed in the Federal Republic of Germany (GSF, Neuherberg, 111) and in the UK (NRPB, Chilton, 213). The GSF Personnel Dosimetry Service has analysed the trends in exposure of workers in

various occupations. The annual average dose for most occupational groups was below one-tenth of the dose limit, although a few individuals, especially maintenance workers in nuclear plants and some medical operators, received annual dose equivalents in excess of 20 mSv. An analysis of dosimetric data, obtained since 1980, showed that the annual collective dose from medical applications remained essentially constant (about 8 man Sv), whereas the annual collective dose from industrial applications declined with time.

GSF also carried out a selective analysis of partial body exposure at the workplace for X-ray exposure to physicians and radiographers engaged in medical diagnostic radiology and for beta-ray exposure to workers in nuclear plants. The results show that organ dose limits were sometimes exceeded even when the standard personal dosemeters did not show this; therefore, partial body dose monitoring is indicated in some situations.

More than 94,000 individuals (97% of the population studied) are now incorporated in the UK National Registry for Radiation Workers, 94% of whom were traced in the National Health Service Central Register. Plans for the analysis of the data base were reviewed. This analysis will involve a comparison of mortality rates with those of the general population, and tests for trends in mortality with doses received. Computer programmes to be used were developed and successfully tested for consistency.

A data base of 5,603 radiation workers (85% of the total, of whom about half are miners) was established at the Spanish Nuclear Council (CIEMAT, Madrid, 229) for the period 1975-1986. Mean exposure time was 11.3 years (observation 83,000 person years; exposure 37,000 person years) with a mean accumulated dose of 11.9 mSv corresponding to an annual average dose of the order of the natural background.

Guidance on the implementation of the ALARA principle

NRPB, Chilton (110) evaluated the implications of using, for members of the public, a limit based on averaging the annual dose over a lifetime rather than on the dose in a single year. Derived limits, in terms of radionuclide concentrations in

environmental materials, were calculated for both approaches. It was concluded that, although it was possible to limit the average annual dose over a lifetime by setting effluent discharge limits, it was easier and more conservative to limit the dose on an annual limit.

Analysing present ICRP recommendations on critical groups, NRPB found conceptual problems in their formulation and application when authorised limits were to be established. Indeed, the calculation of mean doses to these groups relies to a large extent on judgement, making it difficult to assess the real degree of protection achieved. In order to calculate the contribution to dose of major foodstuffs, it seems preferable to define the mean of a critical group on the basis of some upper percentile of the distribution of consumption rates in a population, rather than to define the critical group per se and then calculate their mean consumption.

ICRP, in its Publication No. 37, introduced the concept of source upper bounds as an additional constraint on optimisation. As shown in a review by NRPB, Chilton (110), such constraints are established in different ways in various Member States. This explains why the source upper bound concept has not been formally adopted by regulatory authorities and preference given to the more flexible concept of dose targets.

Clearer guidance is required on the implementation of the ALARA concept in radiation protection. A document prepared in a joint effort by CEPN, Fontenay-aux-Roses (105) and NRPB, Chilton (110) explains in simple language the ideas underlying ALARA and practical measures for its implementation. It indicates that ALARA is a workable concept and that tools for structuring optimisation problems and aiding decisions exist and can be effectively applied in practice.

The ALARA concept calls for due consideration not only of economical, but also of social aspects. The CEC-CEA Assoc., Fontenay-aux-Roses (122) assessed the subjective aspects of risk perception by means of questionnaires addressed to the public and groups of experts. Answers showed that, in addition to fear and anxiety, consideration must be given to the ideological and cultural backgrounds. This is a complicated area requiring further analysis and evaluation.

Conclusions

Analysis of occupational exposure data is a prerequisite for the proper implementation of the ALARA concept. Improvements in data collection are necessary and, where possible, should be harmonised on a Community level. The different approaches used to apply optimisation under normal and accident situations need to be investigated in more detail, especially in view of the forthcoming recommendations of ICRP and the revision of the EC Basic Safety Standards. While site- and country-specific considerations will continue to influence ALARA judgements and practices, especially with respect to the more subjective elements. The search for common approaches to optimisation on a Community scale is imperative to enable radiation to be used in an atmosphere of confidence and with minimal risk.

The methodologies for determining what constitutes ALARA in normal operations, both for public and occupational exposure, are now well established. For potential exposures that may arise in accidents or from releases from waste disposal sites far in the future, the determination of ALARA is more complex as probabistic aspects are then involved. Further development is needed to achieve a comprehensive methodology that is applicable to all areas of radiation protection. This is necessary to obtain optimal protection in situations where balances have often to be made between exposures of varying magnitude to different groups and having different probabilities of occurrence.

e) Risk assessment from epidemiological data

Data from human populations provide the most direct information on radiation risks. Most of these data originate, however, from people exposed to high doses at high dose rates, such as the survivors of the atomic bombs at Hiroshima and Nagasaki, or, as studied in the Programme, from patients treated with ^{224}Ra or thorotrast for medical reasons (for the epidemiology of ^{224}Ra see page 141). Collection and interpretation of data from populations exposed to low doses, such as people exposed to enhanced levels of radon, workers in nuclear industries or medicine, children exposed in utero or parent exposure prior to conception, are

fraught with great uncertainties. Co-operation on a Community or international scale is needed to obtain statistics of sufficient power, and the Programme has strongly stimulated European and international co-operation in this area, in particular with the US Department of Energy and the International Agency for Research on Cancer in Lyon.

INSERM, Paris (126) developed new statistical methods to analyse associations between spatially defined variables or joint variations of risk factors, such as low dose radiation or industrial pollution and with some health indicators such as cancer mortality at specific sites. Modified tests of simple and partial correlation were assessed by Monte Carlo simulations for two variables. Many geographical, medical or ecological applications exist in which variables are dependent on spatial location, but standard assessment procedures cannot consider spatial correlations of both variables. The simulation runs for two models, fixed grid sizes or administrative entities respectively, and type I error testing demonstrated that the power of the statistics is satisfactory and allows account to be taken of possible spatial auto-correlation. Implementation of these tests to geographical data confirmed their suitability for studying problems in geographical epidemiology. The underlying assumption for these methods is that data are normally distributed, but this may be too restrictive, and non-parametric tests of much lower power must be used. New approaches in this respect are being investigated.

The pattern of radiation-induced cancers in populations exposed to high doses of radiation can be modelled as a relative (or multiplicative) risk projection model. These are based respectively on a constant relative cancer risk or an absolute (or additive) risk projection model based on the assumption that the annual absolute excess cancer risk remains constant over time (NRPB, Chilton, 116). It was demonstrated that, generally, the data on solid cancers are consistent with a relative risk model (eventually with a tailing-off with time) rather than with an absolute risk model. These considerations become critical when, based on the new DS86 dosimetry and newly available data, health effect models and radiation protection regulations have to be updated. At the Univ. Würzburg (083), the Monte Carlo simulation code SIRIS, developed during the previous contract, was used to generate

synthetic epidemiological data for radiation induced leukaemia risk. The data were then analysed by means of the Cox proportional hazard model and contingency tables. Both analytical methods appeared to be acceptable.

A computer programme, ARFAR (At Risk For Any Reason), was developed (NRPB, Chilton, 116) which allows stratification of person-year-at-risk data for cumulative radiation dose and standard variables such as age, calendar period, etc. This model will be used for analyzing the data of the United Kingdom National Registry for Radiation Workers and has been satisfactorily run on trial data bases.

The geographical distribution of childhood cancer in the UK in relation to nuclear installations is investigated by the Committee on Medical Aspects of Radiation in the Environment (COMARE). The different methodologies used, particularly the choice of geographical units employed, were reviewed by NRPB, Chilton (116) in several studies. Computer simulation was used to check dispersion from a Poisson distribution and the applicability of the Potthoff-Whittinghill test for the analysis of the data base on the geographical distribution of childhood leukaemia and lymphoma established by the Childhood Cancer Research Group in Oxford. Cancer risks following irradiation in utero were re-assessed and the relative risks were confirmed to be around 1.4 (Univ. Birmingham, 129). NRPB, Chilton (116) estimated a risk of cancer incidence following low LET in utero exposure for diagnostic radiology of 6% Gy^{-1}, with 2.5% Gy^{-1} for leukaemia and 3.5% Gy^{-1} for other cancers.

A cohort study (ISS, Rome, 313) on underground pyrite miners (1,357 individuals) revealed a significant increase in overall mortality (348 deaths observed versus 217 expected) and cancer mortality (95 observed versus 59 expected). For an average duration of underground work of 18 years, and a median value of exposure to radon daughters of 0.5 WL, an excess of 13 cases per 10^6 person years per WLM was estimated, a value consistent with other reported estimates.

The risk associated with radon exposure in the home is being assessed in a case-control study in southwest England. Over the past two years, 648 lung cancer cases were identified of which, according the study criteria (sufficient residence in the region, acceptable health condition and co-operation), 285 were fully interviewed.

A total of 381 potential hospital controls were identified of which 215 received a full interview. Radon detectors were installed in the homes of 401 of the 500 interviewed cases and controls. The number of lung cancers identified is lower than expected but the scope of the radon study was enlarged, meanwhile, through similar studies in France, Belgium, Luxembourg and the Federal Republic of Germany.

The German Thorotrast study (DKFZ, Heidelberg, 123) started in 1968 and comprised 2,326 thorotrast patients and 1,890 controls, of which 2,151 and 1,493 respectively died. The final fate of 185 patients and 397 controls is being followed with a view to allowing the full calculation of the thorotrast late effects thus enabling a differentiation to be made between the various risk model proposed. Over the most recent years, significant excess rates were observed for malignant liver tumours, liver cirrhosis, myeloid leukaemia, bone marrow failures, and, most recently, non-specific mortality. Malignant liver tumours are appearing, after a latency period of 16 to over 45 years, about 200 times more frequently in thorotrast patients than in controls. For calculating the relationship between dose rate and effect, three cohorts with increasing administered volumes of thorotrast showed increasing cumulative rates of malignant tumours with the volume administered. Similar patterns were seen for four groups which had been injected at different ages with a marked increase of liver tumour incidence rate 30 to 40 years after injection.

The Danish Thorotrast Study (DCS, Copenhagen, 333) consists, after the reestablishment of the original data, of 1,092 recorded patients, 256 of which were still alive in 1988. The Danish cancer registry allows the evaluation of cancer and other health effects, and complements the German study through a different methodology. The preliminary finding of an increased risk of non-squamous cell lung cancer (6 fold increase after 20 years) is surprising and may have a bearing on radiation protection standards for exposure to indoor radon. The calculation of lung doses will be an important part of the follow-up, as will the evaluation of health effects in the offspring of female patients.

Conclusions

Radiation epidemiology remains an important field of research where a co-ordination of Community and other efforts is required. In recent years, and especially for environmental radon epidemiology, standardised protocols and harmonised data collection have been achieved, and this has greatly enhanced the quality of the various investigations and their outcomes. The recovery of the original Danish thorotrast data will supplement the German study. Geographical epidemiology is becoming increasingly important and methods of evaluation need to be further developed and optimised.

f) Reduction of patient exposure in medical diagnostic radiology

Improved health care is not conceivable without methods and techniques using ionising radiation. Diagnostic radiology, in particular, demands continuing efforts to optimise the radiation protection of the patient without impairing the diagnostic information and the clinical management of the patient. Special attention is given to diagnostic radiology since it contributes the greatest proportion of exposure from man-made sources to the overall exposure of the population. In the EC, each person receives, on average, about 0.5 mSv annually, but a few individuals who need frequent examinations might receive up to 1 Sv per year. Community efforts for optimising the use of ionising radiation in diagnostic radiology involve:

- regulations by establishing, updating and promoting the Council Directive of 3 September 1984 laying down "basic measures for the radiation protection of persons undergoing medical examination or treatment" (O.J. L 265, 5 October 1984);
- research studying ways and means to achieve optimal diagnosis while reducing patient exposure to levels as low as reasonably achievable.

Compared to the 1980-1984 Programme, this research area has been strengthened and has achieved a remarkably greater cohesion among contractors. New activities were initiated, in particular with regard to quality assurance of radiographic techniques and images. The results of this research are now being progressively introduced into everyday radiological practices.

Evaluation of radiological practices

General radiological practices were surveyed in Spain in the densely populated region of Madrid where health care is readily available (Univ. Complutense, Madrid, 214) and in Portugal, as a NEXT (National Evaluation of X-ray Trends) Programme (LNETI, Lisbon, 299). Several other surveys were re-evaluated in the light of new insights, data treatment or updated enquiries so that data of frequency of examinations, number of films and the corresponding values for the genetically significant dose (GSD) and the effective dose equivalent per caput (EDE) could be

Table I Practices and exposures of patients in EC Member States

CEC Member States	Number of X-ray examin. per 1000 inhabitants per year (1)	Mean number of films per examination (2)	GSD µSv	EDE µSv	References	Contract Nr. BI6-
Feder.Rep.Germany	1200	2.2	400	1000	F.E.Stieve 1989	
France	825	3.6	295	1580	C.Maccia et al.,1988	(132)
UK	444	2.3	120	282	B.Wall et al.,1981	(135)
Ireland	460	2.2	164	-	J.Cunningham et al., 1988	
North-East Italy	665	3.1	248	763	G.Contento et al., 1988	(136)
Spain (Madrid reg.)	680	2.2	252	1210	E.Vano et al., 1989 L. Arranz, 1989	(214)
Portugal	480	2.3	-	-	Galvao et al., 1989	(299)

(1) without dental examinations
(2) remainder organs included

GSD = Genetically Significant Dose
EDE = Effective Dose Equivalent per caput

updated (see Table I). A more detailed analysis of the differences noted in surveys in France, Italy and the UK (CEA/CEPN, Fontenay-aux-Roses, 132; USL No 7, Udine, 136; NRPB, Chilton, 135) revealed some reasons for the differences in the values for GSD and EDE, which could, in part, be attributed to the justification of the examinations, the radiological practices and the age distribution of the patients as well as to the introduction of quality assurance programmes and the use of new technical means and procedures.

Specific types of examinations were surveyed: mammography in France (CEA/CEPN, Fontenay-aux-Roses, 132), the Netherlands (TNO, Rijswijk, 138) and Portugal (LNETI, Lisbon, 299), intravenous urography in North-East Italy (USL No 7, Udine, 136). Consideration was given to specific patient groups: paediatric radiology in France (CEA/CEPN) and Germany (Univ. München, 211) or to new techniques such as Computer Tomography (CT) in Denmark, France, Germany, Italy, Portugal and the UK (Univ. Aarhus, 317, CEA/CEPN, Fontenay-aux-Roses, 132; GSF, Neuherberg, 133; USL No 7, Udine, 136; NRPB, Chilton, 135; LNETI, Lisbon, 299). These surveys provided, besides detailed information on the state of technique, practice and exposure conditions, a baseline of data against which the effects of quality assurance and dose reduction measures can be evaluated. The repeated survey of intravenous urography in northeast Italy showed, for example, that five years after quality assurance measures were introduced, the EDE dropped from 0.091 mSv/year to 0.051 mSv/year as a result of fewer examinations performed (replacement by ultrasound), use of higher speed film-screen combinations and fewer exposures per examination.

Methods and models for dose calculation and measurement

New realistic phantoms were developed based on data from whole body computed tomography which allowed more accurate calculation of doses (GSF, Neuherberg, 133), and Monte Carlo calculations were extended to cover the characteristic geometry of CT (NRPB, Chilton, 135). A comparison of organ doses conversion factors for certain CTs using a flat filter (GSF, Neuherberg, 133 and NRPB, Chilton, 135) agreed within about 2.5% for all important organs. The free-in-air axial dose profile for a single slice at the centre of rotation has been accepted as a basis for dose measurements in CTs with flat filter, but the problems arising for CT systems with shaped filters will require another comparison exercise. Polymethylmethacrylate (PMMA) was found to be suitable as phantom material for depth-dose determination in breasts, including thin compressed breasts which differ with respect to tissue composition (TNO, Rijswijk, 138). Organ doses were calculated for children and compared with data in the USA, but there the distribution of the red bone marrow and the localisation of organs were modelled in

a different way (GSF, Neuherberg, 133; 337). TLD material (CaF) was chosen which was sufficiently sensitive to serve in a survey in paediatric radiology (Univ. München, 211; GSF, Neuherberg, 337). Doses from radiotherapy or nuclear medicine to organs outside the target region were assessed (GSF, Neuherberg, 133; TNO, Rijswijk, 138) and it was found that breasts in women over 40 years can receive significant doses of 0.16-0.34 mGy during radiotherapy of other organs whereas the breast dose from nuclear medicine is insignificant.

The assessment of risk related to organ and tissue doses from routine and special radiological examinations

No general agreement yet exists concerning the quantities relevant for risk assessment in diagnostic radiology. An approach was developed (NRPB, Chilton, 135) to assess the factors for somatic and genetic risks from diagnostic examinations and compare them with the risk factors generally accepted in radiation protection. The extra risk for induction of breast cancer in women aged between 35 and 75 years screened annually by mammography was calculated to be about 1% of the natural incidence (TNO, Rijswijk, 138). This is a small risk compared to the potential benefit of annual mammography. It is hoped that when more data on the efficacy of diagnostic procedures based on optimised imaging processes and patient exposure becomes available that a more relevant assessment of relative risk will become possible.

Determination of dose-increasing and dose-reducing factors

The factors and practices that influence dose to patients are germane to all studies in the area of medical exposure, in particular those which, as revealed in the surveys, cause unnecessarily high doses to the patient. In this context, one should mention the skill of the operator, the age of the equipment, the establishment of standards as well as the frequency of standardised performance and constancy tests. Such investigations were carried out at the Univ. Erlangen, 137; Univ. Madrid, 214; LNETI, Lisbon, 299. A set of parameters which had the largest impact on patient dose was identified and discussed during the CEC Workshop "Technical and Physical

Parameters for Quality Assurance in Diagnostic Radiology; Limiting Values and Tolerances of the Measuring Methods".

Some digital techniques now increasingly used were evaluated for the associated patient exposure and possibilities for dose reduction. Several operational parameters and applications of CT were assessed to identify the causes for the differences in patient exposure. Cardiac cine-angiography and a digital cardiac imaging system were compared with respect to performance and patient exposure for different clinical indications (Fed. Dublin Vet. Hosp., 134). The resolution obtainable by digital luminescence radiography was studied in order to detect details of 0.2 mm diameter for mammography in relation to dose, and this method is now being compared with conventional methods (Univ. Erlangen, 137). The relevance and accuracy of the ionographic image-forming process and the numerical data obtained by a digitally compatible transducer applied to plain film radiography were investigated. The data were applied to assessing image quality under a variety of radiographic operating conditions including patient exposure (Christie Hospital and Univ. Manchester, 140). Preliminary results indicate that the ionographic system compares favourably in all performance aspects with screen-film systems.

In some cases, diagnostics using ionising radiation can be replaced by methods involving less or no radiation exposure. The diagnostic value and patient exposure of examinations to detect heart muscle diseases or certain tumours based on nuclear medicine or immuno-scintigraphy with monoclonal antibodies were compared with methods of conventional X-ray and ultrasound (Univ. Pisa, 139). However, it is extremely difficult to establish objective criteria for the diagnostic benefit of such examinations and to relate them satisfactorily to exposure data.

Establishment of quality criteria of radiographic techniques, radiographic image and patient exposure

The need for more precise data on image quality related to patient exposure was recognised at the Seminar on "Criteria and Methods for Quality Assurance in Medical X-ray Diagnosis", Udine, 1984. Subsequently, a study group "Medical Exposure" consisting of contractors in this area and some invited radiologists

elaborated a list of quality criteria for diagnostic radiographic images for typical projections of six conventional examinations - chest, skull, lumbar spine and lumbo-sacral junction, pelvis, urinary tract and breast - with regard to:

- "diagnostic requirements" for the radiologists, enumerating the anatomical features which should be recognisable on the normal radiograph;
- "guidance to good image performance" describing the image details which should at least be detectable on the radiograph and giving a reference dose value which can be achieved when respecting sound radiographic technique;
- an "example for good radiographic technique" by which the items under the above paragraphs can be realised.

The quality criteria were tested in a trial on about 1,000 patients by 25 radiological departments in 10 European countries and discussed and updated at a Workshop on "Optimisation of Image Quality and Patient Exposure in Diagnostic Radiology", Oxford, 1988.

Several contractors investigated problems encountered when these quality criteria were brought into practice. For instance, it was found to be difficult to define unambiguously speed classes of film-screen combinations for an optimal selection (PTB, Braunschweig, 316) or to detect, as early as possible, a degradation of certain equipment and to introduce automatic corrective measures (Univ. Newcastle upon Tyne, 315). The quality criteria are being developed for paediatric radiology (Univ. München, 211) and for CT by all the above-mentioned groups working on CT. With respect to digital fluoroscopic imaging, the contribution of various sub-components of the image intensifier TV-fluoroscopy system to image quality and patient exposure was investigated and it was shown that a need exists for defining quality criteria and optimising certain parameters and systems components, e.g. uniformity, signal to noise ratio, automated exposure control (Fed. Dublin Vet. Hosp., Dublin, 134).

Conclusions and perspectives

The reduction of patient exposure and optimisation of medical diagnostic radiology is a task which the Programme has commenced successfully in some areas of radiology but which is far from being accomplished. In particular, quality criteria have so far only been established for some key procedures whereas many other important areas, e.g. paediatric radiology, CT, nuclear medicine, application of

radiopharmaceutica, still need particular attention. These efforts are particularly urgent in view of the rapidly expanding application of some of these procedures, the still largely unexplored potential in dose saving that can be achieved by them and, finally, the economic savings and better health care that improved quality of diagnostic radiology can provide. Co-ordination between institutes and clinics in different Member States and with other countries is the most appropriate means for developing and bringing into everyday practice the achievements in dose reduction and quality improvement, and this is greatly aided by the new structure of multinational contracts and by the co-ordinated research programme the Commission is implementing together with the IAEA in this area.

C. Annexes

Annex I

Members and Experts 1985-1989

Management and Coordination Advisory Committee

"RADIATION PROTECTION"

Belgique - België

S. Hallez °
N. Henry °
J. De Brabandere °
J. Gillard
R. Kirchmann
P. Lejeune °
O. Vanderborght
P. De Schouwer °
A.M. Prieels °
A. Lafontaine
R. De Vre
M. Meert

Bundesrepublik Deutschland

W. Gössner °
H.J. Hardt °
A.M. Kellerer
H.H. Landfermann °

Danmark

H.L. Gjorup °
K.A. Jessen
N.O. Kjeldgaard ° Chairman 1985-86
J. Visfeldt °

Elliniki Dimokratia

D. Maïntas °
E.G. Sideris °

España

J.L. Butragueño Casado
E. Iranzo
F. Mingot Buades °
B. Sánchez Murias °
L. Arranz

France

L. Fitoussi °
H. Jammet °
B. Jampsin
J. Lafuma °
P. Pellerin °
H. Métivier
M. Bertin
M. Gras

Ireland

T. Colgan
J.D. Cunningham ° (Chairman 1989-)
M. Gillick °
C.P. O'Toole °
A.W. Moore +

Italia

A. Cigna ° (Chairman 1987-1988)
C. Camerucci
V. Covelli
F. Giorcelli °
F. Morselli °
F. Di Mauro

° Member

Luxembourg

P. Kayser °

Nederland

G.W. Barendsen
B. Bosnjakovic °
M.J. Frissel °
H.R. Leenhouts
A.T. Natarajan
F.H. Sobels
D.W. Van Bekkum
P.H.M. Lohman
J. Schneider °

Portugal

M. Brites Santos Patricio °
M. De Menezes Vilhena °
E. Mendes Magalhaes
J. Pistacchini Galvâo °

United Kingdom

G.E. Adams
R.J. Cole °
J.A. Dennis °
J. Metters °
E.D. Rubery °
R.J. Berry
G. Meekings
A.N.B. Stott
J.W. Stather
H. Walker °
A. Eggleton
D. Goodhead

Commission

H. Ebert
H. Eriskat
G. Gerber
J.M. Mousny secretariat
H. Schibilla

Annex II. List of Contractors Classified by Sector

A) Radiation Dosimetry and its Interpretation

Allisy ICRU BI6-A-027-US.
Quantities, units and measurement techniques for ionising radiation.

Allisy ICRU BI6-A-217-US.
Environmental monitoring needs connected with nuclear reactor accidents.

Allisy ICRU BI6-A-322-US.
Quantities, units and measurement techniques for ionising radiation.

Blanc ADPA BI6-A-001-F
Theoretical support to calibration of neutron area monitors in radiation protection.

Blanc Université Paul Sabatier BI6-A-180-F
Simulation of low-energy electron transport as a function of time. Application to microdosimetry and radiobiology.

Blanc ADPA BI6-A-292-F
Development of a general method allowing the complete modernisation of proportional counters.

Broerse TNO Radiobiolog. Institute BI6-A-002-NL
Neutron dosimetry instrumentation for radiation protection and radiobiology.

Chambers H.H. Wills Physics Laboratory BI6-A-006-UK
A programme of study to examine the microdistribution of alphaemitting radionuclides in man and the development of fast neutron spectrometry and dosimetry.

Coppola ENEA BI6-A-004-I
Study of radiobiological effects at low doses.

Dalpiaz INFN BI6-A-193-I
Stochastic variables in the energy deposit and their meaning in the hazard of neutrons.

Decossas Université de Limoges BI6-A-192-F
Study and realisation of a high performance personal neutron dosemeter.

Dennis EURADOS-CENDOS BI6-A-026-NL.
Collaboration on research and development concerned with the methodology and data of radiation dosimetry.

Descours CEN de Grenoble BI6-A-005-F
Study on a transfer dosemeter for the determination of dose in tissue close to beta-radiation sources

Dietze PTB Braunschweig BI6-A-215-D
Evaluation of Neutron Area Dosemeter Intercomparison

Ettinger University of Aberdeen BI6-A-014-UK
Study and development of microelectronic devices for radiation protection.

Feinendegen Kernforschungsanlage Jülich GmbH BI6-A-007-D
Application of microdosimetric methods to radiation protection.

Fernández Moreno Universitat Autónoma Barcelona BI6-A-232-E
Heating by laser of thermoluminescent dosemeters; application for the measurement of low energy beta rays.

Franconi Universita degli Studi di Roma BI6-A-302-I
Studies of radical formation in tracks and measurement of the activity of alpha emitters.

Furetta Università di Roma "La Sapienza" BI6-A-306-I
Development of an universal personal dosemeter using semiconductor sensors for mixed radiation fields.

Gasiot Université Sciences Techn.Languedoc BI6-A-231-F
Heating by laser of thermoluminescence dosemeters; application to the measurement of low energy beta rays.

Gibson UKAEA BI6-A-019-UK
Gamma-ray dosimetry, neutron dosimetry and spectrometry.

Goebel CERN BI6-A-307-CH
Development of an universal personal dosimeter using semiconductor sensors for mixed radiation fields.

Goodhead MRC BI6-A-009-UK
Biophysical studies of relations between radiation dose, quality and biological effect.

Hansen Risø National Laboratory BI6-A-028-DK
Investigation of alanine as an accident dosemeter and interpretation of dose-effect relationships by model description.

Hunt NPL BI6-A-003-UK
Development and investigation of a reproducible multisphere system for radiation protection purposes, and its use to correct personnel dosemeter measurements.

Jacobi GSF Neuherberg BI6-A-011-D
Track structure calculations.

Jacobi GSF Neuherberg BI6-A-172-D
Radiation exposure analysis and biological dosimetry.

Kellerer Julius-Maximilians-Universität BI6-A-013-D
Development of the twin detector method and of microdosimetric concepts and methods for radiation protection.

Kramer PTB Braunschweig BI6-A-305-D
Development of an universal personal dosemeter using semiconductor sensors for mixed radiation fields.

Leenhouts RIVM BI6-A-008-NL
Comparative risk assessment of radiation and other mutagenic agents. Low dose relative risk of different ionising radiations and comparison with UV radiation.

Lembo ENEA BI6-A-023-I
Track-structure detectors for neutron and alpha dosimetry.

Marshall NRPB BI6-A-015-UK
The implementation of new ICRU operational quantities for use in radiation protection.

McKinlay NRPB BI6-A-216-UK
TLD Environmental Intercomparison

McKinlay NRPB BI6-A-301-UK
Investigation of methods for improving the thermoluminescence properties of thin dosimeters for specific application to beta and low energy photon dosimetry

Menzel Universität des Saarlandes BI6-A-010-D
Dosimetric research and radiation protection dosimetry with proportional counters and physical and biological accident dosimetry.

Morgan UKAEA BI6-A-017-UK
Development of improved X-ray counters for the assessment of plutonium in lungs.

Norris Polytechnic of the South Bank BI6-A-025-UK
Computation of the radiation dose due to the daughter products of radon deposited in the lung.

O'Riordan NRPB BI6-A-016-UK
Calculation of doses from external radiation. Thermoluminescence dosimetry studies.

O'Riordan NRPB BI6-A-018-UK
The development of realistic phantoms to assist in the interpretation of in vivo measurement of low-energy photonemitting radionuclides in bone.

Portal CEN-IPSN de FAR BI6-A-020-F
Neutron individual and area dosimetry, realisation of neutroncalibration sources, beta-particle dosimetry, accident dosimetry of clothes.

Rechenmann Université Louis Pasteur BI6-A-021-F
Heavy charged particle track structure in tissuelike media, incidence on microdosimetric interpretations.

Scharmann Justus-Liebig Universität Giessen BI6-A-022-D
Beta-ray individual dosimetry using exoelectron emission.

Siffert Inst.Nat.de Physique Nucléaire BI6-A-304-F
Development of a universal personal dosemeter using semiconductor sensors for mixed radiation fields.

Taylor Kernforschungszentrum Karlsruhe BI6-A-029-D
Microdosimetry and local dosimetry of 226-Radium, 239-Plutonium and 241-Americium in the beagle dog skeleton.

Uggerhoj University of Aarhus BI6-A-303-DK
Development of an universal personal dosemeter using semiconductor sensors for mixed radiation fields.

Wagner PTB Braunschweig BI6-A-012-D
Investigation and development of neutron spectrometers and investigation and implementation of dose equivalent quantities.

Watt University of St.Andrews BI6-A-024-UK
Specification and measurement of radiation effectiveness.

B) Behaviour and Control of Radionuclides in the Environment

Aarkrog — Risø National Laboratory — BI6-B-030-DK
Behaviour of long-lived radionuclides in terrestrial and marine (North Atlantic Region) environments.

Aarkrog — IUR — BI6-B-052-B .
Promotion of research and exchange of information in radioecology.

Apostolakis — Greek Atomic Energy Commission — BI6-B-293-GR
Behaviour of long-lived radionuclides in soil-plant systems of the Mediterranean region.

Bächmann — Technische Hochschule Darmstadt — BI6-B-183-D
Investigation of the lead 210 pathways via waste air and waste water of uranium mining sites.

Bell — Imperial College of Science — BI6-B-032-UK
Time-dependent transfer of radionuclides from atmosphere and soil to crops, following simulated reactor accidents.

Bonka — Technische Hochschule Aachen — BI6-B-033-D
Improvement of models for the calculation of the dry deposit of radionuclides and radioiodine bound to aerosol particles.

Brenk — BRENK Systemplanung — BI6-B-055-D
Modelling of the deposition and postdeposition behaviour of accidentally released radionuclides in urban and suburban environments.

Bunnenberg — Niedersächsisches Institut — BI6-B-345-D
Transfer of radionuclides in the food chain.

Cremers — KUL — BI6-B-035-B
Dynamics of radionuclide chemistry in soils and sediments.

Cunningham — Nuclear Energy Board — BI6-B-218-IRL
Assessment of the radioactivity levels in Irish soils and their transfer into agricultural produce as a result of the Chernobyl accident.

Damiani — ENEA — BI6-B-034-I
Laboratory and field research on long-lived radionuclides in the marine environment.

Decallone — UCL — BI6-B-042-B
Description of the interactions and processes that are involved in Tc-99movement and cycling.

Derwent — UKAEA — BI6-B-046-UK
Distribution and transfer of radionuclides in terrestrial and sea environments.

Duursma — Delta Institute for Hydrobiolog. Res. — BI6-B-191-NL
Transfer processes and modelling of plutonium species and gamma emitters in the Scheldt estuary; redox and organic speciation in relation toaqueous and particulate fractionation.

Duursma Netherlands Institute BI6-B-199-NL
Biological and geochemical investigation in relation to the deep sea dumping of low level radioactive waste.

Frissel RIVM BI6-B-036-NL
Countermeasures to the uptake of radionuclides from soils by food crops; the long-term availability of radionuclides.

Führ Kernforschungsanlage Jülich GmbH BI6-B-053-D
Simulation of transfer via the soil-plant food chain after accidental release.

Führ Kernforschungsanlage Jülich GmbH BI6-B-189-D
Conversion of elementary tritium (HT) in agriculturally used soils, oxidation of HT to HTO and synthesis to organically bound tritium.

Galvào LNETI BI6-B-198-P
Behaviour of radionuclides and model development in aquatic ecosystems.

Grauby CEN de Cadarache BI6-B-037-F
Behaviour of radionuclides in marine, freshwater and terrestrial environments.

Grauby CEA-CEN de Cadarache BI6-B-325-F
Rehabilitation of soil and surface after an accident.

Hamilton NERC BI6-B-038-UK
The role of surfaces in the transport of radionuclides in the marine environment.

Heal NERC BI6-B-233-UK
The relationship between soil organic matter and the actinide elements.

Heaton University of Aberdeen BI6-B-318-UK
The dynamics of caesium-137 from Chernobyl in upland peat moorland ecosystems.

Hislop UKAEA BI6-B-044-UK
The remobilisation and transport of actinides from sediment deposits in West Cumbria.

Hoppenheit Biologische Anstalt Helgoland BI6-B-039-D
Speciation and availability of Am in tidal water.

Kirchmann Faculté des sciences agronomiques BI6-B-327-B
Study of the transfer of accidentally released radionuclides in agricultural products with the aim of devoloping appropriate countermeasures

Kühn Niedersächsisches Institut BI6-B-041-D
Transfer of radionuclides in the food chain.

Martin Associated Nuclear Services BI6-B-194-UK
Experimental programme to support the development of dynamic models describing carbon-14 (and other B-emitters) in soil-plantanimal systems.

Martin. CNRS BI6-B-234-F
Artificial radionuclides transfer from the Rhône delta to the Mediterranean

McAulay — The University of Dublin — BI6-B-043-IRL
Radioactivity in the sea and food in Ireland.

Mingot Buades — CIEMAT — BI6-B-195-E
Behaviour of plutonium and americium in the marine environment.

Moser — GSF Neuherberg — BI6-B-056-D
Investigation of the behaviour of radioiodine in aquatic and terrestrial environments under the influence of biogeochemical processes.

Parmentier — CEA-IPSN de FAR — BI6-B-045-F
Consequences of sea disposal.

Pentreath — MAFF — BI6-B-200-UK
Studies of the geochemical behaviour of artificial and natural radionuclides in coastal waters.

Pieri — Université de Nantes — BI6-B-047-F
Ligands of technetium and transfer.

Postma — Netherlands Institute — BI6-B-054-NL
Biological and geochemical investigation in relation to the deep sea dumping of low level radioactive waste.

Roed — Risø National Laboratory — BI6-B-326-DK
Design and development of a skim and burial plough for reclamation of contaminated land.

Silva — Università del Sacro Cuore — BI6-B-329-I
Chemical treatments to reduce the transfer of caesium radioisotopes to the human foodchain after a serious nuclear accident.

Stather — NRPB — BI6-B-048-UK
Behaviour of radionuclides in the environment.

Van den Hoek — Landbouwhogeschool — BI6-B-051-NL
Dynamic environmental cycling of HTO/HT/OBT. Experimental studies and modelling. Incorporation and metabolism of OBT, HT and Carbon 14 in mammals.

Van der Ben — Institut Royal des Sciences — BI6-B-049-B
Behaviour of technetium in the marine benthic environment. Experimental studies and modelling.

Vandecasteele — CEN/SCK — BI6-B-040-B
Behaviour of radionuclides in terrestrial and freshwater environments.

Vanderborght — CEN/SCK — BI6-B-050-B
Bioavailability of transuranium nuclides in aquatic environments.

Zettwoog — CEN-IPSN de FAR — BI6-B-182-F
Preliminary study of the contamination by lead-210 in the environment of uranium mines.

C) Non-stochastic Effects of Ionizing Radiation

Bazin UCL BI6-C-187-B
Role of B lymphocytes in chronic radiation damage.

Bortin Medical College of Wisconsin BI6-C-084-US.
Donors for bone marrow transplantation: HLA mismatched related vs HLA matched unrelated.

Coggle St. Bartholomew's Hospital BI6-C-057-UK
Stochastic and non-stochastic effects of alpha and beta radiation onmouse skin.

Daburon CEN-IPSN de FAR BI6-C-058-F
Problems related to skin and underlying tissues after accidents involving local irradiation. Experimental study in the pig.

Dean The Medico-Social Research Board BI6-C-176-IRL
Risk of developing cataract from superficial radiotherapy to the eye.

Doria ENEA BI6-C-059-I
Radiation damage and recovery of the immune system.

Dumont ULb BI6-C-188-B
Thyroid irradiation: consequence of irradiation in experimental systems and in humans.

Field MRC BI6-C-060-UK
RBE for normal tissues at low doses and low doses fraction in normal and potentially sensitive populations, with emphasis on parenchymal andvascular damage in late and chronic radiation damage.

Fliedner Universität Ulm BI6-C-061-D
Impairment of the hemo-lymphopoietic cell system and its microenvironment by ionising radiation. Pathogenesis of non-stochastic and neoplastic effects and conditions for a long term restoration.

Healey CEGB-BNL BI6-C-082-UK
The establishment of radiological protection criteria for non-uniform skin exposure.

Hendry Paterson Laboratories BI6-C-062-UK
Cellular analysis and dose-response relationships in long-term radiation injury to mouse bone marrow.

Hopewell Churchill Hospital BI6-C-063-UK
Early and late effects of radiation on the skin.

Humphries Trinity College BI6-C-309-IRL
Rapid techniques for graft assessment following bone marrow transplantation designed for large scale use following accidental lethal exposure to radiation.

Jammet Centre Internat.de Radiopathologie BI6-C-065-F
Non-stochastic effects of irradiation in man: diagnosis, prognosis andtreatment of acute radiation injury.

Kaul Institut für Strahlenhygiene BI6-C-066-D
Radiation-induced changes in lymphocyte populations and their functions as biological indicators of radiation damage.

Léonard CEN/SCK BI6-C-069-B
Morphological and cytogenetic studies on the sensitivity of the mammalian embryo to low doses of radiation.

Maisin CEN/SCK BI6-C-071-B
Late somatic effects of radiation in mammals.

Masse CEN-IPSN de FAR BI6-C-073-F
Contribution of flow cytofluorimetry for the assessment of overexposure to ionising radiation.

Métivier CEA BI6-C-310-F
Fetal dosimetry: Measurement of the effects induced after in utero chronic irradiation as a function of dose rate and gestation age.

Morgan UKAEA BI6-C-074-UK
Macrophage involvement in actinide-induced lung disease.

Schmahl GSF Neuherberg BI6-C-068-D
Morphological and immunological characterisation of cells from typicalfocal CNS lesions in the rat following prenatal X rradiation and their elationships to ethylnitrosourea neurocarcinogenesis.

Streffer Universitätsklinikum Essen BI6-C-077-D
Investigation into biological dosimetry: chromosomal damage and eratogenic effects following irradiation of one cell mouse embryos.

van Bekkum TNO Radiobiolog. Institute BI6-C-079-NL
Development of conditions allowing restoration of hemopoiesis by allogenic purified and in vitro multiplied pluripotent hemopoietic stem cells.

Vanderborght CEN/SCK BI6-C-081-B
Comparison of damage from internal alpha irradiation to the hemopoietic and stromal system in adult and pre- and postnatal animals.

D) Stochastic Effects of Ionising Radiation

Adams MRC BI6-D-064-UK
Studies on myeloid leukaemia and osteosarcoma induced in mice by Ra-224.

Barendsen TNO Radiobiolog. Institute BI6-D-067-NL
Relative biological effectiveness for the induction of malignant characteristics in cells by fast neutrons and of lung cancer by radon.

Becciolini Università degli Studi di Firenze BI6-D-070-I
Radiation carcinogenesis.

Bentvelzen TNO Radiobiolog. Institute BI6-D-072-NL
Molecular-biological studies on the activation of cellular transforminggenes in radiation carcinogenesis.

Broerse TNO Radiobiolog. Institute BI6-D-075-NL
Late effects in rhesus monkeys after whole body irradiation with X-rays and fission neutrons.

Broerse	Academic Hospital Leiden	BI6-D-219-NL

Analysis of dose-effect relations for radiation carcinogenesis by various mathematical models.

Campos Venuti	Istituto Superiore di Sanità	BI6-D-341-I

Radionuclide transfer factor for human milk.

Chalabreysse	CEN-IPSN Vallée du Rhône	BI6-D-088-F

Studies into the actual toxicity of uranium compounds under conditions prevailing in the industry with a view to reexamining ICRP norms.

Cobb	MRC	BI6-D-076-UK

Local retention and translocation of particles in the respiratory tract.

Dumont	ULB	BI6-D-220-B

Thyroid Radiation:Carcinogenesis in experimental models and effects of low doses in humans for risk assessment.

Duplan	Fondation Bergonié	BI6-D-078-F

Mechanism of radiation-induced leukemogenesis and osteosarcomagenesis.

Duplan	EULEP	BI6-D-099-D.

Late somatic effects of ionising radiation on the mammalian organism.

Gössner	GSF Neuherberg	BI6-D-080-D

Pathogenesis of late somatic effects of radiation.

Gössner	GSF Neuherberg	BI6-D-083-D

Epidemiological studies of radiation carcinogenesis and its biophysical basis.

Gössner	GSF Neuherberg	BI6-D-221-D

Investigation of the cataract incidence in the German Radium-224 patients.

Hagen	GSF Neuherberg	BI6-D-085-D

Molecular and cellular mechanisms of neoplastic cell transformation.

Healey	CEGB-BNL	BI6-D-095-UK

Filtered neutron beam studies (biological effects).

Kaldor	IARC	BI6-D-319-F

Survey on childhood leuknaemia.

Kjeldgaard	University of Aarhus	BI6-D-086-DK

Characterisation of somatic mutations during radiation induced osteosarcomagenesis.

Kriegel	GSF Neuherberg	BI6-D-087-D

Decorporation and interruption of transfer of radionuclides, especially of Sr and Ba.

Lohman	Rijks Universiteit Leiden	BI6-D-202-NL

Genetic and molecular characterisation of stages in X-ray induced malignant transformation.

Maisin	CEN/SCK	BI6-D-090-B

Mechanism of radiation-induced leukemogenesis and osteosarcomagenesis.

Malone Federated Dublin Volunt. Hospitals BI6-D-093-IRL
Radiation response of the thyroid : survival and alteration towards malignancy in cell culture and human systems.

Masse CEN-IPSN de FAR BI6-D-096-F
Experimental approach of absolute and relative risk concepts in radio-induced cancers.Role of combined effects.

Métivier CEN-IPSN de Bruyères-le-Châtel BI6-D-098-F
Metabolism and effects of incorporated actinides.

Morgan UKAEA BI6-D-100-UK
Synergistic effects of cigarette smoke in the induction of lung tumours by inhaled actinides.

Morgan UKAEA BI-D-235-UK
Consequences to lung and bone of exposure to actinides.

Mothersill St. Luke's Hospital BI6-D-092-IRL
Inter-related studies on dose dependence and mechanisms of radiation induced carcinogenesis and environmentally induced and radiation promoted carcinogenesis.

Oberhausen Univ. des Saarlandes BI6-D-335-D
Study of the possibility of an epidemiological research with the aim to determine the morbidity and mortality risks to thyroid gland carcinoma.

Parmentier CEN-IPSN de FAR BI6-D-101-F
Lung modelling contribution:deposition and clearance studies in man.

Planel Université Paul Sabatier BI6-D-201-F
Biochemical and biophysical studies on the effects of very low doses of ionising radiation on cells.

Pohlit GSF Neuherberg BI6-D-236-D
RBE values of monoenergetic electrons in the range of several 100 eV to 10 keV for cell transformation.

Ramsden UKAEA BI6-D-102-UK
Plutonium exposures in man. Direct monitoring of the lung, reassessment of the ICRP lung model and 'solubility' studies.

Rommelaere ULB BI6-D-178-B
Cooperation between radiation and oncogenes in malignant transformation of mammalian cells.

Rossi Istituto Superiore di Sanità BI6-D-103-I
Radiation carcinogenesis in animals: search for and role(s) of oncogenes.

Stather NRPB BI6-D-089-UK
The dosimetry and metabolism of incorporated radionuclides.

Strom Università di Roma "La Sapienza" BI6-D-196-I
Regulation of DNA methylation in cell differentiation, transformation and repair.

Tallone-Lombardi Università degli Studi di Milano BI6-D-177-I
Radiation carcinogenesis in vitro.

Taylor Kernforschungszentrum Karlsruhe BI6-D-091-D
The fractionation and speciation of plutonium and other actinide elements in vivo.

Tipton Trinity College BI6-D-184-IRL
Interaction between radiation and environmental carcinogens, studies on human cells in vitro.

van de Vate Netherlands Energy Research BI6-D-203-NL
Induction of myeloid leukaemia in mice by irradiation with fission neutrons as a function of dose-rate.

Van der Eb Rijks Universiteit Leiden BI6-D-185-NL
Studies on the molecular basis of radiation-induced carcinogenesis.

Vanderborght CEN/SCK BI6-D-094-B
Relation between decorporation of osteotropic alpha-emitters and long term prevention of radiation harm.

Williams Welsh National School of Medicine BI6-D-097-UK
Studies of the mechanism and prevention of low dose radiation carcinogenesis of the thyroid.

Zurcher TNO Instit. Experim. Gerontology BI6-D-212-NL
Flow cytometric analysis, computer aided morphometry and histopathology of radiation-induced rat mammary neoplasms as parameters for their biological behaviour.

E) Genetic Effects of Ionising Radiation

Baan Organisation for Health Research BI6-E-148-NL
The genetic and biochemical basis of radiation sensitivity in cultured human and other mammalian cells.

Barendsen. University of Amsterdam BI6-E-330-NL
Automated detection of radiation induced chromosome aberrations by slit-scan flow karyotyping

Bianchi Università degli Studi di Milano BI6-E-204-I
Development of biochemical and immunological assays for DNA recombination and repair

Bootsma Erasmus University Rotterdam BI6-E-141-NL
The genetic and biochemical basis of radiation sensitivity in human andother mammalian cells in culture.

Bridges MRC BI6-E-142-UK
The genetic and biochemical basis of radiation sensitivity in cultured human and other mammalian cells.

Bryant University of St. Andrews BI6-E-294-UK
Molecular mechanisms of radiation damage to chromosomes of human and rodent cells.

Cattanach MRC BI6-E-143-UK
Mutation studies upon spermatogonial stem cells of mammals and genetic tests for non-disjunction in the mouse.

Cortes-Benavides Universidad de Sevilla BI6-E-311-E
Adaptive response to radiation damage in human lymphocytes induced by hydrogen peroxide and its modulation by antioxidant agents.

Devoret CNRS BI6-E-145-F
Induction of SOS functions from procaryotes to higher eucaryotes.

Dutrillaux CEN-IPSN de FAR BI6-E-149-F
A qualitative study of radiation-induced chromosomal breakage and development of a test for radiation sensitivity.

Dutrillaux I.C. Institut Curie BI6-E-147-F
Somatic cytogenetics of normal humans and people suspected of having adefect in the repair of DNA damage.

Ehling GSF Neuherberg BI6-E-156-D
Radiation-induced mutations in mammals.

Elli Università di Roma "La Sapienza" BI6-E-205-I
Response to radiations of human cells modified by pR plasmid that confers radioresistance in bacteria.

Evans MRC BI6-E-157-UK
Spontaneous and radiation-induced chromosome mutation and deletions of specific chromosome regions of the human karyotype which contain genes of known clinical importance.

Falaschi Consiglio Nazionale BI6-E-158-I
Molecular and genetic analysis of DNA damage.

Frankenberg GSF Neuherberg BI6-E-159-D
RBE-values of monoenergetic electrons for DNA double-strand breaks, chromosome aberrations and lethality and point mutations.

Goffeau UCL BI6-E-160-B
The role of recombination in yeast mitochondrial DNA repair. Influence of ionising radiation.

Houghton University College Galway BI6-E-162-IRL
A study of the effects of radiation on the chromosomes of human gametes.

Kraft GSI BI6-E-197-D
Genetic changes in mammalian cells following heavy ion irradiation.

Léonard CEN/SCK BI6-E-146-B
Radiation-induced structural chromosome aberrations in mammalian somatic cells.

Lohman Rijks Universiteit Leiden BI6-E-166-NL
Radiation sensitivity in cultured mammalian cells, the genetic effects of radiation in eukaryotes and chromosome aberrations in human lymphocytes.

Lohman Rijks Universiteit Leiden BI6-E-226-NL
Studies on spontaneously-arising genetic and partially genetic disorders in man within the framework of the evaluation of genetic radiation hazards.

Morgan UKAEA BI6-E-190-UK
Cellular radiobiology.

Moustacchi Institut Curie BI6-E-151-F
Comparison of the fate of X-rays and DNA cross-linking agents induced lesions: Fanconi's anemia as a model of human repair defect. Genetic and biochemical analysis.

Natarajan Rijks Universiteit Leiden BI6-E-338-NL
Cytological follow-up of individuals exposed in the Goiania (Brazil) accident.

Obe Freie Universität Berlin BI6-E-152-D
Evaluation of the frequencies of chromosomal aberrations induced in human blood lymphocytes by low doses of X rays (1-10 rad).

Obe Universität-GSH Essen BI6-E-223-D
The production of chromosome aberrations in human lymphocytes by low doses of X-rays.

Olivieri Università di Roma "La Sapienza" BI6-E-186-I
Adaptive response to low doses of radiation: studies in human cells of a possible radiation-stimulated repair.

Palitti Consiglio Nazionale BI6-E-171-I
Evaluation of the frequencies of chromosomal aberrations, induced in human blood lymphocytes by low doses of X rays (1-10 rad).

Pohlit GSF Neuherberg BI6-E-153-D
Assessment of genetic damage at low doses of ionising radiations.

Radman Université Paris VII BI6-E-154-F
Molecular basis of radiation-induced mutagenesis from bacteria to humans. New Experimental Systems.

Radman ULB BI6-E-155-B
Mutagenic effects of ionising radiation in bacteria and mammalian cells.

Sarasin CNRS BI6-E-163-F
Molecular analysis of mutagenesis in mammalian cells treated by radiations and chemical carcinogens.

Savage MRC BI6-E-164-UK
Analysis of cell cycle radiosensitivity in normal and mutant cells using replication banding techniques.

Searle MRC BI6-E-150-UK
Use of methods for detection and analysis of deletions and dominant visible mutations in the mouse.

Sideris Greek Atomic Energy Commission BI6-E-224-GR
Radiobiological damage induced into mammalian and human cells by low energy monoenergetic protons and calculations of the RBE factors for risk estimations.

Stather NRPB BI6-E-165-UK
The production of chromosome aberrations in human lymphocytes by ionising radiations.

Stather NRPB BI6-E-225-UK
The production of chromosome aberrations in human lymphocytes by low doses of X-rays.

Streffer Universitätsklinikum Essen BI6-E-312-D
Formation of micronuclei in human lymphocytes after partial and whole body irradiation.

Tease MRC BI6-E-173-UK
Karyotypic analyses of spontaneous and radiation-induced chromosome anomalies in mouse foetuses.

Thacker MRC BI6-E-144-UK
DNA repair genes and the molecular basis of mutation and recombination in mammalian cells.

Thomou-Politi Greek Atomic Energy Commission BI6-E-331-GR
Construction and use of eucaryotic indicator cell lines,for the assessment of radiation induced alterations leading into new defined phenotypes.

van de Putte Rijks Universiteit Leiden BI6-E-167-NL
Processing of radiation induced and spontaneous genetic damage in prokaryotes and eukaryotes.

van der Eb Rijks Universiteit Leiden BI6-E-169-NL
The genetic and biochemical basis of radiation sensitivity in human and other mammalian cells in culture.

von Wettstein Carlsberg Laboratory BI6-E-168-DK
Chromosome pairing, crossing over and disjunction in human meiosis.

Westergaard University of Aarhus BI6-E-170-DK
The molecular basis for the interaction of radiation and carcinogens with the eukaryotic genome and the mechanism of repair. Studies on human and other eukaryotic cell cultures.

Zannos Greek Atomic Energy Commission BI6-E-206-GR
A new analysis of radiation-induced cytogenetic damage in human lymphocytes using the PCC technique, and its implications for biological dosimetry and the understanding of cell-cycle dependent radiosensitivity fluctuations

F) Assessment of Risks and Optimisation of Radiation Protection

Alonso Universidad Politécnica de Madrid BI6-F-227-E
Off-site economic consequences of nuclear reactor accidents.

Artalejo CIEMAT BI6-F-229-E
Health effects of chronic exposure to low dose ionising radiation on workers of the Spanish Nuclear Energy Institute (Junta de Energia Nuclear).

Birkhofer GRS BI6-F-125-D
Methodology for probabilistic uncertainty analysis of computational assessments.

Charalambous Aristotle Univ. of Thessaloniki BI6-F-104-GR
Radioactivity escaping from Coal Power Plants. Pollution and Risks.

Charuau CEA-CEN Saclay BI6-F-344-F
Réalisation d'un banc d'étalonnage de radon-222 et de ses produits de filiation à vie courte dans l'air.

Clarke NRPB BI6-F-295-UK
Investigation of the relationship between lung cancer and radon in houses.

Comba Istituto Superiore di Sanità BI6-F-313-I
Epidemiological study on respiratory cancer among miners with low radiation exposures.

Delpoux Université Paul Sabatier BI6-F-122a-F
Comparative genotoxicity of the principal environmental agents.

Delpoux Université Paul Sabatier BI -F-122c-F

Deruytter Rijks Universiteit Gent BI6-F-112-B
Evaluation of the impact of the domestic environment on the population exposure to radon daughters.

Duursma Netherlands Institute BI6-F-328-NL
Research on processes controlling the regional distribution of Po-210,Pb-210,Ra-226,Pa-231 and Thorium isotopes in estuaries.

Facchini Università degli Studi di Milano BI6-F-174-I
Measurements of radon emission from soil of anomalous sites and investigation of radon concentration in the air of buildings in these areas.

Fagnani CEPN BI6-F-105-F
Optimisation of occupational exposure and implementation of the ALARA principle.

Fagnani CEPN BI6-F-122b-F
Analysis of post-Chernobyl countermeasures

Fagnani CEPN BI6-F-207-F
Comparison of methodologies for risk management applied to nuclear and non-nuclear industrial activities.

Fourcade CEA-IPSN de FAR BI6-F-332-F
Development of a calibration standard for Radon-224 and its short-lived daughter products in air.

Galvào LNETI BI6-F-208-P
Evaluation of the population exposure to radon in the vacinity of uranium mining facilities.

Gjorup Risø National Laboratory BI6-F-175-DK
Shielding for plume radiation and assessment of factors influencing indoor exposure.

Goddard Imperial College of Science BI6-F-108-UK
Pathways and systems pertaining to the urban environment.

Goddard Imperial College of Science BI6-F-228-UK
Experimental studies on aerosol transport processes in dwellings using inactive tracer techniques.

Govaerts CEN/SCK BI6-F-106-B
Optimisation of dose assessment models including the interface with environmental survey, for use in case of accidental releases.

Grauby CEN de Cadarache BI6-F-109-F
Preliminary evaluation of the radiological consequences of a PWR accident.

Hayns UKAEA BI6-F-131-UK
Evaluation and development of models used in assessing the consequences of accidental releases of radioactivity.

Healey CEGB-BNL BI6-F-209-UK
An analysis of uncertainties in inhalation and ingestion dose estimates arising from uncertainties in dosimetric and foodchain transfer data.

Hémon INSERM BI6-F-126-F
Statistical methods for the analysis of geographical correlations, application to the analysis of the correlation between population radiation exposure and cancer mortality.

Hill NRPB BI6-F-110-UK
Establishment of authorised limits for effluent releases and implementation of the ALARA principle.

Hill NRPB BI6-F-127-UK
Methodology for evaluating the radiological consequence of radioactive effluents released in accidents.

Jacobi GSF Neuherberg BI6-F-111-D
Quantification of radiation risks, optimisation procedures and analysis of occupational exposure.

Jensen Danish Cancer Society BI6-F-333-DK
Late effects of Thorotrast among Danish patients 1932-1947

Jonassen Technical University of Denmark BI6-F-113-DK
Investigation and development of methods to control the level of radon daughters in indoor air.

Kessler Kernforschungszentrum Karlsruhe BI6-F-128-D
Methodology for evaluating the radiological consequences of radioactive effluents released in accidents.

Knox University of Birmingham BI6-F-129-UK
Geographical variations of medical and non-medical radiation exposures, and risk of cancer in children.

Kollas Greek Atomic Energy Commission BI6-F-114-GR
Individual and social radiation risks resulting from the operation of nuclear facilities and assessment of risks derived from enhanced natural and artificial radioactivity in Greece

Madelaine CEN-IPSN de FAR BI6-F-115-F
Characterisation of radon daughters and carcinogenesis.

McLaughlin University College Dublin BI6-F-117-IRL
Assessment of the population dose indoors from natural radiation in Ireland with particular emphasis on radon daughter properties and behaviour.

Mikkelsen Risø National Laboratory BI6-F-296-DK
Validation experiments for near-site region atmospheric dispersion models.

Miles NRPB BI6-F-230-UK
Third European intercomparison of active and passive dosemeters for the measurement of radon and radon decay products.

Miles NRPB BI6-F-336-UK
Intercomparison of passive radon detectors.

Morlat Centre de Développement des Etudes BI6-F-121-F
Comparative risk evaluation on a regional scale.

O'Riordan NRPB BI6-F-118-UK
Impact assessment of artificial and enhanced natural radioactivity in the outdoor and indoor environment.

Parmentier CEN-IPSN de FAR BI6-F-119-F
Assessment of population doses from accidental releases of radioactivity and socio-economic cost of evacuation.

Pineau COGEMA BI6-F-340-F
Second European intercomparison of measurement devices and techniques of Radon-222 and of its decay products in an underground mine atmosphere.

Plocq SCOPE BI6-F-339-F
Biogeochemical pathways of artificial radionuclides.

Porstendörfer Isotopenlaboratorium f. biologische BI6-F-130-D
The aerosol size distributions and the unattached fraction of the radon daughters for estimation of the radiation exposure risks in houses.

Quindos Poncela Universidad de Santander BI6-F-314-E
Natural exposure to radon and radon progeny in Spanish houses.

Roed Risø National Laboratory BI6-F-107-DK
Behaviour of accidentally released radionuclides in urban areas.

Sénye Univ. Politécnica de Catalunya BI6-F-297-E
Regional real time modelling of atmospheric transport and its coupling to transfer with a view to the evaluation of the consequences of nuclear accidents.

Siemssen Kernfysisch Versneller Instituut BI6-F-120-NL
Investigation of the mechanisms leading to radon concentrations in dwellings.

Siemssen Kernfysisch Versneller Instituut BI6-F-210-NL
Measurements on, and control of infiltration of radon into dwellings.

Smith ICRP BI6-F-124-UK
Development of fundamental data for radiation protection.

Smith ICRP BI6-F-324-UK
Development of fundamental data for radiation protection

Stather NRPB BI6-F-116-UK
Procedures to assess intakes of radionuclides from samples of airborne radioactivity and statistical studies of radiation risk.

Stather NRPB BI6-F-213-UK
The risks of radiation work: analysis of registry data.

Uzzan CEN-IPSN de FAR BI6-F-122-F
Consequences of irradiation of population and workers.

van Kaick DKZ BI6-F-123-D
Thorotrast - investigations to evaluate the long term effects caused by artificial radiation in man (Thorotrast patients) - follow-up study.

van Kaick DKZ BI6-F-298-D
Thorotrast - investigations to evaluate the long term effects caused by artificial radiation in man (Thorotrast patients) - follow-up study.

Zettwoog CEN-IPSN de FAR BI6-F-181-F
Control of radon-222 sources at underground workplaces through draining of the encasing rock.

Dose Reduction in Medical Diagnostic Radiology

Broerse TNO Radiobiolog. Institute BI6-FA-138-NL
Absorbed dose assessments in diagnostic radiology, nuclear medicine and radiotherapy with respect to the female breast.

Donato Università degli Studi di Pisa BI6-FA-139-I
Limitation of patient exposure to radiation from emerging medical diagnostic procedures in high morbidity disease areas.

Drexler GSF Neuherberg BI6-FA-337-D
Quality criteria for diagnostic radiographic images and patient exposure in paediatrics

Fagnani CEPN BI6-FA-132-F
Analysis of the patient exposure to radiation from medical diagnosis: exposure data and quality assurance.

Faulkner Newcastle General Hospital BI6-FA-315-UK
Automated quality assurance and patient dosimetry in diagnostic radiology.

Fendel Ludwig-Maximilian-Universitaet BI6-FA-211-D
The principles and the practicability of quality control and quality assurance in paediatric radiology.

Galvào LNETI BI6-FA-299-P
Dose assessment and quality assurance in diagnostic radiology.

Hoeschen PTB Braunschweig BI6-FA-316-D
Reduction of dose in X-ray diagnostics by the choice of the optimal screen-film combination.

Jacobi GSF Neuherberg BI6-FA-133-D
Analysis of exposure in radiology

Jessen Aarhus University Hospital BI -FA-317-DK
The impact from quality assurance on dose reduction in computerised tomography in Denmark

Kaul BGA Instit. Strahlenhygiene BI6-FA-342-D
Integration of a newly aquired whole body counter into a European network of personal measurement devices, particularly useful in case of an accident.

Malone Federated Dublin Volunt. Hospitals BI6-FA-134-IRL
Specification of uniformity and noise limited exposure reduction in radiological image intensifier - TV systems as an adjunct to quality control and optimisation of exposure.

McKinlay NRPB BI6-FA-135-UK
Evaluation of the radiation doses and risks associated with diagnostic X-ray examinations in Britain.

Moores Victoria University BI6-FA-140-UK
An assessment of the effect of digital technology on quality assurance procedures, including the evaluation of risks, in X-ray medical diagnosis.

Padovani Unitá Sanitaria Locale BI6-FA-136-I
Refinement of methods for the assessment of organ doses, and possible reduction of patient exposure.

Pauly Universität Erlangen-Nürnberg BI6-FA-137-D
The effective dose equivalent due to X-ray diagnostic examinations and the impact of quality control on medical exposure.

Schmidt Universität Erlangen-Nurnberg BI6-FA-343-D
The effective dose equivalent due to X-ray diagnostic examinations and the impact of quality control on medical exposure.

Vano Carruana Universidad Complutense BI6-FA-214-E
Optimisation of Protection in Medical Diagnostic Radiology.

Annex III. Geographical Distribution of Contracts

Belgium

Bruxelles	BI6-B-049-B
	BI6-C-187-B
	BI6-C-188-B
	BI6-D-178-B
	BI6-D-220-B
	BI6-E-155-B
Gembloux	BI6-B-327-B
Gent	BI6-F-112-B
Heverlee	BI6-B-035-B
Louvain-la-Neuve	BI6-B-042-B
	BI6-E-160-B
Mol	BI6-B-040-B
	BI6-B-050-B
	BI6-C-069-B
	BI6-C-071-B
	BI6-C-081-B
	BI6-F-106-B
	BI6-D-090-B
	BI6-D-094-B
	BI6-E-146-B
	BI6-F-106-B

Switzerland

Genève	BI6-A-307-CH

Federal Republic of Germany

Aachen	BI6-B-033-D
	BI6-B-055-D
Braunschweig	BI6-A-305-D
	BI6-A-012-D
	BI6-A-215-D
	BI6-F-316-D
Darmstadt	BI6-B-183-D
	BI6-E-197-D
Erlangen	BI6-F-137-D
	BI6-F-343-D
Essen	BI6-C-077-D
	BI6-E-152-D
	BI5-E-223-D
	BI6-E-312-D
Frankfurt/Main	BI6-D-236-D
	BI6-E-153-D
	BI6-E-159-D
Garching	BI6-F-125-D
Giessen	BI6-A-022-D
Göttingen	BI6-F-130-D
Hamburg	BI6-B-039-D
Hannover	BI6-B-041-D
	BI6-B-345-D
Heidelberg	BI6-F-123-D
	BI6-F-298-D
Homburg	BI6-A-010-D
	BI6-D-335-D
Jülich	BI6-A-007-D
	BI6-B-053-D
	BI6-B-189-D
Karlsruhe	BI6-A-029-D
	BI6-D-091-D
	BI6-F-105-F
	BI6-F-115-D
München	BI6-F-211-D
Neuherberg	BI6-A-011-D
	BI6-A-172-D
	BI6-B-056-D
	BI6-C-066-D
	BI6-C-068-D
	BI6-D-080-D
	BI6-D-083-D
	BI6-D-085-D
	BI6-D-087-D
	BI6-D-221-D
	BI6-E-156-D
	BI6-F-111-D
	BI6-F-133-D
	BI6-F-337-D
	BI6-F-342-D
Ulm/Donau	BI6-C-061-D
Würzburg	BI6-A-013-D

Denmark

Aarhus	BI6-A-303-DK
	BI6-D-086-DK
	BI6-E-170-DK
	BI6-F-317-DK
Copenhagen	BI6-E-168-DK
	BI6-F-333-DK
Lyngby	BI6-F-113-DK
Roskilde	BI6-A-028-DK
	BI6-B-030-DK
	BI6-B-326-DK
	BI6-F-107-DK
	BI6-F-175-DK
	BI6-F-296-DK

Spain

Barcelona	BI6-F-297-E
Bellaterra Barcelona	BI6-A-232-E
Madrid	BI6-B-195-E
	BI6-F-227-E
	BI6-F-229-E
	BI6-F-214-E
Santander	BI6-F-314-E
Sevilla	BI6-E-311-E

France	
Ambazac	BI6-F-340-F
Bordeaux	BI6-D-078-F
Bruyères-le-Chatel	BI6-C-310-F
	BI6-D-098-F
Cadarache	BI6-B-037-F
	BI6-B-325-F
	BI6-F-109-F
Fontenay-aux-Roses	BI6-A-020-F
	BI6-B-045-F
	BI6-B-182-F
	BI6-C-065-F
	BI6-C-073-F
	BI6-D-096-F
	BI6-D-101-F1
	BI6-E-149-F
	BI6-F-119-F
	BI6-F-122b-F
	BI6-F-122-F
	BI6-F-128-F
	BI6-F-181-F
	BI6-F-207-F
	BI6-F-332-F
	BI6-F-132-F
Gif-sur-Yvette	BI6-E-145-F
	BI6-F-344-F
Grenoble	BI6-A-005-F
Jouy-en-Josas	BI6-C-058-F
Limoges	BI6-A-192-F
Lyon	BI6-D-319-F
Montpellier	BI6-A-231-F
Nantes	BI6-B-047-F
Paris	BI6-B-234-F
	BI6-E-147-F
	BI6-E-151-F
	BI6-E-154-F
	BI6-F-121-F
	BI6-F-339-F
Pierrelatte	BI6-D-088-F
Strasbourg	BI6-A-021-F
	BI6-A-304-F
Toulouse	BI6-A-001-F
	BI6-A-180-F
	BI6-A-292-F
	BI6-D-201-F
	BI6-F-122a-F
	BI6-F-122c-F
Villejuif	BI6-F-163-F
	BI6-E-126-F

Greece	
Athens	BI6-B-293-GR
	BI6-E-206-GR
	BI6-E-224-GR
	BI6-E-331-GR
Attiki	BI6-F-114-GR
Thessaloniki	BI6-F-104-GR

Italy	
Bologna	BI6-A-023-I
Firenze	BI6-D-070-I
La Spezia	BI6-B-034-I
Legnaro	BI6-A-193-I
Milano	BI6-D-177-I
	BI6-E-174-I
	BI6-F-204-I
Pavia	BI6-E-158-I
Piacenza	BI6-B-329-I
Pisa	BI6-F-139-I
Roma	BI6-A-004-I
	BI6-A-302-I
	BI6-A-306-I
	BI6-C-059-I
	BI6-D-103-I
	BI6-D-196-I
	BI6-D-341-I
	BI6-E-171-I
	BI6-E-186-I
	BI6-E-205-I
	BI6-F-313-I
Udine	BI6-F-136-I

Ireland	
Dublin	BI6-B-043-IRL
	BI6-B-218-IRL
	BI6-C-176-IRL
	BI6-C-309-IRL
	BI6-D-092-IRL
	BI6-D-093-IRL
	BI6-D-184-IRL
	BI6-F-117-IRL
	BI6-F-134-IRL
Galway	BI6-E-162-IRL

The Netherlands	
Amsterdam	BI6-E-330-NL
Bilthoven	BI6-A-008-NL
	BI6-B-036-NL
Den Burg	BI6-B-054-NL
Groningen	BI6-F-120-NL
	BI6-F-210-NL
Leiden	BI6-A-002-NL
	BI6-D-075-NL
	BI6-D-185-NL
	BI6-D-202-NL
	BI6-D-219-NL
	BI6-E-166-NL
	BI6-E-167-NL
	BI6-E-169-NL
	BI6-E-226-NL
	BI6-E-338-NL
	BI6-F-138-NL
Petten	BI6-D-203-NL
Rijswijk	BI6-C-079-NL
	BI6-D-067-NL

	BI6-D-072-NL
	BI6-D-212-NL
	BI6-E-148-NL
Rotterdam	BI6-E-141-NL
Wageningen	BI6-B-051-NL
Yerseke	BI6-B-191-NL
	BI6-B-199-NL
	BI6-F-328-NL

Portugal

Sacavém	BI6-B-198-P
	BI6-F-299-P
	BI6-F-208-P

United Kingdom

Aberdeen	BI6-A-014-UK
Ascot, Berkshire	BI6-B-032-UK
Berkeley	BI6-C-082-UK
Berkeley	BI6-D-095-UK
Berkeley	BI6-F-209-UK
Birmingham	BI6-F-129-UK
Brighton	BI6-E-142-UK
Bristol	BI6-A-006-UK
Cardiff	BI6-D-097-UK
Chilton, Didcot	BI6-A-009-UK
	BI6-A-015-UK
	BI6-A-016-UK
	BI6-A-018-UK
	BI6-A-026-UK
	BI6-A-216-UK
	BI6-A-301-UK
	BI6-B-048-UK
	BI6-D-064-UK
	BI6-D-076-UK
	BI6-D-089-UK
	BI6-E-143-UK
	BI6-E-144-UK
	BI6-E-150-UK
	BI6-E-164-UK
	BI6-E-165-UK
	BI6-E-177-UK
	BI6-E-225-UK
	BI6-F-110-UK
	BI6-F-116-UK
	BI6-F-118-UK
	BI6-F-127-UK
	BI6-F-213-UK
	BI6-F-230-UK
	BI6-F-295-UK
	BI6-F-336-UK
	BI6-F-135-UK
Edinburgh	BI6-E-157-UK
Epsom Surrey	BI6-B-194-UK
Fife Scotland	BI6-E-294-UK
Grampian Scotland	BI6-B-318-UK
Grange-over-Sands	BI6-B-233-UK
Harwell, Didcot	BI6-A-017-UK
	BI6-A-019-UK
	BI6-B-044-UK
	BI6-B-046-UK
	BI6-C-074-UK
	BI6-D-100-UK
	BI6-D-235-UK
	BI6-E-190-UK
London	BI6-A-025-UK
	BI6-C-057-UK
	BI6-C-060-UK
	BI6-F-108-UK
	BI6-F-228-UK
Lowestoft, Suffolk	BI6-B-200-UK
Manchester	BI6-C-062-UK
Newcastle u.Tyne	BI6-F-315-UK
Oxford	BI6-C-063-UK
Plymouth Devon	BI6-B-038-UK
St.Andrews	BI6-A-024-UK
Teddington	BI6-A-003-UK
Warrington	BI6-F-131-UK
Winfrith	BI6-D-102-UK
Withington, Manch.	BI6-F-140-UK

International

Milwaukee (IBMT)	BI6-C-084-US
Bordeaux (EULEP)	BI6-D-099-D
Chilton (ICRP)	BI6-F-324-UK
	BI6-F-124-UK
Roskilde (IUR)	BI6-B-052-B
Sèvres (ICRU)	BI6-A-217-US
	BI6-A-027-US
	BI6-A-322-US

Annex IV.

List of Proceedings of Scientific Meetings[4]

and other Publications on Radiation Protection

- Radiation Protection Quantities for External Exposure

  Proceedings, edited by J. BOOZ, G. DIETZE
  Report EUR 9645 EN, published in Radiation Protection Dosimetry, Vol. 12, No. 2, 1985, 236 pages
  Price: US$ 25

- Exposure to Enhanced Natural Radiation and its Regulatory Implications

  Proceedings, edited by B. BOSNJAKOVIC, P.H. VAN DIJKUM, M.C. O'RIORDAN, J. SINNAEVE
  Report EUR 10122 EN, published in The Science of the Total Environment, Vol. 45, 1985, 700 pages
  Price: HFL 450

- Ninth Symposium on Microdosimetry

  Proceedings, edited by J.A. DENNIS, J. BOOZ, B. BAUER
  Published in Radiation Protection Dosimetry, Vol. 13, No. 1-4, 1985, 400 pages
  Price: US$ 85

- The modelling of gravitational settling in the assessment of the consequences of accidental releases of radioactivity

  Report EUR 10097 EN, edited by B.Y. UNDERWOOD, published by EUROFFICE,
  2985 Luxembourg, 1985,
  155 pages
  Price: ECU 11.17

- The relative tissue-kerma sensitivity of thermoluminescent materials to neutrons - A review of available data - CENDOS

  Report EUR 10105 EN, edited by J.A.B. GIBSON, published by EUROFFICE, 2985 Luxembourg, 1985, 79 pages
  Price: ECU 6.65

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[4] Workshops, Seminars or Symposia organised, co-organised or co-sponsored by the Commission of the European Communities during the 1985-1989 Programme.

- An intercomparison study of thermoluminescent dosemeters for environmental measurements

  Report EUR 10330 EN, edited by A.F. MCKINLAY, published by EUROFFICE, 2985 Luxembourg, 1985, 21 pages
  Price: ECU 4.47

- Progress Report 1980-1984 of the Radiation Protection Programme

  Report EUR 9733, published by EUROFFICE, 2985 Luxembourg, 1985, Vol. I&II, 2300 pages
  Price: Vol. I&II ECU 119.39

- Progress Report 1985 of the Radiation Protection Programme 1985-1989

  Report EUR 10452, published by EUROFFICE, 2985 Luxembourg, 1986, 1407 pages
  Price: ECU 74.64

- Radiation Protection Programme, Synthesis of Results 1981-1984

  Report EUR 10394 EN, published by EUROFFICE, 2985 Luxembourg, 1986, 174 pages
  Price: ECU 12.40

- Methods for Assessing the Off-site Radiological Consequences of Nuclear Accidents (I)

  Proceedings, edited by J. SINNAEVE, F. LUYKX
  Report EUR 10397 EN, published by EUROFFICE, 2985 Luxembourg, 1986, 1022 pages, 223 figures, 101 tables
  Price: ECU 56.05

- Methods for Assessing the Off-site Radiological Consequences of Nuclear Accidents (II)

  Final joint report EUR 10243 EN, published by EUROFFICE, 2985 Luxembourg, 1986, 221 pages, 25 figures, 6 tables
  Price: ECU 17.94

- Speciation of Fission and Activation Products in the Environment

  Proceedings, edited by R.A. BULMAN, J.R. COOPER
  Report EUR 10059 EN, published by Elsevier Applied Science Publishers, 1986, 437 pages
  Price: £ 48

- The Radiological Exposure of the Population in the Meuse Basin

  Report EUR 10670 EN, published by EUROFFICE, 2985 Luxembourg, 1986, 166 pages
  Price: ECU 12.50

- Radiation Risks to the Developing Nervous System

  Proceedings, edited by H. KRIEGEL, G.B. GERBER, W. SCHMAHL, F.E. STIEVE
  Report EUR 10414 EN, published by G. Fischer Verlag, 1986, 435 pages
  Price: DM 110

- Cell Transformation in Radiobiology

  Proceedings, Report EUR 10416 EN, published in International Journal of Radiation Biology, 49, 501-547, 1986
  Price: £ 23

- Dosimetry of Beta Particles and Low Energy X-rays

  Proceedings, edited by J. BOOZ, W.A. JENNINGS, G. PORTAL
  Report EUR 10192 EN, published in Radiation Protection Dosimetry, Vol. 14, No. 2, 1986, 204 pages
  Price: US$ 25

- Application of Distribution Coefficients to Radiological Assessment Models

  Proceedings, edited by T.H. SIBLEY, C. MYTTENAERE
  Report EUR 10121 EN, published by Elsevier Applied Science Publishers, 1986, 430 pages
  Price: £ 42

- Radiation Damage to Skin: Fundamental and Practical Aspects

  Proceedings, edited by H. JAMMET, F. DABURON, G.B. GERBER, J.W. HOPEWELL
  Report EUR 10415 EN, published in British Journal of Radiology, Suppl. No. 19, 1986, 160 pages
  Price: £ 18

- Gaseous effluent treatment in nuclear installations

  Proceedings, edited by G. FRASER, F. LUYKX
  Report EUR 10580 EN, published by Graham & Trotmen Ltd, 1986, 1075 pages
  Price: £ 120

- Environmental and Human Risks of Tritium

  Proceedings, edited by G.B. GERBER, C. MYTTENAERE, H. SMITH
  Report EUR 10510 EN, published in Radiation Protection Dosimetry, Vol. 16, No. 1-2, 1986, 192 pages
  Price: US$ 50

- Results of environmental radioactivity measurements in the Member States of the European Community for air - deposition - water - milk 1982-1983

  Radiation Protection - No. 34, Report EUR 10235 DA/DE/GR/EN/FR/IT/NL, published by EUROFFICE, 2985 Luxembourg, 1986, 274 pages,
  Price: ECU 21.30

- The Radiobiology of Radium and Thorotrast

  Proceedings edited by W. GÖSSNER, G.G. GERBER, U. HAGEN, A. LUZ
  Report EUR 9096 EN, published by Urban & Schwarzenberg Verlag, 1986, 219 pages
  Price: DM 118

- Methods of Assessing the Consequences of Population Irradiation

  Radiation Protection - No. 35, Report EUR 10289 EN/FR, published by EUROFFICE, 2985 Luxembourg, 1986, 188 pages
  Price: ECU 20.85

- Results of the second CEC Intercomparison of Active and Passive DosEmeters for the Measurement of Radon and Radon Decay Products

  Edited by J.C.H. MILES, J. SINNAEVE
  Report EUR 10403 EN, published by EUROFFICE, 2985 Luxembourg, 1986, 60 pages, 21 figures, 101 tables
  Price: ECU 5.66

- Aims and Practices of Transfrontier Emergency Planning within the EC Countries in case of an Accident in a Nuclear Installation

  Document V/2138/86 EN/FR, 1986, 47 pages, DG-XI-A-1, CEC, Luxembourg

- Progress Report 1986 of the Radiation Protection Programme 1985-1989

  Report EUR 10953, published by EUROFFICE, 2985 Luxembourg, 1987, 1963 pages
  Price: ECU 85

- Radiological Mass Screening within the Member States of the European Communities, Regulations, Practices, Effectiveness

  Proceedings, edited by J. LOCHARD
  Report EUR 11059 EN, Radiation Protection - No. 37, 494 pages
  Price: ECU 37.20

- A Preliminary Assessment of the Radiological Impact of the Chernobyl Reactor Accident on the Population of the European Community

  M. MOREY, J. BROWN, J.A. WILLIAMS, M.J. CRICK, J.R. SIMMONDS, M.D. HILL
  Report EUR 11523 EN, 1987, 44 pages, DG-XI-A-1, CEC, Luxembourg

- The Transfer of Radionuclides through Foodchains following Accidental Releases to Atmosphere

  J.R. SIMMONDS, C. STEINHAUER, S.M. HAYWOOD
  Report EUR 11255 EN, published by EUROFFICE, 2985 Luxembourg, 1987, 35 pages, 5 figures, 4 tables
  Price: ECU 4.60

- Occupational Radiation Dose Statistics from Light Water Power Reactors operating in Western Europe

  I.R. BROOKES, T. ENG
  Radiation Protection - No. 36, Report EUR 10971 EN, published by EUROFFICE, 2985 Luxembourg, 1987, 228 pages
  Price: ECU 16.40

- Exposure to Natural Radiation in Dwellings in the European Communities

  J.P. McLAUGHLIN
  Document V/6683/87, 1987, 115 pages, DG-XI-A-1, CEC, Luxembourg

- Real-time Computing of the Environmental Consequences of an Accidental Release to Atmosphere from a Nuclear Installation

  Proceedings, Document V/2943/86, 1987, 700 pages, DG-XI-A-1, CEC, Luxembourg

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