4. CREMPA - Report 1994 on the Potentialities and Activities of the WHO Collaborating Center for Radiation Emergency Medical Preparedness and Assistance, Ulm, Director, Dr Th. Fliedner, (CREMPAN, basic support by the German Ministry of Health)

4 1 Introduction

The CREMPA Ulm was appointed at the Department of Clinical Physiology, Occupational and Social Medicine of the University of Ulm in April 1992. For its potentialities and activities (see terms of reference) it works closely together with the following departments and institutions.

- At the University of Ulm: Department of Internal Medicine, Hematology and Oncology (including the divisions of Bone Marrow Transplantation and Blood Stem Cell Transfusion), Department of Transfusion Medicine at the DRK Blood Transfusion Service, including the HLA-Typing Service and access to EURO-Transplant.

  In addition, the CREMPA Ulm can mobilize on short notice all other clinical services of the University of Ulm required for taking care of radiation accident victims, such as emergency medicine services, nuclear medicine services, accident surgery services, dermatology services.

- In Germany: The Director of CREMPA Ulm is an active member of the Advisory Board of the Institute for Radiation Protection Medicine of The Workmen Compensation Board and Chairman of the Radiation Emergency Medical Team of the Burn-Center of the Workmen Compensation Board at Ludwigshafen-Oggersheim, the central hospital in Germany ready to accept radiation accident victims any time (24 hours a day, 7 days a week). Through this activity, CREMPA Ulm is incorporated into the "Regional Radiation Protection Centres" of Germany that are located in several areas of Germany prepared to assist in radiation emergency questions any time.

- In Europe: CREMPA Ulm is part of the EURATOM network of radiation protection research since several decades and contributes actively to the EURATOM radiation protection programme.

4.2 Terms of reference

On the basis of the potentials and actions, the CREMPA Ulm worked also in 1994 to fulfill the following "terms of reference".

- to take part in the general development of radiation protection and medical preparedness for radiation accidents within the framework of WHO REMPAN,

- to promote the improvement of existing and development of new approaches to assess the degree of individual radiation exposure with the aim of developing appropriate therapeutic measures;

- to participate in the development of a data base registering the clinical signs and symptoms of all individuals who have ever been accidentally exposed to acute whole body irradiation,

- to develop an expert system for facilitating decision-making by medical doctors in case of a radiation accident;
- to support training activities for the management of radiation accidents,
- to participate in the preparation of relevant national and WHO documents and guidelines;
- to exchange information with WHO on developments in radiation protection;
- to assist in the elaboration of radiation emergency plans;
- to act as a focal point in Germany for communication with the national system for radiation emergency preparedness and assistance which was established by the Federal Ministry of the Environment and the Workmen Compensation Board for Electricity (Berufsgenossenschaft der Feinmechanik und Elektrotechnik).

In all these areas the CREMPA Ulm was very active in 1994 and has reported about its acitivities at the 5th REMPAN meeting at Paris, France, which was held from December 5 through 8, 1994.

4.3 Overview of activities 1994 relating to the terms of reference

4.3.1 Participation in the general development of radiation protection and medical preparedness for radiation accidents

The CREMPA Ulm has pursued in 1994 several activities, which are of importance to the general development of radiation protection and medical preparedness for radiation accidents. These include the exchange of information with the officers of WHO relating to this topic under particular consideration of the programme of WHO in the field of Post-Chernobyl In addition, the activities related to contacts with research and clinical groups in Kiev, in St. Petersburg and in Chelyabinsk as well as to the participation in the further development of the national and the European programmes relating to the improvement of the radiation protection programme and the medical preparedness for radiation accidents.

4 3.2 Improvement of existing and development of new approaches to assess the degree of radiation exposure

The CREMPA Ulm has a relatively large programme on the development of new approaches to assess the degree of individual radiation exposure. In this field the Ulm group has in its own facilities all possibilities to diagnose the effects of radiation on the human organism It has developed all tools for the hematological assessment of radiation effects, including blood cytology as well as bone marrow cytology and histology. In addition, the CREMPA Ulm has a very active programme on cytogenetics, using all modern facilities, and is working very intensely on the development of new approaches to assess the degree of radiation damage at the DNA level, using the single-cell-gel-electrophoresis. In addition, the molecular biology programme of CREMPA is in the process of developing new approaches to assess the extent of radiation damage to the hemopoietic stem cell population using molecular biology approaches.

These activities alone and in collaboration with other centres in Ulm, in Europe and worldwide resulted in the preparation, execution and publication of an international workshop on "Biological Indicators of Radiation Exposure" that was held under the sponsorship of the SEARLE-Foundation

- to develop an expert system for facilitating decision-making by medical doctors in case of a radiation accident;
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and in close collaboration with WHO and the European Radiation Protection Programme at the International Institute for Scientific Cooperation, Schloß Reisensburg, at the end of September 1994. The proceedings of this workshop are going to be published early in 1995 and will form the basis of the development in 1995 of a new protocol for the assessment of radiation affects on the human organism after acute, subacute and chronic effects of ionizing radiation (programme see annex 1).

It can be said that the CREMPA in Ulm alone and in collaboration with relevant departments of the University of Ulm is prepared to take on any task relating to the assessment of radiation affects on the human body as a basis for the initiation of therapeutic measures.

4.3.3 Improvement of existing and development of new approaches for the treatment of overexposed persons

The Department of Clinical Physiology, Occupational and Social Medicine has a significant experimental programme which allows the group to develop further preclinical models relevant to the treatment of overexposed persons. In particular, the group is supported by the German Federal Ministry of the Environment to develop further the use of cytokines to improve the recovery of hemopoiesis after total body irradiation. In addition, another federal programme is supporting an activity of the Department of Clinical Physiology in the field of studying the recovery mechanisms of human megakaryocytopoiesis after radiation exposure. All these activities that were carried out in 1994 contribute extensively to the preparedness to treat overexposed persons.

The Department of Clinical Physiology, Occupational and Social Medicine is also in close collaboration with the Department of Internal Medicine, Hematology and Oncology in the field of bone marrow transplantation and blood stem cell transplantation for the initiation of hemopoietic recovery after total body irradiation. Together with this department, the CREMPA in Ulm is prepared any time to accept patients for the treatment of radiation overexposure and is prepared to transplant stem cells collected from bone marrow and from peripheral blood. In addition, due to the close collaboration with the Department of Transfusion Medicine and its Division of Histocompatibility Typing and access to the European Bone Marrow Transplant Registry, the CREMPA in Ulm is at any time prepared to search for suitable stem cell donors in case of radiation accident

In summary, the CREMPA in Ulm is participating in the development of new approaches for the treatment of overexposed persons, but in collaboration with the clinical departments of the university hospitals it is prepared any time to take care clinically of overexposed persons. This is also due to the fact that close collaboration activities exist with the Department of Nuclear Medicine, the Department of Dermatology as well as the Departments of Emergency Medicine and Traumatology.

4.3.4 Development of a data base for radiation exposed persons

The CREMPA Ulm, which is part of the Department of Clinical Physiology, Occupational and Social Medicine, is working on a data base for persons accidentally exposed to ionizing radiation This activity was pursued very vigorously in 1994 in close collaboration with the Institute of Biophysics in Moscow, the Ural Research Center for Radiation Medicine and the Institute for Radiation Medicine in Kiev.

In 1994 more than 120 Chernobyl acute radiation accident case histories have been included into the data base. From other reported accidents in the world again more than 120 case histories are now included in the "Moscow - Ulm radiation accident data base". These more than 240 completed radiation accident case histories form an invaluable material for the further analysis of radiation accident case

histories and a basis for the improvement of diagnostic and therapeutic tools. In 1994 the attempts for the data base were extended. While at the moment, the data base consists of reports on the first 100 days after acute radiation exposure, the attempts started in 1994 to develop a "follow-up" data base to find out what has happened to those persons that are registered in the data base. This will be eventually possible for 237 persons of the Chernobyl accident that were treated either in Moscow or in Kiev. The attempt is now to establish the clinical data base for follow-up of these patients between 1986 and 1993. An agreement has been reached with the Institute of Biophysics in Moscow and the Institute in Kiev for the follow-up questionnaire to register all medical visits of exposed persons until 1993. In 1994 we have now the first 10 cases where a follow-up information from 1986 until 1993 is available in the so-called pre computer case report form. This will form the basis to make a serious attempt to get follow-up data on all 237 accident victims.

In addition, the CREMPA Ulm is preparing together with the Ural Research Center on Radiation Medicine a data base for survivors of the Chelyabinsk catastrophe of the last 40 years. Several thousands of persons were exposed by the incorporation of radioactive nuclides through the drinking water of the Techa river and many of these persons developed a "chronic radiation disease". In order to study the pathophysiological mechanisms involved, the Ulm group together with the Chelyabinsk group is preparing a basic study on these persons to include new diagnostic tools to assess the radiation effects on these people In 1994 several exchange visits between Chelyabinsk and Ulm occurred in order to promote this concept.

A research plan was developed to establish between Ulm and Chelyabinsk a pilot telemedicine service to exchange information on radiation exposed persons in a regular fashion as a basis for preparing a multimedia data base for chronically irradiated radiation accident victims. The project will go into its active phase in 1995. The basis of it was reported to the 4th REMPAN meeting which was held at the University of Ulm in December 1992.

4.3.5 Development of an expert system for decision making by medical doctors in radiation accident cases

Members of the Ulm team (laboratory for data bases and informatics) are well on their way to develop an assistance system for decision making by medical doctors in cases of radiation accident. This work has progressed to a large extent in 1994 and will be submitted as a thesis for a Doctor of Engineering Sciences in 1995 to the appropriate faculty of the University of Ulm. The scientific basis for this expert system will thus be published in 1995.

4.3.6 Support training activities for the management of radiation accidents

The CREMPA in Ulm is continuously participating in training activities for the management of radiation accidents.

First of all, the Ulm group is conducting in the framework of the Baden-Württemberg Academy for Occupational and Social Medicine courses on radiation accident management. In addition, the members of the group are participating in training activities of the "Gesellschaft für Strahlenforschung" in Munich. However, in particular the Ulm group is having in regular intervals research workers from several parts of the world, including the former Soviet Union, in the field of radiation accident training We had training visitors, not only from Russia, the Ukraine and China, but also from other parts of Europe.

The Ulm group is preparing for 1995 a training course on the management of radiation accidents in close collaboration with the European Communities.

4.3.7 Participation in the preparation of relevant national and WHO documents and guidelines

The CREMPA Ulm through its director, Prof. Dr. T. M. Fliedner, is participating in several national activities.

In 1992 the German Radiation Protection Commission held a workshop at the University of Ulm, prepared by the group in Ulm, on radiation accident management. The manuscripts of this workshop are currently under preparation for publication.

In addition, the Ulm group is participating in the new edition of Volume 4 of the publications of the German Radiation Protection Commission entitled "Medizinische Maßnahmen bei Kernkraftwerksunfällen (Medical Measures in Case of Accidents in Nuclear Establishments)". This publication is meant to address itself to radiation emergency preparedness and medical assistance in radiation catastrophic events, such as the nuclear excursion in radiation facilities (nuclear power plants).

Furthermore, the Ulm group is participating in the preparation of another publication of the German Radiation Protection Commission, entitled "Der kleine Strahlenunfall" (the Small Radiation Accident). In this publication the medical management options are outlined for small radiation accidents as they may occur in scientific, medical or industrial settings, involving only a small number of persons.

4 3.8 Exchange of information on radiation protection

The Ulm group participated at regular intervals in interacting with the WHO office in radiation protection services. This resulted in an exchange of information on the international plan for the Chernobyl consequences. In addition, the Ulm group participated in the 5th meeting of REMPAN and gave several presentations at that meeting in December 1994.

4.3.9 Assistance in radiation emergency plans

. In October/November 1994 the Ulm group was called to assist in a radiation accident that happened in Tallinn in Estonia. Several persons were exposed to most likely Cäsium 137 which had been stolen from a dumping place. One person died as a consequence of radiation exposure to this radiation source. Other persons were involved since the radiation source apparently was brought to a home. In that home several persons were exposed, especially a 13 year old boy, being treated at the children's hospital. The Ulm group was asked to assist in the diagnostic procedure of this patient and is in day-to-day contact with the children's hospital there. As it appears, the cytogenetic analysis indicated an exposure dose, most likely protracted exposure over several days in the order of 100 to 200 cGy. This resulted in a pancytopenia including leucopenia, thrombocytopenia and a mild degree of anemia. At the present time (December 1994) the boy is alive, local wounds due to the touching of the radiation source are healing and it is now the question whether cytokines should be administered. The Ulm group was able to take a look at bone marrow sections and bone marrow smears of this patient and thus, was able to help in detail in the management of this particular patient.

4.3.10 Communication in Germany and Europe as a focal point for radiation emergency preparedness and assistance

The Ulm group is in constant interaction with all the German activities in radiation accident preparedness and assistance This is due to the fact that Prof Fliedner is member of the Advisory Board of the Institute of Radiation Protection Medicine of the Workmen Compensation Board for Electricity. This Institute of Radiation Medicine has established at the Burn Center in Ludwigshafen-Oggersheim a facility to take care of radiation accident victims, regardless whether they are contaminated, whether an incorporation of radionuclides has occurred or whether total body exposure might have occurred. In this case, the hospital at Ludwigshafen is prepared to accept any patient at any time. This will then lead to the activation of an advisory board of medical experts, under the chairmanship of Prof. Fliedner. In addition, there are several regional radiation protection medicine centres that are able and active to give advice in problem questions any time. The Ulm group is an active part of this network and again in 1994 members of the Ulm group participated in the post-graduate training of members of this German assistance network.

In addition, the Ulm group is participating in radiation accident networks in Europe under the support of the radiation protection action of the European Communities. A close collaboration exists and is pursued with the research groups in Rotterdam, Paris and Rome. The Ulm group is a coordinator for a research programme on radiation accident management with these groups. It is also participating in a programme coordinated by the University of Rotterdam in trying to link the Western European efforts to similar efforts in Russia and the Ukraine.

4.4 Conclusions and Perspectives for 1995

The report for 1994 indicates that the CREMPA in Ulm continued in 1994 to strengthen its role as a collaborating centre in the network of WHO collaborating centres spread all over the world.

Its particular strength lies in the combination of clinical practice with research and training.

From this viewpoint the CREMPA, in collaboration with the relevant departments of the university, is prepared any time to accept the challenge to help in the diagnoses and treatment of radiation accident victims anywhere. The Department of Clinical Physiology is fully equipped in all diagnostic procedures relating to the evaluation of radiation effects on the hemopoietic as well as the immune system. In collaboration with other departments of the university, any problem that may arise in connection with exposure of human beings to ionizing radiation can be addressed constructively.

Such a radiation accident clinical preparedness is due to the fact that the Department of Clinical Physiology, Occupational and Social Medicine is pursuing several lines of research. This research includes preclinical studies in total body irradiated dogs that are studied to improve the recovery of hemopoiesis using appropriate cytokines. In addition, studies at the cellular level using human cells are being pursued to study the replicative and proliferative potentials of hemopoietic stem cells using appropriate molecular biological tools. These research studies enable the group in Ulm to develop further biological indicators for radiation exposure.

Of particular value in 1994 was the organization of a workshop on "Biological Indicators of Radiation Exposure". Experts from all parts of the world assembled at the International Institute for Scientific Cooperation, Schloß Reisensburg, to discuss the availability and research developments of biological indicators of radiation exposure. The proceedings of this workshop will be published in 1995 and will form the basis for the development of an extended protocol for the assessment of radiation

effects of radiation accident victims This protocol is being tested in heavily radiation exposed uranium miners in collaboration with other German institutes.

For 1995 the CREMPA Ulm as part of the Department of Clinical Physiology, Occupational and Social Medicine will continue to work on 5 areas. These include the study of the physiology and pathophysiology of cellular replication and differentiation using hemopoietic cell renewal systems as examples. Furthermore, cytogenetic and cytotoxic analysis of suitable normal and altered cells after exposure to ionizing radiation.

In another area, there will be studies on mammalian organism after exposure to ionizing radiation. These will lead to the improvement of existing and development of new biological indicators.

Finally, there will be more systems research in occupational medicine on the basis of the development of a computerized data base for acute and late somatic effects after total body exposure.

In 1995 special emphasis will be given to the continued day-to-day availability of diagnostic and therapeutic tools for the assessment and treatment of radiation accident victims. There will be also further activities in the field of training for German, European and overseas persons requiring training in the management of radiation accident victims. This will be done especially in collaboration with the European Communities. Finally, the research work will continue in collaboration with the European laboratories and in collaboration with institutions in Russia as well as in the Ukraine.

International Searle-Foundation Workshop on Biological Indicators of Exposure to Ionizing Radiation at the International Institute for Scientific Cooperation, Schloss Reisensburg near Ulm in Germany

September 26, 1994 - September 30, 1994

Scientific Committee: T.M. Fliedner, V.P. Bond, E.P. Cronkite,

Scientific Secretaries: B. Ziegler and U. Plappert

This workshop was initiated by the International Institute for Scientific Cooperation, Schloss Reisensburg in close cooperation with the Department of Clinical Physiology, Occupational and Social Medicine of the University of Ulm and its WHO-Collaborating Center of Radiation Emergency Medical Preparedness and Assistance as well as the Medical Department, Brookhaven National Laboratory, Upton, L.I., New York.

The workshop was made possible by a grant of the Searle-Foundation for Medical Prevention and Epidemiology, Ulm.

Further support was obtained by the University of Ulm and its University Hospital, by the European Communities, the Federal Government of Germany, the State Government of Baden-Württemberg, the World Health Organization, Geneva, as well as the Department of Energy, Washington.

Scientific Committee: T.M. Fliedner, V.P Bond, E.P. Cronkite

Scientific Secretaries: B. Ziegler and U. Plappert

Asst. Scientific Secretaries: D. Densow, L. Rutzen-Loesevitz, Ch. Selig, M. Weiss

Programme

Arrival of participants

Monday, September 26, 1994

19.00 Reception

19.30 Welcome Dinner

Tuesday, September 27, 1994

08.30 **Opening Session**

T.M. Fliedner. Purpose and goals of the workshop:
The need for an expanded protocol for the examination of radiation exposed persons

08.50 **Special address**:

W. Kreisel, Executive Director, WHO, Geneva.
International Programme on the Health Effects of the Chernobyl Accident (IPHECA)

Welcome addresses:

J. Dreier, Vice Minister for Science and Research Baden Württemberg
G. Simnacher, President of the Swabian Region
W. Pechhold, Rector of the University of Ulm

09.30 **Key note addresses:**
Moderators: E.P. Cronkite and J. Maisin

V.P. Bond:
Imparted energy, absorbed dose and effect severity in assessing biological effects

B.D. Goldstein:
The concept of biological markers in the field of toxicology

10.30 Coffee Break

11.00-13.00 **Scientific Session I:** Case Studies
Moderators: A. Guskova and H. Jammet

D. Preston. Hiroshima/Nagasaki
E.P. Cronkite: Marshall Islands
A.V. Akleyev: Radiation incidents in the Urals and their effects on the health of the residents

13.00-14.30 Lunch

14.30-15.30 **Scientific Session I (cont.)**

A.B. Baranov: Chernobyl Experience
K.Friedrich/G. Enderle : East German Uranium Miners

15.30 Coffee Break

16.00 Panel Discussion
Chair: T.M. Fliedner, Asst. Scientific Secretary: D. Densow

Common denominators for the development of somatic late effects in the presented as well as other case studies:

What primary or secondary effects were observed in spite of different scenarios?

What are the pathophysiological mechanisms resulting in the observed effects?

Are there obvious biological indicators of value to predict non-neoplastic and neoplastic effects in relevant organ systems?

18.30 Cocktails

19.00 Concert Helios-Trio Stuttgart: Chamber Music

20.00 Dinner

Wednesday, September 28, 1994

08.30-10.45 **Scientific Session II**: Biological markers at the molecular level including the immune system as a critical parameter
Moderators: B. Goldstein and H.J. Seidel

B. Ziegler: Hemopoietic stem cell markers

R. D. Thomas: Markers relevant to effects on the immune system

C. Peschle: Biological functions of homeobox genes

M. Montenarh: Marker genes for cytotoxic exposure: P 53

N. Dainiak: Utility of biological membranes as indicators for radiation exposure: alterations in membrane structure and function over time

10.45-11.15 Coffee Break

11 15-13 00 **Scientific Session II (cont.)**.

G. Wagemaker: Surface markers and growth factor receptors of immature hemopoietic stem cell subsets

V. Liu/D. Weaver Cell cycle checkpoints and repair of ionizing radiation damage

P. Vincent: Apoptosis and the assessment of radiation injury

J. Boniver: Spontaneous and induced Apoptosis after whole body exposure: experimental approaches

13.00-14.30 Lunch

14.30-15.30 **Scientific Session III**: Biological markers at the cellular level
Moderators: A. Akleyev and N. Dainiak

M. Bender: Cytogenetic research in radiation biology

M. Bauchinger: Cytogenetic research after accidental radiation exposure

W.F. Blakely: Application of the PCC assay for partial-body radiation exposures

B. Heinze. Stable chromosome aberrations. investigations performed in patients after total body irradiation

15 30-16.00 Coffee Break

16.00-17 15 **Scientific Session III (cont.)**

R. Tice: The comet assay in its significance as a biological marker

U. Plappert DNA-damage detection in man after radiation exposure

W.U. Müller. Micronucleus determination as a means to assess radiation exposure

17.15-18.30 Panel discussion
Chair: G. Wagemaker
Asst. Scientific Secretaries: U. Plappert/L. Rutzen-Loesevitz

Which biological markers at the molecular and cellular level can be used to detect exposure (acute, subacute, chronic) to ionizing radiation early and late after exposure?

What is their diagnostic and prognostic value?

19.00 Dinner

Thursday, September 29, 1994

08.30-10.30 **Scientific Session IV**. Biological markers at the cell system level
Moderators: V. Covelli and M.M. Kossenko

L. Feinendegen: Cellular repair mechanisms after radiation exposure and their consequences for cell system responses

G. Wagemaker: Heterogeneity of radiation sensitivity of hemopoietic stem cell subset

A. Chuchalin, A. Cherniaev: The delayed respiratory consequences of inhaled radionuclides in population exposed to nuclear catastrophe

10.30-11.00 Coffee Break

11.00-12.00 **Scientific Session IV (cont.)**:

J. E. Trosko: Tumor vs. non-neoplastic effects induction and promotion mechanisms after radiation exposure

M. Rezvani/J. Hopewell: Initiation of non-neoplastic late effects: the role of endothelium and connective tissue

I. Emerit: Radiation-induced clastogenic factors in Chernobyl-exposed children and accident recovery workers

12.00-13 00 Panel discussion
Chair: W. Gössner, Asst. Scientific Secretary: Ch. Selig

Which markers at the cell system level are of use to assess the biological consequences of radiation exposure?

13.00-14.30 Lunch

14.30-15.30 **Scientific Session V**: Cell System Responses
Moderators: L. Feinendegen and V.G. Bebeshko

Hematopoiesis:
W. Nothdurft: Response of hemopoiesis in dogs to continuous low dose rate total body irradiation

B. Tibken: Application of a biomathematical model of granulopoiesis to estimate stem cell numbers

15.30-16.00 Coffee Break

16.00-18.00 **Scientific Session V (cont.)**

Immune System:
P.-R. Wüstermann/E.P. Cronkite: - Pathophysiological Aspects
E. Hofer: An approach to a biomathematical model of lymphopoiesis

Tumor Development:
P. Möller: Pathophysiological aspects of tumor development
W. Düchting: Modeling of tumor growth and radiogenic responses of normal and malignant tissue induced by fractionated irradiation

19.30 Bavarian music

20.00 Workshop Banquet

Friday, September 30, 1994

8.30-12.00 **Scientific Session VI**

Panel Discussion
Chair: T.M. Fliedner
Asst. Scientific Secretaries : M. Weiss/B. Ziegler

- What biological markers of radiation exposure are relevant
  - at the molecular level
  - at the cellular level
  - at the cell system level

- Which markers should be used in the biomedical evaluation of radiation exposed persons/populations?

- What is the research agenda in this field for the future?

12.00 Closing Remarks

5. CREH - Brief Description of WHO Collaborating Centre for Radiation Effects on Humans, Radiation Effects Research Foundation, RERF, Hiroshima and Nagasaki, Japan, Director, Dr Yutaka Hasegawa

5.1 Introduction

The WHO Collaborating Centre for Radiation Effects on Humans is based on the Radiation Effects Research Foundation (RERF). RERF was established on 1 April 1975 as a non-profit foundation under Japanese Civil Law and according to an agreement between the Governments of Japan and the USA.

The objective of RERF is to conduct research and studies, for peaceful purposes, on the medical effects of radiation on humans with a view to contributing to the maintenance of the health and welfare of the atomic bomb survivors and to the enhancement of the health of all mankind.

RERF has been designated as the WHO Collaborating Centre for Radiation Effects on Humans (CREH) since May 1979. The terms of reference of the Centre are as follows:

1) to provide WHO with all results of its scientific investigations on radiation effects on man, irrespective of the source of exposure;

2) to provide WHO with expert advice on relevant tasks, if requested;

3) to collaborate with WHO in special investigations relevant to the subject of radiation effects on humans. The kind and extent of collaboration will be agreed in each separate case and will depend on priorities set by WHO as well as the Radiation Effects Research Foundation.

CREH has been a member of REMPAN since October 1988 when the second meeting of REMPAN took place in Oak Ridge, U.S.A.

The main role of CREH in REMPAN is to provide advice on the methods for a long-term follow-up of health effects of the population affected by radiation accidents.

5.2 Recent activities of CREH as a WHO Collaborating Centre

5.2.1 Work performed in relation to the terms of reference

1) Term of reference 1

"To provide WHO with all results of its scientific investigations on radiation effects on man, irrespective of the source of exposure;"

All the RERF publications including its technical reports (TRs), commentary and review series (CRs), the annual report and newsletters "Update" have been provided to WHO.

2) Term of reference 2

"To provide WHO with expert advice on relevant tasks, if requested;"

CREH has provided WHO with its expert advice on its relevant tasks whenever requested, e.g. when WHO requested any comments of CREH on the draft WHO documents, etc.

CREH has also done this on the occasions when its staff members have attended WHO meetings. For example, during the last year (1993), the following staff members have participated in WHO meetings and provided WHO with their expert advice:

- Dr Itsuzo Shigematsu, RERF Chairman, attended the WHO Meeting on Chernobyl Projects Coordination, which was held at the WHO Headquarter in Geneva, from 16-28 May 1993.

- Dr Shizuyo Kusumi, Chief, Division of Clinical Laboratories, attended the WHO Workshop on International Health-Related Studies Following the Chernobyl Accident, which was organized by the WHO European Centre for Environment and Health and held in Rome, from 14 to 17 December 1993

3) Term of reference 3

"To collaborate with WHO in special investigations relevant to the subject of radiation effects on humans. The kind and extent of collaboration will be agreed in each separate case and will depend on priorities set by WHO as well as the Radiation Effects Research Foundation "

No work has been done with regard to this term of reference since when CREH was first designated as a WHO collaborating centre in 1979. This is because no proposal for a special investigation of relevance has come up between WHO and CREH

5.2.2 Other activities relating to WHO

1) Participation in the REMPAN meetings

- Dr Y. Hasegawa (Head of CREH) participated in the second meeting of REMPAN in Oak Ridge, U.S.A., in October 1988.

- Dr Y. Hasegawa participated in the third meeting of REMPAN in Leningrad, then USSR, in May 1990.

- Dr N. Nakamura (a research scientist of CREH) participated in the fourth meeting of REMPAN in Ulm, Germany, in December 1992.

2) Hosting a WHO meeting

CREH hosted the first meeting of the WHO Scientific Advisory Committee on International me on Health Effects of Chernobyl Accident (IPHECA) that took place at CREH in Hiroshima, Japan, from 23-26 October 1990.

3) Collaboration with other WHO collaborating centres

Since July 1989, CREH continues a to exchange its major publications with those of other WHO collaborating centres in the field of radiation, which include the WHO collaborating centres in Australia (Australian Radiation Laboratory), Germany (Institute of Radiation Hygiene) and New Zealand (National Radiation Laboratory).