THE THIRTY FIRST BOARD MEETING
RADIATION EFFECTS RESEARCH FOUNDATION

CONTENTS

	Page (Eng)	Page (Jpn)
Agenda(Tentative)	i	i
List of Participants(Tentative)	ii	ii
Schedule	iv	iv
I. Minutes of the 30th Meeting of the Board of Directors, 5 - 7 June 1996, Hiroshima	1	(1)
II. Items for Information		
1. Status report of RERF	22	(22)
2. Report on progress made since the presentation of the Blue Ribbon Panel's recommendations	23	(23)
3. Present personnel status	24	(24)
4. FY-96 salary revision, etc.	36	(36)
5. Labor Union's FY-97 demands for improvement of working conditions, etc.	43	(44)
6. Others (1) International collaboration	51	(49)
(2) Development of an A-bomb related materials database system	57	(54)
(3) Others	58	(55)
III. Items for Deliberation and Action		
1. Recommendations of the 23rd meeting of the Scientific Council	59	(56)
2. Responses to recommendations of the 23rd meeting of the Scientific Council, and "Five Year Strategic Research Plan and Program Management"	65	(63)
3. FY96 research activities report and audit report, etc.	223	(222)
4. FY96 settlement of accounts and audit report	273	(223)
5. FY97 working budget	274	(224)
6. Outline of FY98 budget request	275	(225)
7. Revision of Act of Endowment	276	(226)
8. Revision of rules and regulations	278	(228)
9. Election／Appointment of directors and others	295	(246)
10. Schedule of next board meeting	296	(247)
IV. Any other business		

We hope you will take into account the fact that the Marshall Islands in a young, but strong, democracy, and a close friend of the United States. With the active cooperation of the Marshall Islands Government, we maintain very extensive missile testing facilities at Kwajalein Atoll that are vital to our national security. We are informed that the Marshall Islands has recently agreed to the establishment of an additional missile launch site to accommodate the requirements of our ballistic missile defense testing program, and another such site is under consideration. This is indicative of the commitment of the Marshall Islands to continued cooperation in our bilateral relationship.

On such critically important international issues as the permanent, unconditional extension of the Nuclear Non-Proliferation Treaty, the Marshall Islands, at our request, has provided strong support for our national policies. We note that, as stated in the report of the recently concluded NPT conference, the international community "acknowledges the existence of a special responsibility towards the people of the former United Nations Trust Territories who have been adversely affected as a result of nuclear weapons tests conducted during the period of the Trusteeship."

In requesting that the Administration support the proposed *feasibility study*, we wish to be very clear. We are not proposing that the Administration commit funds to the study, nor even provide technical assistance for its conduct. Rather, we are simply requesting a policy of support in principle. We emphasize that the issue is not one of whether to support the establishment of a nuclear waste disposal facility; the feasibility of such a project is precisely what the study proposes to determine in a preliminary way. By the same token, we feel strongly that the factors we have outlined in this letter compel the conclusion that the proposal of as study merits a positive response, not neutral non-support, from the United States.

As a political matter, it is questionable whether the proposed study could be expected to proceed in the absence of a policy of support on the part of our government. If we expect the Marshallese who were displaced by the testing to actually return to their home atolls utilizing federal trust funds established primarily for those purposes, we should do all we can to facilitate radiological rehabilitation of the islands and resettlement through sound nuclear disposal practices. In that light, a policy of non-support for the proposed study could not be reconciled with our special responsibility towards the people of the former Trust Territory and our desire to see them reestablish and inhabit safe and functional communities.

Sincerely,

GEORGE MILLER, CALIFORNIA, CHAIRMAN
[illegible]

U.S. House of Representatives
Committee on Natural Resources
Washington, DC 20515-6201

[illegible]

March 28, 1994

Honorable Hazel R. O'Leary
Secretary of Energy
Washington, D.C. 20585

Dear Secretary O'Leary:

The Republic of the Marshall Islands recently provided me with the enclosed proposal for a long term-term storage and permanent disposal facility for nuclear materials. I am writing to request that the Department evaluate this proposal as it raises serious policy and safety issues.

Specifically, I would appreciate your providing me with answers to the following questions by May 2, 1994.

1. Please identify the roles the Clinton Administration and the U.S. Congress have in establishing such a facility in the Marshall Islands. What approvals are required by law?

2. With respect to nuclear waste from the United States, please describe the geographic source of the material, the nature of the waste itself, and the systems required for its safe transportation.

3. Please evaluate and describe the manner in which waste would be handled and transported, including identification of methods of transport, and need for roads, ports, and other related facilities.

4. The Marshall Islands proposal suggests that wastes from [illegible] nations, including Russia, may be secured for this site. Pl[illegible] identify all issues related to the co-mingling or co-storage [illegible] nuclear wastes.

5. Please list all U.S. and international laws, including treaties or similar agreements, to which such a proposal would be bound.

6. Has the Marshall Islands government presented this proposal to the Administration, and if so, what is the Administration's position with respect to this proposal?

[illegible]

THE THIRY-FIRST BOARD MEETING
RADIATION EFFECTS RESEARCH FOUNDATION

Date: 11 - 12 June (Wednesday - Thursday), 1997
Place: Board Room, National Academy of Sciences, Washington, D.C.

List of Participants (Tentative)

DIRECTORS

Dr. Itsuzo Shigematsu, Chairman

Dr. Sheldon Wolff, Vice Chairman and Chief of Research

Dr. Shigenobu Nagataki, Permanent Director

Dr. William J. Schull, Permanent Director (Retirement on January 1997)

Dr. Toshiyuki Kumatori, Chairman, Radiation Effects Association

Mr. Kazuaki Arichi, Permanent Director, Japan Institute of International Affairs

Dr. Masumi Oike, Permanent Director, National Social Insurance Societies Association

Dr. Warren K. Sinclair, President Emeritus, National Council on Radiation Protection and Measurements

Dr. Patricia A. Buffler, Dean, Professor of Epidemiology, School of Public Health, University of California, Berkeley

Dr. Jonathan M. Samet, Chairman, Department of Epidemiology, The Johns Hopkins University School of Hygiene and Public Health

SUPERVISOR

Mr. David Williams, Senior Financial Advisor, National Academy of Sciences

SCIENCE COUNCILLORS

Dr. Clark W. Heath, Jr., Vice President for Epidemiology and Statistics, American Cancer Society

OBSERVERS

Dr. Hidesuke Kobayashi, Director-General, Health Service Bureau, Ministry of Health and Welfare

Mr. Masayuki Kimura, Director, Planing Division, Health Service Bureau, Ministry of Health and Welfare

Dr. Hiroshi Maruyama, Assistant Director, Planing Division, Health Service Bureau, Ministry of Health and Welfare

Mr. Masaki Orita, Director-Genenal, North American Affairs Bureau, Ministry of Foreign Affairs

Mr. Tadamichi Yamamoto, Director, First North American Affairs Division, North American Affairs Bureau, Ministry of Foreign Affairs

Mr. Yutaka Aoki, Assistant Director, First North American Affairs Division, North American Affairs Bureau, Ministry of Foreign Affairs

Dr. Paul Seligman, Deputy Assistant Secretary for Health, U.S. Department of Energy

Mr. Frank C. Hawkins, Director, Office of International Health Studies, U.S. Department of Energy

Mr. Joseph Weiss, Japan Project Team, Office of International Health Studies, U.S. Department of Energy

Mr. Milton Eaton, DoE Representative, U.S. Embassy, Tokyo

Dr. Paul Gilman, Executive Director, Commission on Life Sciences, National Research Council, National Academy of Sciences

Dr. Evan Douple, Director, Board on Radiation Effects Research, Commission on Life Sciences, National Research Council, National Academy of Sciences

Ms. Catherine S. Berkley, Administrative Associate, Commission on Life Sciences, National Research Council, National Academy of Sciences

Ms. Robin Morris, Accounting Office, National Academy of Sciences

Operating Committee Members of RERF

Mr. Yasukiyo Hirano, Chief of Secretariat

Mr. Richard D. Sperry, Administrative Advisor, Secretariat

Assistant to Chief of Research

Dr. Akio Awa

Secretariat

Mr. Hiroyuki Tominaga, Assistant Chief of Secretariat

Mr. Torao Sasaki, Assistant Chief of Secretariat

Interpreter

Ms. Eiko Ishizaki

Ms. Naomi Umehara

Ms. Miyuki Hosoya

財団法人 放射線影響研究所
第 31 回理事会（米国 ﾜｼﾝﾄﾝ D.C.）
The 31st RERF Board Meeting (Washington D.C.)

平成 9 年 6 月 11－12 日
11－12 June 1997

日　程　表
Schedule

第 1 日目 6 月 11 日(水)
1st Day: 11 June (Wed.)

		報告または説明者 Presenter
午前の部 Morning Session		
09:30－09:40 (10)	開会の挨拶 Opening words	重松理事長 Chairman Shigematsu
09:40－09:55 (15)	第 30 回理事会 議事録承認 Minutes of the 30th RERF Board Meeting	重松理事長 Chairman Shigematsu
報 告 事 項 Items for Information		
09:55－10:30 (35)	放影研の現状報告 Status report of RERF	重松理事長 Chairman Shigematsu
10:30－10:50 (20)	コーヒーブレイク Coffee break	
10:50－11:40 (50)	ブルーリボン委員会勧告後の経過報告 Report on progress made since the presentation of the Blue Ribbon Panel's recommendation	重松理事長 Chairman Shigematsu
11:40－12:00 (20)	記念撮影 Group photograph	
12:00－13:30 (90)	昼　食 Lunch	
午後の部 Afternoon Session		
13:30－14:10 (40)	役職員等の現状報告 Present personnel status	平野事務局長 Chief of Secretariat Hirano

In the United States, proposals have been made to increase storage capacity for plutonium at tl Pantex facility in Texas. Other sites have also been identified for that purpose. The Oak Ridg facility is considered of adequate dimension to accommodate the anticipated additional HEU, bu there is a question as to whether the complex is suitable for large scale storage of plutonium. Th Savannah River site offers another possibility for additional plutonium storage, however, th capacity of the facility for that purpose is very limited. Los Alamos could provide storag capacity, but also only on a limited basis. Hanford and Rocky Flats would not appear to b candidates. Military bases have been considered, but there are daunting problems involved. A 1993 report to the U.S. Congress from the Office of Technology Assessment (OTA) details th profoundly unsatisfactory storage situation, and takes note of the fact that there are no credibl plans in existence for resolving the problem.

Plutonium exists in vast amounts in civilian spent fuel. According to the NAS, 130 tons of plutonium have been separated from spent fuel, of which amount, 80-90 tons are in storage. In excess of 500 metric tons of additional plutonium could be extracted from the tens of thousands of tons of spent fuel that remain in the civilian sector, worldwide. Of course, the supply of spent fuel is growing constantly. RAND estimates that 300 metric tons of plutonium will be separated from spent fuel by enrichment plants by 2003, "and a lot more in subsequent years". RAND analysts state, "We believe that these plants and materials pose a serious proliferation threat."

It is well known that adequate long-term storage facilities for spent fuel are non-existent in the United States and Russia. As in the case of plutonium, there is no permanent disposal facility for spent fuel in either country.

Although there is debate as to whether plutonium is an asset to be utilized for power production, there is no dispute that the substance cannot be entirely eliminated by "burning". A highly toxic

waste remains for storage and disposal. Moreover, processing for use in power plants results in the production of contaminated scrap, and until the plutonium is utilized and the waste and scrap are finally disposed of, a severe proliferation threat remains. For those who advocate preclusion of the use of plutonium for electrical power production (the current U.S. policy), there are various options. Vitrification, with or without mixing with highly toxic radioactive waste to discourage conversion to weapons purposes, is a partial answer. Nevertheless, storage and disposal must be secure, as the process can be reversed, although with some difficulty.

Russia, several European countries, and Japan are, at present, committed to continuing the production of plutonium for various purposes. If the United States policy of discouraging the civilian use of plutonium prevails, there will be a further, considerable exacerbation of the storage and disposal problem. If the U.S. policy fails, there will remain both a stream of new plutonium requiring continuing storage, and as noted, a flow of residual plutonium and associated highly radioactive waste from the various civilian operations.

Apart from the issue of whether plutonium should be maintained in a retrievable form for future civilian use, there is a less disputed military requirement to maintain a stockpile of the substance. It appears that, although no plutonium has been declared surplus, there is a supply that far exceeds any predictable military demand. Long-term storage and permanent disposal of the declared surplus will have to be provided.

Plutonium "pits", which are the "primary" or fission components of nuclear weapons, can be stored and disposed of intact or in pieces. There is dispute as to which approach is preferable, but security remains essential in either case, as the plutonium substance is not eliminated and can be recovered for weapons production. In addition, there are plutonium oxides, residues, and scraps, as well as contaminated metal, glass, and ceramic components, for which long-term storage and permanent disposal must be provided.

Minutes of the 30th Meeting of the Board of Directors, 5 - 7 June 1996, Hiroshima

within the scope of Basel, it is interesting to note that this OECD-to-non-OECD ban approach has been incorporated into the latest version of a proposed treaty to control the movements of wastes in the South Pacific region. The latter proposal, which will be considered at the next meeting of the South Pacific Forum, DOES include radioactive wastes within the scope of coverage. Clearly, there is a strong sentiment in the region to afford protection from risks associated with transport, storage and disposal of hazardous chemical and radioactive waste.

d. Any repository for high level nuclear wastes originating from international sources, in addition to being subjected to detailed technical review, also would require a multilateral legal framework addressing proposed safeguards of the sub-surface strata, secure transportation specifications, legal liability issues, cost sharing, and contract specifications. Although a preparatory study was conducted by the DOE with Japan in 1980-82, to date no arrangement of this type has been successfully completed nor has such a facility been established anywhere in the world.

e. The U.S. does not currently have the legal authority to dispose of its waste in the RMI. The National Energy Policy Act of 1992 subsequently deleted the Marshall Islands from the list of approved states which may participate in Federally negotiated siting for the establishment of nuclear waste storage facilities, in accordance with the Nuclear Waste Policy Act (NWPA). In addition the 1980 "Matsunaga" Amendment prohibits the disposal of U.S. nuclear wastes in the Pacific Basin without prior Congressional approval.

f. Moreover, although the Nuclear Waste Policy Act (NWPA), Section 122, provides for a period of retrievability of any nuclear fuel placed in a nuclear waste storage repository for purposes of accountability, public safety, and economic value recovery, it does not specifically address the use of a repository facility located outside of direct USG control. Any proposal such as the use of the Marshall Islands for a repository would therefore require a major change in current USG nuclear waste management policy, concurrent with an international agreement with the RMI to allow the right of retrieval of spent nuclear fuel of U.S. origin from such an international repository. These concerns for the retrievability of commingled U.S.-origin nuclear waste from an international repository at a remote location may also be a relevant concern for other participant nations in the RMI proposal.

[illegible] territory or the United States itself. We are not currently aware of the existence of any specialized terrorist threats to the type of nuclear repository proposed by the RMI. We therefore are unable to project whether there may be specialized defense requirements. This possibility, however, must be a factor in the consideration of any such proposal.

CONCLUSIONS/RECOMMENDATIONS

15. The USG does not support the RMI pre-feasibility study for the establishment of a high-level nuclear waste repository in the Marshall Islands. The USG does not currently have domestic legal authority to participate in the proposal, and the significant environmental and safety risks, and technical, economic, and political concerns associated with the proposal are of such a magnitude that the Administration does not plan to seek such authority. Additionally, on 29 April 1994 the USG rejected a request from RMI Ambassador Kendall in Washington to provide technical assistance funding from the Department of Interior for two persons from USGS to travel to the RMI to conduct soil stability surveys as part of the pre-feasibility study.

It is against this background of mounting concern over government mismanagement of nuclear power that all proposals, no matter how practical, to arrange for long-term storage and permanent disposal at any location in the United States have been met--and will continue to be met--by a firestorm of protest from state officials, public interest groups, and by those communities which would be affected. This strong resistance threatens to turn what is now intended to be interim storage into de facto long-term storage that will not assure protection of the environment and human health and safety nor properly guard against the threat of nuclear weapons proliferation.

A Possible Solution

The Republic of the Marshall Islands, located in the central Pacific Ocean, may present an opportunity to establish facilities for the long-term storage and permanent disposal of nuclear materials. The nation is comprised of two parallel chains of coral atolls, with a total land area of less than 80 square miles, spread out over an ocean area of some 750,000 square miles. These island formations, which descend 18,000 feet into the abyssal depths of the ocean, are considered geologically stable. Many of the islands are both uninhabitable and distant from any human population.

The history of the relationship between the Marshalls and the United States is a long one. After World War II, the Marshall Islands were placed under U.S. administration, as part of the United Nations Trust Territory of the Pacific Islands. Although the country gained independence as a sovereign and democratic nation in 1986, a Compact of Free Association with the United States ensured a continued, close political, economic, and security relationship. With the support of the United States, the Marshalls gained membership in the United Nations, the World Bank, the International Monetary Fund, and the International Atomic Energy Agency, among other important international organizations.

governments officially decided to establish a BRP. The panel met twice this year and plans to submit an official report in July. At this board meeting, Dr. Clarke will present a summary of its interim report. After Dr. Shigematsu explained the above progress and sought comments on any addition and revision, the minutes were approved.

II. Items for information

1. Status report of RERF

(1) US-Japan meetings (presented by Dr. Shigematsu)

Dr. Shigematsu gave the following explanation about the meetings that had been held between MHW and DOE, asking for statements from the representatives of the two governments later:

A total of seven US-Japan meetings were held from the first meeting in February 1994. Dr. Pettengill and Dr. Galson visited Hiroshima to attend these meetings, and earnest discussions were made until March 1995. The entrustment contract between DOE and NAS was extended for two years until 1997. Main progress after the previous board meeting includes the official agreement reached at a meeting in San Francisco in September 1995 on the establishment of the BRP, which began its activities thereafter.

Dr. Shigematsu mentioned that the nature of the meetings of the Panel and the details of the discussion would be explained by Dr. Clarke in the presentation of the interim report on its recommendations.

(2) Present personnel status (presented by Mr. Hirano)

Because of the budgetary constraints at RERF due to the budgetary situation in the US government and the fluctuation of the exchange rate since FY95, significant personnel reduction has been progressing since two years ago, and the policy of personnel reduction will be continued in the future. The personnel strength as of 1 April 1996 comprised 3 directors, 1 chief of secretariat, 44 research scientists, and 283 general employees, totaling 331, which represents a drastic decrease by 42 from 373 last year. Taking into account 72 mandatory retirements in the next five years and assuming 10 voluntary retirements per year, the total number will be 231 in the year 2000.

Continued personnel reduction may hinder the progress of research. Although the number of research scientists will not change greatly with only two of them due for retirement in the next five years, reduction of general staff may impede the activities of the research departments. The foundation is coping with the situation by reorganization and personnel transfer. During the past two years, the number of directors was reduced by two and the positions of the administrators in the secretariat were abolished. Further, the secretariat was reorganized, and the number of sections in Hiroshima was reduced from 6 to 4. Also, by combining the Department of Epidemiology and Department of Epidemiologic Pathology, a total of two departments were abolished in Hiroshima and Nagasaki. Such reorganization will be continued in view of personnel changes.

of an array of critical issues. This is an important point, as it may be desirable or necessary to c locate processing, analysis, and fabrication operations with storage facilities, for certain nucle components and materials.

In sum, the RMI might be in a position to make a major contribution to the U.S. and other nuclea waste-producing countries, as well as to the international community at large, by providing long-term storage facility and a permanent repository for nuclear substances, with stringen safeguards to protect the environment, human health and safety, and to promote the goal o nuclear non-proliferation. In so doing, the RMI would gain revenues that would help its peopl achieve economic self-sufficiency. These are revenues that the Government of the Marshall Islands might possibly share with neighboring Pacific Island states.

The proposal to establish facilities for the storage and disposal of nuclear substances in the Marshall Islands could well lend itself initially to a joint United States-Marshall Islands initiative. Clearly, an expansion of the project to include other nations, Russia in particular, would be of major importance.

In examining this possible solution to the nuclear waste challenge, an essential first step would be the undertaking of a preliminary feasibility study to address the broad outlines of economic, engineering, environmental, health, safety, and security considerations. This analysis would provide the basis for a definitive decision to go ahead with a detailed feasibility study of a single atoll identified as the optimal prospective site for storage and disposal of nuclear materials.

As a rough estimate, construction of a subsurface facility, set into basaltic rock, for the disposal of a volume of plutonium reasonably estimated to become surplus, would cost about $1.5 billion. This estimate takes into consideration the monitoring and materials-handling equipment required for state-of-the-art disposal. A much larger facility would be required to dispose of the vastly

greater quantities of nuclear waste from civilian nuclear reactors. Of course, economies of sca would be important to any calculation of the cost of the construction of the larger facility.

A long-term storage facility of modest capacity would require perhaps an additional seve hundred million dollars. As one would expect, the scope of the mission of that facility would b major factor in its eventual construction cost.

It would seem that the overall project could be economically competitive with facilities currer used to hold nuclear materials, and thus, could be financed by the private sector on the basis expected revenues from users. Both technology and engineering expertise could be rea secured for such a project. The availability of private financing and technology and engineer expertise should not be blurred by present preoccupation with existing, costly and faulty stor facilities, nor by doubtfully credible proposals for their improvement and replacement in United States and other nuclear nations.

It is reasonable to expect that a decision to proceed with a feasibility study would involv degree of controversy. It should be recognized, nevertheless, that there is a compell countervailing interest in exploring this plausible possibility of establishing facilities in Marshall Islands that would greatly reduce the risks of nuclear proliferation, environme contamination, and radiation-induced illnesses.

Selected References:

"Management and Disposition of Excess Weapons Plutonium", Committee on Internati Security and Arms Control, National Academy of Sciences, National Academy P Washington, D.C., 1994

styles on health. Also, the information is important in elucidating the interaction between the effects of radiation and life styles.

Recommendation (1) Collection of data on mortality and cancer incidence should be continued and the activities of the Department of Epidemiology should be strengthened.

Recommendation (2) Researchers at RERF should promote joint studies with epidemiologists in the world, so that valuable information already collected can be analyzed.

[Statistics]

The Department of Statistics is closely interlinked with the Departments of Epidemiology and they jointly form the central core of RERF. Through its extensive body of work, the Statistics Department has become a source of great strength for the entire organization and has had great influence on other radiation studies worldwide.

Recommendation (1) The Department of Statistics should continue to produce analyses of the risks of radiation exposure in collaboration with the Epidemiology Departments and the high quality of the research in the Statistics Department should be maintained.

Recommendation (2) Apart from research studies, the Department of Statistics should develop software in order to make available basic data sets on mortality and cancer incidence for analysis by other groups.

[Information Technology] The move from mainframe computing to a distributed network has led to significant economies and has improved the method for data management and processing. Efficient data management and computing by the Department of Information Technology are the backbones to the success of research at RERF.

Recommendation Strong support should continue to be given to the Department of Information Technology because it is essential that the large body of data collected over many decades is properly stored, documented and accessible to researchers at RERF.

[Clinical Studies]

An important function of the Clinical Studies Program is to bind the exposed populations in Hiroshima and Nagasaki to the scientific program of RERF. The AHS provides them with a visible service, one which they obviously value, as indicated by the high level of voluntary participation. The AHS should be considered as one of the important measures directly beneficial to the health of the survivors.

The importance of the AHS is of a wide range since it augments or supplements the findings of the Life Span Study by supplying additional clinical and laboratory data and provides biological materials essential to other investigations at RERF.

The contributions of the studies at the Department of Clinical Studies may be described in the following categories:

1) Provision of enormous data on the role of radiation exposure in the development of fatal and non-fatal carcinomas and non-malignant diseases;

2) In-depth investigations of associations with various radiation-related diseases to be

Question 1: Please identify the roles the Clinton Administration and the U.S. Congress have in establishing such a facility in the Marshall Islands. What approvals are required by law?

While the Nuclear Waste Policy Act of 1982, as amended (NWPA) limited site characterization activities to Yucca Mountain, Nevada, it did allow the Marshall Islands, among others, to be considered as a site for a potential repository or monitored retrievable storage facility under a negotiated volunteer siting process. However, the Energy Policy Act of 1992 removed the Republic of the Marshall Islands from this negotiated siting process. Under the Compact of Free Association, any storage or disposal of radioactive materials by the United States in the Marshall Islands must be in accordance with the laws of the United States and implementing regulations, as well as international guidelines accepted by the United States. Further, the United States must apply the National Environmental Policy Act of 1969 (NEPA) to its activities under the Compact and related agreements as if the Marshall Islands were the United States. The United States must also comply in the conduct of any activity requiring preparation of an environmental impact statement under NEPA with standards substantively similar to those required by various United States environmental laws. Finally, there is no specific authority for the United States to participate in the proposal. Legislative action would thus be required before the United States could participate.

The attached State Department memorandum of July 21, 1994, has identified treaties such as the Basel Convention which prohibits the export of hazardous wastes from OECD to non-OECD countries, and the "Matsunaga" Amendment which bans the disposal of United States nuclear wastes in the Pacific Basin without prior Congressional approval.

A more detailed discussion of the applicable regulations is included in the response to Question 5 in this report.

Question 2: With respect to nuclear waste from the United States, please describe the geographic source of the material, the nature of the waste itself, and the systems required for its safe transportation.

The geographic sources and the physical characteristics of nuclear waste in the United States are derived from the EIA Service Report, Spent Nuclear Fuel Discharges from U.S. Reactors 1992 (May 1994).

Geographic source of the nuclear waste and spent fuel for storage and disposal:

Commercial Spent Fuel	107 Reactor Sites in 34 States
DOE Reactor Irradiated Nuclear Material	8 Sites in 6 States
Commercial High-Level Waste	1 Site in 1 State
DOE Defense High-Level Waste	3 Sites in 3 States

the council should take a more active role.

Also, appointment to the council should be for 5 year terms, with no more than a single reappointment.

(6) National and international collaborations

While RERF is internationally known as a center for radiation research, its research results need to be more widely disseminated in the global scientific community.

Recommendation (1) Formal links should be strengthened to universities or other research institutions in Japan and especially to the local universities, with RERF department chiefs having visiting or part-time professorships and PhD students being involved in projects at RERF.

Recommendation (2) In view of the accumulated knowledge at RERF, it should be developed as an information center to promote informed public understanding.

That ended Dr. Clarke's report on the preliminary results of the BRP.

Discussion was made concerning Dr. Clarke's report in the afternoon.

[Discussion]

Dr. Abrahamson raised a question dealing with financial issues, which were not touched in the report, seeking Dr. Clarke's agreement on the need that RERF should be protected from financial instability caused by outside sources including fluctuation of the exchange rate. Dr. Clarke commented that, although the financial issues were beyond the charge of the BRP, research should be conducted under stable financial conditions.

Dr. Clarke made a specific recommendation that the Adult Health Study, which has been continued for 38 years, especially the health surveillance program which provides the bases for some of the current studies, should be continued.

Mr. Jablon raised a question on the role of the Scientific Council and the nature of the proposed peer review. Although it is recommended that the councilors should be reappointed no more than once, the term may be too short for them to be actively involved in the research activities and to take the leadership in the review groups, since the research projects at RERF are highly sophisticated.

Dr. Clarke said that the councilors could serve up to two terms, i.e., 10 years, which should be long enough. What the panel was recommending was strengthening of the roles of the councilors.

Dr. Matsunaga asked about the nature of the proposed F_1 screening. Dr. Clarke said that the clinical study contemplated was a follow-up of health with focus on multifactorial diseases considered to occur mainly in adulthood. Dr. Schull stated that, in view of the costly F_1 studies in the past and the limited budget, studies based on the recommendations should be conducted efficiently by considering the possibility of using the samples collected already. Dr. Kumatori mentioned that in the past some US councilors had proposed discontinuing the AHS because they felt the study was not fruitful. He was glad that the AHS had been continued and

that the BRP recognized its value. However, he added that bias against A-bomb survivors still existed.

With regard to the expert review of each department once in five years, Dr. Schull expressed his concern about the increase of the burden of researchers and other staff considering the preparation required for meetings of the board and the Scientific Council and workload due to involvement of multiple departments in one research project. In response, Dr. Clarke mentioned that the departments had agreed to this new system, under which they could proceed at their discretion toward the target set for the five years.

Directors and department chiefs raised other detailed questions on research. Finally, Dr. Clarke said that he would give due consideration to the discussion at this meeting in the preparation of the final report to be submitted in July.

3. **Reassessment of DS86** (presented by Drs. Sinclair and Fujita)

At the beginning, Dr. Shigematsu said that Dr. Sinclair, chairman of the US Dosimetry Committee and Dr. Shoichiro Fujita, assistant chief of the Department of Statistics, on behalf of Dr. Tajima, chairman of the Japanese Dosimetry Committee, will report on the joint meeting of the US and Japan Dosimetry Committees.

Dr. Sinclair reported on the US Dosimetry Committee meeting held in September last year. At the said meeting, neutron transport calculation was discussed and the following two recommendations were made: 1) Measurements of the neutron cross section of iron, which are in progress at the Los Alamos Laboratory, should be continued and 2) ^{63}Cu ^{63}Ni reaction should be assessed to allow direct measurement of neutrons.

Subsequently, Dr. Sinclair reported on the joint meeting of the US and Japan RERF Dosimetry Committees held on 22 and 23 May this year. He said that six presentations were made by the Japanese delegation led by Dr. Fujita. Dr. Fujita's explanation of the exposed materials which are stored at RERF was of great interest to the US Dosimetry Committee. Dr. Shizuma reported on europium and cobalt activation in Hiroshima and Nagasaki. His understanding that the disagreement between calculation and measurement in Hiroshima also existed in Nagasaki led to lively discussions. After Dr. Preston read a paper entitled, "Dosimetry Issues from the Response Perspective," Dr. Straume gave a presentation under the title, "The Cu (n,p) Ni Reaction as a Dosimeter for Fast Neutron Exposure at Hiroshima," which is a report of his preliminary study. This study showed that examination of the copper reaction is useful for short distance studies. Lastly, cross-section measurements in iron, which have been done at the Los Alamos Laboratory as a modeling study for RERF dosimetry, were reported. The measurements have been completed, and the data obtained will be analyzed.

Each of the US and Japan RERF Dosimetry Committees discussed the reports presented and made the following recommendations:

(1) That investigators pursue experiments that will lead to improved confidence in a revised DS86.

(2) That investigations to resolve the neutron uncertainty be pursued, including

1) Evaluation and intercomparison of measurements of thermal neutrons in the U.S. and in Japan to assess background problems (including the use of samples from long distances) and to assess total uncertainty in each measurement. Since europium, chlorine, and cobalt are being measured by various researchers at present, background and uncertainty of measurements vary. A small team consisting of experienced researchers, one American and one Japanese, should be established to evaluate discrepancies between the values measured under different backgrounds.

2) Application of the Cu-Ni reaction for fast-neutron measurements by both the US and Japan. While Dr. Straume uses mass spectrometry, Dr. Shibata uses a scintillation counter. The results of these two studies will be combined to obtain better results. To this effect, it is necessary to collect copper samples. It is important to collect copper samples up to 500 m to get more accurate measurements. Collection of samples is expected to be difficult since 50 years have already passed. Samples at defined positions will be collected in Hiroshima and Nagasaki.

3) Calculations of weapon leakage and cross-section experiments. This is to complete the work which is in progress at the Los Alamos Laboratory. However, even if this work is completed, it is not certain whether the problem in Hiroshima will be solved or not.

(3) If DS86 is to be revised, the revision should include a reevaluation of gamma rays at Hiroshima, of which measurements are larger than calculations by 10 - 15%, yield, height of burst, the US Army map (survivor locations), and shielding.

(4) That a strong effort be initiated to quantify uncertainties in all phases of DS86 and any later revision with a view to upgrading all estimates of uncertainty that are an integral part of the dosimetry system. When DS86 was employed, a team to evaluate uncertainties was established. However, since the members of the team were not radiation experts, the work was not accomplished. A working group of DS86 evaluated uncertainties and the details were reviewed by Dr. Kaul of SAIC and others, which were followed by the neutron problems. In 1990, uncertainties were evaluated and the further study should be continued based on this evaluation.

Subsequently, Dr. Fujita reported the Japanese committee's activities.

Exposed materials have been collected and the residual radioactivity has been measured in Hiroshima and Nagasaki. Efforts to develop a database for exposed materials, measurements, and literature have been initiated. Recent major activities were reported at the joint meeting of the US and Japan RERF Dosimetry Committees reported by Dr. Sinclair. The Japanese Dosimetry Committee will continue with its activities including actions on the issues agreed upon at the said meeting. It was reported that RERF was actively involved in the collection of

exposed materials in Hiroshima and Nagasaki. A list of the materials collected by RERF for gamma and neutron measurements was presented. It was reported that the samples have been sent to the research institutes both in Japan and the US so that residual radioactivity can be measured using the same samples.

Subsequently, efforts to collect copper samples which had also been discussed at the joint meeting were introduced. It was reported that the lightning rods of the Hiroshima Rest House located at 130 m from the hypocenter and the Hiroshima branch of the Bank of Japan located at 400 m from the hypocenter examined were found to be unsuitable for measurements. Although 50 years have passed since the A-bombings, efforts to collect exposed materials will be continued. It was mentioned that RERF would like to take part in the dosimetry reassessment activities, such as reevaluation of survivor locations and shielding histories and solution of the uncertainties of DS86.

Dr. Shigematsu, in response to the presentation, commented that RERF's active involvement in the dosimetry issue was included in the recommendations of the BRP which were presented by Dr. Clarke on the same day. He concluded the session by expressing hope that further efforts will be made to solve the uncertainties of DS86 as much as possible.

4. **FY95 salary revision** (presented by Mr. Hirano)

The pay scales were revised by using as a guide the revision of the pay scales applicable to national government employees. The base pay for professional employees and that for general employees were increased by 0.68% (¥4,263) and 0.85% (¥3,082) on average, respectively, whereas the increase for national government employees was 0.9% (¥3,097). Dependents' allowance and housing allowance were revised.

Revision of the pay scale applicable to the directors, which is decided by using the pay scale applicable to national government employees in designated positions, due in FY95 was suspended. It is expected to be effected as of 1 April 1996.

5. **Labor union's FY96 demands for improvement of working conditions, etc.** (presented by Mr. Hirano)

The RERF Labor Union is affiliated with the All Japan Prefectural and Municipal Workers' Union consisting of 1.1 million members. The RERF Labor Union is 202 members strong, representing an enrollment rate of 93%. This accounts for 61% of all the directors and staff combined (331).

FY96 demands focus on improvement of the US-Japan equal-sharing system and contained the following specific points: 1) establishment of a council for monitoring actions of the RERF board of directors, allowing participation of representatives of A-bomb survivors' organizations, labor unions, and RERF employees; 2) establishment of a new system under which the Japanese government assumes the principal role in providing funds; 3) participation of representatives of A-bomb survivors' organizations in the board of directors; and 4) promotion of RERF relocation and reopening of the department that provides treatment.

In addition, improvement of working conditions such as salary increases, filling of vacancies, and an equitable personnel system are demanded.

6. Others

(1) International Collaboration (presented by Dr. Shigematsu)

International collaboration has increased since the Chernobyl accident. It was reported that RERF participates in international collaborative activities to the extent that this does not disrupt regular research activities. Explanation was given using the material that listed visitors related to Chernobyl, Chelyabinsk, and other places. It was reported that RERF received 288 official visitors from abroad in FY95. Also, last year a WHO Meeting on Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) was held at RERF.

(2) Development of an A-bomb Related Materials Database System (presented by Dr. Hasegawa)

RERF, entrusted by MHW, has worked on developing an A-bomb related materials database system since FY91. The actual work is done by the Committee on A-bomb Materials and Information Network. The database system will be situated in the "A-bomb Dead Memorial and Peace Praying Hall" to be built in Hiroshima in FY98 and in Nagasaki in FY99. In relation to the development of the database system, the committee has prepared a draft home page to introduce and publicize the activities of the halls through the Internet. It was reported that the home page was planned to be connected to the reference database of A-bomb related materials.

(3) Recent Advances in Research Projects (presented by Dr. Abrahamson)

The following four researchers made presentations on recent advances in their respective research projects.

Researcher	Project
Dr. Tokuoka, consultant, Dept. of Epidemiology	Site-specific cancer incidence — Salivary gland tumor
Dr. Delongchamp, research scientist, Dept. of Statistics	Mortality among in-utero survivors
Dr. Nakamura, Asst. Chief, Dept. of Genetics	ESR in tooth enamel and chromosome aberration
Dr. Asakawa, senior research scientist, Dept. of Genetics	F1 DNA study

At board meetings, unlike Scientific Council meetings, detailed reports are not made on research activities. Thus, the participants raised various questions and comments after each presentation, showing their strong interest in specific research projects.

Level Radioactive Waste);

- Title 49 (Transportation) Parts 171 (Hazardous Materials Regulations, General Information, Regulations, and Definitions); 172 (Hazardous Materials Table, Special Provisions, Hazardous Materials Communications, Emergency Response Information , and Training Requirements); 173 (Shippers - General Requirements for Shipments and Packagings); 174 (Carriage By Rail); and 177 (Carriage By Public Highway).

- Title 40 (Protection of Environment) Part 191 (Environmental Radiation Protection Standards for Management and Disposal of Spent Nuclear Fuel, High-Level and Transuranic Radioactive Wastes);

Question 6: Has the Marshall Islands government presented this proposal to the Administration, and if so, what is the Administration's position with respect to this proposal?

- The current proposal was presented to Dr. Tara O'Toole, the Department's Assistant Secretary for Environment, Safety and Health, by representatives of the Republic of the Marshall Islands on February 23, 1994.

- Following an interagency review involving the Departments of State, Defense, Interior and Energy, the Clinton Administration does not support the proposal for an international high-level radioactive waste repository in the Republic of the Marshall Islands. The United States has no specific legal authority to participate in the proposal, and the potentially significant environmental and safety risks, liability issues, and technical, economic and political concerns associated with the proposal are of such a magnitude that the Administration does not plan to seek such legislation.

Question 7: Has the Department evaluated previous nuclear waste repository proposals from the Marshall Islands? If so, please provide a copy of the Department's evaluation of such proposals.

- In December 1987, President Kabua of the Republic of the Marshall Islands offered to enter into consultation with the United States to evaluate the utility of conducting a feasibility study on the storage and disposal of high-level nuclear wastes on uninhabitable islands in the Marshalls. At the time, the 1987 amendments to the NWPA had just been passed in which Yucca Mountain was named as the sole site for characterization by the Department for suitability as a repository. However, the Act also allowed for independent siting attempts through the Office of the Nuclear Waste Negotiator. The Republic of the Marshall Islands was included in the definition of States eligible to participate in the volunteer siting process. The Marshall Islands proposal was supported by, among others, Rep. Barbara Vucanovich of Nevada. (See Attachment 1).

- The Republic of the Marshall Islands entered into free association with the United States on October 21, 1986. The status of free association recognizes that the Republic of the Marshall Islands is now a sovereign, self-governing state. Thus the Energy Policy Act of 1992 deleted mention of the Marshall Islands in the list of States and Indian Tribes which may participate in federal negotiated siting in accordance with the Nuclear Waste Policy Act.

Question 8: In general, what concerns will the United States need to consider during a review of this proposal?

- The Republic of the Marshall Islands, formerly part of the Trust Territory of the Pacific Islands, entered into free association with the United States on October 21, 1986. The status of free association recognizes that the Republic of the Marshall Islands is now a sovereign, self-governing state; by the terms of the compact of free association, the United States is responsible for defense, and for extending agreed-upon amounts of economic and service assistance. The United States has an agreement with the Republic of the Marshall Islands for use of a missile range at Kwajalein Atoll for 30 years. Another subsidiary agreement provides for the settlement of all claims arising out of the nuclear testing programs conducted by the United States at Bikini and Enewetak Atolls from 1946 to 1958. These historical agreements notwithstanding, given the fact that the Marshall Islands constitute a fully independent Republic, and given the framework of laws and regulations governing the United States radioactive waste management program, any repository in the Marshall Islands could not be considered part of the NWPA program, but instead must be considered to be an "international repository." International regulations governing such an enterprise are almost nonexistent (there are IAEA guidelines for the international transport of nuclear materials); however, unilateral or even bilateral attempts at siting a repository for U.S. nuclear wastes outside United States borders would very likely attract controversy.

- The nuclear testing policies of previous Administrations (predecessors of the Department of Defense and the Department of Energy) have, from both environmental and social perspectives, impacted the Republic of the Marshall Islands. Further, since production of spent nuclear fuel and defense high-level radioactive wastes occurs in the coterminous United States, any proposal for a repository in the Republic of the Marshall Islands would be scrutinized for the equity of such an action. Executive Order 12898 on Environmental Justice (signed February 11, 1994) calls for the identification of adverse impacts of Federal actions on minority or low-income populations before decisions implementing these actions are made.

- Disposal of waste in an island repository is one of a number of methods for managing high-level radioactive waste studied by the Federal Government. Disadvantages associated with island disposal concept include the risks associated with ocean transport under adverse weather conditions and the fact that geologic foundations of many islands are composed of permeable rock types of volcanic origin. The intrusion of sea water into an island repository through these permeable geologic structures could increase the chances that high-level radioactive waste would come into contact with the biosphere.

- Many islands experience frequent and intense seismic and volcanic activities. Such activities could discharge waste into either lava flows or into the atmosphere.

- The humid Marshall Islands climate has a pronounced monsoonal season, with correspondingly high precipitation values. The highly fractured (and transmissive) volcanic rocks typical of the Republic of the Marshall Islands would provide fast-pathways for infiltrating waters, potentially inundating any subsurface repository.

- The proposal suggests study of the feasibility of using the Marshall Islands as a site for either temporary storage or long-term disposal of high-level radioactive waste and other nuclear materials. The considerations outlined above relate principally to the option of a repository site in the Republic of the Marshall Islands. As to the possibility of using an island site for only a temporary storage site, with a repository in the United States, logistics involved in such a scenario would render the proposition prohibitively expensive.

Question 9: Who are the principals involved in this proposal?

- Since 1987, President Amata Kabua of the Marshall Islands has proposed storing United States nuclear wastes in either the Bikini or Enewetak lagoons. Both of these were taken over by the United States for early nuclear weapons tests after the residents were removed. Representative Barbara Vucanovich has also urged the Administration to open negotiations with the Marshall Islanders. Jonathan Weisgall is an attorney who has represented the Bikinians since 1975 and has been quoted in the press as a proponent of these proposals. Ambassador Wilfred Kendall of the Republic of the Marshall Islands has been named by President Kabua to head a Commission charged with studying the proposal.

Question 10: Finally, please describe all risks associated with the transportation and storage of nuclear wastes in the Marshall Islands.

The risks generally associated with the transport and storage of high-level radioactive waste and spent fuel in the U.S. also apply to the specific case of the Marshall Islands. These general risks are described below:

- Transportation of SNF or other radioactive material has an excellent safety record for shipments within the U.S. and for those limited shipments that have occurred over the seas by or for foreign countries. However, for a country, such as the Republic of the Marshall Islands, embarking for the first time on such an endeavor, the question of safe shipments would require careful scrutiny.

  Generally, there are two categories of risks associated with transportation. First, the routine exposure of radiation from normal operations to both workers and the general public. The NRC regulations limit exposure to 10 millirem per hour at any point 2 meters from the cask. Second, there are risks to the workers, the general public, and the environment in the rare event of an accident. Spent nuclear fuel casks are

designed to provide radiological safety under specific hypothetical accident conditions which include impact, fire, puncture, and deep immersion. Radiological safety criteria address containment, shielding, and subcriticality. It should be noted that for sea transport of spent nuclear fuel, risks to the general public are insignificant due to the lack of population receptors over the ocean. Risks to the public, workers, and the environment are controlled by international treaties in international waters, and are strictly controlled by numerous Federal, state, and local regulations within the United States.

- There are site-specific risks associated with the shipment of large quantities of SNF to the RMI, whether for storage or for permanent disposal. These include the logistics of making ocean-going barge shipments over a period of 40 years or more. The large numbers of voyages would increase the risks of loss at sea due to collision, weather-related incidents, or the deliberate diversion of SNF.

F 1325.12
93)

U.S. DEPARTMENT OF ENERGY
CORRESPONDENCE CONTROL FORM
OFFICE OF THE EXECUTIVE SECRETARIAT

CI

ACTIVITY CHANGE DO NOT DETACH FROM ORIGINAL CORRESPONDENCE 08/01/94 OE
SOURCE CODE CC CONGRESSIONAL
SPEC INT: CONTROL NO: ES94-009775
DATE CORR: 03/28/94 DATE RECD: 03/29/94 DATE CNTRL: 03/29/94 DATE DUE: 05/
LETTER: X MEMO: _ TWX: _ OTHER: _ TO: SECY: X DEP SEC: _ UN SEC: _ OTHER: _

FROM: MILLER, GEORGE CA O
CHAIRMAN
COMMITTEE ON NATURAL RESOURCES

SUBJ: APPOINTMENT SCHEDULING
QUESTIONS & ANSWERS
SUBMITS PROPOSAL FOR LONG-TERM
STORAGE AND PERMANENT DISPOSAL
OF NUCLEAR MATERIALS

REMARKS:

FOR USE BY ACTION OFFICE ONLY

	ACTION REFERRED TO	DATE	RETURN TO
1			
2			
3			

ACTION TO: PO TYPE ACTION: Prepare final reply SIG OF: S
CONCURRENCE:
INFORMATION:
FILE CODE: CCMILLER-ES94009775 CONTROL ANALYST: B Atcherson

ALL DOCUMENTS FOR THE OFFICE OF THE SECRETARY
MUST BE FORWARDED TO THE OFFICE OF THE EXECUTIVE SECRETARIAT FOR FINAL PROCESSING

Printed with soy ink on recycled paper

U.S. GOVERNMENT PRINTING OFFICE: 1993-357-188 56783

be made for securing the services of research scientists required for the desired level of research and for increasing the budget.

5. **Revision of rules and regulations** (presented by Mr. Hirano)

Revision of rules and regulations was proposed as follows, and each of the proposed revisions was approved.

(1) Regulations Concerning Organization of the Laboratory (Research Departments)

The library not only handles publications but also collects, accumulates, and provides information. With completion of the construction of a computer network within RERF and greater use of computers, the library & archives will be transferred to the Research Information Center to enable speedy contact with outside research organizations and transmission of information. Also, the names of the center and its sections and units will be changed to reflect the work done more accurately.

[Hiroshima]

1) The name of the Research Information Center will be changed to Information Technology Department, and the Library & Archives under the Publication & Documentation Center will be transferred to the department.

2) Information System Laboratory and Computer Section will be combined, and the name of the new section will be Systems Integration Section.

3) Names of Management Unit, First Operations Unit and Second Operations Unit under the Systems Integration Section will be changed to Systems Administration Unit, Application Development Unit and Data Administration Unit, respectively.

4) Printing & Photography Unit under the Editorial & Publications Section, Publication & Documentation Center, will be abolished. (Effective date: 1 October 1995)

[Nagasaki]

For more efficient research activities, the Nagasaki Department of Radiobiology will be abolished and its activities will be transferred to Hiroshima. (Effective date: 1 April 1996)

(2) Regulations Governing Salaries of Directors and Chief of Secretariat

The base pay of the directors and the chief of the Secretariat will be increased by 0.86% on average, based on the revision of the National Government Pay Scale for Designated Positions. (Effective date: 1 April 1996)

(3) Employee Wage Regulations

1) Base pay of employees will be increased using as a guide the revisions effected for national government employees (0.85% for general employees and 0.68% for research scientists).

2) Dependents allowance: When, among the children who are employee's dependents, there are children who have attained 15 years of age and the first 1st April after their date of birth has passed, a sum of ¥2,500 (currently ¥2,000) will be added for each of those children to the monthly amount of the dependents allowance.

3) Housing allowance: The rented housing allowance for family members will be one half of the amount allocated prior to relocation of the employee, who is receiving family-separation allowance. (Effective date: 1 April 1995 for the base pay increase and the revision of dependents allowance and 1 January 1996 for the revision of housing allowance.)

6. **Election/appointment of directors and others** (presented by Dr. Shigematsu)

Before deliberation, it was announced that the appointment of Dr. William J. Schull as permanent director effective 7 May and as successor to Dr. Donald R. Harkness, the Chief of Research who resigned as of 31 August last year, had been unanimously approved by mail ballot.

Deliberation was made after Dr. Shigematsu explained mid-term resignations of a director, a Scientific Councilor, and a supervisor and appointment of operating committee members.

(1) Election of a director

Election of Dr. Jonathan M. Samet, professor at the Department of Epidemiology, School of Hygiene and Public Health, Johns Hopkins University, as of 1 July as successor to Director Jablon, who was due for resignation as of 30 June, was recommended and approved. The election has been recommended by NAS and DOE and agreed by MHW. Also, with the resignation of Dr. Seymour Abrahamson as Vice-Chairman and chief of research as of 27 June, it was proposed that Dr. Schull assume these two roles as of the same day. The proposal was approved without any objection.

(2) Election of a supervisor

It was reported that Supervisor Shishido was due to resign as of 30 June. Dr. Shudo Yamazaki, director, National Institute of Health, was recommended as his successor, and his appointment as of 1 July was approved.

(3) Election of a scientific councilor

Dr. Susan Preston-Martin, Professor at the Department of Preventive Medicine, University of Southern California School of Medicine, was recommended as successor to Scientific Councilor Herzenberg, who was due to resign on 30 June. Her appointment as of 1 July was approved.

(4) Appointment of operating committee members

It has been agreed that the numbers of US and Japanese members of the Operating Committee be the same, and the committee presently consists of four members each. It was approved that the numbers of the US and Japanese members will be three each after the resignation of Dr. Abrahamson as of 27 June and the mandatory retirement of Mr. Tadashi Nakaoka, Nagasaki Chief of Administration, on 30 June.

As in the above, the proposed actions concerning election/appointment of officers and others were approved.

7. Schedule of the next board meeting

It was agreed to schedule the next meeting for 3 days from the 25th until the 27th June 1997 at the Hiroshima Laboratory.

Upon completion of discussion of all items on the agenda, Dr. Shigematsu declared the meeting closed.

Date: 28 Oct. 1996

Radiation Effects Research Foundation

Chairman: _____
Itsuzo Shigematsu

Signatory of Minutes: _____
Yutaka Hasegawa

Signatory of Minutes: _____
William J. Schull

Items for Information

Status Report of RERF

STATUS REPORT OF RERF

(1) Prioritization of RERF Research Programs

RERF has been in a difficult situation for the past few years for financial reasons owing to the stringent budget of the United States and the strong yen. However, the report submitted by the Blue Ribbon Panel in July last year (1996) has given us hope. The report highly appraises the research studies that RERF has conducted, and urges that its research programs be further strengthened in the future. Regarding the budget, which would be a bottleneck in implementing the recommendations, the Governments of Japan and the United States have indicated that they would respect to the utmost the recommendations of the panel. However, since the stringent budgetary situation can be expected to continue, measure such as prioritizing the research programs will be necessary.

(2) ABCC/RERF 50th Anniversary Commemorative Symposium to Be Held at NAS

ABCC/RERF 50th anniversary commemorative symposium is scheduled for June 13 and 14 at NAS's auditorium. The efforts made by NAS, which will host the symposium, are very much appreciated. RERF also has provided every possible support in preparing for the event.

(3) Hiroshima Facilities Relocation Issue

In addition to the original plan proposed by Hiroshima City to relocate the Hiroshima facilities to the former site of Hiroshima University Faculty of Engineering, which has been tabled due to lack of funds, there has surfaced a plan to have the Hiroshima Prefectural Government's proposed, "Hiroshima International Peace Praying Cancer Center" (tentative name) cooperate with RERF, and this is being carefully reviewed at present.

REPORT ON PROGRESS MADE AFTER THE BLUE RIBBON PANEL PRESENTED ITS RECOMMENDATIONS

(1) Endorsement by the Scientific Council of RERF's Proposed Responses to the Recommendations

RERF drafted responses to the 21 recommendations of the Blue Ribbon Panel and a Five-year Strategic Plan, and submitted them to the 23rd Scientific Council meeting held last November. The council reviewed them and presented comments to the effect that it endorses them, together with its recommendations. The recommendations focus on three issues in particular which are regarded as the most important: 1) F_1 study, 2) the role of the Scientific Council and the process by which it will review and evaluate studies in the future, and 3) adjustment of the organizational structure of RERF to that considered to be best suited for it to pursue its research studies.

(2) Change of Terms of Office of Scientific Councilors

In response to the recommendations of the Blue Ribbon Panel, the Scientific Council discussed the councilors' term of office and agreed that it should be five years, with reappointment to be approved exceptionally once when the Board deems it especially necessary, and that the system of two councilors changing annually should be introduced. If this plan is approved at this Board meeting, all councilors will resign on June 30 with the transition to the new system in July this year, and the terms of office of the new councilors, limited to appointment at the beginning of the new system on July 1, will be one, two, three, four and five years for one Japanese and one American councilor, respectively.

This material will be distributed at the meeting

Report on progress made since the presentation of the Blue Ribbon Panel's recommendations

This material will be distributed at the meeting

Present Personnel status

放射線影響研究所　役職員構成表
COMPOSITION OF RERF PERSONNEL

平成９年４月１日
As of 1 April 1997

常勤役職員　Full-time Officers

区　分 Classification	広　島 Hiroshima	長　崎 Nagasaki	合　計 Total
役　員 Director	3		3
事務局長 Chief of Secretariat	1		1
研 究 員 Research Scientist	35	4	39
一般職員 General Staff	206	68	274
合　計 Total	245	72	317

非常勤役員　Part-time Officers

区　分 Classification	広　島 Hiroshima	長　崎 Nagasaki	合　計 Total
役　員 Directors	8		8

顧問・専門委員・非常勤研究員
Consultans, Expert Advisers, Research Scientists

区　分 Department	顧　問 Consultants	専門委員 Expert Advisers	非常勤研究員 Visiting Research Scientists	合　計 Total
臨床研究部 Clinical Stsudies	28	5	26	59
遺伝学部 Genetics	7	1	2	10
放射線生物学部 Radiobiology	8		1	9
疫 学 部 Epidemiology	14	14	3	31
統 計 部 Statistics	6	3	1	10
情報技術部 Information Technology Dep.	3	1	1	5
事 務 局 Secretariat	4		1	5
合　計 Total	70	24	35	129

人員構成表
PERSONNEL COMPOSITION

1997年 4月1日現在
AS OF 1 APRIL 1997

	部名	DEPARTMENT	役員等 DIRECTORS AND ETC.	研究員 RESEARCH STAFF	A 事務職 STATISTICAL, CLERICAL, ETC.	B 作業・技能職 MANUAL AND GEN. TECH.	C 医療技術職 I LABORATORY TECHNOLOGISTS	D 医療技術職 II NURSES AND OTHERS	合計 TOTAL	来所研究員 VISITING SCIENTISTS	臨時職員（委託経費） TEMPORARY (ENTRUST FUND)
	役員	DIRECTORS	3						3		
	事務局長	CHIEF OF SECRETARIAT	1						1		
広	研究担当理事補	ASSOCIATE CHIEF OF RESEARCH									
	臨床研究部	CLINICAL STUDIES		6	20	1	10	12	49		
	遺伝学部	GENETICS		9	3	2	15		29	1	
	放射線生物学部	RADIOBIOLOGY		10	4	2	13		29	1	
	疫学部	EPIDEMIOLOGY		4	35		2		41	1	1
	統計部	STATISTICS		6	5				11		
	情報技術部	INFORMATION TECHNOLOGY			17				17		
	出版・資料センター	PUB AND DOC CENTER			20				20		
	放射性同位元素使用施設	RADIOISOTOPE FACILITY					1		1		
	放影研顧問等	RERF CONSULTANT									
	事務局	SECRETARIAT			36	8			44		
	広島計	HIROSHIMA TOTAL	4	35	140	13	41	12	245	3	1
	研究担当理事補	ASSOCIATE CHIEF OF RESEARCH									
	臨床研究部	CLINICAL STUDIES		2	15	1	11	7	36		
	疫学部	EPIDEMIOLOGY		2	17		3		22		3
	放射性同位元素使用施設	RADIOISOTOPE FACILITY									
	放影研顧問等	RERF CONSULTANT									
A	事務局	SECRETARIAT			14				14		
	長崎計	NAGASAKI TOTAL		4	46	1	14	7	72		3
	合計	GRAND TOTAL	4	39	186	14	55	19	317	3	4

1. 来所研究員欄（　）数は有給者数を示し、定員に含める。
2. 事務職 186名中、136名は研究支援部門に属し、50名が事務局職員である。
3. 人件費臨時職員（育休代替等）　3名を除く。

1. Figures in ( ) in the column for visiting scientists are the number of those paid by RERF and included in the number of regular staff in the same.
2. Of the 186 statistical, clerical and other, 136 are in the research departments and 50 in the secretariat.
3. 3 temporary employees (relief for child care leave) whose salaries are paid out of regular personnel budget are excluded.

役職員の構成内訳　Personnel Composition

			広島 Hiroshima		長崎 Nagasaki		合計 Total	
1. 役員等 Directors and etc.			4				4	
2. 研究員 Research Staff			35		4		39	
内訳 Items	医師研究員 Medical	博士 D.Msc.	8	11	2	3	10	14
		その他 Other	3		1		4	
	非医師研究員 Non-Medical	博士 Ph.D.	22	24	1	1	23	25
		修士 M.Sc.	1				1	
		その他 Other	1				1	
3. 一般職員 General Staff			206		68		274	
内訳 Items	事務職 Stat., Clerical, etc.		140		46		186	
	作業・技能職 Manual and Gen. Tech.		13		1		14	
	医療技術職（一） Lab. Technologists		41		14		55	
	医療技術職（二） Nurses and other(II)		12		7		19	
合計 Total			245		72		317	
来所研究員 Visiting Scientists			3				3	

1. 来所研究員欄（　）数は有給者数を示し，定員に含める。
   Figure in ( ) in the column for Visiting Scientists are the number of those paid by RERF and included in the number of regular staff in the same.
2. 事務職 186名中 136名は研究支援部門に属し，50名が事務局職員である。
   Of the 186 Statistical, Clerical and other, 136 are in the research departments and 50 in the Secretariat.
3. 人件費臨時職員（育休代替等）3 名を除く。
   3 temporary employees (relief for child care leave) whose salaries are paid out of regular personnel budget are excluded.

予算定員と現員との推移
CHANGES IN BUDGETARY PERSONNEL SLOTS ACTUAL PERSONNEL STRENGTH

As of 1 April 1997

区分 Classification ＼ 年度別 Fiscal year		昭和50年度 1975	51年度 1976	52年度 1977	53年度 1978	54年度 1979	55年度 1980	56年度 1981	57年度 1982		58年度 1983		59年度 1984	60年度 1985	61年度 1986	平成62年度 1987	63年度 1988	元年度 1989	2年度 1990
予算定員 Badgetary Perssonnel Slots		579	△2 577	△5 572	△10 562	△15 547	△13 534	△10 524	前期 1st half △5 519	後期 2nd half △5 514	前期 1st half △5 509	後期 2nd half △3 506	△8 498	△8 490	△9 481	△8 473	△8 465	△8 457	△8 449
現員 Actual Personnel Strength		588	575	567	559	541	523	524	517		503		491	486	474	472	462	435	427
内訳	役員 Directors	4	4	4	4	4	4	3	4		5		5	6	6	6	4	6	6
	研究員 Research Staff	40	40	44	(1) 47	(4) 48	(3) 47	(3) 54	53		50		(1) 52	(2) 58	(3) 62	(2) 63	(2) 66	(2) 63	(1) 57
	一般職員 General Staff	544	531	519	508	489	472	467	460		448		434	422	406	403	392	366	364

注： Note:

1. 休職者及び無給来所研究員は定員外とし除外する。
   Employees on protracted leave and visiting scientists not on RERF payroll are excluded from budgetary personnel slots.
2. 有給来所研究員は研究員欄へ含め（　）書で示す。
   Visiting Scientists who are on RERF payroll are counted in the number of research staff. Their number is shown in the parentheses.
3. ＊ 事務局長を含む。
   Chief of secretariat included.

区分 Classification ＼ 年度別 Fiscal year		平成3年度 1991	4年度 1992	5年度 1993	6年度 1994	7年度 1995	8年度 1996	9年度 1997	昭和50年度との比較 with 1975
予算定員 Badgetary Perssonnel Slots		△7 442	△4 438	△4 434	△4 430	△52 378	△43 335	△23 312	△267
現員 Actual Personnel Strength		433	437	435	412	373	331	317	△271
内訳	役員 Directors	6	5	6	6	5*	4*	4*	0
	研究員 Research Staff	(1) 61	(1) 64	62	57	48	44	39	△1
	一般職員 General Staff	366	368	367	349	320	283	274	△270

定年退職者予定者数
NUMBER OF EXPECTED MANDATORY AGE RETIREMENTS

1997年以降5年間の、規定による定年退職者数は次のとおりである。
The following is the number of mandatory age retirements expected yearly during the 5-year period from FY1997 according

		平成9年度 FY1997	平成10年度 FY1998	平成11年度 FY1999	平成12年度 FY2000	平成13年度 FY2001	合計 Total
広島 Hiroshima	男 Male	7 (6)	7 (4)	4 (3)	3 (1)	3 (1)	24 (15)
	女 Female	10 (3)	3 (2)	2 (1)	7 (1)	4	26 (7)
	計 Total	17 (9)	10 (6)	6 (4)	10 (2)	7 (1)	50 (22)
長崎 Nagasaki	男 Male	4 (3)	3 (2)	2 (2)	0	2 (2)	11 (9)
	女 Female	4 (1)	1 (1)	2	2	1	10 (2)
	計 Total	8 (4)	4 (3)	4 (2)	2	3 (2)	21 (11)
合計 Total	男 Male	11 (9)	10 (6)	6 (5)	3 (1)	5 (3)	35 (24)
	女 Female	14 (4)	4 (3)	4 (1)	9 (1)	5	36 (9)
	計 Total	25 (13)	14 (9)	10 (6)	12 (2)	10 (3)	71 (33)
課長以上 Sec. Chief or above		13	9	6	2	3	33
課長補佐 Asst. Sec. Chief		8	2	0	6	3	19
係　長 Unit Supervisor		4	2	2	3	3	14
その他 Others		0	1	2	1	1	5
合　計 Total		25	14	10	12	10	71

注：　（　　）内の数は課長以上を再掲
退職者 71名中研究員は4名である

Note: The number in the parenthesis includes personnel in the position of Section Chief of above.
Of the 71 retireas in the next 5 years, there are 4 professional staff members.

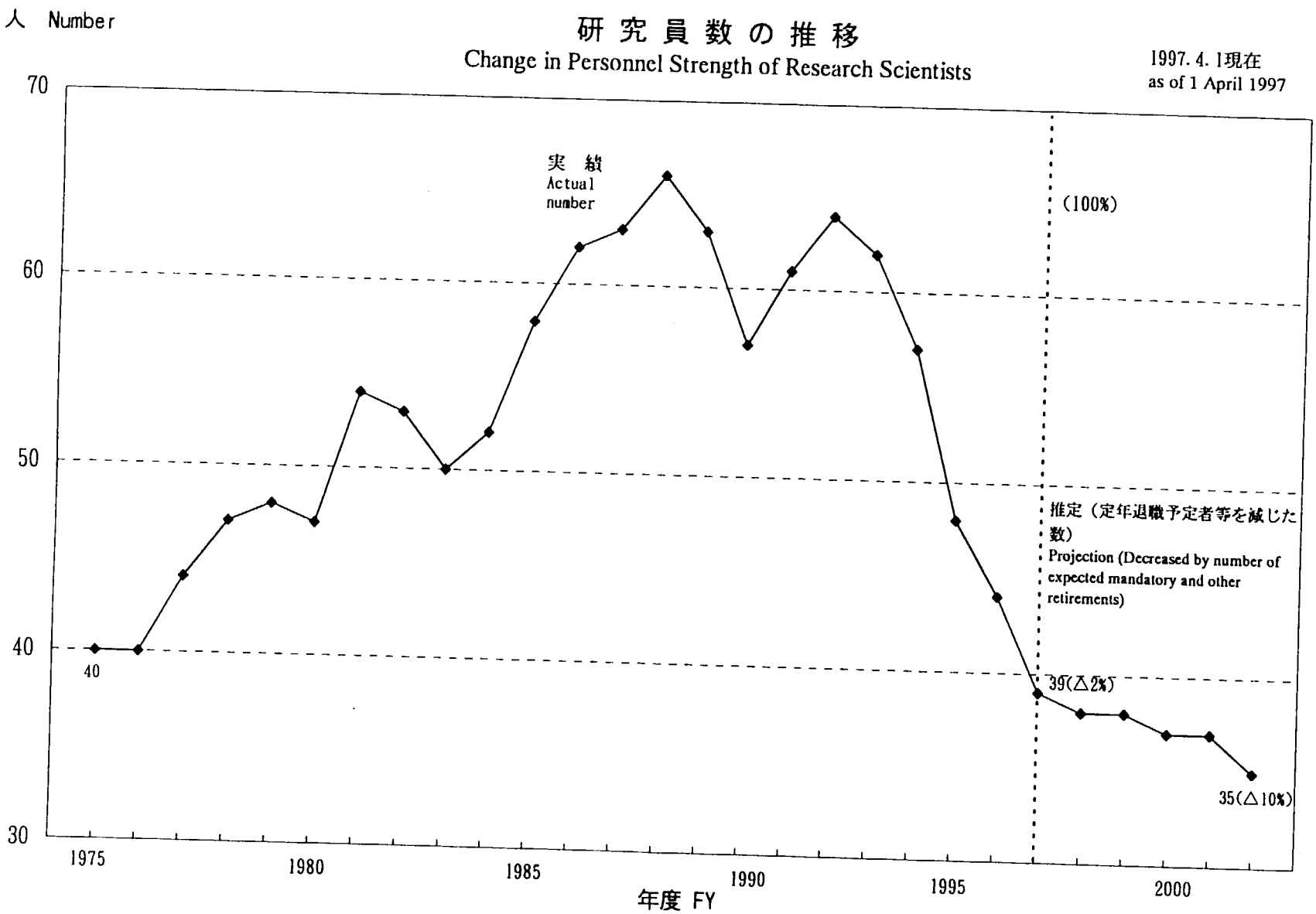
過去5年間の定年・選択定年退職者数

Number of Mandatory Age Retirements / Optional Retirements in The Past Five Years

		平成4年度 FY1992	平成5年度 FY1993	平成6年度 FY1994	平成7年度 FY1995	平成8年度 FY1996	合計 Total
広島 Hiroshima	研究員 Research Scientist			1	2 (1)		3 (1)
	一般職員 General Staff	8 (2)	11 (1)	13 (2)	15 (2)	6 (1)	53 (8)
	小計 Sub Total	8 (2)	11 (1)	14 (2)	17 (3)	6 (1)	56 (9)
長崎 Nagasaki	研究員 Research Scientist		1	1 (1)			2 (1)
	一般職員 General Staff	13 (2)	2	5 (1)	17 (1)	5	42 (4)
	小計 Sub Total	13 (2)	3	6 (2)	17 (1)	5	44 (5)
合計 Total	研究員 Research Scientist		1	2 (1)	2 (1)		5 (2)
	一般職員 General Staff	21 (4)	13 (1)	18 (3)	32 (3)	11 (1)	95 (12)
	小計 Sub Total	21 (4)	14 (1)	20 (4)	34 (4)	11 (1)	100 (14)

注：（　）書は、選択定年者数を示す。

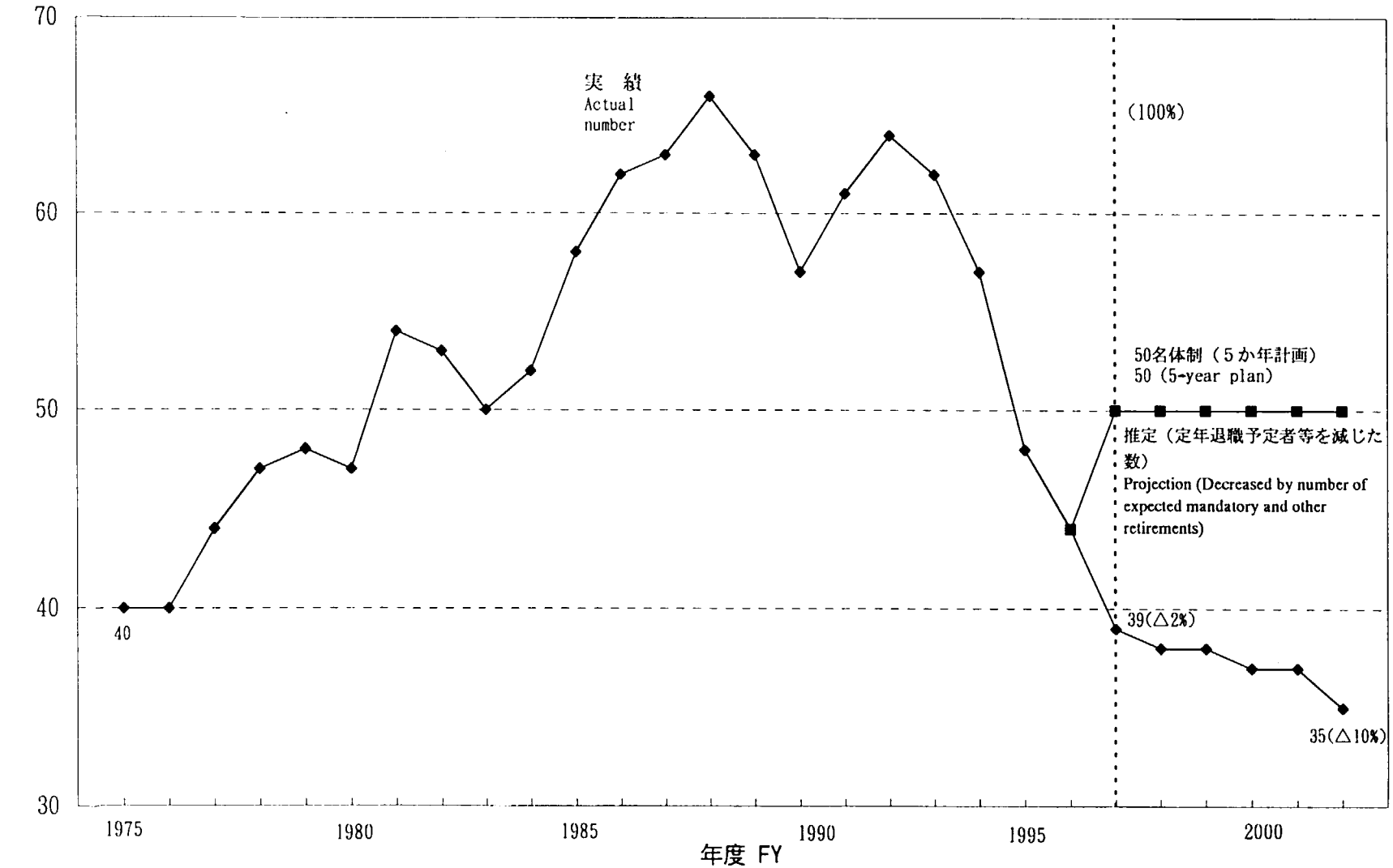
Note: The number in the parenthesis indicates optional retirements.


人 Number
研究員数の推移
Change in Personnel Strength of Research Scientists
1997. 4. 1現在
as of 1 April 1997
70
60
50
40
30
実績
Actual
number
(100%)
推定（定年退職予定者等を減じた数）
Projection (Decreased by number of expected mandatory and other retirements)
40
39(△2%)
35(△10%)
1975
1980
1985
1990
1995
2000
年度 FY

研究員数の推移

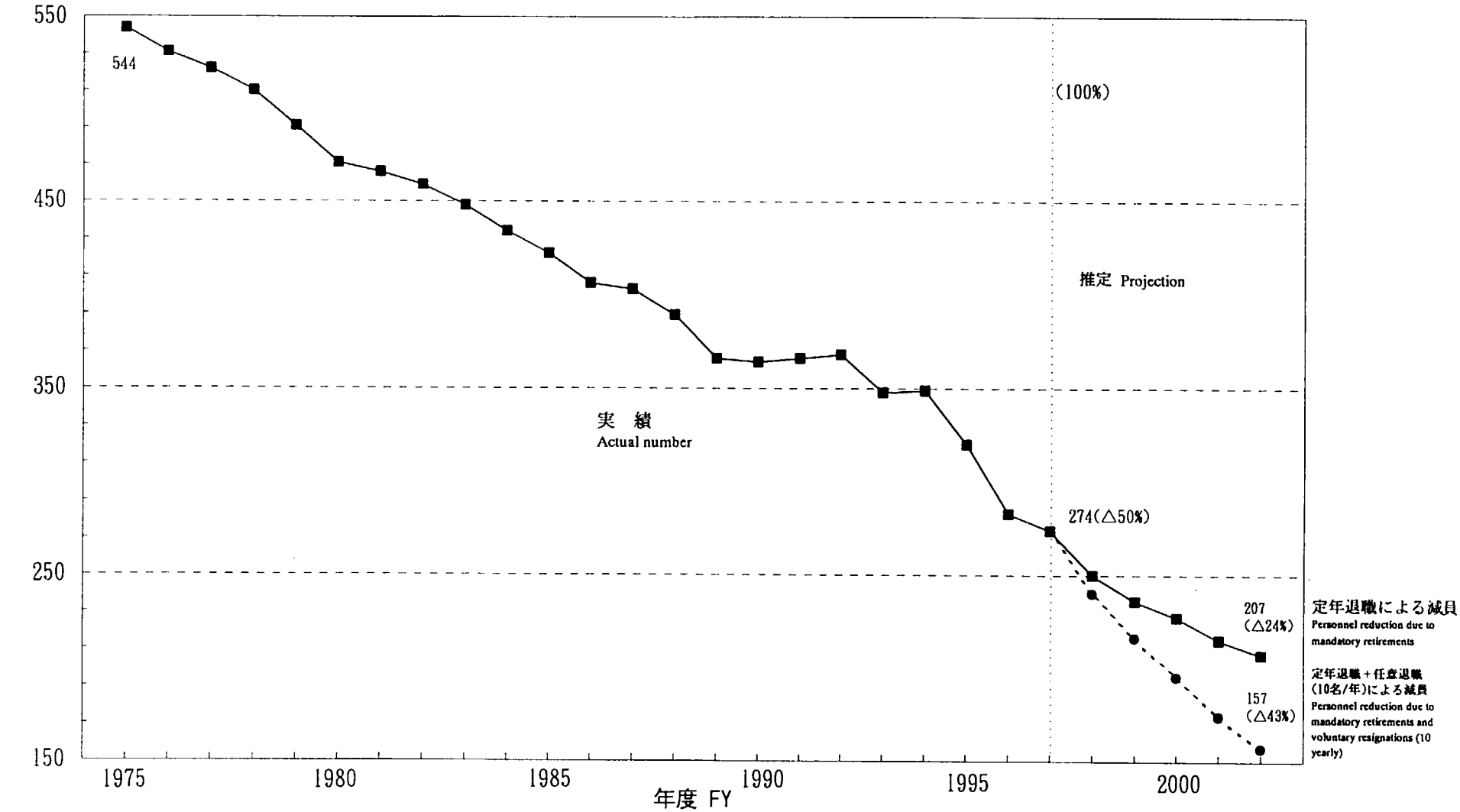
Change in Personnel Strength of Research Scientists

1997. 4. 1現在
as of 1 April 1997



一般職員数の推移
Change in Personnel Strength of General Staff

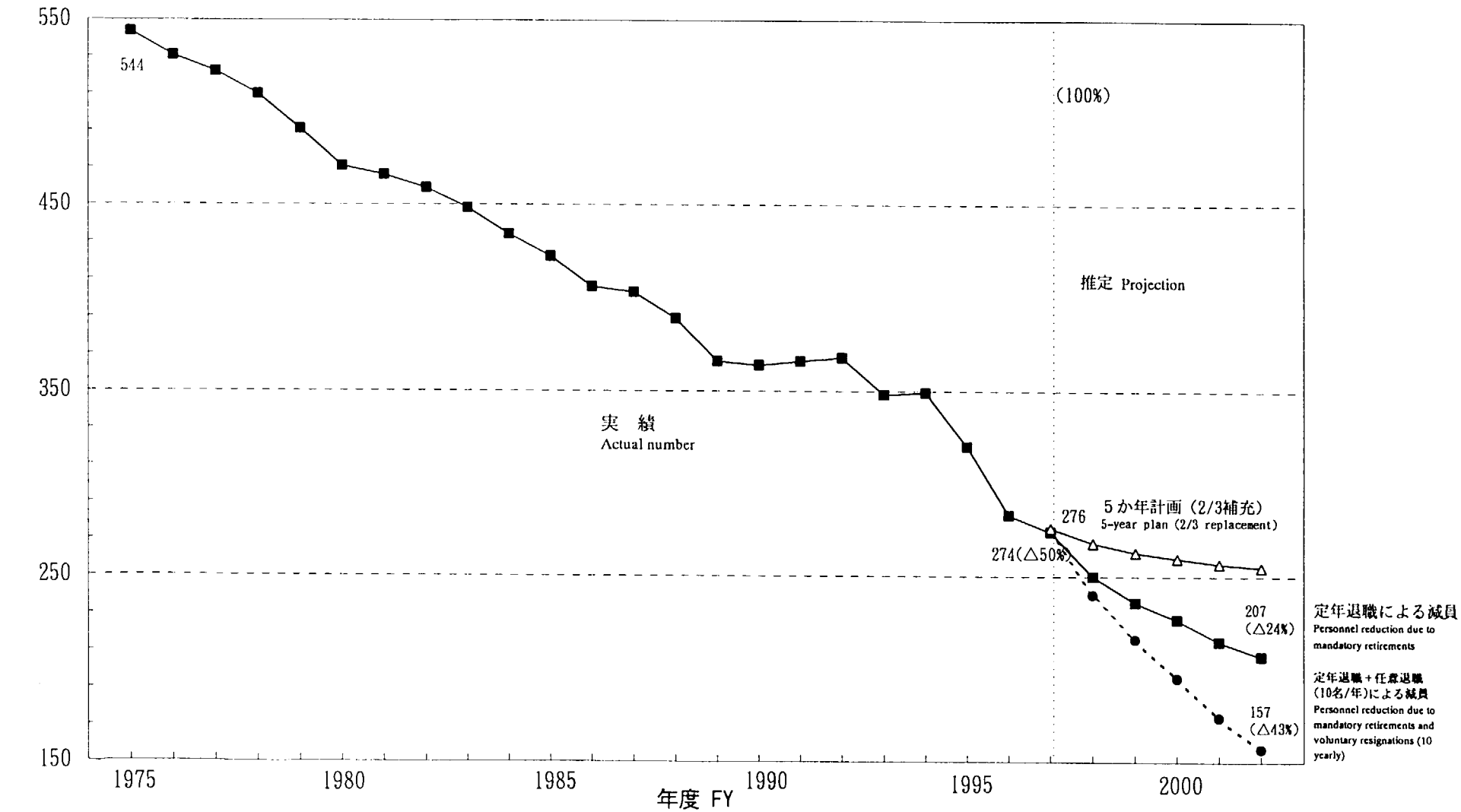
1997. 4. 1現在
as of 1 April 1997

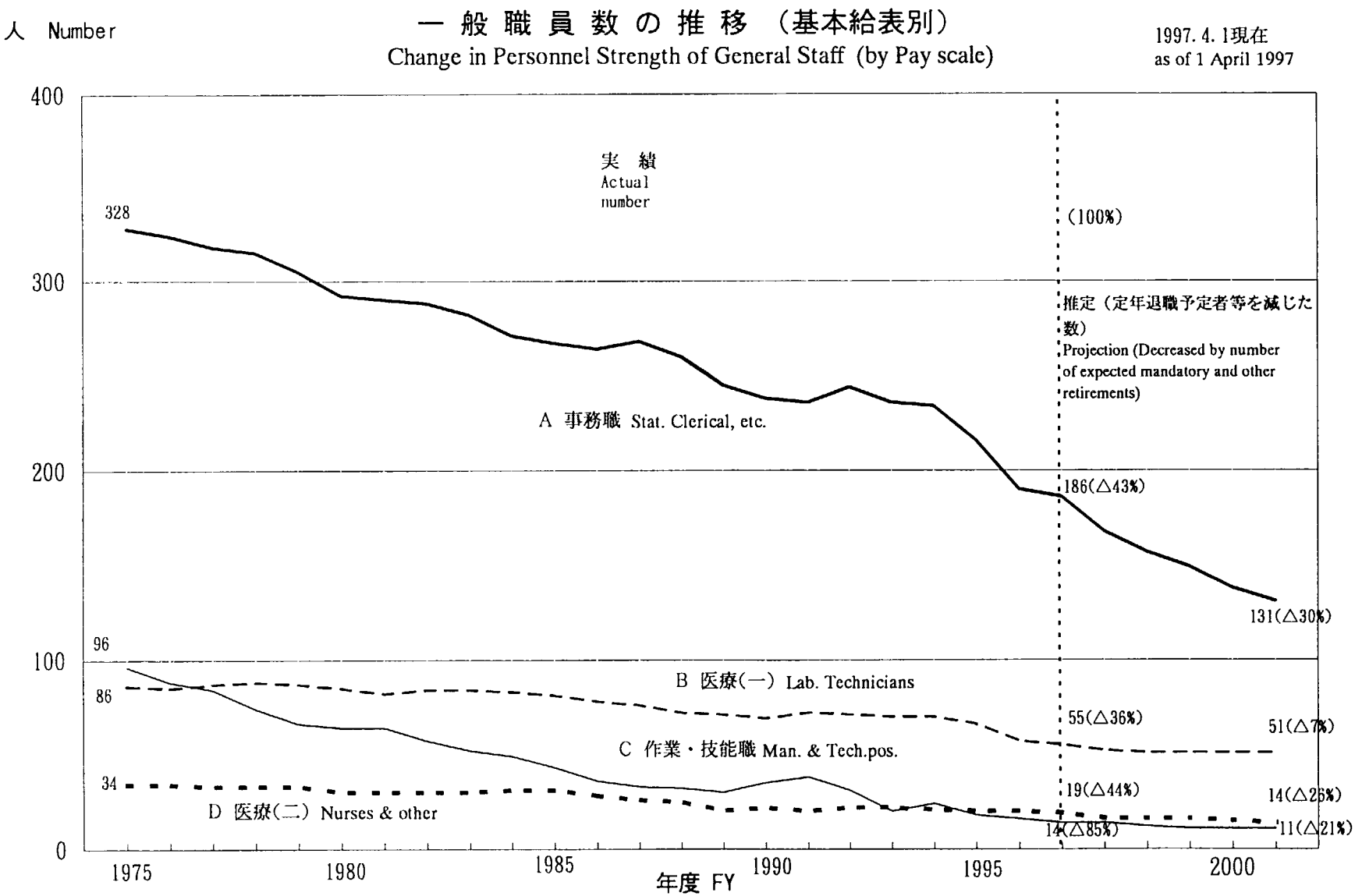


一般職員数の推移

Change in Personnel Strength of General Staff

1997. 4. 1現在
as of 1 April 1997



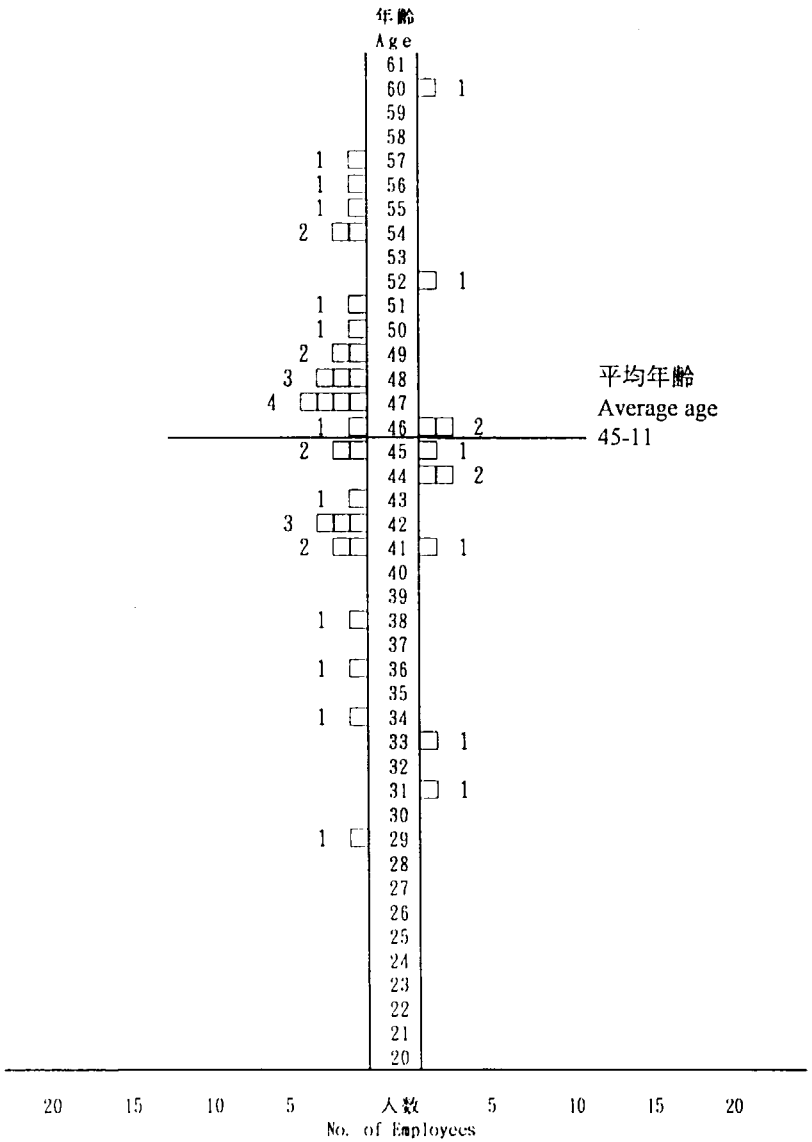

人 Number
一般職員数の推移（基本給表別）
Change in Personnel Strength of General Staff (by Pay scale)
1997. 4. 1現在
as of 1 April 1997
400
300
200
100
0
実績
Actual number
328
(100%)
推定（定年退職予定者等を減じた数）
Projection (Decreased by number of expected mandatory and other retirements)
A 事務職 Stat. Clerical, etc.
186(△43%)
131(△30%)
96
B 医療(一) Lab. Technicians
86
55(△36%)
51(△7%)
C 作業・技能職 Man. & Tech.pos.
34
19(△44%)
14(△26%)
D 医療(二) Nurses & other
14(△85%)
11(△21%)
1975
1980
1985
1990
1995
2000
年度 FY

年齢別男女別構成表　Personnel Composition by Age & Sex

1997年 4月 1日 現在
1 April 1997

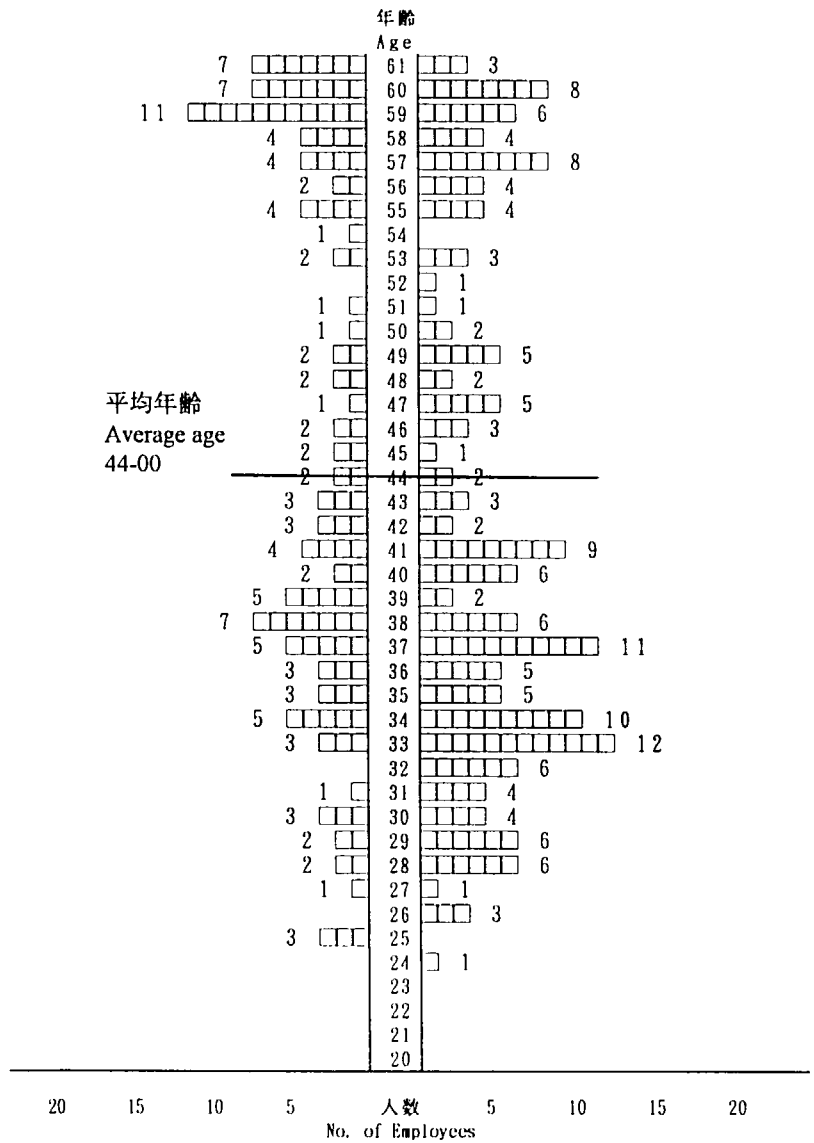
研究職（両市） Professional Employees (Both Cities)

男性 Male 29　　合計 Total 39　　女性 Female 10



一般職（両市） General Employees (Both Cities)

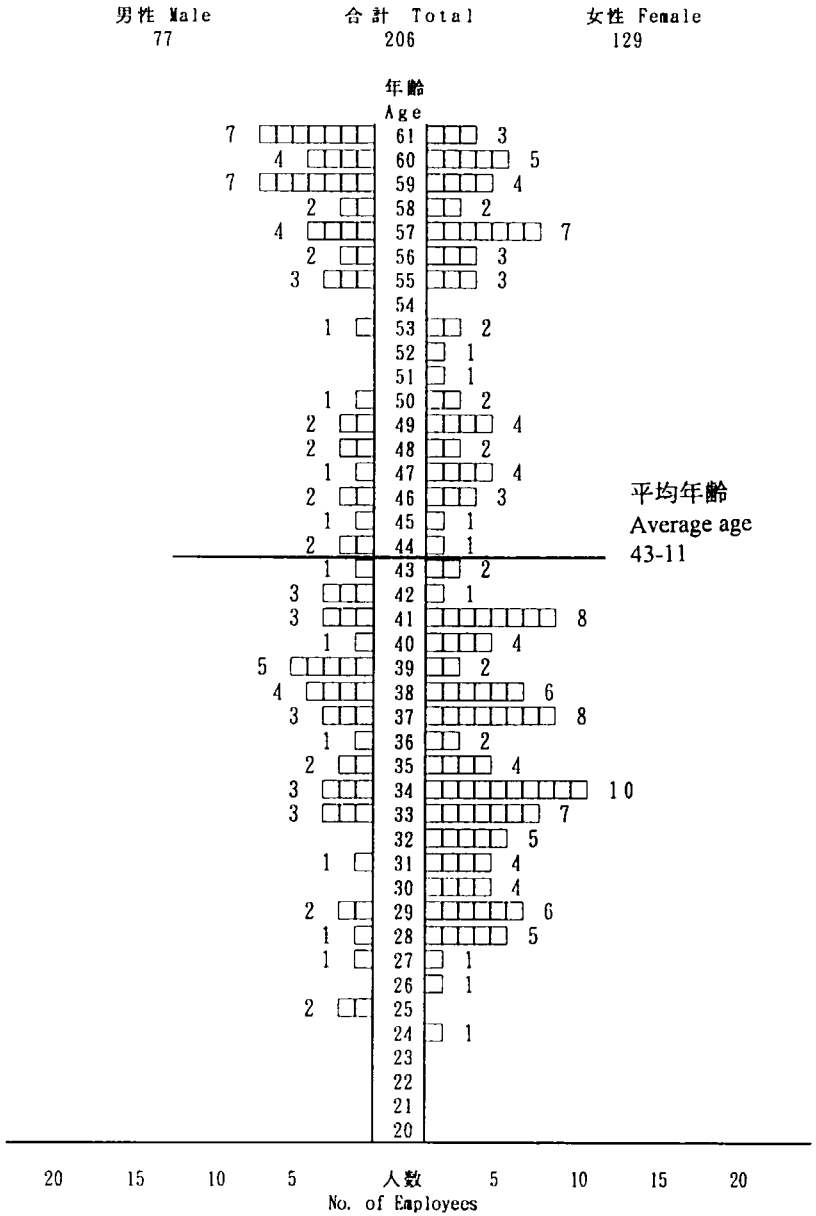
男性 Male 110　　合計 Total 274　　女性 Female 164



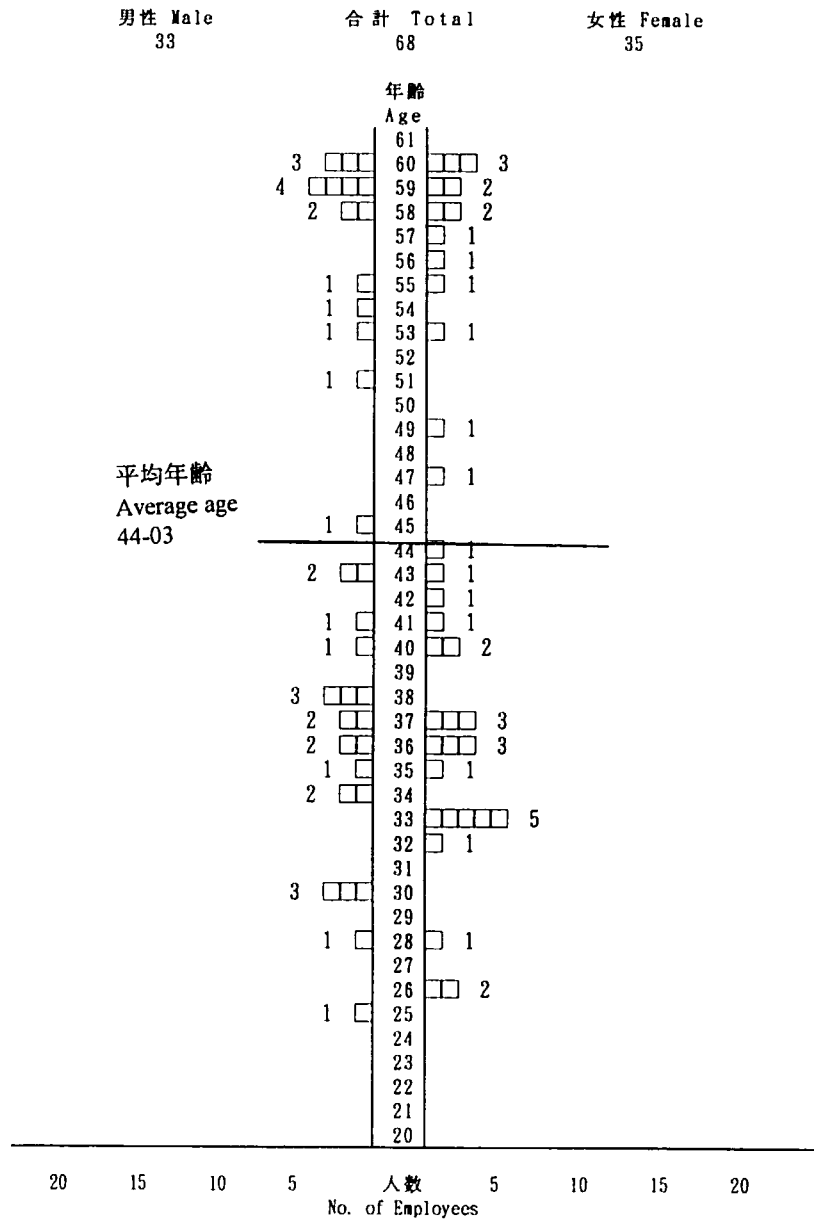
年齢別男女別構成表　Personnel Composition by Age & Sex

1997年 4月 1日 現在
1 April 1997

一般職（広島） General Employees (Hiroshima)



一般職（長崎） General Employees (Nagasaki)



FY-96 salary revision

(Translation)

FY96 Salary Revision and Others

Using as a guide the revision of pay scales for national government employees based on the recommendations of the National Personnel Authority issued on 1 August 1997, the FY96 salaries of the directors and professional and general employees were revised as follows:

I. Salary revision for professional and general employees

1. Revision of base pay

Base pay will be increased as shown in the attached sheets (I for professional employees and II for general employees)

Rate and amount of increase of base pay

Description	Mean age (years)	Amount of pay increase				Rate of increase (%)
		Monthly base pay (yen)	Allowances (yen)	Others (yen)	Total (yen)	
Research scientists	45.00	4,149	221	131	4,501	0.71
General employees	43.06	3,399	52	103	3,554	0.97
National government employees	39.60	3,054	124	158	3,336	0.95

(2) Allowances

(1) Revision of dependents allowance

The amount of the dependents allowance payable additionally for employee's dependent children who have attained 15 years of age and passed the first April 1 following their 15th birthday will be increased from the current ¥2,500 per person to ¥3,000 per person.

(2) Transportation allowance

Full cost of transportation payable to employees who use public transportation will be changed from the current ¥40,000 to ¥45,000 (The maximum of one-half the cost exceeding this amount payable will be unchanged.)

(3) Effective date

1 April 1996.

II. Revision of salaries of directors and others

1. Base pay

(Unit: ¥)

	Current	Revised	Amount of increase
Chairman	1,249,000	1,253,000	4,000
Vice Chairman	1,125,000	1,129,000	4,000
Permanent Director	970,000	974,000	4,000
Chief of Secretariat	836,000	839,000	3,000
	694,000	701,000	7,000

2. The revised regulations will be effected from 1 April 1997. However, the revised salary of chief of secretariat will be effected from 1 April 1996.

III. Improvement of working conditions

1. Using as a guide the government's regulations for the protection of mothers, the following leave benefits (special leaves) will be made available anew as measures for health management of female employees during pregnancy or after childbirth and for the health and safety of employees.

(1) Leave will be granted to female employees during pregnancy or after childbirth as shown below to allow them to undergo health examinations: However, the frequency of leave will be as especially indicated by the doctor as necessary.

1) Up to and through the 27th week (7 months) of pregnancy Once every 4 weeks

2) From the 28th week (8 months)
through the 35th week (9 months) of pregnancy Once every 2 weeks

3) From the 36th week (10 months) to the time of delivery (childbirth) Once a week

4) Once within the first year after childbirth

(2) When an employee wishes to undergo a comprehensive health examination, time necessary for this not to exceed one day will be granted as leave.

(3) Effective date 1 January 1997

2. Introduction of the Welfare Pension Fund

Based on approval at the Twenty-sixth Board of Directors meeting, negotiations with concerned parties had been held on the welfare pension fund as a system to enrich life in old age, and it was decided to join the Hiroshima Prefecture Hospitals Welfare Pension Fund (established on 1 April 1986, 116 member groups and 6,300 members) as of 1 April 1997.

（財）放射線影響研究所

別表一

（第１１条関係）　RADIATION EFFECTS RESEARCH FOUNDATION

研究員基本給表 REVISED BASE PAY SCALE FOR RESEARCH STAFF				平成8年4月1日 1 April 1996
級 Grade	1 級 Grade 1	2 級 Grade 2	3 級 Grade 3	4 級 Grade 4
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1	299,900	316,800	380,300	438,500
2	314,000	333,200	398,100	454,300
3	326,400	349,700	416,000	470,100
4	338,900	366,200	433,900	486,000
5	351,300	383,200	447,600	501,600
6	360,000	400,000	460,800	518,300
7	368,300	416,900	473,500	535,200
8	376,600	429,400	485,800	552,700
9	385,000	440,900	498,000	570,200
10	393,400	451,700	510,200	587,500
11	401,700	461,700	522,000	604,800
12	410,100	470,500	533,600	622,000
13	418,200	478,800	545,300	638,800
14	426,200	486,900	556,900	655,100
15	432,500	494,900	568,200	671,400
16	438,500	502,700	579,300	687,600
17	442,900	510,400	590,200	703,900
18	447,100	517,500	601,100	718,300
19	451,300	523,900	610,600	729,200
20	455,500	529,900	619,900	738,700
21	459,500	535,600	626,900	746,500
22	463,500	541,000	633,000	753,400
23	467,400	546,300	638,100	758,800
24	471,300	550,800	643,200	
25	475,300	555,100		
26	479,200	559,400		
27	483,100	563,700		
28	487,100			
29	491,000			
30	495,000			
31	499,000			

備考：　この表は研究員に適用し表別区分は別に定める基準による.

（財）放射線影響研究所

別表二①
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

事務職基本給表
BASE PAY SCALE FOR ADMINISTRATIVE POSITIONS

平成8年4月1日
1 April 1996

級 Grade	1級 Grade 1	2級 Grade 2	3級 Grade 3	4級 Grade 4	5級 Grade 5	6級 Grade 6	7級 Grade 7	8級 Grade 8	9級 Grade 9	10級 Grade10	11級 Grade11
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1			184.800	218.400	237.500	256.500	276.000	297.400	332.500	371.500	420.800
2	134.900	171.000	191.700	226.600	246.100	265.500	285.300	307.400	344.600	384.000	435.500
3	139.300	177.700	198.700	235.000	254.800	274.600	294.900	317.600	356.700	396.600	450.200
4	143.800	184.800	205.700	243.900	263.800	283.700	304.600	328.100	368.600	409.100	465.000
5	148.900	190.600	213.300	252.800	272.800	292.800	314.400	338.600	380.400	421.800	479.800
6	154.700	195.700	221.200	261.400	281.800	302.100	324.300	349.000	392.300	434.200	494.600
7	160.700	200.800	229.000	269.800	290.700	311.500	334.300	359.100	404.200	446.500	509.400
8	166.900	205.900	236.400	278.200	299.600	321.000	344.200	368.900	416.200	458.700	524.500
9	171.400	210.600	242.900	286.400	308.500	330.500	353.900	378.700	428.100	470.700	539.50
10	174.900	215.100	249.300	294.500	317.300	340.000	363.400	388.400	439.600	482.600	554.600
11	177.900	219.500	255.600	302.400	326.000	349.600	372.800	398.100	450.500	493.200	566.500
12	180.600	223.900	261.400	309.900	334.500	359.100	381.900	407.800	461.100	503.000	574.300
13	183.300	228.200	267.000	317.200	342.800	368.400	390.700	417.400	469.800	511.200	581.800
14	185.500	231.600	272.200	324.300	350.900	377.500	398.300	426.600	477.200	518.400	588.000
15	187.600	234.700	277.400	330.700	358.200	385.600	404.900	433.600	484.500	523.000	592.800
16	189.200	237.800	282.100	336.800	364.400	392.000	410.900	440.300	489.600		
17		240.900	286.300	341.200	369.700	398.200	416.000	444.700	494.200		
18		243.800	290.000	345.100	373.800	402.400	420.300	449.200	498.500		
19		245.800	293.400	348.800	377.700	406.500	424.600	453.500			
20			296.300	351.900	381.200	410.500	428.700	457.400			
21			299.200	355.000	384.800	414.500	432.600	461.200			
22			302.100	358.100	388.300	418.400	436.300				
23			305.000	361.200	391.700	422.100					
24			307.900	364.300	395.000	425.700					
25			310.800	367.400	398.400						
26			313.700	370.500	401.700						
27			316.600	373.600							
28			319.500	376.700							
29			322.400								
30			325.200								
31			328.000								
32			330.800								

備考：　この表は主として事務系業務に従事する職員で別に定める基準により適用する．

（財）放射線影響研究所

別表二②

（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

作業・技能職基本給表

BASE PAY SCALE FOR MANUAL & GENERAL TECHNICAL POSITIONS

平成8年4月1日
1 April 1996

級 Grade	1級 Grade 1	2級 Grade 2	3級 Grade 3	4級 Grade 4	5級 Grade 5	6級 Grade 6
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1		164,600	182,900	200,400	226,600	255,000
2	120,900	171,200	188,700	206,400	233,500	262,300
3	124,600	177,000	194,600	212,800	240,400	269,700
4	128,300	182,800	200,400	219,700	247,400	277,700
5	131,800	188,000	206,300	226,500	254,300	285,800
6	135,800	193,100	212,600	233,200	261,100	294,200
7	140,600	198,200	219,200	239,400	267,800	302,700
8	145,300	203,300	225,500	245,300	274,000	311,100
9	151,300	208,600	231,700	251,100	279,900	319,300
10	157,400	213,900	237,500	257,000	285,600	327,200
11	164,400	219,400	243,200	262,400	291,200	335,000
12	171,000	224,500	248,800	267,700	296,800	342,800
13	176,700	229,300	254,100	272,800	302,200	350,400
14	182,100	234,200	259,300	277,900	307,400	357,200
15	186,800	239,000	264,300	282,800	312,600	363,900
16	191,200	243,300	268,900	287,800	317,800	370,500
17	195,700	247,500	273,800	292,200	322,800	376,800
18	199,700	251,400	278,600	296,200	327,400	382,700
19	203,200	254,800	283,100	299,700	331,900	388,100
20	206,300	257,500	287,100	303,000	336,000	392,900
21	209,300	260,200	290,200	306,200	339,800	397,700
22	212,400	262,900	293,100	309,200	343,300	402,000
23	215,300	265,600	296,000	312,200	346,400	405,400
24	218,100	268,300	298,900	315,200	349,500	
25	220,500	271,000	301,800	318,200	352,600	
26	222,800	273,700	304,700	321,200	355,700	
27	225,000	276,400	307,600	324,200	358,800	
28	227,200	279,100	310,500	327,200		
29	229,300	281,800	313,400	330,200		
30	231,300	284,400	316,300	333,200		
31	233,200	287,000	319,200	336,200		
32	235,000	289,600				
33		292,200				

備考：　この表は機器の運転操作、施設の保全、その他の業務に従事する職員で別に定める基準により適用する。

（財）放射線影響研究所

別表二③
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

医療技術職基本給表（一）

BASE PAY SCALE FOR MEDICAL TECHNICAL POSITIONS (I)

平成8年4月1日
1 April 1996

級 Grade	1 級 Grade 1	2 級 Grade 2	3 級 Grade 3	4 級 Grade 4	5 級 Grade 5	6 級 Grade 6	7 級 Grade 7
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1			205,700	235,600	265,500	307,400	343,200
2	139,500	176,800	212,600	243,800	275,000	317,600	355,000
3	145,000	183,300	219,800	252,200	284,500	327,800	366,800
4	151,700	189,800	227,800	261,000	294,100	337,900	378,600
5	158,400	196,300	235,900	269,800	303,700	347,900	390,400
6	165,900	202,700	244,200	278,800	313,400	357,800	402,200
7	173,400	209,200	252,500	287,900	323,300	367,600	414,400
8	179,600	215,600	260,800	297,000	333,100	377,400	426,600
9	185,800	222,400	269,200	306,000	342,800	387,300	438,600
10	191,000	229,700	277,600	315,000	352,300	397,300	449,900
11	196,200	236,700	285,900	323,800	361,700	407,200	460,800
12	201,300	243,400	294,100	332,400	370,600	416,800	469,800
13	206,300	249,900	302,200	340,900	379,500	426,200	477,200
14	210,900	256,400	310,100	348,900	387,700	433,400	484,500
15	215,400	262,200	317,700	356,100	394,500	440,200	491,800
16	219,800	267,700	325,000	363,000	401,000	444,700	496,300
17	224,100	272,900	331,800	369,200	406,500	449,200	500,600
18	228,400	278,100	338,300	375,000	411,700	453,500	
19	231,900	282,800	343,000	379,500	415,900	457,400	
20	235,000	287,300	347,600	383,800	420,000	461,200	
21	238,000	290,600	351,300	387,700	424,100		
22	240,500	293,500	354,400	391,100	427,800		
23	242,500	296,400	357,500	394,500	431,400		
24		299,300	360,600	397,800			
25		302,200	363,700	401,200			
26		305,100	366,800	404,500			
27		308,000	369,900	407,900			
28		310,900	373,000				
29			376,100				
30			379,200				

備考：　この表は薬剤師、診療放射線技師、臨床検査技師及びこれらに準ずる業務に従事する職員で別に定める基準により適用する。

（財）放射線影響研究所

別表二④
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

医療技術職基本給表（二）　平成8年4月1日
BASE PAY SCALE FOR MEDICAL TECHNICAL POSITIONS （Ⅱ）　1 April 1996

級 Grade	1 級 Grade 1	2 級 Grade 2	3 級 Grade 3	4 級 Grade 4	5 級 Grade 5
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1			221,100	243,400	274,700
2	152,600	179,400	227,900	250,800	283,200
3	158,200	187,900	235,700	258,200	291,700
4	164,100	197,000	243,100	265,600	300,200
5	170,200	202,700	250,400	273,100	308,800
6	178,300	208,500	257,800	280,900	317,400
7	186,800	214,400	265,100	288,700	326,000
8	195,300	220,800	272,400	296,600	334,400
9	200,300	227,600	279,800	304,600	342,300
10	205,500	235,000	287,400	312,600	350,100
11	210,600	242,300	295,100	320,500	357,900
12	215,900	249,600	302,800	328,200	365,600
13	221,500	256,900	310,300	335,500	373,400
14	227,100	264,200	317,600	342,700	381,400
15	232,800	271,400	324,800	349,900	389,400
16	238,400	278,600	331,500	356,900	397,300
17	244,100	285,800	338,100	363,900	404,800
18	249,700	293,000	344,600	370,700	411,400
19	255,400	299,900	351,100	377,400	416,600
20	261,000	306,800	357,500	383,400	421,400
21	266,300	313,600	363,900	389,100	426,200
22	271,400	319,900	369,800	394,600	430,300
23	275,700	326,000	375,200	398,900	433,800
24	280,300	332,200	380,500	402,800	437,400
25	284,600	338,100	384,900	406,500	
26	288,700	342,800	388,600	410,100	
27	292,300	346,800	392,100	413,600	
28	295,700	350,600	395,500	417,100	
29	298,500	354,000	398,900		
30	301,000	357,300	402,300		
31	303,400	360,600	405,700		
32	305,600	363,900			
33	307,900	367,200			
34	310,000	370,500			
35	312,100	373,800			
36	314,200	377,100			
37	316,300	380,400			
38	318,500	383,700			
39	320,700				
40	322,900				
41	325,100				

備考：　この表は保健婦、看護婦、及び準看護婦で別に定める基準により適用する.

Labor Union's FY-97 demands for improvement
of working conditions, etc.

(Translation)

HOEIKEN-ROHON-HATSU No. 8

3 March 1997

To: Dr. Itsuzo Shigematsu
Chairman, Radiation Effects Research Foundation

From: Satoshi Kudamatsu
President, All Japan Prefectural and Municipal Workers Union Hiroshima Office

Noboru Ueda
Executive Chairman, RERF Labor Union Headquarters

Subject: FY1997 demands regarding how RERF should be, salary increase, and improvement of working conditions

Demands for improvement of the Japan-US equal-sharing system for operation of RERF, establishment of a democratic operation system, realization of relocation, and development of the foundation as an organization contributing to international peace and relief of victims of nuclear accidents

The A-bomb survivors and we have struggled together for many years, demanding that the Japanese government stop committing ABCC/RERF to the charge of the United States, enact the A-bomb Survivors' Relief Law based on the spirit of state compensation and establish the legal status of the foundation under this law, revise the Japan-US equal-sharing system, establish a democratic operation system, realize relocation and construction of a new laboratory building, and develop the foundation as an institution contributing to international peace and to the relief of A-bomb survivors and victims of nuclear accidents. As a result, we have seen the fruition of our struggle in the "enactment of the A-bomb Survivors' Relief Law and establishment of the legal status of RERF thereunder (effective from July 1995)." During the struggle, however, the concerns the A-bomb survivors and we had about RERF deriving from the binational equal-sharing system, became real and serious due to its structural defects, and RERF faced a real "crisis," which could have led to layoffs, nonpayment of salaries, etc.

However, we are deeply moved that "establishment of legal status of RERF and supplementary resolution" solidly follow the "recommendations of the Blue Ribbon Panel" and action has been taken for their implementation, which could overcome the "crisis of RERF." Therefore, we ask you to further endeavor for the realization of the following demands of the A-bomb survivors and ours to rescue the stability of RERF, and thus fulfill your responsibilities.

1. Demand for reorganization discontinuing the Japan-US equal-sharing system and democratization of RERF

1) The provisions "equal participation" and "equal funding in principle" in the "notes verbale exchanged between Japan and the US" concerning RERF be deleted, and the act of endowment amended accordingly.

2) The membership of the Board of Directors be mainly Japanese, with no retired high-ranking officials, and a representative of A-bomb survivors be elected to it.

3) Membership in the Scientific Councilors be, not necessarily limited to Americans and Japanese, but be widely opened to the world.

4) A council be established based on the September 20 cabinet resolution to supervise the Board of Directors and others, allowing the election of representatives of A-bomb survivors and RERF employees to it.

5) Discontinuation of equal sharing of the budget and making the Japanese side bear the major portion

6) Reorganization of the Human Investigation Committee and placement of the human investigation committee members in workplaces.

2. Demand concerning relocation of RERF

Realization of establishment of RERF based on the recommendations of the Blue Ribbon Panel and the Scientific Council along with the "Hiroshima Peace Memorial Cancer Center" envisaged by Hiroshima Prefecture

3. Demands for FY1997 wage increase and improvement of working conditions

It is nothing else than unjust that hefty remunerations by the standards of the first-class public corporations are paid to the Chairman and directors, while the wage standards of national government workers, whose status is guaranteed and who are completely free of the fear of discharge or unemployment, are forced upon us RERF workers who are exposed to the uncertainty of employment with no guarantee of status. Furthermore, the Laspeyre's index and the disposable income vis-à-vis national government workers are inferior.

We would like to give due credit to your sincere responses last year regarding issues which included improvement of promotional standards for administrative positions, addition of Grade 7 to medical technical positions (I), introduction of welfare pension fund, protection of human rights and prevention against recurrence of sexual harassment. However, particular efforts yet need to be made to improve wages of manual & general technical and medical technical (II) positions. Therefore, we strongly demand wages and working conditions exceeding the levels for national government employees, as follows, and firmly oppose drastic rationalization by non-employment of replacements for retirements, and demand that you on your responsibility employ long-term temporary workers as regular employees and employ new school graduates.

Demands

1. Wage increase

1) Increase of base pay by ¥13,000 or more for each and every employee (Standardized demand of Japanese Trade Unions Confederation and All Japan

Prefectural & Municipal Workers Union

2. Increase of starting salaries and equitable salary adjustments of present employees

Increase of starting salaries and salary adjustments of all employees on the payroll

3. Improvement of pay scales

1) The base pay scale for manual and general technical positions be replaced with that for administrative positions and their wage be increased to the level of Grade 7 for administrative positions.
2) The pay scales for medical technical positions (I) and (II) be improved to a point that grades comparable to Grade 10 on the pay scale for administrative positions will be made available.
3) Pay scale step increases to be ¥5,000 or more.

4. Improvement of the salary increase system

1) Abolition of the system to postpone regular salary increases for aged workers
2) Expansion of the 15% quota of special salary increases and its implementation from the standpoint of improving the working conditions and remedying unfairness and imbalance

5. Improvement of the promotion system

1) Improvement of the table of standard duties and its flexible and positive application such as 80% application of the standard table of qualifications by grade
2) Approval of grade increases before employees arrive at the pay scale steps at which they will fall into the category of the so-called twins and triplets or will qualify for specified grades
3) Establishment of an automatic promotion system up to the following grades in case of a worker in an administrative position who graduated from a junior college and was employed at age 20 (already enforced by the Prefecture)

   i) Grade 4 at age 30
   ii) Grade 5 at age 35
   iii) Grade 6 at age 40
   iv) Grade 7 at age 50 or over

   Grades corresponding to those of administrative positions should be applied to other positions.

4) Where there are a number of persons with identical qualifications for promotion, comparable titles be made available for the purpose of promotions.
5) Adjustments for employees resulting from the improvement of the promotion system recommended by the National Personnel Authority in 1991 be made from age 27 without following the criterion "above starting grade," which expands the difference between job types. The imbalance be corrected.

6. Improvement of wages of those employed in midcareer and those suffering from rationalization

   1) Improvement of the standards for starting salaries for midcareer employment
   2) Wages not less than 90% of the wages of standard employees be paid to those who were employed in midcareer and have worked for three years or more and 100% to those who have worked for five years or more.
   3) Wages of workers transferred to a different type of job be improved by recalculating wages as if they had been working in the new position from the beginning.
   4) Improvement of salaries of employees suffering a drastic wage decrease due to reduction of overtime duty for rationalization

7. Improvement of allowances

   1) Establishment and payment of a new allowance for supplementation of the working conditions, such as status, employment, annuity, welfare, etc., which are inferior to those of national government workers
   2) Increase of the 3% adjustment allowance to 8%, the standard of payment applied to national government workers in a one million population city
   3) Inclusion of position allowance in the base pay to increase the Laspeyre's index, and review of the allowance for managerial positions
   4) Housing allowance exceeding that of national government employees was established as the second base pay in the days of ABCC. Thus, the portion over and above the government's level should be included in base pay to increase the Laspeyre's index. When an employee living in a rented house or who is not a household head acquires a house of his/her own, ¥27,000 be paid for the next five years. Also, abolition of discriminatory practice in terms of job type (professional and non-professional).
   5) Improvement of transportation allowance (including support for use of toll road), hazard allowance, which has not been improved for many years (¥230 for working four hours or more a day), outside duty allowance (¥2500 at maximum per month), night duty allowance (¥1000 per night), and other allowances
   6) Establishment of new allowances for holders of licenses required by law for the operations and management of RERF
   7) Fees for various association and academic society affiliations required in connection with duty be born by RERF.

8. Effective date

   The aforementioned demands to be effected retroactively to 1 April 1997 and the demand in item 5 of paragraph 5 retroactively to 1 April 1992.

9. Seasonal allowances

based on age.

10. Improvement of the personnel management system including promotions and reshuffles

    1) No skipping, arbitrary action, or discrimination by sex in terms of promotions
    2) Amicable settlement by explanation and consultation in advance with the Union and the party concerned in cases of reshuffle, transfer and promotion.

11. Use of annual leave

    1) Encouragement of complete use of annual leave
    2) Further instructions be given to department and section chiefs and other employees for full use of annual leave. Punishment of department and section chiefs who negate the right of the workers to use annual leave, break the agreement on overtime work, and infringe upon human rights
    3) Review of special leave and expansion of its application.

12. Improvement of child care leave and bedside care leave systems

    1) A minimum of 60% of the salary be paid during child care leave, and introduction of partial leave system.
    2) Improvement of the bedside care leave system using improvement of the child care leave system as a guide
    3) Period of child care leave and bedside care leave be regarded as period worked so that periodical salary increase, grade increase, promotion, or calculation of termination allowance will not be effected.

13. Improvement of welfare benefits

    1) The agreement on employee welfare be revised.
    2) Increase of RERF loans and lowering of interests
    3) Improvement of long service award (vacation trip supported by RERF, etc.)

14. Improvement of labor safety and hygiene
    1) Resting lounges for men like those for women be established.
    2) VDT guidelines be established to promote health management.

15. Establishment of standards for the filling of vacancies and full employment of the authorized number of personnel

    1) Authorized strength be based on full use of annual leave and not on the guidelines for administrative reform and securing of, at the minimum, the budgeted strength approved by the Government.
    2) Employment of temporary employees as regular employees.
    3) Improvement of wages and working conditions of temporary and part-time employees

16. Raising of mandatory retirement age

    1) With the revision of welfare pension receiving age, the mandatory retirement age

and the welfare pension receiving age be linked (based on the 1984 recommendation of the Local Labor Relations Committee)..

2) The present employment continuation system for the aged be improved as follows:

i) Employment be guaranteed for all employees who desire to work.

ii) Continued employment be considered separately from the current budgetary personnel slots.

iii) Working conditions including wages (duty, job type, working hours, etc.) be agreed upon between management and labor.

3) Systematization of participation in lifetime designing seminar, etc.

17. Reinstatement of the A-bomb anniversary as a rest day

18. Article 3 (scope of union members) of the Labor Agreement (concluded on 18 December 1987) be revised.

We request that you answer to the above in writing on March 12.

As of 1 April 1997

General State of RERF Labor Union

I. Organization

1. Number of Union members : 184 (H = 134, N = 50)

2. Organization Rate

   (1) Persons eligible to join the Labor Union:

   Number of Union members(184)/ number of employees eligible to join the Union(199) = 92%

   (2) Directors and staff:

   Number of Union members(184)/ total number of directors and staff (317) = 58%

3. Non-members:

   Breakdown

(1)	Persons ineligible to join the Union:	118
1)	Directors	3
2)	Chief of Secretariat	1
3)	Research scientists(those in supervisory positions included)	39
4)	Section chiefs and those in equivalent or higher positions	30
5)	Unit Supervisors and those in equivalent or higher positions of the General Affairs Section, Personnel Section, Accounting Section, and Secretariat of Nagasaki	19
6)	Directors' secretaries, interpreters, and employees responsible for personnel and labor affairs	9
7)	Contract employees	16
8)	Employees during probational employment	1
(2)	Others(employees unaffiliated with the Labor Union)	15

4. Total number of and staff: 317

II. Higher organization with the RERF Labor Union is Affiliated

Hiroshima Prefectural Headquarters, All Japan Prefectural and Municipal Workers' Union

Hiroshima Prefectural Confederation, Japanese Trade Union Confederation

Others (1) International collaboration

(2) Development of an A-bomb related materials database system

(3) Others

RERF FY 96: International Collaborative Activities

I. Participation in International Collaborative Activities by RERF Directors and Staff Members (excluding participation in international scientific meetings)

1. Chernobyl accident-related collaborative activities

1) International Atomic Energy Agency (IAEA) and Hiroshima International Council for Health Care of the Radiation-Exposed (HICARE)

* RERF Chairman Itsuzo Shigematsu and Kiyohiko Mabuchi, chief, Department of Epidemiology, participated in the International Meeting for the 10th Anniversary of the Chernobyl Accident in Vienna, Austria. Mabuchi also participated in the 9th General Meeting of International Commission on Radiological Protection, at which he introduced the activities of HICARE. (Austria, April, 1996)

2) Sasakawa Memorial Health Foundation

* Yoshisada Shibata, chief, Department of Epidemiology and Biometrics (Nagasaki), participated in the Post- Chernobyl Accident: 10 Year Anniversary Symposium in Kiev, Ukraine. Also, he participated in the memorial ceremony held in Moscow, Russia. (Ukraine, Russia, April 1996)

* Yoshisada Shibata, chief, Department of Epidemiology and Biometrics (Nagasaki), provided on-site technical guidance to the Chernobyl Medical Cooperation Project. (Belarus, May 1996)

* Yoshisada Shibata, chief, Department of Epidemiology and Biometrics (Nagasaki), provided on-site technical guidance to the Chernobyl Medical Cooperation Project, and also participated in the 1996 Chernobyl workshop. (Russia, June - July 1996)

* RERF Chairman Itsuzo Shigematsu and Yoshisada Shibata, chief, Department of Epidemiology and Biometrics (Nagasaki), participated in the Fifth Chernobyl Medical Cooperation Symposium. Shibata also provided on-site technical guidance to the Chernobyl Medical Cooperation Project. (Ukraine, Russia, Belarus, October 1996)

* Yoshisada Shibata, chief, Department of Epidemiology and Biometrics (Nagasaki), participated in the research project coordination meeting of the Chernobyl Medical Cooperation Project. (France, January 1997)

3) Radiation Effects Research Foundation

* Kazuo Neriishi, chief, Division of Medicine, Department of Clinical Studies, participated in the first meeting on the oxidized stress after exposure to radiation in Chernobyl and on antioxidant treatment.
(France, September 1996)

2. Chelyabinsk-related cooperation

1) RERF-URCRM-FIB-1 collaboration agreement

* Kiyohiko Mabuchi, chief, Department of Epidemiology, and Seishi Kyoizumi, chief, Immunology Laboratory, participated in the international joint research project on health effects of chronic exposure to low dose rate radiation among the exposed population in the Southern Ural region.
(Russia, July 1996)

* Dale L. Preston, chief, Department of Statistics, conducted an analysis of the joint research study with Urals Research Center for Radiation Medicine (URCRM) and Branch N1, Institute of Biophysics (FIB-1).
(Russia, March 1997)

3. Other International collaborative activities

1) World Health Organization (WHO) and Hiroshima International Council for Health Care of the Radiation-Exposed (HICARE)

* Permanent Director Yutaka Hasegawa, participated in preparation of the proceedings of the Sixth WHO/REMPAN meeting report and in the preparatory meeting for the WHO/ HICARE joint symposium (scheduled in August 1996).
(Switzerland, May 1996)

II. Acceptance of visitors from overseas for briefing and training
(total in FY 96: 339 persons)

【RERF Hiroshima: 319 persons】

1. 64 visitors related to HICARE

(1) 36 visitors related to Chernobyl

1) Japanese Ministry of Foreign Affairs. One specialist respectively from Novozybkov and Obninsk (dose group), the Russian Federation on 8 April; two doctors from Tallin, the Republic of Estonia, two doctors from Riga, the Republic of Latvia, and one doctor respectively from Kaunas and Vilnius, the Republic of Lithuania from 19 to 28 March 1997; one doctor respectively from St. Petersburg and Obninsk, the Russian Federation, one doctor from Gomel, the Republic of Belarus, and two doctors from Kiev, Ukraine from 6 to 28 March.

2) HICARE. One specialist from Kiev, Ukraine from 15 May to 9 August; one doctor from Vilnius, the Republic of Lithuania from 19 September to 14 October; one doctor respectively from Kiev, Ukraine, Gomel, the Republic of Belarus, and Riga, the Republic of Latvia from 20 to 27 September; one doctor from Novosibirsk, the Russian Federation from 7 to 11 March 1997.

3) University of Kuopio, the Republic of Finland. Two specialists from Kuopio, the Republic of Finland on 29 July.

4) Sasakawa Memorial Health Foundation. Three specialists from Mogil'ov, the Republic of Belarus and one specialist from Moscow, the Russian Federation on 23 August.

5) Nagasaki Association for Hibakushas' Medical Care (NASHIM). One doctor from Kiev, Ukraine on 29 August.

6) National Institute of Radiological Sciences. Two doctors from Moscow, the Russian Federation on 24 January 1997; Two specialist from St. Petersburg, the Russian Federation and one specialist from Bangkok, Thailand on 10 February.

7) Japanese Red Cross Society, Hiroshima Branch. One doctor respectively from Bryansk, the Russian Federation, Gomel, the Republic of Belarus, and Kiev, Ukraine from 27 to 28 January.

8) Radiation Effects Research Foundation. One specialist respectively from Geneva, Switzerland and Paris, France from 26 to 28 March.

(2) 11 visitors related to Chelyabinsk

1) RERF/Branch N1, Institute of Biophysics (FIB-1) collaboration agreement. One doctor from Ozyorsk, the Russian Federation from 17 September to 14 October; two specialists from Ozyorsk, the Russian Federation from 25 September to 18 October.

2) RERF/Urals Research Center for Radiation Medicine (URCRM) collaboration agreement. Two specialists from Chelyabinsk, the Russian Federation from 17 September to 14 October.

3) Marubeni Utility Services, Ltd. Two specialists from Moscow, three specialists from Ozyorsk, and one specialists from Snezhinsk, the Russian Federation on 7 October.

(3) Other visitors (17 persons)

1) Japan Atomic Energy Research Commission. For training, seven trainees from the 1996 Nuclear Medicine Study Meeting of Nuclear Medicine from the People's Republic of China, Southeastern Asian and African countries on 10 September.

2) Community Hygiene Services, Department of County Public Health, San Francisco. One doctor from San Francisco, USA from 20 to 27 September.

3) Faculty of Medicine, Osaka University. For training, eight trainees from the "Course of Advanced Medical Radiological Technology, FY96" from Central and South American, African and Southeast Asian countries on 12 December.

4) International Atomic Energy Agency (IAEA). One doctor from Ankara, Turkish Republic from 11 to 13 March 1997.

2. 55 visitors related to Japan International Corporation Agency (JICA)

1) Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association. For training, fifteen trainees from the "1996 Group Training Course in Tuberculosis Control for Administrative Medical Officers" from the People's Republic of China, Southeast Asian, African and Central and South American countries on 27 May.

2) Japan Atomic Energy Research Commission [same as (3), 1)]. For training, seven trainees from the 1996 Nuclear Medicine Study Meeting from the People's Republic of China, Southeastern Asian and African countries on 10 September.

3) Japan Chemical Analysis Center. For training, five trainees from the "Course of Environmental Radioactivity Analysis and Measurement, FY96" from Southeast Asian countries on 4 October.

4) National Cancer Center Research Institute. For training, ten trainees from the "Course of Clinical Oncology Ⅱ, FY96" from Central and South American, Southeast Asian and African countries on 17 October.

5) National Cardiovascular Center Research Institute. For training, nine trainees from the "Cardiovascular Diseases Course, FY96" from Central and South American, African and Southeast Asian countries on 6 November.

6) Faculty of Medicine, Osaka University [same as (3) 3)]. For training, eight trainees in the "Course of Advanced Medical Radiological Technology, FY96" from Central and South American, African and Southeast Asian countries on 12 December.

7) International Atomic Energy Agency (IAEA) [same as (3) 4)]. One doctor from Ankara, Turkish Republic from 11 to 13 March 1997.

3. Other visitors (216 persons)

1) Hiroshima University School of Medicine. Three medical students from the US on 11 April; one doctor from Surrey, England on 13 May; seven Hiroshima University international exchange students on 22 August; one doctor from Melbourne, Australia on 29 August; one doctor from Nairobi, the Republic of Kenya on 25 February 1997; twenty-one Hiroshima University international exchange students on 12 March 1997.

2) International Exchange Center, Meiji Gakuin University. Sixteen exchange students from the University of California, USA on 1 May.

3) Radiation Effects Association. One doctor from Ferrara, Italy on 12 July.

4) Hiroshima International Cultural Foundation, Inc.
Three reporters and others in the "Asian Reporters Invitation Project" from the People's Republic of China and Kazakhstan on 1 August.

5) Hiroshima Peace Culture Foundation. Twenty visitors from the '96 UN Disarmament Fellowship Project from countries of North, Central and South America, Southeast Asia, Africa, former Soviet Union, Europe, Middle and Near East and Oceania on 15 October.

6) Japan Atomic Energy Research Commission. Two specialists from Ozyorsk, the Russian Federation on 12 December.

7) Nagasaki Association for Hibakushas' Medical Care (NASHIM).
One doctor from Kiev, Ukraine on 4 March 1997.

8) Radiation Effects Research Foundation. Seventeen visitors from the Workshop on Biological Dosimetry and ESR including two doctors from Moscow, the Russian Federation, one doctor respectively from Chelyabinsk and , the Russian Federation, Munich, Germany, Washington, DC, and San Francisco, USA.

9) Others
122 researchers, doctors and others visited RERF individually.

【RERF Nagasaki: 20 persons】

1. 14 visitors accepted through Nagasaki Association for Hibakushas' Medical Care (NASHIM)

(1) 11 visitors related to Chernobyl

1) Japanese Ministry of Foreign Affairs. One doctor respectively from Novozybkov and Obninsk, the Russian Federation on 11 April.

2) Nagasaki Association for Hibakushas' Medical Care (NASHIM).
One doctor from Mogilyov, the Republic of Belarus, and one chief nurse respectively from Gomel, the Republic of Belarus, Klintsy, the Russian Federation, and Kiev and Korosten, Ukraine on 18 April.

3) Sasakawa Memorial Health Foundation. Two specialists from Mogilyov, the Republic of Belarus and one specialist from Moscow, the Russian Federation from 29 July to 18 September; one specialist from Kiev, Ukraine from 22 February to 16 March 1997.

(2) Other visitors (3 persons)

1) Nagasaki University School of Medicine.
Two doctors from São Paulo, Brazil on 17 April.

2) Republic of Korea Red Cross Society.
One doctor from Seoul, the Republic of Korea on 19 September.

3. 6 visitors related to Japan International Corporation Agency (JICA)

1) Okinawa Prefectural Institute of Health and Environment.
Six trainees from countries of Southeast Asia, North, Central and South America, Oceania and Europe enrolled in the "Public Hygiene and Environmental Contamination Analysis Course for FY96" on 22 November.

(RERF Translation Office - 16 Apr 97)
seuh-6

Development of an A-bomb related material database system

Under a contract with the Japanese Ministry of Health & Welfare (JMHW) and with the advice of the Committee on the A-bomb materials and Information Network composed of the experts outside RERF, RERF has developped a system to provide the services of atomic bomb exposure-related materials and information since 1991.

These services are expected to start to be offered at the two A-bomb deceased memorial and peace praying halls, one of which is to open in Hiroshima in 1998 and the other, in Nagasaki in 1999.

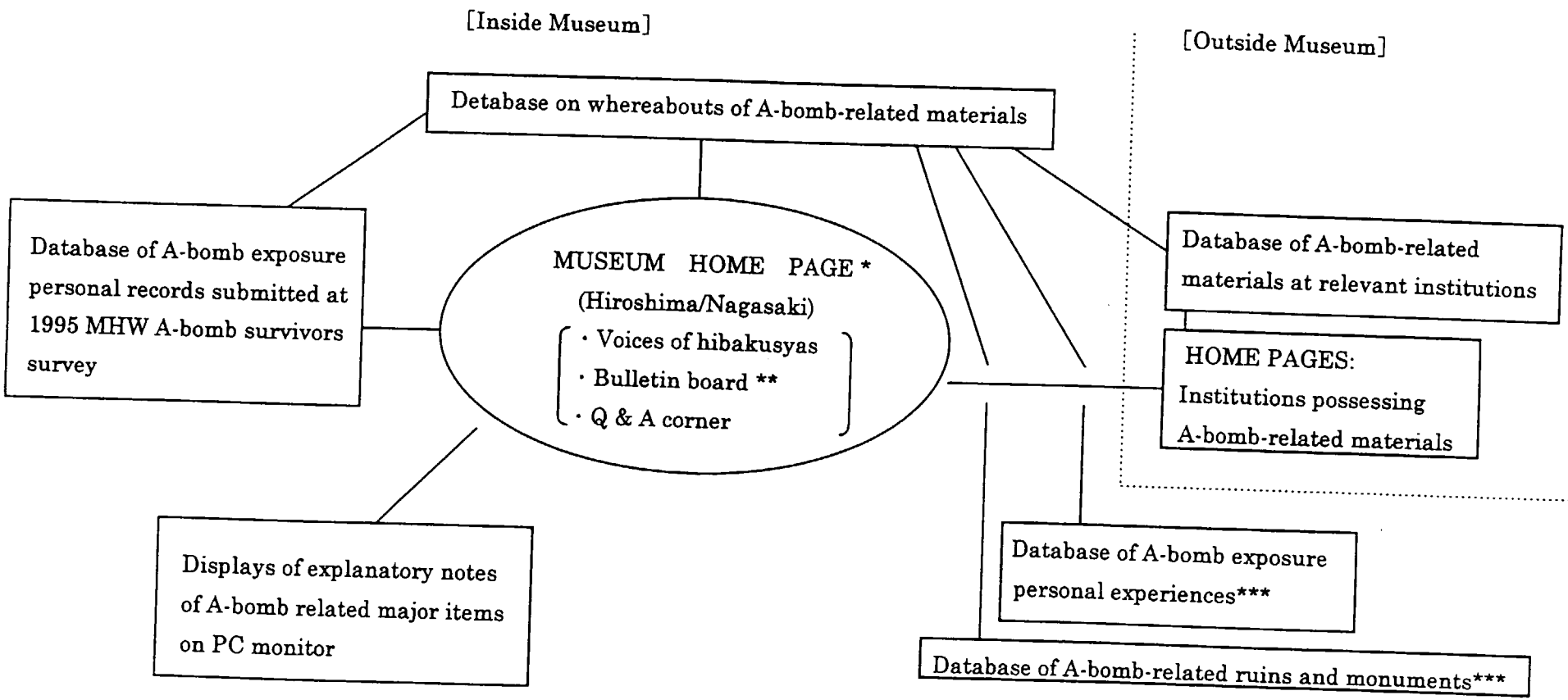
A conceptional illustration of the services is shown in the attached figure.

During FY96, RERF conducted the following pieces of work according to the above-mentioned contract;

1. Inputting about 2,000 data in order to construct a database on whereabouts of A-bomb-related materials
2. Recording by either optical filing or CD-R method the entered questionnaires from the A-bomb Survivors Actual Conditions Surveys of JMHW conducted in 1965, 1975 and 1985.
3. Recording by CD-R method the memoirs of the experiences of A-bomb exposure which was investigated by JMHW in 1995.
4. Construction of a database system for the management, retrieval and mutual uses of A-bomb-related materials.
5. Preparation of displays of explanatory notes of A-bomb-related major items on PC monitor.

Figure1.Information Service of Atomic Bomb Deceased Memorial and Peace Praying Museum

(Conceptional Illustration)



* Includes introductions of institutions that possess A-bomb-related materials, but have not yet set up their own home pages.

** Provisions of information on valuable A-bomb-related materials that have not been noticed.

*** To be started.

[Off-line databeses: Database of information on A-bomb deceased, Database of MHW A-bomb Survivors Survey Data, Database of A-bomb Victims' Medical Data, etc.]

Recommendations of the 23rd meeting of the Scientific Council

23rd Meeting of the Science Council
Radiation Effects Research Foundation
Irvine, CA, U.S.A.
13-15 November 1996

COMMENTS AND RECOMMENDATIONS

The Science Council this year has met under truly exceptional circumstances. Not only is it the first time that the meeting has occurred outside Japan (and we do thank the National Academy of Sciences for its excellent arrangements), but it is perhaps the first time that the meeting has occurred late in the calendar year, thereby missing one entire fiscal year cycle. This was done, of course, so that an independent multinational Blue Ribbon Panel could convene to evaluate the entire RERF mission and to chart its future direction. The deliberations of that Panel have been likened in importance to the two earlier landmark evaluations which occurred some 20 and 40 years ago and which have strongly shaped the remarkable progress of the atomic bomb survivor studies over time. We particularly appreciate the work of the Blue Ribbon Panel since the creation of that Panel followed directly on the specific suggestions which the Science Council made at its last meeting in April 1995. The present meeting of the Council, therefore, has been of special significance. It is important to note that all Councilors were present, except Dr. Motulsky who was detained at the last minute but who provided active input through written comments and telephone contact.

Since the setting for our meeting has been unusual, we shall depart from our regular practice of commenting mainly on specific research activities within specific RERF departments. Instead, we will focus on certain over-riding organizational issues and research philosophies which underlie the Blue Ribbon Panel's recommendations, ideas which are also reflected in the responses made by the RERF staff in their thorough and careful presentation of future strategic plans. By making such a departure, we believe we can best fulfill the central mission of the Council at this particular time which is to assess RERF research progress and to advise on its future course. This has practical importance since, although the Blue Ribbon Panel has strongly indicated how future work should proceed, the practical constraints on resources which limit RERF productivity are still a difficult reality.

We therefore propose first to comment on the Blue Ribbon Panel recommendations, together with the RERF responses to them. We will then consider the general panorama of strategic planning which the staff has presented, including some selected comments on particular departmental activities. Along the way, however, we will particularly focus on three matters which we believe are of critical concern at present: first, the proposed F_1 survivor studies; second, the future functions of the Science Council itself and their relation to formal processes of peer review; and third, specific organizational arrangements by which future RERF research can best be guided.

The Blue Ribbon Panel Report

The 21 recommendations contained in the Blue Ribbon Panel report cover the entire spectrum of RERF activity. **We approve of virtually all the recommendations as they stand and of the staff responses to them.** Fourteen of the 21 recommendations address the importance of specific ongoing research activities: the central role of epidemiologic and statistical work (Recommendations 1, 2, 3); the critical value of the LSS and AHS upon which virtually every research investigation depends (Recommendations 5, 6, 12); the need for obtaining and preserving biologic specimens derived from the various survivor populations (Recommendations 8, 9, 15); and the many laboratory-based research investigations involving genetic and radiobiologic techniques (Recommendations 7, 10, 11, 13, 14). In particular, we would highlight Recommendations 6 and 7 which recognize the direct benefits of the AHS and the FI Survey for the welfare of survivors and their offspring.

The remaining seven recommendations concern support and guidance of research: the information systems and data management needs of RERF (Recommendations 4, 21); the importance of collaborative work with outside research groups (Recommendations 19, 20); the constant and ongoing requirements of strategic research planning (Recommendation 16); and the essential nature of candid outside evaluations regarding research quality and productivity (Recommendations 17, 18). As already suggested, two pairs of recommendations have received our particular attention: Recommendations 7 and 13 which concern the matter of F_1 follow-up and Recommendations 17 and 18 which concern restructuring the Science Council and instituting formal departmental peer reviews.

F_1 Follow-up

The Blue Ribbon Panel suggests the possible scientific value of F_1 studies in clarifying radiation-induced genetic effects in relation to the occurrence of common multifactorial diseases. In response to that suggestion, and recognizing the widespread and long-standing concern about possible F_1 effects, RERF proposes a feasibility study to ascertain disease and disability among F_1 adults. **That proposal requires more planning and refinement before implementation.** Data presented by RERF scientists indicate that the majority of F_1 adults will not reach the age at which the major non-cancer diseases become prevalent for at least one or two decades. Therefore, the scientific basis for a comprehensive study in the near term is weak. In addition, rough estimates suggest that atomic bomb radiation is not likely to increase multifactorial disease by more than about one percent. Detecting such a small increase would require a population sample larger than the entire F_1 cohort. **Nevertheless, the Science Council does recommend that a tightly focused study be undertaken.** Such a study should have two components: 1) clinical examination of those F_1 adults who were previously examined in the Biochemical Genetics Study, and 2) a mail questionnaire survey of a sample of F_1 adults in which disease risk factors (smoking habits, etc.), are ascertained. Sample size should provide sufficient power to be useful in analyzing the F_1 mortality data already being collected. The survey should avoid asking health outcome questions, since such questions would be subject to considerable

observer bias. Sampling might first select those persons whose parents had clearly increased exposure by DS86 measurements, and then draw a limited sample from the remaining F_1 cohort. This approach would have a greater chance for achieving full follow-up than surveying the entire cohort. Considerable difficulty can be anticipated in tracing F_1 members since ongoing contact has not been maintained over the years. **Before the study is initiated, its protocol should be carefully evaluated and approved by a bioethics review committee** to assure the protection of the rights and welfare of the F_1 adults and their families. In that context, **increased attention should be given to providing full information to survivors and the public regarding the actual extent of atomic radiation exposures and their health effects.**

The Science Council and Peer Review

The Science Council agrees with the Blue Ribbon Panel that the terms of the Councilors should be limited and staggered. As indicated by the Panel, each Council member should be appointed for a 5-year term only, with the possibility of renewal for a second 5-year term in special cases. It is important to have a continually rotating Council that will bring new Councilors with new ideas and expertise to the Council at regular intervals. Councilors will be appointed by the RERF, in consultation with the Ministry of Health and Welfare (for Japanese Councilors) and the Department of Energy through the National Academy of Sciences, (for American Councilors), and with an eye to maintaining a distribution of disciplines appropriate to the RERF research agenda.

The Science Council also agrees that an in-depth, multinational peer review of each of the major Departments should be carried out every 5 years on a rotating basis. This review should be the responsibility of the Science Council which will choose appropriate panels of reviewers from Japan, the United States, and elsewhere in consultation with the National Academy of Sciences and perhaps members of the Blue Ribbon Panel itself. It is important to assure diversity of input in these reviews. Each review will be co-chaired by two members of the Science Council (one Japanese, and one American). These reviews will take place separately from the regular meetings of the Council; the report from the Peer Review Committee will be presented to the Council at its next regular meeting. Reviews will be of such central importance for the RERF scientific program that they should be fully supported, despite budgetary stringencies.

The regular annual meetings of the Science Council should continue and should be clearly distinct from the peer reviews. They should have two objectives: 1) to receive and discuss the recommendations of any peer review conducted in the preceding year; and 2) to conduct programmatic reviews of RERF activities. The latter review would focus on projects or programs that are interdepartmental in nature. Such programmatic reviews, along with the in-depth departmental peer reviews, should enable the Council to improve its assessment of the overall RERF program and to play a more active role in guiding RERF research.

The Strategic Research Plan

The 5-year plan developed by RERF staff in response to Recommendation 16 from the Blue Ribbon Panel is remarkable both in its comprehensive detail and in the speed with which it has been assembled. We applaud the logical structure of the plan and its consistent awareness of the need to consider a full research agenda and yet to recognize priorities. The detailed accounts of particular research projects are too numerous for us to review usefully one by one, so we would only comment on general principles which need to guide the 5-year planning process and which are already evident in the plans presented. In addition to prioritization, especially in the face of diminished resources, we would stress the importance of focusing each research project on specific, concrete outcomes, emphasizing work which directly addresses the unique data resources of RERF (the survivor populations) and resisting the temptation to over-reach specific objectives. Project-oriented workshops, held from time to time, and involving suitable international experts from outside RERF may help in developing well-focused research. Workshop topics might include: 1) feasibility and design of F_1 studies; 2) molecular epidemiology and oncology; 3) non-cancer diseases, including benign tumors; 4) dosimetry issues, including differences between Hiroshima and Nagasaki; 5) new DNA technology for mutation detection; and 6) storage and utilization of biological materials. Since workshop scientists often have little prior awareness of the facilities, data, biological specimens, and other resources available at RERF, a videotape designed to provide such orientation might be useful. The video could be sent along with other materials to all workshop participants well in advance of the workshop so that valuable workshop time would not need to be spent providing such background information.

LSS and AHS data collection. Ongoing collection of data on mortality and cancer incidence in the LSS cohort must continue to have highest priority. While the interpretation of such data may be affected by some continued uncertainty in estimates of neutron dose, hopefully those uncertainties can soon be resolved through clarifications in physical dosimetry and integration with biologic measures. In the meantime, close attention to those cohort members who were young or in utero ATB is of increasing importance as they enter the adult years when cancer and other diseases are most common. Clinical studies of the aging AHS cohort are of equal importance, as are the maintenance of tumor and tissue registries linked to the cohorts in the Nagasaki and Hiroshima areas. Proper preservation and pathology review of tissue specimens is critical in this process, with adequate linkage to epidemiologic data. If in the future RERF is relocated near the planned cancer center in Hiroshima, collaborative links with medical schools and major hospitals, including qualified pathology centers, should be fostered. It would also be valuable to establish a tissue collection and use committee to guide this tissue registry work.

Non-cancer outcomes. Much attention in our meeting, and in fact at every Council meeting in recent years, has focused on possible radiation-related non-cancer outcomes. Clearly, the survivor populations offer a special opportunity to look at such health outcomes, although studies must be done with close attention to possible confounding factors. While we realize the importance of this topic because of the frequency of non-cancer diseases,

particularly as populations age, **we believe that RERF research priorities still rest principally with cancer and with specific genetic damage.** The absence of concrete evidence regarding mechanisms of radiation action in non-cancer outcomes and the lack thus far of corroborative evidence from other population studies leave this topic much in limbo and hence of lower priority, we think, than cancer and genetics. This should not preclude continued research analyses, of course, and perhaps organizing an exploratory workshop, but it should re-emphasize priorities.

Family aggregations. Another recurring theme in recent Council meetings has been that of discrete familial aggregations within the survivor populations and their potential value for radiobiologic or genetic research. Here we believe there is a need to focus on particular family sets (sib-sib or parent-child pairs, for example) which may provide opportunities for discrete genetic studies of related persons in whom particular cancer outcomes are documented against a background of known radiation exposure and genetic relationship. The broader undertaking of constructing a full database documenting all family relationships among LSS subjects is not necessary in this context and in fact would divert critical resources away from higher priority research objectives.

Molecular epidemiology. The recurring topic of molecular epidemiology is of pervasive importance. Certainly the many RERF data sets, at least on the surface, lend themselves particularly well to this promising research approach. It is therefore all the more important, when any molecular epidemiology or molecular oncology study is contemplated, to develop a concrete research plan designed to test a clearly defined hypothesis. Such a plan must include use only of markers which are fully documented and are closely relevant to the stated research objectives. The need to focus research plans in this way is of paramount importance, whether or not resources are restricted.

RERF Organization and Staffing

We have given special attention to matters concerning RERF organization, because such matters directly influence resource utilization and hence effectiveness of the 5-year planning process. The recent budget crisis has shaken the underlying infrastructure of RERF. **The Council cannot emphasize strongly enough the importance of rebuilding and maintaining adequate support for research.** Even with the restoration of job slots for professional personnel, the budget over the next several years will be flat and thus in effect will not allow the usual annual increases required just to keep pace. For this reason, further economies, including further reductions in staff and resources, will be required in the future. The question remains, how to maintain a strong scientific program in this context?

One move toward achieving greater economy with minimal loss of scientific productivity would be to combine the Departments of Genetics and Radiobiology. The Radiobiology Department was formed relatively recently, and its role in the RERF research program is not yet clearly defined. Since the nature of its program (molecular epidemiology, molecular oncology, and immunology) seems to interdigitate well with that of the Genetics

Department, **the Science Council suggests that RERF consider merging the Genetics and Radiobiology Departments into a single consolidated unit.** This change could take place at the time of the retirement of Dr. Satoh in 1997. This reorganization would permit a unified attack in the important areas of molecular epidemiology and oncology, as well as an integration of the studies of genetic and cytogenetic endpoints which are presently proposed in both departments (the immunology program might continue as a separate research area in the new department). It is becoming more and more the case that both disciplines involve use of similar laboratory facilities and procedures. A merger would therefore allow for a pooling and eventual sharing of resources such as equipment, reagents, and even personnel. The possible economies are compelling.

We strongly endorse plans of the various departments to replace key professional personnel lost by attrition over the past few years. For some departments, such as the Department of Epidemiology which has lacked a critical mass of professional staff for the past several years, the goals outlined in their strategic plan cannot be realized unless such hiring occurs. In this context, the plans to institute new hiring practices are also encouraged. Such practices include both hiring professionals under contract for specified finite periods and recruitment of postdoctoral fellows from abroad and from Japanese universities. The latter approach would particularly strengthen the ties of RERF with academic communities in Japan. The timing may be ripe for such a change, as Japanese universities are becoming more flexible in allowing joint appointments with other institutions. The hiring of professional personnel under contract would secure the help needed from experts in areas where RERF staff lacks expertise (e.g., for the Department of Statistics in the analysis of longitudinal data, image analysis, and genetic epidemiology, and for the Department of Information Technology in the design and implementation of data security systems and the training of departmental personnel in the use and management of such systems). Contract hiring would also allow a period of a few years in which to try out a scientist before offering him or her a permanent position.

The Council urges the rapid reinstitution of a second full-time American Director. The two full-time U.S. Directors have had integral roles in the successful operation of the RERF research program. Continuation of a strong and productive research effort is also critical for the welfare of both survivors and their offspring. Dr. Schull (and Dr. Abrahamson before him) had no choice but to do the job of both U.S. Directors single-handedly, aided fortunately by long prior experience working at the RERF. In a few weeks, however, Dr. Wolff, who is a newcomer to RERF, will be taking over as the sole American Director. At best, his situation is likely to be difficult.

The prospect that RERF may relocate in close proximity to the proposed Hiroshima Cancer Center is most welcome. This further integration of the Foundation into the local medical and research community is highly desirable, and it will help to strengthen the research program of the RERF in the face of continuing resource restrictions.

Responses to recommendation of the 23rd meeting of the Scientific Council, and "Five Year Strategic Research Plan and Program Management"

20 January 1997

Responses to the Science Council Recommendations

At the 23rd Meeting of the Science Council of the Radiation Effects Research Foundation held in Irvine, California on 13-15 November 1996, the Councilors reviewed the Five Year Strategic Research Plan and Program Document as well as the recommendations of the Blue Ribbon Panel and the Foundation's responses to the latter. As an outgrowth of that review, the Council made a series of comments and recommendations. Specifically, they were the following:

"We approve of virtually all the recommendations (of the Blue Ribbon Panel) as they stand and of the staff responses to them."

As to the proposed F_1 Follow-up, the Council noted "that proposal requires more planning and refinement before implementation." They further stated that "Nevertheless, the Science Council does recommend that a tightly focused study be undertaken." However, they opined "Before the study is initiated, its protocol should be carefully evaluated and approved by a bioethics review committee" and that "increased attention should be given to providing full information to survivors and the public regarding the actual extent of atomic radiation exposures and their health effects."

With regard to the proposed changes in the terms of appointment of the Councilors, they observed that "The Science Council agrees with the Blue Ribbon Panel that the terms of the Councilors should be limited and staggered." They further noted that "The Science Council agrees that in-depth, multinational peer review of each of the major departments should be carried out every 5 years on a rotating basis." However, "The regular annual meetings of the Science Council should continue and should be distinct from the peer reviews."

The Council further observed, with respect to the studies of noncancer mortality and morbidity" that "we believe the RERF research priorities still rest principally with cancer and specific genetic damage."

"The Council cannot emphasize strongly enough the importance of rebuilding and maintaining adequate support for research."

"The Science Council suggests that RERF consider merging the Genetics and Radiobiology Departments into a single consolidated unit."

"We strongly endorse plans of the various departments to replace key personnel lost by attrition over the past few years."

Finally, "The Council urges the rapid reinstitution of a second full-time American Director."

Although we appreciate all of these suggestions and recommendations, some lie outside the Foundation's capacity to effect. For example, although we strongly support the reinstitution of a second full-time American Director, this matter involves a decision on the parts of the Ministry of Health and Welfare and the Department of Energy and not the Foundation. Until the realization of a second director, we are considering the appointment of an "Associate Chief of Research," who will assist the Chief of Research in the scientific activities of the latter office. Similarly, we cannot ensure the availability of adequate support for the Foundation's research program, we can only urge that it be forthcoming from the funding agencies. Nonetheless, we value the support these suggestions imply and will do all that rests within the Foundation's authority and ability to implement them.

Three of the above comments and recommendations are clearly within the scope and abilities to implement.

First, as to the restructuring of the Science Council, steps have already been taken to secure the approval of the Board of Directors to make the recommended changes. Similarly, with the cooperation of the staff, the National Academy of Sciences, the Ministry of Health and Welfare and the Department of Energy, we have begun the identification of reviewers for the recommended peer review process. Hopefully, the first of these reviews can occur late in the autumn of 1997.

Second, concerning the F_1 study, a new sampling strategy has been devised (see annexes 1 and 2), and a committee has been appointed to prepare the survey questionnaire and a research protocol for evaluation by the Human Investigations Committee and the Research Protocol Committee. The drafting committee includes representatives from the two cities as well as the four departments involved in the proposed study, namely, the Departments of Clinical Studies, Epidemiology, Genetics and Statistics. We will take cognizance of the Council's recommendation that the questionnaire not include self-appraisals of health status nor self-reported diseases. However, at the urging of the Councilors and the members of the F_1 cohort, questions will be included regarding reproductive performance.

Third, as to the suggested merger of the Departments of Genetics and Radiobiology, we recognize the intent of this suggestion. The Executive Committee, while taking into account the possibility of merging the two departments in the future, proposes to reorganize the Department of Radiobiology so as to focus its research activities more sharply and define better intra-departmental responsibilities. The intent is to follow the model that has proven successful in the Department of Genetics, namely, to establish two interacting but partially autonomous laboratories each with clearly defined research objectives and responsibilities. To strengthen the program in molecular biology and more specifically in molecular oncology, the Department of Radiobiology has revised its Five Year Plan focusing on human related research and activities that can only be done at the Foundation (see annex 3). While the revised plan needs further honing, the plan as it presently stands is appended to these responses, and we seek the reactions of the Councilors. Before any decision with regard to a merger of the two departments can occur, it will be necessary to resolve the following inherent problems: (a) the dramatic expansion

of personnel in one department which would result, (b) the loss in identity of the Genetics Program, one of our stronger research activities at the Foundation, and (c) the deterioration of scientific morale as a result of a merger.

Finally, as recommended by the Blue Ribbon Panel and endorsed by the Science Council the Foundation has initiated steps to strengthen its relationship to other academic and research institutions in Japan. Two such initiatives are especially worthy of note. First, the Foundation is actively involved in the planning of the projected new Prefectural Cancer Center, and has been encouraged to play a major role in the epidemiological research at this Center (see Annex 4). This association promises to be an especially fruitful one, and will ultimately provide an opportunity to collect more complete cancer incidence data than is presently possible, and access to tissue specimens of substantial value to the Foundation's research in molecular oncology. Second, collaborations have been initiated with the Department of Computing Science and Intelligent Systems at Oita University and the Department of Intelligent Systems at the recently established Hiroshima City University. In both instances the intent is to provide a source of recruitment, training, and computational consultation in areas of the computing sciences of immediate relevance to the research and supportive services of the Foundation. We will continue to explore and define other collaborative programs with institutions both in Japan and elsewhere. These efforts will not be restricted to the Foundation needs in the computing sciences but will extend to all research departments.

ANNEX 1

放影研
RERF

Radiation Effects Research Foundation

Inter-Office Memorandum

December 16, 1996

To: I Shigematsu, WJ Schull, S Wolff

From: D.L. Preston, K. Mabuchi, Y Shibata

Subject: F1 mail survey sampling plan and budget estimate

In our original plan for the F_1 "feasibility" included a mail survey of the full F_1 cohort (~88,000 people). The Science Council endorsed the idea of a mail survey but felt that this survey should be limited to a "sample of F_1 adults". The Science Council also recommended that the mail survey "avoid asking health outcome questions". We have developed a modified plan for an F_1 mail survey taking into account the recommendations of the Science Council. This note provides some background data on parental exposure status and dose estimates for the full F_1 cohort and outlines a sampling plan for the mail survey that would provide us with sufficient data for subsequent analyses of mortality and cancer incidence in the cohort. This memo includes a rough estimate of the costs of conducting a survey based on the proposed sample. We do not address the types of questions to be asked in survey in this note. This topic will be discussed elsewhere.

Based on the plan and cost estimates outlined below we propose to survey about 39,000 members of the F_1 cohort with a budget of about ¥48,000,000 (excluding personnel costs) and would require two to three years to complete.

The F_1 Cohorts.

The F_1 cohort includes 88,484 people in four overlapping subcohorts that were defined on the basis of four sample selections. The cohorts are:

F_1 Study Cohorts

Cohort	Size	Description
F1 Mortality Cohort	76,814	Used as the basis for mortality and cancer incidence analyses.
Biochemical Genetics Study (BGS) Cohort	23,675	People who were selected for and examined in the course of the BGS study that was carried out between 1976 and 1984(?).
Cytogenetics Study (CS) Cohort	16,392	People who were selected for and examined in the F_1 cytogenetics studies carried out between 1967 and 1985
Peripheral Lymphocyte Culture Study (PLC) Cohort	3,690	People who were selected for the PLC studies. In contrast to the BGS and CS groups, this cohort includes all people who were selected as potential candidates for PLC, whether or not cultures have been obtained. The cohort was defined in 1986 and the study is continuing.

All members of the last three cohorts listed above have, at some time, been invited for a clinical examination at RERF and, thus, are aware of RERF's interest in their vital status and health. We will refer to these cohorts collectively as the F_1 clinical cohort. While, as indicated above, the clinical cohorts are not distinct, they are also not nested. There are total of 26,401 people in the combined clinical cohorts, which will be referred to collectively as the *clinical cohort* herein.

The sample selections from which these cohorts were defined are described in the following table:

F_1 Selection Samples

Sample	Year	Size	Description
F_1 Mortality Original Sample	~1960	53,519	People born between to May 1946 and December 1958 with one parent in the cities at the time of the bomb. Formed using ABCC records to define a cohort of all children with at least one proximal parent (< 2 km) from the hypocenter ATB together with age, sex, and city matched controls from two groups: 1) one or both parents between 2.5 and 10 km from the hypocenter ATB; 2) neither parent in the city ATB.
F_1 Mortality Extension Sample	1975 - 1984	23,298	All people with at least one parent in the extended Life Span Study (LSS) cohort who were born between 1959 and 1984.
BGS Extension Sample 1	1975	5,544	People born between May 1946 and December 1958 at least one of whose parents is in the extended LSS cohort.
BGS Extension Sample 2	~1980 - 1984	6,123	People born between May 1959 and December 1984 at least one of whose parents is in the Nagasaki distal extension to the LSS cohort.

Mortality follow-up is carried out on a routine basis only for those people included in the F_1 Mortality Original and Extension samples and not for the 11,670 people identified on the basis of the BGS extensions. The following tables summarizes the relationships between the F_1 selection samples and the study cohorts.

Composition of F_1 Cohorts by Selection Sample

	Study Cohorts		
Selection	**Mortality**	**Clinical Cohort**	**Total Selected**
F1 Original Mortality	53,519	14,520	53,519
F1 Mortality Extension	23,295	8,258	23,298
BGS Extension 1	0	2,248	5,544
BGS Extension 2	0	1,375	6,123
Total	***76,814***	***26,401***	***88,484***

Composition of F_1 Clinical Sub-Cohorts by Selection Sample

	Clinical Sub-Cohorts		
Selection	**BGS**	**Cytogenetics**	**PLC**
F1 Original Mortality	12,316	11,740	1,332
F1 Mortality Extension	7,892	2,627	1,980
BGS Extension 1	2,093	1,474	378
BGS Extension 2	1,374	551	0
Total	***23,675***	***16,392***	***3,690***

Parental Exposure Status and Doses in the F_1 Cohorts.

In order to develop a sampling plan for the mail survey it is important to examine information on the distribution of parental doses. The following tables summarize these distributions for both the full F_1 cohort and the clinical cohort. In these tables the category of *< 0.005* includes parents who are known to have been outside the cities at the time of the bombs (ATB). The *No Info* category includes people for whom RERF's records contain information about location at the time of the bomb. It is likely that most of these people were not in the cities ATB. The *Unknown* category includes people who were exposed but for whom it is not possible to compute a DS86 dose estimate. All of these people are

reported to have been within 2000m of the hypocenters ATB and are likely to have received appreciable doses. (Results of analyses of the LSS cancer data suggest the mean doses for these people are typically 1 Gy or more).

Parental Exposure Status and Dose Estimates
Full F_1 Cohort

Mother's Dose (Gy)	Father's Dose (Gy): No Info	< 0.005	0.005 - 1	1+	Unknown	Total
No Info	72	5,987	5,902	494	687	13,142
< 0.005	6,719	36,386	3,891	654	1,780	49,430
0.005 - 1	7,381	9,116	2,707	169	557	19,930
1+	507	856	96	43	46	1,548
Unknown	786	3,103	333	40	172	4,434
Total	15,465	55,448	12,929	1,400	3,242	88,484

The gray-shaded region indicates the group to be selected as the "exposed" group for the mail survey. The mail survey comparison group will be defined as a sample of the group whose parents have known low (< 0.005 Gy) exposures (black shading).

Parental Exposure Status and Dose Estimates
Combined Clinical Cohorts

Mother's Dose (Gy)	Father's Dose (Gy): No Info	< 0.005	0.005 - 1	1+	Unknown	*Total*
No Info	24	1,818	1,908	189	251	4,190
< 0.005	1,930	7,989	1,625	411	547	12,502
0.005 - 1	2,320	3,901	1,107	96	181	7,605
1+	168	528	45	26	13	780
Unknown	230	926	104	14	50	1,324
Total	4,672	15,162	4,789	736	1,042	26,401

The shaded region indicates the group to be selected for the mail survey. As discussed below all members of the clinical cohort whose parents have known DS86 doses will be included in the mail survey.

Size And Structure of the F_1 Mail Survey Sample

The Science Council recommended that the sample for the mail survey include "those persons whose parents had clearly increased exposure by DS86 measurements" and a "limited sample from the remaining F_1 cohort." To implement this recommendation we need to define what is meant by a "clearly increased exposure".

In order to insure complete coverage of the groups of most interest, we suggest that the "exposed" group be defined to include the 18,791 people in the following groups:

1. people for whom the exposure status of both parents is known and who had at least one parent with a DS86 dose of 0.005 Gy or more (17,532 people);

2. all other people for whom the estimated dose for one parent is 1 Gy or more (1087 people);

3. all other people both parents were exposed but the DS86 dose is unknown (172 people)

An equal number of controls would be selected from the group of 36,386 F_1 cohort members with known parental exposure status for whom neither parent's dose exceeds 5 mGy. Controls would be matched to the exposed on the basis of sex, city, and birthdate (within 30 days). In addition to the matched controls it would also be useful to obtain survey data on all unselected members of the clinical cohort for whom the exposure status of both parents is known. This would lead to the addition of about 4000 people.

This definition of the F_1 mail survey sample leads to a sample size of about 41,000, which is comparable to the size of previous mail surveys of survivors carried out by ABCC and RERF (most recently, the 1991 LSS mail survey). At this time about 6% of the members of F_1 cohort are known to have died, so the actual number of people to be surveyed would be about 39,000. The following table summarizes the size and structure of the proposed sample of surviving members of the cohort by city.

F_1 Mail Survey Sample by Sample Group and City

Survey Sample Group	Total	Hiroshima	Nagasaki
Exposed	17460	11355	6105
Matched controls	17460	11355	6105
Unmatched controls *	3800	2100	1600
Total	***38720***	***24810***	***13810***

* Unmatched controls are members of the clinical cohort who were not selected in the matching process

This design insures that virtually all F_1 cohort members whose parents were heavily exposed are asked to participate in the survey. This latter point is important because a key use of the mail survey data will be to assess the role of confounding and bias on any radiation effects that might be seen in future F_1 mortality and incidence studies. In order to avoid biases associated with the fact of selection for earlier clinical studies, it is important for the survey to include F_1 cohort members who are not included in the clinical cohort. Care must be taken, however, when contacting those F_1 cohort members who have not previously been contacted by RERF.

Cost Estimates

We estimate that conduct of this survey will cost about ¥1250 per person. About ¥450 per person will be spent to determine current addresses. (This includes ¥350 for the koseki check and ¥100 for postage). Under the assumption that 75% of those surveyed will respond after an average of 2 contacts per person, we estimate it will cost ¥800 per person for sending and receiving questionnaires. (These costs include ¥90 for printing and ¥700 for postage and ¥10 per person for telephone contacts.) The contact and response rate figures are based on the results of the 1991 LSS mail survey. It is also estimated that 2 FTE clerks will be necessary for handling of survey documents, data entry and other administrative work.

Taking this estimate of the cost per subject (excluding personnel costs) together with the sample size estimate from the last section we arrive at the budget estimate shown in the following table:

Budget Estimate for F_1 Mail Survey

		Total Costs (1000's of yen)		
	Yen per person	Total	Hiroshima	Nagasaki
Address determination	450	17420	11160	6210
Questionnaire	800	30980	19850	11050
Total	1250	48400	31010	17260

Thus, we estimate that a budget of about 27 million yen (exclusive of personnel costs) is needed to carry out the proposed F_1 mail survey. A more detailed breakdown of these is being prepared at this time.

During the first year efforts would center on selection of the sample and the determination of current address for those to be surveyed. The questionnaire would be mailed during the second year.

ANNEX 2

放影研
RERF

Radiation Effects Research Foundation

Inter-Office Memorandum

January 13, 1997

To: K. Mabuchi, Y. Shibata, M. Dote
From: Dale Preston
Subject: F_1 mail survey subject list with control samples

In a previous note I described files that contained basic information on exposed persons in the F_1 cohort and unexposed members of the F_1 clinical cohort who will be included in the F_1 mail survey if it is carried out according to the plan that Dr. Mabuchi, Dr. Shibata, and I outlined in our December 16, 1996 memo. I have now selected additional "control" cases to be included in the survey.

The controls were selected from among F_1 cohort members who do not have a date of death recorded in the research database deaths table and for whom the weighted genital doses for each parent is less than 5 mSv. Controls were matched to the 17,460 "exposed" cohort members on sex, city and date of birth. The selected controls included 4203 members of the F_1 clinical cohorts and 13,257 F_1 cohort members who are not members of the F_1 clinical cohorts. The total number of people in the mail survey sample is summarized in the following table:

	People		
Group	Hiroshima	Nagasaki	Total
Exposed	11355	6105	17460
Matched Controls	11355	6105	17460
Others from clinical cohorts	2138	1517	3655
Total	24848	13727	38575

I have updated the lists described in the previous memo to include all of the people selected for inclusion in the mail survey sample. As before the list, includes SYSID, master file number, city, sex, and birth date. The list is contained in two files: `hirofl.dat` (24,848 people)and `nagafl.dat` (13,727 people). Since not all of the members of the F_1 cohort are included in the routine mortality follow-up and since the frequency with which the death date table in the database is updated is unclear, the list includes a small number of people who are dead.

These lists were created from an MS Access data base that I created using data from the RERF research data base. The controls were selected using a program that was written specifically for this purpose. The database and control selection program will be documented in a later memo.

Cc: S. Funamoto
W.J. Schull
S. Wolff

ANNEX 3

Department of Radiobiology

In line with the recommendation of the Scientific Council that the Foundation's research priorities rest principally with cancer and genetics, we propose streamlining the Department of Radiobiology. The department's role will be primarily to document, at the cellular and molecular levels, the clinical and epidemiological data on cancer morbidity and mortality that have been documented and that are currently being observed among the A-bomb survivors.

Program objectives

As a two pronged attack, the department will be composed of the Laboratory of Molecular Epidemiology and the Laboratory of Immunology. Fundamentally, the Laboratory of Molecular Epidemiology will investigate the molecular changes induced by radiation in cancer tissues of the survivors using paraffin-embedded archival materials. The results from such retrospective studies can provide evidence for the molecular mechanisms of cancer development in the survivors. And the Laboratory of Immunology will investigate the accelerated rate of aging-related-immunosuppression induced by radiation as an etiological factor behind the increased incidence of tumors in the survivors through use of blood samples from the AHS participants. A longitudinal study using cryopreserved and fresh blood samples taken at various intervals in the life of the individual is intended to reveal changes in radiation induced immune dysfunction as the survivor population ages and develops cancer. The results generated in the department will be used to help interpret the increased incidence of cancer and related disorders that have been ascertained in the past and that are currently being observed in the clinical and epidemiological studies of the LSS and AHS at the Foundation.

Workshops

As an aid to orient and focus research in the two proposed core programs in the Department of Radiobiology, holding of molecular epidemiology and tissue collection workshops is of utmost importance for the smooth transition of the department to its more well defined duties.

Core programs

A. Molecular epidemiology

Cancer development is believed to be a multi-step process. The steps are not known but major roles appear to be played by oncogenes and tumor suppressor genes. The former act to accelerate cell growth and the latter to suppress it. Radiation can potentially damage either or both which can lead to uncontrolled growth -- a hallmark of cancer. Such damage is presumed to be the key to the increased risk of various cancers in the survivors. Differences in the frequencies of mutations or types of mutations involving oncogenes and tumor suppressors between the tumor tissues of the exposed and unexposed are anticipated.

A-1. Molecular analyses

The usefulness of preserved tissue specimens from A-bomb survivors has been demonstrated by means of the PCR method which allows the amplification of DNA by over a million fold. Thus PCR makes it possible to study the genes of A-bomb survivors using microscopic quantities of archival tissues from as far back as 1950. There are currently four active Research Protocols based on the epidemiological evidence for an increased risk of cancer among the survivors. These are for the molecular analysis of skin, liver, thyroid, and female breast cancers.

A-1-1. Skin cancer (RP3-93)

We have already prepared DNA from 60 tissue samples of skin cancer and are currently studying the molecular structure of the ras and p53 genes, two of the most commonly mutated oncogenes and tumor suppressor genes, respectively, in human cancers. We will continue this analysis and begin an analysis of the patched gene, which has recently been cloned and found to be frequently mutated in skin cancer.

A-1-2. Liver cancer (RP2-94)

In addition to skin cancer, molecular analyses of liver cancer (total sample number is approximately 800) are on going. Currently, studies of mutations in the p53 tumor suppressor gene, genomic integration of the hepatitis B virus, and the existence of hepatitis C virus RNA in tissue specimens are being carried out. It may take two or more years to complete these analyses.

A-1-3. Thyroid cancer (RP7-93)

Thyroid cancer will be analyzed at the molecular level since it is among the cancers with highest risk seen in the A-bomb survivors, implying that this cancer may be one of the best candidates in the search for an A-bomb radiation-induced unique fingerprint. Thyroid samples will initially be analyzed for RET proto-oncogene aberrations, uniquely associated with thyroid carcinogenesis and likely radiation-induced carcinogenesis, by immunohistochemistry using monoclonal antibodies against the RET protein, which is not expressed in normal thyroid tissues.

A-1-4. Female breast cancer (RP7-92)

Breast cancer has one of the highest increased risks in the survivors. The average excess relative risk (ERR) at 1 Sv is 1.6. This risk is even higher for those survivors exposed at a young age with an ERR at 1 Sv of 3.21 and 2.61 for age ATB of 0 - 9 years and 10 - 19 years, respectively. Moreover, breast cancer is a potential familial cancer that may predispose some women to radiogenic breast malignancies. Thus far, BRCA 1 and 2 have been shown to be the best prospects as genes in the cause of the disease. Since antibodies to detect mutations are commercially available, samples will initially be screened for BRCA 1 mutations by immunohistochemistry.

A-2. Tissue Collection

The success of this core program depends heavily on our ability to obtain appropriate samples from LSS cohort members who are diagnosed with cancer. It is possible to obtain archival material through the tissue registries in Hiroshima and Nagasaki; however better methods

are needed to ensure the availability of the necessary materials from newly diagnosed cases. To achieve this end, RERF is seeking support from the local medical community for the establishment of a community-wide tissue/DNA bank in Hiroshima. This bank would maintain tissue specimens or preserved DNA that could serve as a resource for all interested groups. One of our major roles will be to take responsibility in the preparation of DNA from the samples.

Tissues to be collected will have to have an associated RP describing their use. Once the collected tissue samples are registered in the tissue bank, they will be available for use internally or by outside collaborators. Registration will include entry of the tissues into a database that will catalogue and link them to relevant RERF cohorts.

B. Immunology

A well known effect of whole body irradiation is destruction or damage of the immune system. Furthermore, exposure to ionizing radiation can potentially accelerate immune system aging. Previous analyses of immune function in groups of AHS participants have revealed dose dependent decreases of T-cell immunity which is also associated with aging of the survivors. Such immunosuppression can lead to a variety of diseases of varying severity especially as the person ages. The Laboratory of Immunology will focus on immune function against cancer among the survivors; the working hypothesis being that the cancers were induced by radiation through suppression of the immune system as is supported by a number of clinical observations. The core activity in this laboratory will be tumor immunology involving the retrospective longitudinal analysis of blood samples from A-bomb survivors with and without cancer to detect correlative changes in immune function and latent cancer development. Availability of cryopreserved and fresh blood samples will be crucial in conducting the studies.

B-1. Longitudinal and multidimensional analysis of immune function (RP3-87, RP1-93)

The continued study of T-cell and stem cell function is important because it is one of the few parameters which has demonstrated clear radiation effects. The precision of techniques developed and honed in the somatic mutation studies are usefull too in the detection of significant changes in the T-cell and stem cell populations that are associated with aging and possibly cancer.

It will be vital to establish a comprehensive database on past, present, and future studies of immune function for elucidating the association of altered immune function and radiation-related diseases, especially cancer, as soon as possible. The inclusion into the database of data from the somatic mutation projects, such as the GPA study, and from the HLA typing project will enable investigation of the relationships between radiation-induced immune dysfunction and the degree of stem cell pool reduction and genetic background, respectively. As correlations between certain parameters and diseases are observed using the database, the longitudinal study will be refined to focus on these parameters. For these refined studies, detailed retrospective analyses using cryopreserved blood samples will be utilized.

B-2. Blood cell preservation (RP2-90)

To ensure that appropriate materials will be available for future studies of the late effects of exposure to A-bomb radiation, and to allow the exploitation of potential future technological

advances and scientific discoveries, we are cryopreserving live blood cells from AHS participants in Hiroshima and Nagasaki. From 1990 to 1996 (3 AHS cycles), lymphocytes and granulocytes from 4,420 Hiroshima and 3,766 Nagasaki survivors were cryopreserved. We will continue this effort to complete all AHS participants. In the near future, retrospective studies will also be possible, therefore, as well as follow-up for the survivors who now do not have cancer but who will eventually develop the disease.

Personnel requirements

The staff will be divided into a ratio of approximately 2 to 1 in the Laboratories of Molecular Epidemiology and Immunology, respectively. These two laboratories will be able to carry out their responsibilities with a smaller staff than now obtains. The projected reduction in personnel over the next five years is as follows:

	Present	1997	1998	1999	2000	2001
Research associates						
Molecular epidemiology	5	6	6	6	6	6
Immunology	5	3	2	2	2	2
Technicians						
Molecular epidemiology	3	7	7	7	6	6
Immunology	10	5	4	4	3	3
Technician helpers	2	2	1	1	1	1
Clerks	5	4	3	3	2	2
Total	30	27	23	23	20	20

Equipment budget (x ¥ 1,000)

The current budget for equipment and consumables in the department is approximately ¥27,500,000. With the discontinuation of the somatic mutation studies and refinement of the projects, the department will be able to manage with ¥18,500,000. A five year projection for the equipment budget is given below.

Fiscal year	New/Repl	Item	Q'ty	Unit Cost	Total
1998	R	Autoclave	1	700	700
	R	Laser for FACStar	1	3,500	3,500
1999	R	Deep Freezer	1	2,200	2,200
	R	Power Supply	1	550	550
2000			0	0	0
2001	R	Thermal Cycler	2	850	1,700
			Total		8,650

ANNEX 4 (Draft)

Gist of Hiroshima International Peace Praying Cancer Center (tentative name) Development Plan

Hiroki Nakatani, M.D., Chief, Welfare Health Department, Hiroshima Prefecture

Hiroshima Prefecture has made plans for putting up a cancer center as a high-level specialized medical care facility which the prefecture plans to develop in the near future and is now discussing where the location and its functions should be. In the basic plans which have been developed, the basic features of the cancer center given are 1) the cancer center should have functions of a high level to the point of being acceptable internationally and have in its sight the needs not only of Hiroshima Prefecture but of the Chugoku-Shikoku region as well, and 2) importance is stressed of gainfully using the scientific expertise and findings Hiroshima has accumulated to this date for future development of the cancer control measures of this country and of the world's.

Also it is proposed that the cancer center be prepared to offer, as its basic functions, services in the areas of cancer diagnosis, therapy, palliative care, research (particularly epidemiological research), international cooperation, and education and training.

Considering the above-mentioned basic characters and functions of the cancer center, the resources with which the characteristics of Hiroshima can be made the best use of would be, in the area of diagnosis and treatment, the experiences gained in the medical care of A-bomb survivors and, in the area of research, ABCC/RERF's cumulative achievements in its epidemiological studies of the health effects of radiation which have been continued over the past half a century.

RERF has both the cumulative achievements of epidemiological studies of the health effects of radiation and the experience in medical care of the A-bomb survivors, and it can be considered to be a very important requisite for the realization of the basic feature of 2) that the cancer center be provided its know-how and human resources. And, since RERF is an international institution in terms of its organization and research, the "internationalization," which the cancer center will strive for in its research, can be attained at the same time.

Furthermore, advancement and strengthening of the local cancer registries, the earliest registries in Japan, would be indispensable for the epidemiological studies at the cancer center to promote prevention of cancer among the people of Hiroshima Prefecture. RERF has made many achievements in studies of cancer incidence in the Life Span Study using prefectural tumor registry data with the cooperation of the Hiroshima Prefectural Medical Association and is well-versed in making effective use of these data. Furthermore, the most up-to-date techniques are indispensable in making advanced scientific research. RERF is already conducting molecular epidemiological studies to elucidate the mechanism of carcinogenesis in A-bomb survivors. The cooperation of RERF in this field is to be desired.

As mentioned above, cooperation with RERF in research would be indispensable for the realization of the basic plans of the cancer center. Hiroshima Prefecture hopes that RERF will give serious consideration to scientific cooperation with the cancer center when it develops its future plans.

RADIATION EFFECTS RESEARCH FOUNDATION

FIVE YEAR

STRATEGIC RESEARCH PLAN

AND

PROGRAM MANAGEMENT, 1997-2001

SUBMITTED BY THE RERF EXECUTIVE COMMITTEE

FOREWORD

The Foundation recognizes that it functions in a climate of limited resources, and if these resources are to be used cost-effectively and if the Foundation is to fulfill its mission efficiently, there is a need for continued program planning and management. To conduct all of the research that is deemed important within the current funding level and probable future ones, priorities must be established, some research activities will need to be redirected or terminated, and recruitment of additional scientific personnel may be necessary. The intent of this document is to provide a framework for the establishment of research priorities to guide the allocation of resources and the recruitment of personnel.

Organization of this Strategic Research Plan and Program Management Document

This Strategic Research Plan and Program Management document will give an overview of the origin of the Foundation, its management structure, its mission, its research programs, and its resources. This will be followed by a listing of program objectives, current major research activities and those projected in the next five years, and the related resource requirements for each of the major research departments. This section will be followed by an enumeration of resource and personnel requirements as they relate to the administrative, computer-related, publication and documentation, and radioisotopic services necessary to support the research program. Finally, there will be a section on the maintenance of an adequate infrastructure and a summary and set of conclusions which will also act as the executive summary of this document. Annexes will provide ancillary information too detailed for enclosure in the body of the report.

There are many reasons why a strategic research plan and program management document is timely and necessary. However, the salient ones are the following:

- The members of RERF's survivor cohorts are aging, and the number of cohort members who remain alive will decrease markedly over the next few years. The research program and data collection procedures must reflect these changes. (See Annex A for the current size of the cohort and projections to the year 2020).

- The revolution in biomedical research in the last several decades has opened avenues of research of potentially great relevance to RERF and the understanding of the biological bases of radiation-related damage.

- Recent years and the next several have seen or will see a significant loss in personnel, largely through retirement. This situation requires renewed emphasis on optimizing the proportions of manpower devoted to research and support functions, and the development of innovative ways of achieving the Foundation's aims without increasing the general staff while maintaining a sound level of scientific personnel, for example, through the judicious use of personal services contracts.

- A series of workshops recommended by the Foundation's Scientific Council were conducted between 1988 and 1993 (see Annex B). The recommendations from these workshops have affected RERF's current research and are influencing plans for future research initiatives.

Assumptions used in developing this planning document

In this assessment of the Foundation's needs to support its scientific program, the Executive Committee felt it necessary to adopt certain self-imposed restrictions:

- It was assumed that budgetary limitations will prevent a significant expansion of the Foundation as a whole, that is, the level of support provided by its two funding agencies for research will remain more or less constant (with inflationary increases only).

- It was further assumed that it was critically important to maintain the appropriate array of professional, technical, and clerical skills needed to implement the research.

Within these limitations, the Committee believes that its research activities can still expand through increasing efficiency, through savings created by retirements, and, where possible, through transfer of general personnel positions to research-oriented ones.

The Executive Committee has carefully considered which of all potentially desirable research activities *could only be carried out* by the Foundation, which *could best be carried out* by the Foundation, and which *could be carried out elsewhere*, possibly on a collaborative basis. Prioritization along these lines will avoid the inclusion of research that is not specific to the Foundation's needs and potential, and will therefore reduce needed resources to only those that are most appropriate to RERF.

THE FOUNDATION

In the summer of 1945, the residents of Hiroshima and Nagasaki were in all probability, representative of a typical, heterogeneous wartime population of individuals in Japan. In August of that year, atomic bombs were detonated over these two cities. Soon thereafter a group of Japanese and American scientists, known as the Joint Commission for the Investigation of the Effects of the Atomic Bomb, began the task of assessing the physical damage wrought by the bombings and of identifying the early health effects of exposure to atomic radiation. This Commission, in its final report, strongly recommended the establishment, under civilian auspices, of a program of research to evaluate the long-term health consequences of exposure to ionizing radiation. In November 1946, President Truman approved a directive to the US National Academy of Sciences-National Research Council (NAS-NRC) to initiate the long-term investigation recommended by the Joint Commission. With funding provided by the Atomic Energy Commission (AEC), now the Department of Energy (DOE), the NAS-NRC established the Atomic Bomb Casualty Commission (ABCC) in March 1947, and research began shortly thereafter. The Government of Japan, through the Japanese National Institute of Health, became a partner in this endeavor.

In 1975, the Radiation Effects Research Foundation (RERF) was established and assumed the responsibilities of the ABCC. This private, nonprofit Foundation, a *zaidan hôjin*, is incorporated under Japanese law and its research is equally funded by the Governments of Japan and the United States, through the Ministry of Health and Welfare (MHW) and through the Department of Energy and the National Academy of Sciences, respectively. Administratively, the Foundation is governed by a Board of Directors consisting of 12 individuals, six of whom are Japanese citizens and six of whom are United States citizens. The day-to-day operations are managed by an Executive Committee consisting of four permanent members of the Board of Directors, two from Japan and two from the US, each of whom resides in Japan. The Permanent Directors consist of a Chairman, a Vice Chairman, a Chief of Research, and one other Director, who functions as the head of the Foundation's Nagasaki laboratory. The responsibilities of these individuals, their terms of office, and the like are specified in the Foundation's charter, known as the Act of Endowment.

Functionally, the Foundation consists of five major research departments, namely, the Departments of Clinical Studies, Epidemiology, Genetics, Radiobiology, and Statistics, supported by the Information Technology Department (ITD), the Publication and Documentation Center (PDC), a Radioisotope Facility, and a Secretariat. The ITD is responsible for the maintenance of the computational capabilities of the Foundation; whereas the Publication and Documentation Center and Secretariat are responsible for the publications (print and online) emanating from the Foundation and the administrative details relating to budgeting, personnel, purchasing, and public affairs, respectively. The Radioisotope Facility serves as a resource for those departments, such as Genetics and Radiobiology, requiring the use of radioisotopic materials.

The clinical, epidemiological, statistical, and other investigations are conducted in two laboratories, one in Hiroshima and the other in Nagasaki. The management of both laboratories is the responsibility of the Executive Committee, and the research activities conducted in the two laboratories are coordinated by the Chief of Research. To help conduct RERF's research activities properly there is a series of standing committees such as the Research Protocol and

Human Investigation committees. Review of the research program and recommendations on the relevance and scientific quality of ongoing investigations, as well as future research directions, are provided to the Board of Directors on an annual basis by a Scientific Council. This Council is composed of ten experts in areas of research relevant to RERF, five of whom are from Japan and five of whom are from the United States. As in the instance of the Board of Directors, the process of selection of these individuals, their terms of office, and their responsibilities are specified in the Act of Endowment. In addition, over the last eight years, the Council has been instrumental in the organization of a series of workshops in specific areas of research to provide guidance on promising approaches for possible implementation in the research programs and many of their recommendations have been implemented. (See Annex B for a listing of the recent workshops.)

As of 1 April 1996, the Foundation had 335 employees, 258 in Hiroshima and 77 in Nagasaki. Of these 47 represented the professional research staff, 43 in Hiroshima and 4 in Nagasaki.

The Foundation is housed in Hiroshima in a complex of nine interconnected two-story structures with a gross area of 9,681 square meters (about 105,400 square feet); whereas in Nagasaki, the Foundation occupies a four story building with a gross area of 2,643 square meters (28,780 square feet). The facility in Nagasaki is relatively new, but the bulk of the one in Hiroshima was built in 1950 and is now barely adequate for the Foundation's research needs.

To conduct a broadly based research program involving the collection, processing, and analysis of extensive data on mortality and morbidity in a population as large as that of the survivors and their children, RERF has developed an organization plan (see Figure 1) for the coordination of epidemiological, clinical, and laboratory research conducted in two widely separated laboratories. This plan is periodically reviewed by the Board of Directors and revised as circumstances warrant.

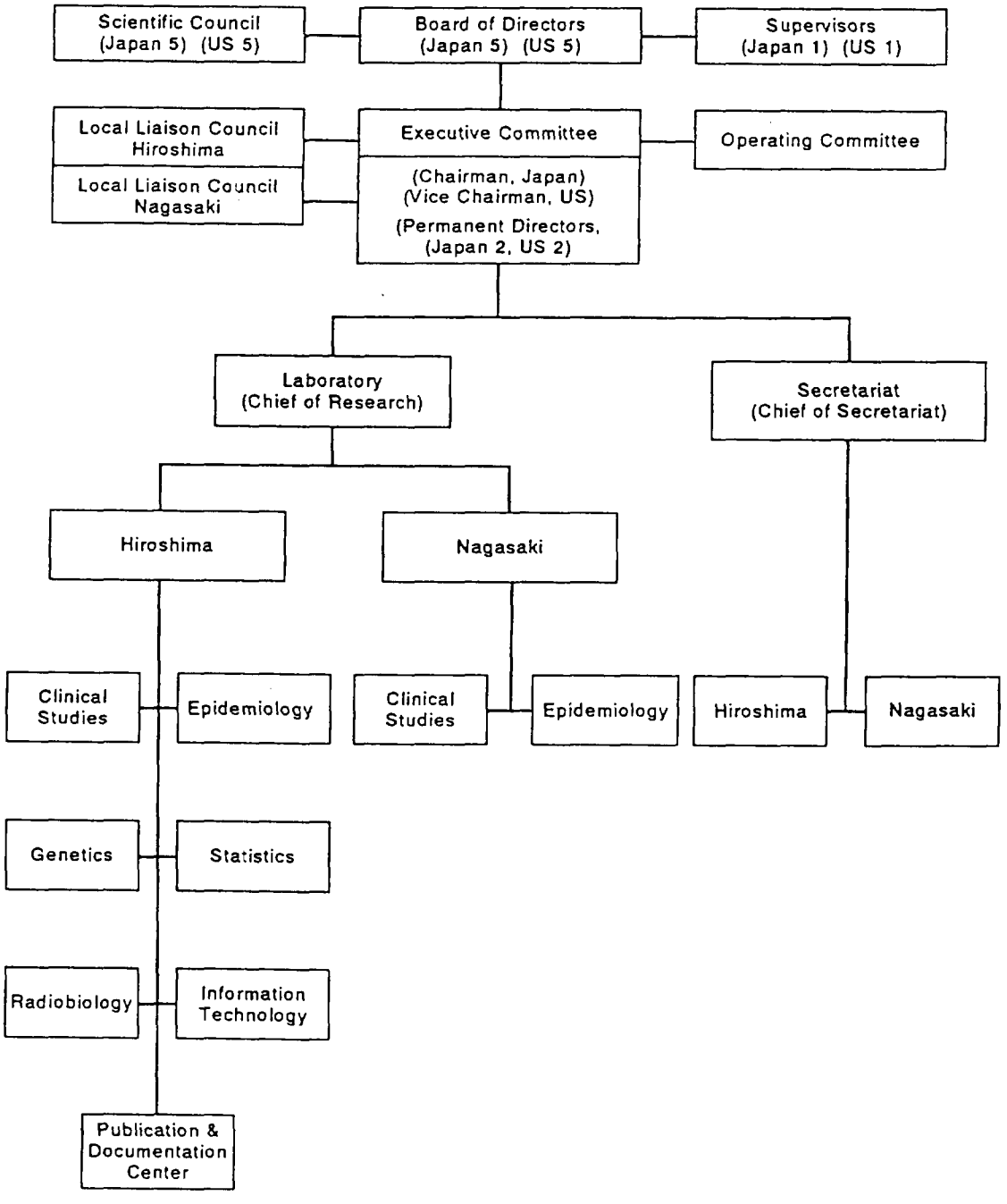
It is important to note that the investigations conducted by the Foundation are the only opportunity in existence for determining the late biological effects resulting from a single exposure to ionizing radiation ranging from very low to high doses. The results obtained in these investigations provide information that will lead to improved health care for the survivors as well as individuals who may be exposed to ionizing radiation elsewhere. Furthermore, the results of these investigations are of fundamental importance to an understanding of the effects of ionizing radiation on human beings and are, therefore, essential for estimating radiation risk and setting safe standards for occupational, medical, and general population exposures. Indeed, the data accumulated by the Foundation is the major source of information on which the standards established by national and international radiation protection bodies rest.

RESEARCH GOALS AND OBJECTIVES

The unique nature and long-term follow-up of this exposed population have provided invaluable information on the early and late health effects of radiation exposure. (See Annex C for some recent summaries of the findings to date.) To ensure that these investigations continue in a productive manner and are focused on radiobiological and health-related issues of importance to the scientific and medical community and the concerned public, it is essential that a careful,

Figure 1.

Organization



continuing evaluation of the research program be made, future directions determined or revised as need arises, and research priorities established. This strategic research plan has been developed to achieve these ends.

To carry out its responsibilities in an orderly and scientifically sound manner and to be responsive to its charter, the broad goals of the Foundation are:

- To determine the late health effects, both somatic and genetic, produced in human beings from exposure to ionizing radiation.

- To obtain information on the temporal pattern of cancer expression and other radiation-related effects and on the role of biological and environmental factors which may modify the effects resulting from exposure to ionizing radiation.

The strategy for addressing these goals is implicit in the following general research objectives:

- To conduct long-term epidemiological studies of a fixed sample of exposed and unexposed individuals to determine the frequency-dose relationships of morbidity and mortality resulting from radiation exposure and to obtain information on the differential sensitivity of various tissues.

- To conduct case-control and other special investigations on cancer induced in specific tissues or organs to determine the cell types affected and the effects of modifying factors.

- To conduct research in molecular and cellular biology to detect somatic mutation, cell transformation, changes in immunological competence and other biological events for use in understanding and estimating radiation risk.

- To utilize all available sensitive and cost-effective approaches for measuring heritable mutation in the children of exposed and unexposed individuals, and for assessing the public health impact of these mutations.

All research at the Foundation aimed at these goals takes place under published research protocols that must obtain the approval of the Chief of Research, the Research Protocol Committee, the Human Investigation Committee, and the Chairman of the Foundation before they are activated. These protocols are of two kinds, the so-called platform protocols that guide the major or core research activities of the Foundation, and special research protocols. The core activities commonly involve more than one department and are collaborative; whereas the specific research activities may or may not be collaborative. A listing of the currently active protocols will be found in Annex I. Of primary importance to the Foundation are, of course, the core activities since ultimately they are the raison d'etre of the institution.

RESEARCH PROGRAM STRATEGY

To conduct a successful long-term epidemiological investigation which addresses the goals of RERF, data must be collected on a continuing, prospective basis using specified samples of

exposed individuals and a matched group of unexposed individuals when a need for a comparison with the latter arises. These data must be collected in a systematic and epidemiologically acceptable manner to reduce the chance of bias or ambiguity affecting interpretation of the results observed.

The first major program to be initiated by ABCC was the Genetics Program, which included observations on the occurrence of major congenital abnormalities, sex, birth weight, viability at birth, and survival during the neonatal period of all newborn infants in Hiroshima and Nagasaki. The study, which began in 1947 and continued until 1954, encompassed some 76,626 infants, with reexamination of a subsample of approximately 20,000 of these infants at age 8-10 months. Although this major clinical program was terminated in 1954, the cohort thus established, with subsequent additions, has been followed for survival since that time, as the F_1 Mortality Study.

Most of the early studies on the survivors themselves were essentially ad hoc, each investigator usually establishing his own study population. In 1955 the Francis Committee reviewed the research on exposed (and unexposed) persons at ABCC and urged the adoption of a Unified Study Program as a permanent research guide. The committee's recommendations were approved and have since provided the basis for much of the current epidemiological and clinical follow-up of the survivors in Hiroshima and Nagasaki. In 1975, prior to the establishment of RERF, a second committee, known as the Crow Committee, reviewed the program and recommended continued investigation of this unique population.

Implementation of the Francis Committee recommendations resulted in the establishment of four major fixed cohorts:

- the Life Span Study (LSS) cohort of survivors and an unexposed comparison group who were alive at the time of the bombings;

- the Adult Health Study (AHS) cohort (a subset of the LSS cohort), whose members are encouraged to participate in a program of standardized biennial clinical examinations carried out at RERF;

- the in-utero (IU) cohort of individuals who were exposed in-utero and matched controls; and

- the F_1 cohort of children born between June 1946 and December 1984 to exposed or unexposed parents.

Follow-up of these cohorts is central to the work of the Foundation. The primary follow-up programs are:

- mortality ascertainment for most members of all of the cohorts through the Japanese family registration (*koseki*) system;

- ascertainment of cancer morbidity through linkage of the cohorts with the Hiroshima and Nagasaki tumor and tissue registries, which are managed by RERF;

- a special registry (the Leukemia Registry) of cases of leukemia and malignant diseases of the hematopoietic system;

- the offering of standardized biennial clinical examinations for members of the AHS cohort and a (fixed) subset of the IU cohort;

- a mail- and telephone-based morbidity surveillance system for AHS cohort members;

- occasional mail surveys carried out within the LSS cohort; and

- an autopsy program (active from about 1960 through the early 1980's but currently inactive).

Analyses of data from the RERF cohorts make use of individual dose estimates. The basic methods used to compute these estimates were originally developed by researchers at Oak Ridge and other national laboratories. The current dosimetry system, DS86, was the result of a binational effort to reassess the physical data and refine the theoretical models that formed the basis for the dosimetry system (T65D) that had been in use at ABCC and RERF since the late 1960's. Japanese and US scientists are currently working to deal with discrepancies between DS86 Hiroshima neutron dose estimates and neutron doses inferred from physical measurements and some biases suggested by RERF biodosimetric data. It is likely that this effort will lead to revised dosimetry within the next five years. As in the past, RERF researchers will be responsible for adapting and applying the new dosimetry for use with the survivors.

CURRENT STATUS OF THE RERF COHORTS

In this section we present some information on each of the major cohorts at this time. This discussion provides a limited amount of historical information about the creation of the cohorts since the primary focus concerns the nature of these cohorts today.

The Life Span Study cohort

The LSS cohort was constructed from a Master Sample of about 284,000 Japanese atomic bomb survivors (159,000 in Hiroshima and 125,000 in Nagasaki) developed from a special nationwide enumeration of A-bomb survivors carried out as a part of the 1950 National Census. As initially defined, the LSS included all survivors in the Master Sample who were within 2000 m of the hypocenter at the time of the bombings (ATB) and alive and residing in Hiroshima or Nagasaki on 1 October 1950 and who met certain other criteria necessary to ensure complete mortality follow-up. There were originally two age and sex matched comparison groups who met the residency and other criteria deemed necessary for adequate follow-up. One of these groups was composed of individuals who were exposed in the cities at distances of 2,500 to 10,000 m from the hypocenter ATB and the other group consisted of individuals who were not in the cities at the time of the bombing. With the introduction of individual dose estimates, the cohort was extended to include all persons in the Master Sample who were within 2,500 m of the hypocenter ATB. Finally, in the early 1980's all remaining distal survivors in Nagasaki (2,500 - 10,000 m from the hypocenter) were added to the LSS to increase the size of the relatively small Nagasaki internal comparison group. With these additions, there are now 120,321 individuals in the LSS

cohort, including 93,473 who were in one or the other of the two cities at the time of the bombing.

As of the fall of 1996, the mortality follow-up records indicate that 49% of the cohort members have died and less than 200 individuals have been lost to follow-up (primarily due to migration out of Japan). The average age of the surviving members of the cohort is 65.4 years. When broken down by age at exposure, it is seen that lifetime follow-up is essentially complete for cohort members who were at least 50 years old at the time of exposure, while more than 90% of those who were under the age of 20 ATB are still alive. (See Annex A.)

The Adult Health Study (AHS) cohort

The AHS cohort is a subset of the LSS cohort. This subset was so defined as to include all members (4,990 individuals) in the original LSS cohort who were within 2000 m of the hypocenter and who reported one or more of the cardinal symptoms associated with acute radiation sickness, that is, epilation, oropharyngeal lesions, and purpura. Three age and sex matched control groups were chosen from among (1) the survivors within 2,000 meters who reported no acute radiation symptoms, (2) survivors who were at distances of 2,500 to 10,000 m from the hypocenter ATB, and (3) unexposed LSS cohort members. With the introduction of individual dose estimates the AHS cohort was augmented by the addition of all remaining members (2,436 persons) of the LSS whose T65D shielded kerma dose estimate was greater than 1 Gy. The examination schedule was set so that in any one month a more or less representative cross section of the entire population would visit the clinic. These examinations are now in the 19th cycle; however, over time, attrition has reduced the population to about 50% of the original sample.

As of the fall of 1996 more than 9,200 of the 17,397 exposed members of the AHS are still alive and about 8,000 of these individuals are living in the clinical contacting catchment area. Among this latter group almost 80% participated in the most recent cycle of AHS examinations.

In Utero Sample

The in-utero cohort was assembled from a roster of more than 10,000 individuals whose date of birth was between the date of the bombings and May 1946. This roster was developed from Hiroshima and Nagasaki birth records, records of early ABCC studies, and data from a special survey conducted in conjunction with the 1960 Japanese national census. As currently defined, the cohort includes data from two overlapping samples: a clinical sample defined in the late 1950's and a mortality cohort defined in the early 1960's. As with the other cohorts these two groups were defined in terms of a core set of individuals whose mothers were close (within 1,500 m for the clinical and 2,000 m for the mortality samples) together with age and sex matched groups of more distal or unexposed people. The cohort includes 3,654 individuals of whom 1,192 were exposed at distances of less than 2,000 m of the hypocenter while 1,356 were exposed at distances of 2,000 to 10,000 m. Complete mortality follow-up is available for all members of the IU cohort other than the 59 individuals who were lost to follow-up due to emigration from Japan or a failure to locate the *koseki* records. There are 755 in-utero survivors who have been included in analyses of IQ and school performance but are not in the main IU cohort. Consideration is being given to initiating routine mortality follow-up for these people. A total of 1,021 members

of the IU cohort are invited to participate in the AHS examinations. (This group overlaps but is not the same as the IU clinical cohort whose members were asked to come to ABCC for annual examinations during their late childhood and adolescence.).

Because of the age of members of this cohort (51 or 52 years in the fall of 1996), there have been few deaths (434) at this time. More than one-third of these occurred during the first few months of life.

The F_1 cohort

The original F_1 cohort included 53,518 children born to survivors between 1 June 1946 and 31 December 1958 selected from among the 76,626 children identified in the course of the Genetics Program that ran from 1947 through 1953 or from other sources, generally the birth records. The F_1 cohort was subsequently extended to include the children of virtually all proximally exposed members of the Life Span Study cohort and the children of some distally exposed members of this cohort. At this time the cohort includes 88,484 persons. However, mortality follow-up is not being carried out for 11,760 cohort members who were selected for some special clinical studies. Follow-up of these individuals should begin within the next year. As of the fall of 1996, 5,316 members of the F_1 cohort are known to have died and 1,434 cohort members have been lost to follow-up. Most of the deaths were infant deaths. The average age of the surviving cohort members is currently about 38 years. As is discussed below, a mail survey of the full F_1 cohort and a small study of the feasibility of an F_1 clinical examination program are being planned.

THE STRUCTURE OF RESEARCH AT THE FOUNDATION

Research at the Foundation can be seen as a matrix with one dimension, the spectrum of health effects resulting from exposure to ionizing radiation, and the other, the disciplinary skills, represented by the research departments, needed to identify and understand the biological events that subtend these effects. This duality of aims is implicit in the Unified Program of research recommended by the Francis Committee and the need to focus most, if not all of the research effort on the fixed samples described above. This focus implies in turn that much of the research is integrative and necessarily collaborative. Indeed, no one of the major research departments at the Foundation stands fully alone; each requires the help of the others either in data collection and management, their analysis, or their biological interpretation. The collaboration can, of course, vary in form. It is instructive, therefore, in describing the Foundation's program of research to view it from both the programmatic perspective and the individual departmental contributions since one illustrates the inherently collaborative nature and broad sweep of much of the research and the other illuminates the individual departmental contributions.

Cancer Studies

Cancer is the best established, and most important late effect of exposure to ionizing radiation among the atomic bomb survivors and other exposed populations. There are, however, several important issues remaining unclear regarding the nature of cancer risk.

Major LSS reports

The series of general reports on cancer mortality and the recent collection of reports on cancer incidence in the atomic bomb survivors in the LSS are the most visible and influential products of the Foundation's research efforts. As previously stated, lifetime follow-up is essentially complete for cohort members who were 50 years of age or older at the time of the bombings, but for those survivors who were less than 20 years of age then 90% are still alive and are now at, or on the verge of, ages of rapid increases in spontaneous cancer rates. While the total number of cancer cases among those exposed as children is not yet large, the data indicate that, despite a possible decrease in the excess relative risks, excess cancer rates associated with the radiation exposure are continuing to increase. The number of cancer cases in the youngest members of the LSS can be expected to double every 5 to 10 years until well into the next century. Thus, additional follow-up and analyses of these data are central to the development of a comprehensive assessment of the long term impact of radiation exposure on cancer risks in the survivors.

During the next five years we will produce a new comprehensive cancer mortality report (LSS Report 13) covering the period from 1950 through 1995 as well as an updated report on solid cancer incidence covering the period from 1987 through at least the end of 1992. While there will undoubtedly continue to be a need for both mortality- and incidence-based risk assessments, efforts will be made to present a more integrated, comprehensive picture of the incidence and mortality data. As these analyses are completed we will continue to make the detailed data sets available to other researchers.

Site-specific incidence studies

The general LSS Reports provide useful summaries of cancer risks in the LSS. However, they cannot provide an in-depth look at the nature of cancer risks for specific tumor types or subtypes. To address this problem, RERF researchers in collaboration with the local medical community and some support from the US National Cancer Institute (NCI) have carried out a number of studies of cancer incidence at specific sites. These studies involve the identification of potential LSS cases from a variety of sources (including tumor and tissue registry records, death certificates, and autopsy reports) using broadly defined selection criteria. The medical records and, where possible, pathologic material for candidate cases are screened by a panel of pathologists in order to arrive at a consensus diagnosis. Cases identified in this way are then analyzed to assess cancer risks.

The results of site-specific studies on cancers of the breast and salivary glands have been published. Reports on skin, CNS tumors, and liver cancer will be completed soon. Over the next several years studies of thyroid cancer, lung cancer, lymphoid malignancies, and an update of the breast cancer series will be completed.

In contrast to the general LSS Reports, which appear in radiation-related journals, we are seeking to publish the results of the site-specific incidence studies in the more general medical literature to increase awareness of the RERF findings in the broader scientific community.

Patterns of excess cancer incidence among those exposed in childhood

As noted above, the excess relative risks associated with radiation exposure among the

youngest survivors are higher than those for other age groups and the data suggest that these relative risks may be decreasing with time. These findings have led to a widely held view that people exposed as children are particularly sensitive to radiation effects. However, for most solid cancers excess absolute rates, at a given attained age, appear to be quite similar to those exposed as adults. This may not be the case for some tumors, notably breast and other endocrine tumors. As those exposed as children reach ages at which rates of cancer increase dramatically it will be possible to carry out more detailed analyses of the nature of solid cancer risks among these survivors. Thus, as in earlier RERF reports on the shape of the dose response and on temporal patterns in the excess solid cancer risk, we will produce a short report focused on solid cancer incidence following childhood exposures. This project is being undertaken in collaboration with NCI.

Issues in modeling excess cancer risks in the LSS

The analysis of the LSS cancer mortality data continues to raise a variety of interesting and challenging statistical problems. A number of innovative methods have been developed to analyze the LSS data. These include extensions of classical regression models for survival analysis to allow for efficient estimation in large cohorts using general relative and absolute risk models, procedures to adjust for biases resulting from random errors in individual dose estimates and to allow for the impact of migration in the analysis of the tumor registry data, and methods for the joint analysis of data on multiple causes.

There is an increasing interest in the application of biologically-motivated models to the data on radiation and cancer risks. Over the next year or so we expect to complete work on a generalization of the Armitage-Doll multistage model that provides some useful insights into the age and time patterns of the excess risk seen in exposed survivors. We are working on the application of the Moolgavkar-Venzon-Knudson two-stage model to the LSS cancer data.

Because of the strong interest in the nature of the dose response at low doses, there is a need to consider more flexible alternatives to linearity than the simple quadratic and threshold models generally used. This will involve the development of regression-adjusted nonparametric smoothers.

Over the next two years studies of inter-site variability in radiation-associated excess cancer incidence and of the comparison of relative risk and absolute rate models in the description of excess cancer risks will be completed.

Effect modification by nonradiation factors

Use of data from the mail surveys conducted by ABCC-RERF over the past 30 years has largely been limited to assessments of smoking and lung cancer risks. However, these surveys also include information on alcohol consumption, nutrition, reproductive history, and socioeconomic factors. Additional cross-sectional and longitudinal data on non-radiation factors have been obtained directly from participants in the AHS examinations. The serum samples from AHS participants that have been collected and stored are also a valuable resource for the study of nonradiation risk factors and for molecular epidemiological studies.

Use of these mail survey and clinical data has been limited in part by the problems in collating data from the various sources. This problem is being addressed as a part of efforts (discussed further below) to modernize the RERF research database. Thus over the next few years we plan to undertake a number of projects that will make more extensive use of the mail survey data. These studies include updated analyses of smoking and the incidence of lung or other smoking-related cancers in the LSS, new analyses of alcohol consumption and liver cancer incidence, and analyses of the impact of socioeconomic factors on comparisons of the exposed and unexposed (not-in-city) groups.

Over the next five years we will conduct a series of case-control studies nested in the AHS to investigate the impact of nonradiation factors on some common but generally nonfatal cancers (breast, thyroid, and skin). The mail survey and clinical data will be useful either directly (as a source of data on risk factors) or indirectly (by providing information enabling more efficient matching of cases and controls) in the design and analysis of such nested case-control studies.

Radiation and benign tumor incidence

Recent AHS data have suggested that there may be radiation-related increases in the risk of various benign tumors including myoma uteri and parathyroid adenoma among AHS participants. A study of the prevalence of uterine myoma based on ultrasonographic examination will be published within a year and reports on the prevalence of several other benign tumors (liver hemangioma, and ovarian tumor) observed using ultrasound will be completed within the next two to three years. Consideration is also being given to the conduct of a study of benign thyroid tumors and other thyroid disorders among Hiroshima AHS participants. If it is deemed feasible, this study would serve to complement the Nagasaki thyroid study, which indicated radiation-related increases in risks for these conditions. Within the next year a 10-year incidence study on hyperparathyroidism among AHS participants will be completed. It is hoped that this study will provide some hints as to the reason for the elevated serum calcium and parathyroid hormone levels in heavily exposed survivors.

Cancer incidence and mortality in the in-utero and F_1 cohorts

A major report on cancer mortality in the in-utero cohort for the period from 1950 through 1992 is now in press. This report will be supplemented within the next year by reports on cancer incidence and general mortality patterns in this cohort. In view of the age of the in-utero population, the number of cancer cases can be expected to increase dramatically with five additional years of follow-up. Thus it would be appropriate to produce an updated report on cancer mortality and incidence in the cohort in about five years.

Mortality follow-up for the F_1 cohort will be extended to include all people who have been selected for the BGS study. Once this is done a new report on cancer incidence and mortality in the cohort will be prepared. This report should be completed within about three years.

Pooling of RERF data with data from other cohorts

While the atomic bomb studies are a major source of information on risk assessment, they cannot address all of the important issues on radiation risks. Comparison of the data on the A-

bomb survivors with that from other exposed populations enables us to examine some of these issues, such as dose rate effects and risk transfer. Under the terms of a contract with the NCI, RERF is working with Russian and US scientists on documenting, updating, and improving the data on cohorts of Russian nuclear workers and the general population exposed to large radiation doses as a result of low-dose rate chronic exposures from the operation of the Mayak plutonium production plant located in the Southern Urals. An important part of this work will be the preparation of initial reports on cancer risk estimates for these cohorts together with some (limited) comparison of these estimates with those seen in the LSS. The initial contract will continue until September of 1998. This contract may be extended for several more years depending upon the results of current work and the availability of funds.

Work being carried out at RERF on a multi-population comparison of breast cancer risks following radiation exposure in six cohorts, including the LSS, should be completed within the next year.

Trends in Hiroshima and Nagasaki cancer incidence

As noted earlier, RERF operates tumor registries in cooperation with the medical associations in Hiroshima city and Nagasaki city and prefecture. The linkage between these general population registries, which are regarded as among the best in Japan, and the LSS, in-utero, and F_1 cohort data is important to the conduct of RERF research. The registries also provide useful information on cancer risks in the Hiroshima and Nagasaki populations. While the Hiroshima and Nagasaki registry data are routinely published in IARC's *Cancer Incidence in Five Continents* volumes, the effort devoted to analysis and publication of these data has been limited (especially in Hiroshima). Over the next five years we will produce a series of short bilingual reports on trends in cancer incidence in these cities and develop procedures for the routine production of summary reports on the status of the registries and the nature of the accumulating data.

Noncancer Studies

Noncancer mortality dose response

The evidence for a significant association between radiation and noncancer mortality is becoming stronger as the follow-up of the LSS cohort continues. Excess risks are seen not only for cardiovascular disease mortality but also for other broad categories of noncancer disease mortality. LSS Report 12 Part 2, which will be completed within the next year, will describe the basic nature of this effect while addressing the uncertainties and limitations of the mortality data. Over the next five years it will be important to extend the mortality follow-up through at least 1995 and to carry out further investigations aimed at clarifying, to the extent possible, issues related to the shape of the dose response and patterns of the excess risk with regard to sex, age and time. Additional follow-up may also help to determine if there are cause-specific differences in risk. Because of the paucity of known biological mechanisms for a radiation effect on noncancer disease we must continue to look for factors that might lead to a spurious association between radiation exposure and noncancer disease mortality in the LSS.

There is a highly significant excess risk for noncancer diseases of the blood, with the

excess relative risk per Sv being larger than for any of the solid tumors. A review of these cases is being undertaken in collaboration with the hematologists associated with the Leukemia Registry. Results of this review should be available in one to two years.

Cardiovascular disease

The AHS data enable us to assess the incidence and prevalence of specific cardiovascular diseases and to undertake analyses of conventional risk factors, and thus are essential for the development of a better understanding of radiation effects on cardiovascular disease (and other noncancer diseases). Studies of AHS data on the incidence of cardiovascular disease and stroke will continue beyond the next five years. Analysis of data on various CVD risk factors and related-endpoints obtained from shorter term studies such as the prevalence of aortic and abdominal arch calcification, isolated systolic hypertension, retinal arteriosclerosis, and coagulation rates have all provided evidence of radiation effects. A major objective for the next few years is to publish initial reports on the first 30 years of follow-up and other findings.

These studies are currently being supplemented with studies of the rate of sudden death, the prevalence of peripheral vascular disease (as determined by pulse wave velocity and ankle-arm blood pressure ratio), plasma fibrinogen levels, and new analyses of conventional risk factors, including blood pressure and cholesterol. Research is being planned on several additional risk factors, including case-control studies of *H. influenzae* and homocysteine and the prevalence of latent atherosclerosis (as determined by ultrasonographic examination of the thickness of the carotid artery).

RERF has had a productive, long-term involvement in the Ni-Hon-San study of cardiovascular disease among Japanese in Japan and the US. This collaboration with the Honolulu Heart Program will continue through the next five years and should lead to several publications on general cardiovascular disease epidemiology.

Noncancer effects hypothesis generation

Because of the lack of a known biological basis for a radiation effect on noncancer morbidity, there is a need to develop ideas and, if possible, testable hypotheses regarding this issue. A workshop, such as that proposed by NAS, that would bring together RERF researchers and scientists from a broad range of disciplines to learn about RERF's findings and to discuss and develop ideas for future research in this area should take place in the near future. This will permit us to develop contacts for future collaboration and may inspire others to undertake research in this area. In addition to such a workshop, we need to establish a continuing dialog involving RERF staff and other scientists (particularly those at Geniken in Hiroshima and Nagasaki University) in order to focus more attention on this issue.

Liver disease

These studies will provide important data relevant to the interpretation of the finding of a radiation-related increased incidence of liver cancer and other liver diseases in the LSS and AHS. The serum assay-based study of the relationship between hepatitis-B and hepatitis-C virus infection and radiation dose, initiated in 1993, will be completed within the next two years.

We plan to investigate the feasibility and power of a nested case-control study using stored sera to compare HCV infection rates and subtypes prior to the diagnosis of liver cancer or cirrhosis and to look for interactions between radiation dose and HCV infection. Of particular interest is the recent report that HCV infection can mask the concurrent presence of HBV infection, leading to an underestimation of the prevalence of the latter infection. Similar studies on HBV infection have been reported, but in the light of the finding just cited may have to be redone.

Longitudinal analysis of clinical and laboratory measurement data

The recent report of an association between radiation and age-related changes in cholesterol levels illustrates the usefulness of modern analytical methods in the study of longitudinal clinical data. These methods will be developed further and applied to other blood chemistry and hematology data as well as to blood pressure and other clinical measurements. We will also consider how these methods might be applied in analyses of longitudinal data from electrocardiograms.

Menopause

Analyses of the Nagasaki menopause incidence study indicate that a decrease in age at menopause is associated with increased radiation dose. A report on these results will be completed in the coming year. The Nagasaki findings have led to the initiation of a longitudinal study of FSH and estradiol levels in peri-menopausal women to characterize better the relationship between self-reported menopause and underlying hormonal changes. Data collection for this study will continue through 1997 with analyses to be conducted in the following two or three years. In Nagasaki, longitudinal observations on peri-menopausal changes in relationship to serum cholesterol and estradiol will continue for the next five years.

Aging

A study of the relationship between age-related changes in cognitive function and radiation dose has been underway since 1992. This study also includes comparison of data on AHS participants with that for Japanese-Americans in Honolulu and Seattle (NI-HON-SEA study). Data collection will continue for about one more year with analyses taking place over the subsequent three years.

Osteoporosis is a common age-related disorder influenced by menopause and parathyroid hormone levels which have been shown to be associated with radiation exposure in the AHS. Dual photon absorptiometric measurements of spinal bone density of AHS participants, made since 1989, suggest that bone density increases as radiation dose increases. In order to provide a more definitive result, measurements of spine and hip bone mineral density using dual X-ray absorptiometry supplemented with data on total body composition are being obtained for selected AHS participants. An analysis of the baseline data is being carried out at this time. As data on these subjects are obtained in future AHS examinations longitudinal analyses of age-related changes in bone mineral density will be made. Data from this study will also be used in the NI-HON-SAN collaboration.

Estimates of physiological age were computed for AHS participants on the basis of grip strength, skin elasticity and other factors measured in the 1970-72 AHS exam cycle. These estimates are being used as covariates in an analysis of rates of mortality and morbidity during the following 20 year period. This analysis should be completed within a year. A new assessment of physiologic age based on a broader battery of measurements is being planned.

Molecular epidemiology

With some effort RERF can play a unique and important role in the search for evidence of so-called finger prints associated with radiation-induced cancers. Work has begun on PCR analyses of the ras and p53 genes using preserved and fresh skin, thyroid, and liver cancer tissues. In the light of recent advances and the relatively large radiation effects for breast and thyroid cancer, studies of tissues from breast and thyroid cancer cases among the high dose survivors have the potential to yield important results. It may also be useful to supplement the search for characteristic gene alterations in cancer cells with a search for evidence of specific mutations associated with cancer development in the blood of cancer-free survivors.

The success of such studies depends heavily on our ability to obtain appropriate samples for LSS cohort members who are diagnosed with cancer. It is possible to obtain archival material through the tissue registries in Hiroshima and Nagasaki; however, better methods are needed to ensure the availability of the necessary materials from newly diagnosed cases. To facilitate this end RERF is seeking support from the local medical community for the establishment of a community-wide tissue/DNA bank in Hiroshima. This bank would maintain tissue specimens or preserved DNA that could serve as a resource for all groups in Hiroshima engaged in studies of the molecular mechanisms of carcinogenesis.

It is important to keep abreast of the rapid progress in knowledge of the molecular basis of cancer. The pace at which this field is developing suggests that future studies may be more important than anything that can be done today. This suggests in turn that it would be worthwhile for RERF scientists to work, possibly in collaboration with other groups, on the development of methods to maintain a broad spectrum of DNA in a form that could be used in future studies. Such samples would be particularly useful when it becomes possible to scan the entire genome for evidence of possible changes.

In view of RERF's limited resources it is important for us to develop a general research plan that defines specific projects that can be done at RERF as well as projects where collaboration is important and establishes mechanisms for seeking this collaboration and, where necessary, support.

Immunology

One of the major sources of tissues from the A-bomb survivors is from the on-going collection of blood samples. This supply of viable cells from the survivors is a resource for the study of many diseases including those with immune system dysfunction. Reduced immune function can potentially lead to a variety of pathologic consequences including cancer, which is known to show heightened risk among the survivors. RERF has a matchless opportunity to investigate the late effects of radiation exposure on the immune system.

We plan to continue our studies of the features and mechanisms of radiation-induced disorders in the hematolymphoid system at the cellular and molecular levels. These studies include radiation effects on the distribution of T-cell subsets in the survivors and of radiation effects on endocrine and hematopoietic growth factor levels as well as the study of stem cells, the progenitors of cells which constitute the immune system.

Heritable Mutations

Permanent lymphocyte cell line cultures

The 1984 Genetic Study Conference endorsed an RERF plan to establish immortalized B-lymphocyte cell lines from 1000 families (500 with at least one parent exposed within 2,000 m). A sampling plan was drafted based on the T65D dosimetry. At this time the Biochemical Genetics Laboratory has established cell lines for 800 families (1600 parents and 1200 children) based on this plan. With the introduction of DS86 doses it was discovered that dose estimates were unavailable for one or more of the parents in the remaining families. Over the next two years 200 additional Hiroshima and Nagasaki families for whom the parental doses are known will be identified and efforts commenced to establish cell lines for these families in order to achieve the goal of 1000 families. This is the largest cohort-based sample for the detection of radiation effects on the human germline anywhere in the world.

Pilot studies of methods for the detection of deletion–insertion–rearrangement mutations (D/I/R)

Methods for genome-level (DNA) analyses are developing rapidly. It is likely that the next five years will see the development of new markers and increasingly powerful methods that can be used in the search for evidence of mutation in the children of the survivors. At this time, we are examining several promising approaches. In each approach, mutations are detected by comparison of a child's gel with that of his or her parents. Indications of a mutation include the absence or dislocation of bands or spots as well as changes in intensity. As we learn of (or develop) additional methods it may be necessary to initiate new pilot studies, in conjunction with researchers outside of RERF when necessary.

<u>Mutations at minisatellite loci</u>

An initial study of 100 families will be extended by the addition of 100 families in order to provide information for further comparisons of the RERF data with the results of a Belarus-UK study (Dubrova et al 1996, Satoh et al 1996) that has been interpreted as providing evidence of an excess of such mutations among Chernobyl victims.

<u>Chemiluminescent bands on Southern filters</u>

Employing a quantitative analysis of chemiluminescent bands on Southern filters, material from the 200 families used in the minisatellite studies will also be screened for evidence of mutation using DNA probes that correspond to the human counterparts of the seven mouse-specific loci and other loci including genes that are suspected to be related to several common chronic diseases, such as hypertension, diabetes mellitus, and hereditary nonpolyposis colorectal cancer.

Two-dimensional electrophoresis (2-DE) methods

The Biochemical Genetics Laboratory has developed a 2-DE technique based on ^{32}P-labeled DNA digests created with three sets of restriction enzymes. This method produces three gels per individual having a total number of roughly 2000 spots (fragments) that are suitable for D/I/R mutation detection. A study using DNA samples from 200 BALB/c mice derived from irradiated spermatogonia, conducted primarily to prove that the 2-DE technique is capable of detecting mutations, will be completed within a year. This study will be followed by an investigation of DNA from the 200 pilot study families. It is expected that this pilot study will take at least five years to complete. If the spontaneous mutation rate is 1×10^{-5} / fragment / generation, we would expect to detect five mutations in the 120 children of the 100 control families.

The study (even in its preliminary phase) involves collaboration of a number of groups, including: the Cytogenetics Laboratory for efforts to localize putative mutations and their normal counterparts using FISH or other techniques, the Information Technology Department for help in data management and software conversion/development, the Department of Statistics in dealing with the pattern recognition and other problems arising in the analyses of these complex data. RERF's long-term collaboration with the University of Michigan is also an essential component of this program.

Genetic markers of hypertension

In accordance with the recommendations of the Blue Ribbon Panel, a protocol is being developed for a pilot study to assess markers for genes potentially associated with hypertension. This study, which will include 200 AHS participants (100 normal and 100 with hypertension as defined by the 1993 WHO/ISH guidelines), will make use of DNA from lymphocytes obtained during the routine AHS examination.

F_1 mail survey and health study feasibility

In response to the recommendations of the Blue Ribbon Panel, we are preparing detailed plans to carry out a mail survey of all surviving members of the F_1 cohort and to conduct a small scale study of the feasibility of an ongoing program for ascertainment of disease and disability in the cohort. The mail survey will provide data that can be used to obtain baseline (self-reported) information on health status and serve as a source of risk factor data that can be used in future analyses of cancer mortality and incidence in this cohort. The small clinical study (500 people) will include biochemical genetic studies of several genes related to common diseases (e.g., hypertension and diabetes). The mail survey and clinical feasibility study will last about two years and will be followed by a workshop to determine what additional studies, if any, should be carried out by RERF.

Genetic epidemiology (family studies)

Efforts are currently underway to define a database of family relationships within the LSS, in-utero, and F_1 cohorts. The initial focus is on the families of breast cancer patients in order to

look for evidence of genetic predisposition among women who were diagnosed with breast cancer before the age of 35. Data on family relationships in the RERF cohorts and the extensive epidemiological and clinical follow-up data for the cohort members will be a unique resource in the study of the impact of genetic factors on disease. Continued development and use of this resource requires support and collaboration with groups outside of RERF who are active in this area. Progress will be highly dependent on the availability of personnel and special financial support.

Dosimetry

Biodosimetric studies

Over the past thirty years, RERF has played a central role in the development and assessment of biomarkers of radiation exposure, including structural chromosome aberrations (using conventional staining, G-banding, and most recently FISH methods); mutation assays (including GPA, T-Cell receptor, HPRT, and others); and electron spin resonance (ESR) of tooth enamel. The availability of physical dose estimates, DS86, makes RERF one of the most important centers for developing and assessing various long-term biological dosimeters useful in other populations. As for the mutation assays, only the GPA assay can detect radiation exposure that occurred several decades earlier. However, the frequency of GPA mutants varies widely and thus the GPA assay has not proven to be a useful alternative to the cytogenetic method of estimating individual doses although it can be valuable in estimating collective dose. Therefore, little, if any, work on the development or application of somatic mutation assays will be done during the next few years, and the extensive programs for the analysis of chromosome aberrations in the survivors using conventional and G-band analyses have also ended. However, these cytogenetic studies, as corroborated by our recent work on ESR of 100 teeth and cytogenetic tests of the tooth donors, are useful in estimating individual doses, and the recently introduced FISH method is even more effective. Accordingly, we plan to obtain FISH data on an additional 1,000 survivors over the next five years. Our aim is two-fold, namely, (1) to clarify the possible systematic bias in the DS86 dose estimates according to shielding category and (2) to determine the extent of random errors among individuals. We hope to supplement this activity with a program to obtain FISH data from all unsampled AHS participants who were under 20 years of age ATB with DS86 dose estimates in excess of 0.6 Gy (about 1,500 persons) and all parents of families selected for molecular heritable mutation screening studies. ESR analyses of 100 additional samples that are currently available will be carried out in the next year. Efforts to obtain more tooth samples (and, when possible, FISH data) from AHS cohort members in Hiroshima will continue.

Over the next few years effort will be directed toward a variety of comprehensive analyses and comparisons of existing biodosimetric data. These analyses will include: an analysis of all available data from the conventional chromosome aberration studies including assessments of more detailed data (e.g. interchromosomal:intrachromosomal aberration ratios); continued comparison of ESR, chromosome aberration data and GPA data as well as comparison of the correlation between these biological markers and the physical (DS86) dose estimates.

While further analyses of the nature of the dose response for the various assays are important, recent comparisons of the ESR and cytogenetic data demonstrate that the data are also

useful for the detection of errors in individual dose estimates. More importantly, the biodosimetric data will become increasingly important for the identification of potential systematic biases and the characterization of uncertainties in the physical dose estimates. For example, the chromosome aberration data suggest that DS86 dose estimates for Nagasaki factory workers may be too high by a factor of two or more.

Revision of the DS86 dosimetry system

Ten years after its introduction, there is increasing evidence of systematic errors in DS86 dose estimates. Much attention has been focused on a distance-dependent discrepancy between measured and calculated values for neutrons in Hiroshima. While estimates based on the best available information suggest that these changes will have little impact on cancer risk estimates derived from the survivor data, the fact that these discrepancies exist has led to some serious questions about the validity of RERF risk estimates. There is also, as noted above, biodosimetric data suggesting that doses may be over-estimated for Nagasaki factory workers (who account for 30-40% of Nagasaki survivors with DS86 doses in excess of 0.5 Gy). It is expected that within the next two to three years the US and Japan senior atomic bomb survivor dosimetry committees will accept a revised dosimetry that will modify the Hiroshima neutrons and, hopefully, address the factory worker problem. Once a consensus has been reached the current RERF dosimetry programs will be revised and doses recomputed for all survivors. This will involve a considerable effort on the part of members of the Department of Statistics and ITD over a period of six months to a year followed by reassessments of the major findings regarding cancer and other risks.

To prepare for the revised DS86 system, to make the basic dosimetry data more easily available (including shielding histories and acute effects), and to resolve several basic questions about exposure status for some in-utero mothers and F_1 parents, we have been working to reorganize and better document the dosimetry data. This effort, which has also included moving the DS86 system to the new RERF computer system, was begun several years ago and will continue for another year. This project should lead to the incorporation of all of the basic dosimetry data into the RERF research database and to a report that thoroughly describes and documents these data.

Database Development

Continued development and documentation of core research database

The introduction of distributed computing has led to great progress in the development of a modern, unified research database. The new database is built around a newly created master list of over 700,000 individuals including all members of the major and minor RERF study cohorts as well as people registered in the tumor and tissue registries. The new system has simplified data handling for the mortality and cancer incidence follow-up and led to improvements in data quality through the elimination of redundant copies of data items. Using the new system researchers have quick direct access to current RERF data and can easily link their data to other items in the system to obtain data needed for analysis using standard statistical programs. At this time the database includes demographic, cohort membership, mortality follow-up, basic dosimetry, and tumor and tissue registry data. However, much additional work is needed to ensure that the database fully serves RERF's research needs. These activities include the development of improved

documentation (on paper and online) and the implementation of additional consistency checks to ensure data quality along with an effort to make researchers more aware of the capability and accessibility of the new system. In addition to these activities, much of the work on database development over the next several years will focus on the areas mentioned in the following subsections.

Clinical follow-up data

These complex and voluminous data include longitudinal information on clinical contacting, routine measurement and laboratory test results, the results of special tests, diagnostic information, and more. Work has progressed on the development of the basic design of the clinical follow-up data tables to be added to the core database. This database will include data on the AHS examinations but also data from other special examinations of the in-utero and F_1 cohorts. It is hoped that the design and implementation of the major tables (focusing on the AHS data) will be completed in a year or two but the effort to incorporate all of the clinical follow-up data can be expected to take several additional years. In addition to incorporating these data to the RERF research database, a modernized version of the AHS patient tracking and clinical management system is being developed that will serve as the front-end for continued updating of the clinical data.

Laboratory data

The data collected in the course of RERF's cytogenetic, biochemical genetic, and radiobiological studies are stored in computer files, laboratory notebooks and other formats. It is not practical to add all of these data into the new database at once. However, as new analyses of archival data are undertaken or new programs are introduced we will incorporate these data in the main research database. At the present time the conventional chromosome aberration data are being cleaned and linked to the core database. Over the next year data on other biodosimetric studies will be added to the system.

The DNA studies being carried out in the Biochemical Genetics Laboratory will generate large amounts of data and analyses will be highly computer-intensive. Thus, there is a need to develop methods for the storage and management of these data. An interdepartmental effort will be undertaken to develop effective methods for handling these data.

Detailed dosimetry data

As noted earlier, efforts are underway to add all of the basic dosimetric data (survivor location, shielding history, and acute effects data) into the research database. This work has involved developing consistency checks and procedures for resolving differences in data from different sources. The basic work on this project has been completed and the new dosimetry data tables should be ready for formal addition to the main database within a few months. Work on documentation of these data will continue for about a year.

Unified inventory of stored samples

Over the last 30+ years more than 120,000 sera and other biological specimens have been

collected and stored for use in future studies. Advances in molecular biology are increasing the value of this unique resource. At present there is no single inventory of these samples. Over the next two to three years we will develop a unified inventory of stored samples. This inventory will be a part of the research database and will be useful in facilitating the planning and conduct of case-control and family studies that employ stored samples and managing this resource more effectively.

Current Status and Future Plans for RERF Follow-up Programs

Mortality ascertainment (koseki check)

RERF carries out a program of active mortality ascertainment for all members of the LSS and most members of the in-utero and F_1 cohorts. As noted earlier, plans are being developed to extend the mortality follow-up to include the 11,760 F_1 cohort members who are not currently included in the routine follow-up. Death certificate information for survivors whose *honseki* (place of family registration) is in Hiroshima or Nagasaki is routinely received by RERF. For cohort members whose honseki is not in either of the cities, requests for information are sent to the appropriate office once every three years. Because of the decreasing number of surviving members of the LSS cohort and more efficient procedures for handling the data, it should be possible to obtain information on vital status and cause of death every two years, especially for members of the LSS cohort.

Hiroshima and Nagasaki tumor and tissue registries

RERF manages the population-based Hiroshima city and Nagasaki city and prefectural tumor registries. These registries are recognized as among the best in Japan. The Foundation's role in the management of these registries has allowed us to create and maintain a direct link between the cancer registry data and the RERF cohorts. Without this connection the increasingly important analyses of cancer incidence among survivors and their children would be difficult, if not impossible. The development of the RERF research database has strengthened the linkage between the tumor registries and the LSS cohorts and further development of the database will make this linkage even more useful. Over the next five years we hope to develop increasingly efficient and effective means for obtaining data on cancer incidence among residents of Hiroshima and Nagasaki.

While it is essential for RERF to continue to play a central role in the management of the tumor and tissue registries, we are working closely with the Hiroshima prefectural government and Hiroshima Medical Association on plans for the development of a new Hiroshima prefectural tumor registry and on the inclusion of the Hiroshima tumor and tissue registry database as an integral part of the proposed new Hiroshima cancer center. It is hoped that in conjunction with these efforts RERF can take a leading role in the creation of a regional tissue bank that would serve as a resource for molecular epidemiological studies carried out at RERF or other institutions, such as Hiroshima University and the Hiroshima Red Cross Hospital. As these plans develop, it should be possible to begin discussions with Nagasaki University and other related groups about the establishment of a similar system in Nagasaki.

The tumor registries are community resources and it is essential that more effort be

devoted to the presentation and analysis of the accumulated data in ways that benefit the communities. Steps are being taken to analyze trends for selected cancer types and to publish regular, standardized summaries of the tumor registry data in a format that will be useful to physicians and others.

Leukemia registry

Special efforts to collect data on cases of leukemia and other hematopoietic malignancies occurring among the survivors were begun by local physicians and ABCC in the late 1940's. Over time these efforts evolved into the Leukemia registry. In recent years virtually all ascertainment of leukemia and related disorders is being done through the tumor registry. It is now felt that the tumor registries are adequate for the identification of new cases of leukemia and related malignant conditions. Hematologists and others associated with the leukemia registry are currently involved in a review of survivor deaths attributed to blood diseases other than leukemia as well as an effort to reclassify all potential LSS lymphoma and myeloma cases using modern diagnostic criteria. Over the next five years we plan to incorporate all of the historical leukemia registry data into the research database.

Standardized biennial clinical examinations

Since 1958 RERF has been giving standardized medical examinations to all participating members of the AHS survivor and in-utero cohorts. This examination currently consists of a complete physical examination that includes systolic and diastolic blood pressures, electrocardiography, radiography, abdominal and thyroid ultrasonography as well as special tests of bone mineral density and cognitive function. Data are also collected on smoking and drinking habits, diet, and other factors. Overall participation remains high (almost 80% of those who were still living in the clinical contacting area participated in the most recent examination cycle). Home visits and hospital examinations are conducted for those survivors too infirm or incapacitated to participate in examinations at the Foundation's clinic. Participation rates do tend to decline sharply among the oldest groups of survivors, and as a consequence of this, thought is being given to plans to increase the examination frequency for some of the older individuals as well as to the development of cost-effective methods of special morbidity surveillance (see next item).

Special one-time examinations have been carried out for selected subsets of the RERF cohorts. The major examination programs, included annual examinations during 1956-63 of in-utero cohort members during adolescence; special examinations of almost 25,000 F_1 cohort members for the biochemical and cytogenetics studies; and most recently the ongoing examinations of the F_1 cohort members and parents in conjunction with the establishment of permanent lymphocyte cell cultures for future genetic studies. As discussed later, plans are being developed to conduct clinical examinations on a limited number of F_1 cohort members in order to assess the feasibility of an ongoing clinical examination program for a subset of the F_1 cohort members.

AHS mail- and telephone-based morbidity surveillance

In response to the recommendations of the 1993 Health Monitoring Workshop, a new AHS morbidity surveillance system was introduced in 1995. This system involves a short mail

survey with subsequent telephone contact at six month intervals. Thus far, response rates have exceeded 90%. To validate the information obtained from this survey a system of periodic hospital and home visits by physicians or public health nurses within the regular two year examination cycle should be introduced.

Mail surveys

Since 1965 a number of mail surveys have been carried out on the LSS or AHS cohorts. These surveys provide important data on risk factors that cannot be determined by means of the routine mortality surveillance program. As described elsewhere, in response to the recommendations of the Blue Ribbon Panel, a new mail survey of F_1 cohort members will be carried out within the next few years.

RESEARCH PLANS BY DEPARTMENT

Research at the Foundation centers on two broad fronts, namely, those programs that will presumably continue well into the future, such as the periodic reports on mortality and cancer incidence in the LSS sample, and are commonly designated as the "core activities," and those programs, the "specific research activities," that are initiated within a single department and are generally time-limited. As previously noted, the core activities are set forth in the so-called "platform protocols" whereas the specific research activities are described in individual research protocols. Largely for convenience, we describe departmental research activities on an individual departmental basis.

Departments of Clinical Studies

The AHS biennial examinations initiated in 1958 continue. The primary purposes of these examinations have been to determine the types of diseases and abnormalities in physiologically or biochemically determined values that may have occurred as a consequence of previous exposure to ionizing radiation and to collate this information with other life experiences and death. The AHS clinical examination is the only point of direct contact with the survivors and functions as a source of biological materials for various special studies.

The AHS has greatly increased in importance in recent years as a result of the accumulation of an enormous body of data on serial medical examinations, with and without the superimposed radiation aspects. Particularly noteworthy is the accumulating evidence that cardiovascular mortality may have a positive radiation-dose response. This potentially important and largely unexpected relationship could never be properly studied using death certificate data alone. Similarly intriguing and potentially important relationships arise from the clinical studies on hyperparathyroidism and serum levels of parahormone, calcium, and alkaline phosphatase. These results suggest that significant deviation in calcium metabolism may be a direct radiation effect and raise further questions about bone density and osteoporosis among the survivors. Still another unexpected finding is the retrospective evidence that radiation is associated with premature menopause and this, in turn, may result in earlier onset of other physiologic conditions such as an increase in cholesterol levels and cardiovascular disease. However, given the age of the survivors, the window of time for such studies is growing shorter, and it is imperative that these opportunities be exploited soon.

The major research elements in the Department's investigations of the AHS sample can be categorized as follows: (1) characterization of cancer types in relation to various confounders of radiation effects, (2) radiation-related noncancer diseases (benign tumors, cardiovascular diseases, and other chronic diseases), (3) aging associated with exposure, (4) radiation-related changes in physiological, biochemical, and hematological measurements, (5) medical dosimetry, (6) psychosocial changes associated with exposure, and (7) health status of the in-utero exposed.

Program objectives

1. To provide biennial comprehensive medical examinations to the AHS cohort subjects to determine disease occurrence and longitudinal changes in physiological or biochemical parameters in relation to exposure to ionizing radiation and to relate this information to effects on life span.

2. To conduct special in-depth studies to determine the association between ionizing radiation and various health outcomes taking into account the possible effects of other health determinants (for example, life-style factors, physiological and biochemical determinants, prior health history, and menstrual and reproductive history for women).

3. To collect and store biological materials for basic science uses.

4. To utilize the accumulated data for epidemiological purposes in general.

Major research activities in the next five years

A. Core activities (Hiroshima and Nagasaki)

Priority 1

A-1. Basic AHS examination (RP 2-75):

The AHS clinical examinations will be continued in their usual format, but to optimize the quality and quantity of the clinical information considering the aging of the population, a new method of morbidity surveillance was introduced in Hiroshima and Nagasaki in 1995 based on the recommendation of the Health Monitoring Workshop in 1993. This method, with modifications if warranted, will be continued. The new morbidity surveillance consists of a mail survey followed by telephone contact every six months. Since its introduction, the response rate has been more than 90%. To validate the information obtained through this new surveillance program, a system of periodic hospital and home visits by either physicians or public health nurses within the examination cycles should be begun as soon as possible. The utility of introducing an annual health examination for older AHS members, such as those who are 70 years old or older, will also be carefully assessed both from the standpoint of the health of the study participants and research needs.

A-2. Application of new methods of longitudinal data analysis:

A new method of analysis of longitudinal epidemiological data (which takes fuller advantage of the 38 years of accumulated serial measurements than is possible with cross sectional analyses) is being developed with support from staff members of the Departments of Statistics and Epidemiology. The creation of a new AHS database (diseases and measurements) for this type of analysis is currently underway.

A-3. Collection and storage of biological materials:

Collection and storage of biological materials, such as serum, plasma, and lymphocytes, will be continued with some modification of the method of storage, if necessary. The collection of teeth extracted for health reasons will be continued to provide materials for ESR measurements through the new AHS surveillance system.

A-4. Improvement of clinical examination procedures:

In addition to the above, clinical examination procedures of recognized benefit to the study participants, such as early cancer detection or health guidance, that will provide more services to the AHS participants as recommended by the Blue Ribbon Panel, will be updated and broadened to maintain a high level of AHS subject participation. However, it is unrealistic to seek to obtain such equipment as a CT scanner or MRI, and where such tests are needed, they should be performed through collaboration with local medical institutions.

Research plan for the next one year (A1-A4):
The plan to produce *AHS Report 8* will be developed. In this report, the study period will be extended to 1994 and analytic methods will place greater emphasis on confounding and bias due to long-term follow-up, migration and nonparticipation. The creation of the new AHS database will be completed. A plan to improve services to AHS participants will be developed.

Research plan for the next three years (A1-A4):
The *AHS report 8* will be completed and the results published. The new information obtained through the AHS surveillance program should become available for use in AHS Report 9. Comprehensive clinical examination procedures of recognized benefit to the study participants will be introduced in an effort to provide more services to the participants.

B. Special research activities (Hiroshima)

Priority 1

B-1. Benign tumors:

a) Hyperparathyroidism (RP 11-86, 2-89):

Screening for hyperparathyroidism, by measuring serum calcium level, has been underway since 1986. Continued screening will provide not only incidence data on

hyperparathyroidism but could also offer a clue to the cause of the slightly elevated levels of serum calcium and parathyroid hormone seen among survivors exposed to higher radiation doses.

Research plan for the next one year:
Data collection for a 10-year incidence study will be completed.

Research plan for the next three years:
The incidence of hyperparathyroidism will be analyzed for radiation effect, using the data accumulated in the 10 years from 1988 to 1997.

In collaboration with the Department of Radiobiology, a protocol for a molecular biological study (PRAD gene analysis) will be developed to elucidate the etiological mechanism underlying parathyroid adenoma and elevated levels of serum calcium and parathyroid hormone among individuals exposed to radiation.

b) Other benign tumor study (RP 6-86):

Systematic detection of various benign tumors such as myoma uteri, ovarian tumor, and liver hemangioma are being undertaken using abdominal ultrasonographic techniques.

Research plan for the next one year:
Results of the prevalence study of uterine myoma will be published.

Analysis of the prevalence of liver hemangioma and ovarian tumor determined by ultrasonography will be completed.

c) Benign thyroid tumors:

In Nagasaki, thyroid tumors and disorders were screened for by means of physical examination, ultrasonography, and thyroid function tests from 1984 to 1987.

Research plan for the next one year:
The feasibility of studying benign thyroid tumors or thyroid disorders in Hiroshima will be examined.

Research plan for the next three years:
If the decision is made to initiate a thyroid study in Hiroshima, a research plan will be developed and data collection begun.

B-2. Cardiovascular disease study (RP 4-85):

A longitudinal cardiovascular study has been underway since 1965, and the results of this study, covering the period of 1958-1990, suggest a positive radiation effect on the incidence of myocardial infarction (MI). The estimated relative risk (RR) at 1 Gy is 1.17 (p=0.02, 95% confidence interval: 1.01-1.36). In a Cox regression analysis including such factors as age, sex, blood pressure, and cholesterol, it was found that exposure dose still

remained a significant factor, though the association was less than that with age, sex, or blood pressure, suggesting that atomic bomb radiation may be involved in the occurrence of MI. In addition, the different endpoints of atherosclerosis available in the AHS database, such as the prevalence of aortic arch calcification, calcification of the abdominal aorta, blood coagulability, the prevalence of isolated systolic hypertension, and the prevalence of retinal arteriosclerosis, were analyzed and all of these endpoints suggested the presence of radiation effects. Studies in progress include those on sudden death and detection of peripheral vascular disease by pulse wave velocity (PWV) measurements and ankle-arm blood pressure ratio using Doppler equipment. The analysis of radiation effects on conventional risk factors, such as blood pressure and cholesterol levels, has been underway for some time. An analysis of plasma fibrinogen is also underway as a part of the NI-HON-SAN Study, which will be described in more detail later. Studies on new risk factors, such as *H. influenzae* infection and homocysteine will be undertaken in the near future either in cross-sectional fashion or by a nested case-control study using stored sera. The feasibility of ultrasonographic measurement of the wall thickness of the carotid artery to detect latent atherosclerosis will be explored. The incidence studies on myocardial infarction and stroke will continue beyond the next five-year period because the necessary information can be obtained through routine AHS data collection and it is worthwhile to continue to try to understand the underlying mechanisms. The other studies are conducted over shorter periods, such as two years.

Research plan for the next one year:
Manuscripts on myocardial infarction, isolated systolic hypertension, calcification of the aortic arch, and pulse wave velocity will be prepared and submitted for journal publication. The analysis of plasma fibrinogen will be completed. Data collection on ankle-arm blood pressure will be completed. The feasibility of studies of new risk factors will be carefully assessed.

Research plan for the next three years:
Data collection on the incidence of myocardial infarction and stroke will continue. Results on plasma fibrinogen will be published. If new proposed studies turn out to be feasible, data collection will be initiated.

B-3. Studies of liver disease (RP 9-92):

Previous studies have shown a higher prevalence of hepatitis B surface (HBs) antigen in highly exposed subjects, but no difference in the prevalence of anti-HBs antibody was observed between the two groups.

With the availability of the serum assay for hepatitis-Be antigen (HBe) and hepatitis-C virus antibody (HCV), a study of liver diseases, such as chronic hepatitis or liver cirrhosis, was initiated in 1993 to determine the relationship between radiation dose and the prevalence of infection by B and C hepatitis virus in the AHS sample.

Research plan for the next one year:
Measurements and analysis of the data on HCV antibody, and HB antigen and antibodies will be completed.

Research plan for the next three years:
The design of a nested case-control study using stored serum will be developed. Using stored serum collected before onset of hepatoma or liver cirrhosis, the prevalence of HCV or subtypes of HCV in cases and controls will be compared.

Priority 2

B-4. Cancer study (RP 2-75):

Cancers continue to be one of the most prevalent diseases among AHS subjects. For example, from 1969 through 1991, approximately 800 gastric cancers, 280 lung cancers, and 200 breast cancers were found among the AHS subjects in Hiroshima.

Cancer screening will continue to be one of the objectives of the AHS, and special emphasis will be placed on screening for cancers which are often not fatal, such as skin, breast, and thyroid. A new analysis including potential confounders and risk modifiers using the information obtained by various questionnaires and clinical measurements at the time of the routine AHS examinations, such as dietary factors and medications, will be initiated. A case-control study will be conducted on various cancers related to nutrients, hormones and potential carcinogens such as viral infections using stored serum. This study will continue beyond the next five years because all of the necessary information is obtained through routine AHS operations.

Research plan for the next one year:
An attempt will be made to create a new data set for longitudinal analysis using currently available information on confounders and/or risk modifiers. An inventory will be initiated of stored sera for each cancer case for use in future case-control studies.

Research plan for the next three years:
If a new data set is constructed, longitudinal analysis will be initiated to identify confounders or risk modifiers of radiation in cancers among atomic bomb survivors. Once the inventory of stored sera on cancer cases is completed, similar steps will be taken for controls. Then, a comprehensive study method will be developed including noncancer diseases for nested case-control studies.

B-5. Aging and radiation:

Priority 1

a) Osteoporosis study (RP 3-91):

Osteoporosis is a common aging-related disorder among Japanese, and bone density is influenced by premature menopause and parathyroid hormone levels which are known to be radiation-related. Measurement of spinal bone density using dual photon absorptiometry has been underway since 1989, and the results suggest a significant positive relationship between radiation exposure and spinal bone mineral density. However, the apparent increase in bone mass measurements may have been a confounding

effect caused by calcification of the abdominal aorta which is positively associated with radiation dose. To solve this problem, bone mineral density in the spine and hip using dual X-ray absorptiometry was begun in 1994. Total body composition (fat, lean body mass, bone) among the selected AHS samples has been measured using the same equipment.

Research plan for the next one year:
Radiation effects on bone mineral density and body composition including various potential risk factors will be analyzed.

Research plan for the next three years:
A longitudinal analysis will be undertaken to look at the radiation effects on changes in bone density with aging.

b) Senile dementia (RP 5-92):

A dementia study was begun in 1992 to assess the association between radiation exposure and a decline in cognitive function and to determine whether the prevalence of senile dementia increases as radiation dose increases. The epidemiological survey method being used was developed through international collaboration under a program known as the NI-HON-SEA study, which will be described later. This study may make it possible to examine the effects of ionizing radiation on the mature central nervous system.

Research plan for the next one year:
Cognitive function tests have been conducted on about 70% of AHS participants at this time; the remainder will be tested next year.

Research plan for the next three years:
Case ascertainment of senile dementia by a neurologist will be complete, and the results of an analysis of the data will be written up for publication.

c) Menopause study (RP 5-93):

Menopause is a general biological marker of aging in women. Information on age at menopause has been obtained in past epidemiological surveys in Hiroshima and Nagasaki. In Nagasaki, self-reported date of last menstrual period has been routinely obtained at the time of the biennial chest X-ray examinations. Incidence of menopause among Nagasaki participants was analyzed in 1993 using this self-reported information. The results suggest that the higher exposed group experienced an earlier onset of menopause. A longitudinal study using hormone measurements as an indicator of menopause was initiated in 1994 and is expected to take four years to complete. The subjects of this prospective study are premenopausal women who were younger than 10 years old or were in-utero when exposed to A-bomb radiation.

Research plan for the next one year:
The level of two important perimenopausal hormones (FSH and estradiol) will be measured every six months until 1997.

Research plan for the next three years:
The relationship between radiation exposure and the levels of these perimenopausal hormones will be analyzed.

Priority 2

d) Physiologic aging study (RP 4-86):

Accelerated aging resulting from irradiation has been a scientific concern for several decades. Earlier studies of the AHS participants have failed to reveal evidence of such an effect; however, these studies were conducted almost twenty years ago. It is important, therefore, to repeat them using a broader battery of physiological measures and several endpoints that reflect aging. The endpoints to be used for analysis are the incidence of myocardial infarction and stroke, cardiovascular mortality, and the prevalence of aortic arch calcification. The physiological measurements to be used are hand grip strength and skin elasticity which are measured as part of the routine AHS examinations in Hiroshima.

Research plan for the next one year:
Data analysis will be carried out using new endpoints, and a manuscript will be prepared.

Research plan for the next three years:
A new research plan including the use of new statistical methods will be developed.

B-6. Medical dosimetry (RP 7-86, 8-86):

Information on exposure to X-irradiation (radiological examinations at ABCC/RERF, radiological examinations elsewhere, and radiation therapy) has been obtained in the course of the AHS examinations. The examination of ionizing radiation exposure for medical reasons may facilitate assessment of the role of medical X-ray exposures in the follow-up studies of the A-bomb survivors. However, this is an issue which requires careful consideration since it will be difficult to incorporate these data into the various analyses conducted at RERF.

Research plan for the next one year:
Data collection will continue.

B-7. Psychosocial studies and others (RP 2-75):

Few studies have been done on the psychosocial effects of exposure to the atomic bombing, although it is well recognized that they vary greatly in association with socioeconomic factors. Nonetheless, it is possible that psychosocial factors may have influenced the occurrence of disease or at least the stage of development when disease is recognized.

Research plan for the next one year:
A study will be designed to assess the frequency and nature of the social and psychological problems experienced by the survivors with the cooperation of psychological specialists.

The possibility of international collaboration with scientists at the State University of New York will be explored.

B-8. Measurements:

Priority 1

a) AHS Clinical measurements (RP 2-75)

In the AHS, an enormous amount of information has been obtained on laboratory measurements, and it has now become possible to analyze the changes in these measurements over time. In collaboration with the Department of Statistics, growth curve analyses of the information on total serum cholesterol and blood pressure showed that heavily exposed individuals had higher levels of total serum cholesterol. This elevated cholesterol level associated with radiation exposure may have been one of the confounding factors in the increased cardiovascular morbidity and mortality seen among atomic bomb survivors.

Research plan for the next one year:
Results of the longitudinal analyses of cholesterol and blood pressure will be published. The other longitudinal data, including height, weight, and hematological information, accumulated since 1958 will be analyzed.

Research plan for the next three years:
Autoanalyzers for biochemical measurements were introduced into the Hiroshima Clinical Laboratory in 1986 and into Nagasaki in 1987. Longitudinal analyses will be performed on twenty different biochemical measurements accumulated from 1987 to 1996.

Priority 2

b) Benign monoclonal gammopathy (RP 6-85):

Benign monoclonal gammopathy has been shown to be suggestively related to radiation dose, a finding of potential importance since this disease has the possibility of being transformed into multiple myeloma. Screening with protein electrophoresis will be continued for detection of cases with monoclonal spike. Cases will be further tested for confirmation.

Research plan for the next one year:
Screening by protein electrophoresis will continue as before.

Research plan for the next three years:
The study of the incidence of this condition will be summarized and the results published.

B-9. National and international collaboration (RP 4-85, 5-92, 3-91):

There are three major international collaborations underway in Hiroshima. These are the

NI-HON-SAN Study, the NI-HON-SEA Study, and the Japan-Hawaii Osteoporosis Study. All of these studies have been beneficial to RERF because the epidemiological methods developed through collaboration have been applied to other radiation research, and they have been producing important results in elucidating effects of radiation on noncancer diseases.

At its outset, the NI-HON-SAN Study was a study of cardiovascular diseases among Japanese men and men of Japanese descent living in Honolulu and San Francisco. It was initiated in 1965. Although follow-up of the San Francisco cohort ceased in the mid-1970s, the Japanese and Hawaiian cohorts are still being studied. A symposium to commemorate the study's 30th anniversary was held on 2 September 1996 in Hiroshima.

The NI-HON-SEA Study is a study of senile dementia among Japanese men living in Japan and men of Japanese descent living in Honolulu and Seattle. It began in 1992.

The Japan-Hawaii Osteoporosis Study was initiated in 1991.

We have been involved in several national collaborative studies sponsored by the Ministry of Health and Welfare. Through these collaborations, it has been possible for us to develop epidemiological methods to study radiation effects on noncancer diseases and to provide diagnostic services to AHS participants that otherwise would not have been possible. For example, we have been able to obtain free use of a modern bone mineral densitometer to conduct studies of osteoporosis as part of a national collaborative study.

<u>Research plan for the next one year:</u>
NI-HON-SAN Study: Results of comparisons of mortality, glucose intolerance, and fibrinogen levels will be summarized and published.

NI-HON-SEA Study: Data sets will be created to compare the prevalence of senile dementia in the different study cohorts.

Japan-Hawaii Osteoporosis Study: In collaboration with the Hawaii Osteoporosis Center, a comparative study of bone mass, bone loss, and potential risk factors of osteoporosis among Japanese and Japanese-Americans will be analyzed.

<u>Research plan for the next three years:</u>
NI-HON-SAN Study: Results of comparisons of ankle-arm blood pressure index, EKG changes, and pulmonary function will be summarized and published.

NI-HON-SEA Study: Results will be summarized and published.

Japan-Hawaii Osteoporosis Study: Results will be summarized and published.

C. New research initiatives (Hiroshima)

Priority 1

C-1. Molecular epidemiological study:

There are many studies describing the importance of oncogenes and tumor suppressors in the development of malignant disorders, but the role of ionizing radiation in the activation or suppression of these genes is still unclear. In addition, recent studies suggest that some of these genes may be involved in the development of atherosclerosis. A molecular epidemiological study on the AHS population will be initiated with inter-departmental collaboration to examine these issues. For this study, collection of fresh biological materials from surgery, such as tissues of cancers, benign tumors, blood vessels and skin, is desirable through a more intensive morbidity surveillance, in addition to the preservation of lymphocytes of the AHS subjects.

Research plan for the next one year:
A study plan will be developed.

Research plan for the next three years:
If a study is thought to be beneficial for RERF, collection of biological materials will be initiated and appropriate techniques for their use will be developed.

C-2. Feasibility of an F_1 clinical study

In response to the recommendations of the Blue Ribbon Panel, the feasibility of a full-scale study of chronic disease among the F_1 will begin with a mail survey involving all members of the F_1 mortality cohort, to be followed by the clinical examination of a small set of these individuals, about 500 persons, and biochemical genetic studies of several genes known to be related to common chronic diseases.

Research plan for the next one year:
The feasibility study will last for two years.

Research plan for the next three years:
A workshop will be convened to determine whether a full-scale study should be conducted.

Priority 2

C-3. Lenticular opacities:

A new system of grading the degree of lenticular opacification, developed by the research group at NASA, will be introduced and grading will be done using illustrations from the cases of cataracts detected in previous ophthalmological surveys. This will be part of an international collaboration with NASA that aims to test hypotheses regarding the relationship between degree of opacification and radiation dose. For those survivors who were young at the time of the bombing and have not been included in previous surveys, we will consider the use of stereolaminographic images of the lens to provide a more objective and permanent basis for the evaluation of changes that may occur in the future.

Research plan for the next one year:
A study plan will be developed.

Research plan for the next three years:
If the study plan is thought to be beneficial, data collection will be initiated.

Project time lines (Hiroshima)

	1997	1998	1999	2000	2,001.00
Core program: AHS (RP 2-75)	→	→	→	→	→
Special studies					
Cancer study (RP2-75)	→	→	→	→	→
Parathyroid (RP11-86)	→	→	→	→	→
Other benign tumor (RP6-86)	→	→	→		
Cardiovascular (RP4-85)	→	→	→	→	→
Liver disease (RP9-92)	→				
Aging and radiation					
Osteoporosis (RP3-89)	→	→	→	→	
Dementia	→	→	→		
Physiologic aging (RP4-86)	→	→	→		
Menopause (RP5-93)	→	→			
Medical dosimetry (RP7-86,8-86)	→	→	→	→	→
Psychosocial (RP2-75)	→	→	→		
Monoclonal gammopathy (RP6-85)	→	→	→		
National-international collaboration					
NI-HON-SAN (RP4-85)	→	→	→	→	→
NI-HON-SEA (RP5-92)	→	→	→		
Osteoporosis (RP3-91)	→	→	→		
Molecular epidemiology	→	→	→	→	→
Cataract		→	→	→	→

Personnel requirements (Hiroshima)

Year	1996	1997	1998	1999	2000	2001
Research Scientists*	6 (5+0.5 x2)	6	6	6	6	6
Assistant Adm. Chief	1	1	1	1	1	1
Nurses*	9	8	7	7	7	7
Technicians (X-ray)	3	3	3	3	3	3
Technicians (Lab)	8.5	8	8	8	8	8
Contactors*,#	9	11	12	12	12	12
Clerks+	13	12	12	12	12	12
Total	49.5	49	49	49	49	49

*: If clinical examination of the F_1 is introduced, the number of physicians, nurses and contactors must be increased.
#: Replacement should be made by nurse or public health nurses.
Need more contactors due to aging of the population and newly introduced surveillance program.
+: Replacement should be made by research assistants.

Space requirements (m^2) (Hiroshima)

	1996	1997	1998	1999	2000	2001
Administration	134.50					
Medicine	78.50					
Nursing	185.30					
Radiology	169.21					
Clinical Lab	236.06	+10*	+30**			
Contacting	59.80					
General affairs	286.83					
Total	1,150.20					1,190.20

* : Room for hematology currently in use needs expansion for smooth daily operation.
**: Additional space for storage of serum and plasma is needed.

Equipment budget (Hiroshima) (x ¥ 1,000)

Fiscal year	1997	1998	1999	2000	2001
Laboratory equipment	3,760	2,533	13,528	0	7,283
Computer equipment	4,612	1,952	2,682	712	4,282

D. Special research activities (Nagasaki)

Priority 1

D-1. Effects of menopause on risk factors for ischemic heart disease - a longitudinal study of the Nagasaki Adult Health Study sample (RP 1-95).

The purpose of this study is to look for an association between perimenopausal changes in the level of total serum cholesterol and its fractions and changes in serum estradiol. The results of this study will produce hypotheses on cardiovascular mortality and its relationship to radiation dose in women, because radiation seems to accelerate the onset of menopause, that is, radiation may cause earlier deterioration of the atherogenic cholesterol profiles.

At the outset of the study 63 of 73 study participants had not yet experienced menopause. This study will continue for 4 to 6 years.

D-2. The Nagasaki Department of Clinical Studies will implement all RPs except for RP 4-86, RP 3-89, RP 3-90, RP 3-91, RP 6-92, and RP 2-95 in the same manner as conducted by the Hiroshima Clinical Studies Department.

Project time lines (Nagasaki)

Project	1997	1998	1999	2000	2001
Menopause	⇒	⇒	⇒	⇒	⇒

Personnel requirements (Nagasaki)

Fiscal Year	1997	1998	1999	2000	2001
Physicians[1]	2.5	2.5	2.5	2.5	2.5
X-ray technicians	3	3	3	3	3
Clinical Laboratory	9	9	9	9	9
Nursing Section	5	5	5	5	5
Contacting Section	9	9	9	9	9
Administration	9	9	9	9	9

[1] Dr. Midori Soda is included as half-time in the Nagasaki Department of Clinical Studies.

Space requirements (m^2) (Nagasaki)[1]

Fiscal Year	1997	1998	1999	2000	2001
Internal Medicine	73	73	73	73	73
X-ray	171	171	171	171	171
Clinical Laboratory	298	298	298	298	298
Nursing Section	143	143	143	143	143
Contacting Section	81	81	81	81	81
Administration	103	103	103	103	103

[1] Personnel strength and floor space must be expanded if a full-scale study of chronic disease among the F_1 is initiated.

Equipment budget (Nagasaki) (x ¥ 1,000)

Fiscal Year	1997	1998	1999	2000	2001
Laboratory	19045	0	0	3000	0
Computer Equip.	1072	1052	2252	452	852

[1] The standard equipment budget was calculated on the basis of the present cost of the respective pieces of equipment. Annual inflation and price increases due to equipment upgrading may affect this five-year projection. Equipment approaching the end of its working life may malfunction and would also alter this estimate as would the initiation of new research protocols.

Departments of Epidemiology

Until the mid-1980s, epidemiology, statistics, and computing were combined in a single Department of Epidemiology and Statistics at the Foundation. It became clear, however, that this was neither an efficient nor cost-effective organization of resources and skills. During 1984-85, these disciplines were established as independent research or support departments. In 1994, the Departments of Epidemiologic Pathology, responsible for the conduct of pathology studies and the tumor and tissue registries, were merged with the Departments of Epidemiology.

Program objectives

The Departments of Epidemiology play a central role in the conduct of the long-term follow-up of the three cohorts, LSS, in-utero, and F_1. The follow-up of these cohorts has long relied on mortality surveillance through the use of the nationwide family registration system, the *koseki*. Recently, cancer incidence data from improved tumor registries in Hiroshima and Nagasaki have become available on these cohorts, adding new dimensions to our studies of radiation cancer risks. Continued follow-up of these cohorts is essential in clarifying the temporal patterns of cancer risk as young subjects reach ages when background cancer risk is increased. In addition, the emerging excess noncancer mortality risk is of particular concern as the nature of the risk is still unclear. Although the numerous mail surveys conducted in the LSS provide potentially valuable data on the role of nonradiation risk factors, little effort has been made to incorporate these data into RERF analyses. We must place increased emphasis on the studies of nonradiation risk factors in relation to cancer and noncancer disease risks.

Because of the nature of the RERF research, the Departments of Epidemiology should and will play a key role in the design and conduct of various interdepartmental research activities. As indicated in the Blue Ribbon Panel report, one of the most important multidisciplinary programs at the present time is the molecular epidemiology of cancer, which will require close interdepartmental and interdisciplinary communication. In addition, the Departments of Epidemiology must also play a more active role in generating new ideas for studies to answer questions arising from the ongoing epidemiological studies, which are being conducted in collaboration with other RERF departments or outside research groups.

The epidemiological research activities in Hiroshima and Nagasaki are carried out following common research protocols and procedures. The professional staff in the Department of Epidemiology in Hiroshima currently consists of three epidemiologists supplemented by one

pathology consultant and one visiting pathology investigator. The professional staff in the Nagasaki Department of Epidemiology consists of one epidemiologist and one physician. The epidemiology staff work closely with the staff in the Department of Statistics in study design, data analysis, and preparation of major reports; they also work with the Departments of Statistics and Information Technology in database design and development.

A. Core activities

The core activities of the Epidemiology research program are as follows:

A-1. Publication of periodic general reports

The Departments of Epidemiology working together with the Department of Statistics will continue to produce periodic and specific reports on cancer and noncancer mortality as well as cancer incidence resulting from continued follow-up of the LSS, in-utero and F_1 cohorts. In view of the uncertainty regarding the cancer risk for the young survivors, continued follow-up of the LSS and in-utero cohorts in the next decade and beyond is considered critical. Principal periodic reports that are expected within the next 5 years include LSS Report 13 on updated cancer and noncancer mortality (through 1995), an updated LSS cancer incidence report (through 1992 or later), an in-utero cancer incidence report, and F_1 mortality and cancer incidence reports.

Investigations of the noncancer mortality data will be particularly challenging because of the multiplicity of factors that must be considered and the paucity of relevant biological models. As the survivors age, further follow-up of the cohort will provide increasingly useful information on this important question. At the same time, it will be equally important to define working hypotheses to account for the excess noncancer disease risks and to develop and carry out research programs in collaboration with other RERF departments and outside research groups.

A-2. Conduct of site-specific cancer studies

Several site-specific cancer studies are currently active. These studies are designed to provide detailed data on pathological features of tumors associated with radiation exposure accompanied by in-depth risk analysis, providing insights into the biological bases of radiation-induced tumorigenesis. A number of reports from this series of site-specific cancer studies will be forthcoming in the next several years.

A-3. Continued management of the Hiroshima and Nagasaki tumor and tissue registries, and development of a tissue bank

The Foundation continues to manage the Hiroshima and Nagasaki tumor and tissue registries which provide high-quality cancer incidence data. They are among the few registries in Japan whose incidence data have been included in several volumes of *Cancer Incidence in Five Continents* (by IARC/IACR), a worldwide compilation of cancer incidence data. The LSS cancer incidence data published in 1993 and 1994 and the current series of site-specific cancer incidence studies would not have been possible

without RERF's direct involvement in the registry operations. While we will continue to publish the Hiroshima and Nagasaki incidence data in future volumes of the above IARC/IACR monograph series, it is important that we also produce our own comprehensive and more detailed analyses of population-based cancer incidence data.

RERF, together with the local medical societies, also continues to manage the tissue registries. These registries have the potential to be developed into a tissue bank linked to the LSS, which will be a tremendously valuable source for molecular oncology studies. Therefore, the Departments of Epidemiology must continue to be involved in the management and further development of the tumor and tissue registries.

A-4. Design and conduct of case-control and other special studies to address specific questions

The Epidemiology department also conducts ad hoc case-control or other studies to investigate specific hypotheses prompted by regular analyses of the A-bomb survivor data or other research developments. Such studies involve personal interviews to elicit specific information, make use of existing information, or require biological samples such as tissues and frozen sera. Case-control studies nested in the cohort are particularly useful for providing answers to the questions of current interest. Illustrative examples include studies of liver cancer and viral hepatitis infection (ongoing), breast cancer and detailed reproductive history (completed), and stomach cancer and serum ferritin (completed). The Department will continue to generate new studies of this kind to gain insights into the nature of cancer and noncancer diseases.

A-5. Studies of radiation and nonradiation factors using mail survey data

During the course of the LSS follow-up several mail surveys have been conducted to obtain epidemiological information on lifestyle factors such as smoking, alcohol intake, diet, and occupation. To date use of this information has been limited to the smoking data as related to cancer. Studies of conventional risk factors are also critically important in elucidating the nature of the excess noncancer vascular, digestive, and respiratory diseases. While some work has been done in the last few years, further effort should be devoted to the study of nonradiation risk factors.

These studies are covered by the following platform research protocols:

Priority 1

Research plan for RERF studies of the life span of A-bomb survivors, Hiroshima and Nagasaki (RP 1-75)

Research plan for RERF studies of the potential genetic effects of atomic radiation: Hiroshima and Nagasaki, Part 1. Mortality study of children born to atomic bomb survivors (RP 4-75)

Tumor registry study in Hiroshima and Nagasaki (RP 18-61)

Detection of leukemia and related disorders (RP 29-60)

Pathology studies in Hiroshima and Nagasaki, revised research plan (RP 5-89: Formerly RP 3-75)

Guidelines for the conduct of site-specific cancer incidence studies among A-bomb survivors, Hiroshima and Nagasaki (RP 9-88)

B. Special research activities

B-1: Site-specific cancer studies

Under the platform protocols regarding tumor and leukemia registries (RP 18-61, RP 29-60) and pathology studies (RP 5-89, RP 9-88), various site-specific cancer studies are now under way. Standardized pathology reviews are conducted by panels of pathologists (from Hiroshima and Nagasaki) using contemporary classification schemes, and special effort is made to ascertain cases beyond those routinely reported to the tumor and tissue registries. Pathology slides and tissue blocks obtained for these studies facilitate the conduct of molecular epidemiological studies. These site-specific studies in various stages of completion are summarized in the next table, followed by a description of the objectives for each study.

Priority 1

Incidence of lymphoid malignancies among the atomic bomb survivors, 1950-90 (RP 3-94):

This study is designed to provide more definitive data on the rather inconsistent evidence thus far available on the risk of lymphoid malignancies in the LSS. The objective is to investigate all lymphopoietic tumors (lymphomas, multiple myeloma, lymphocytic leukemias) between 1950 and 1990 in the LSS. Emphasis is on the confirmation and classification of cases using modern techniques. The study involves both hematologists and pathologists engaged in lymphoid tumor research. Non-Hodgkin's lymphomas are classified by immuno-histochemical studies into T- or B-cell lymphomas, and the diagnosis of adult T-cell leukemia is based on detection of proviral DNA of HTLV-I using archived tissues.

Studies of lung cancer incidence among the atomic bomb survivors, 1950-90 (RP 1-94):

Lung cancer is a late effect of radiation exposure, but several specific issues and questions remain to be addressed. These include the specificity of various cell types involved in radiation- versus smoking-related cancers, confounding and joint effects of smoking in relation to radiation exposure, delineation of the temporal trend with allowance given to the age-at-exposure and attained-age effects. ICRP also has recently published a new report on lung cancer risk from inhaled radionuclides modeled on an anatomical basis in terms of lung "compartments." New information on anatomical distribution of lung cancers resulting from uniformly distributed radiation may be useful for evaluating the ICRP model. This RP was developed to address these questions and issues.

Current and Planned Site-specific Cancer Studies

Site	Year study began	Specific objectives	Current status/Plan
		Currently active	
Liver	1990	Incidence; role of hepatitis infection (case-control)	Preliminary results presented at Jpn. Soc. Path. Mtg., '96; Paper on incidence to be submitted within a year; HCV assays in progress
Salivary gland	1991	Benign & malignant tumors; major & minor glands	Results presented at Jpn. Soc. Path. Mtg., '95 One paper published; another submitted; To be completed within a year
Skin	1991	Cell types and UV effect	Results presented at Jpn. Soc. Path. Mtg., '95; Data presented One paper submitted; another paper in preparation;To be completed within a year
Thyroid	1991	Benign & malignant tumors; microcarcinomas	Ready for analysis; Papers to be prepared in the next 2-3 years
Ovary	1992	Benign & malignant tumors	Preliminary results presented at Jpn. Soc. Path. Mtg., '96; Analysis in progress; To be completed in 2-3 years
Nervous system	1992	Neurilemmoma, meningioma, pituitary tumors; benign and malignant	Results presented at Jpn. Soc. Path. Mtg., "95 Two papers in preparation; To be completed within a year
Breast	1993	Update of the continuing series; risk for young women	Paper in preparation; To be completed within a year
Lung	1994	Topographic distribution, cell types and smoking; time trend	Pathology review in progress; Expected to be completed in 4-5 years
Lymphoid	1994	Lymphoma, multiple myeloma; T-cell and B-cell origin	Pathology review started; Expected to be completed in 4-5 years
		Planned	
Colon		Different sub-sites; parallel molecular study	To be started
Stomach		Histological subtypes; EB virus infection	To be started
Bone/connective tissues		Bone tumors	To be started

Breast cancer incidence study among atomic bomb survivors, 1950-90 (RP 6-93):

This is the latest (started in 1993) of a series of breast cancer incidence surveys, extending the follow-up through 1990. Data collection for this series has been completed, adding 261 newly accessed cases (250 for the period of 1986-1990 and 11 prior to 1986). Of these, 58 cases were exposed at <10 years of age, and this should strengthen risk estimates for this age-at-exposure group.

Incidence of tumors of the central nervous system among A-bomb survivors (RP 4-92):

In the recent solid cancer incidence report, a suggestive dose response was found among those survivors exposed at ages <20 years for tumors of the nervous system except for the brain. These findings prompted the present study. The objective is to ascertain malignant and benign tumors of the central nervous system in the LSS from 1950 to 1987.

Studies of ovarian tumor incidence among the RERF extended Life Span Study cohort, 1950-87 (RP 2-92):

The present study extends the previous ovarian cancer series by 7 years (through 1987) and also includes a systematic ascertainment of benign tumors.

Studies of thyroid tumor incidence among the RERF extended Life Span Study cohort, Hiroshima and Nagasaki, 1950-87 (RP 6-91):

This investigation was started in 1991 with the aim of updating and expanding the earlier thyroid cancer incidence series (through 1979), including both benign and malignant tumor cases diagnosed between 1950 and 1987. The increased number of cases over the extended study period should allow more detailed risk analyses than were available previously.

Studies of skin cancer incidence among the RERF extended Life Span Study cohort, Hiroshima and Nagasaki, 1950-87 (RP 2-91):

The completeness of the ascertainment of skin cancer from the tumor registries is questionable and diagnoses of skin cancer are highly variable among physicians and pathologists. The present study is designed to provide extended case-finding and a standardized pathology review for histological typing of skin tumors. All work related to case ascertainment that began in 1991 has been completed, and analyses have almost been completed. A significant dose response is demonstrated for basal cell carcinoma but not for squamous cell carcinoma of the skin. Noteworthy is the absence of a suspected combined effect of UV and ionizing radiation exposure and a strong effect of age at exposure on basal cell carcinoma.

Studies of salivary gland tumors among the RERF extended Life Span Study cohort, Hiroshima and Nagasaki, 1959-87 (RP 1-91):

This study was initiated in 1991. The objective was to study both benign and malignant

tumors of the major and minor salivary glands diagnosed between 1950 and 1987. All phases of the study are virtually completed. Analysis shows a significant dose response for both benign and malignant tumors. Most of the dose response for malignant tumors is provided by an exceptionally strong dose response for a particular type, mucoepidermoid carcinoma, and most or all of the dose response is attributable to Warthin's tumor.

Primary liver cancer incidence study among atomic bomb survivors, Hiroshima and Nagasaki, 1958-1987 (RP 5-90):

Since diagnostic misclassification is a major concern for liver cancer, the primary objective of this study is to assess the relationship between atomic bomb radiation and liver cancer based on data confirmed by a panel of pathologists. Another objective is to investigate, in a nested case-control study, the possible role of HBV, and possibly HCV, infection in radiation-related liver cancer. The pathology review extends from histologic classification of liver cancer to diagnosis of any accompanying liver cirrhosis and testing for HBV markers. In the companion study conducted in the Department of Radiobiology (RP 5-90), molecular techniques are being used to characterize the HB and HC viruses more precisely.

B-2: Case-control studies in progress

In addition, case-control studies are being conducted to investigate factors other than radiation exposure that may interact with radiation. Information is obtained, primarily by retrospective interview, on personal habits, and other life-style factors, medical history, reproductive factors, and other suspected cancer risk factors.

Priority 1

Interaction between radiation dose and host factors. An epidemiological case-control study of female breast cancer in atomic bomb survivors (RP 14-79):

This study, started in 1979, continues to investigate reproductive and other known risk factors in association with radiation. In a study of 196 breast cancer cases and 566 controls, the risk was found to be positively associated with age at first full-term pregnancy, in agreement with the literature; whereas negative, and partially independent, associations were observed with number of births and total cumulative period of breast feeding. Significant positive associations were also found with history of treatment for dysmenorrhea and uterine or ovarian surgery. Neither age at menarche nor age at menopause was significantly associated with breast cancer. Multiplicative relationships were found between radiation exposure and age at first full-term pregnancy, number of children, and cumulative total period of lactation.

A plan is underway to revise this case-control study by adding reproductive and family information from various Master-File documents kept at RERF (an example of a record-based case-control study).

Priority 2

Thyroid cancer (RP 12-85):

The study includes 365 cases with histologically diagnosed thyroid cancer and their matched controls. Personal interviews have been completed to obtain retrospective information on major risk factors such as diet and nutrition, reproductive experiences and previous medical history. Factors that have been found to be associated with thyroid cancer are: history of cancer in sisters, previous histories of goiter, tonsillectomy, ovariectomy, and breast disease, and increased body mass index. Analysis is almost completed, and a paper is being prepared for publication. Data from this study are included in a pooled analysis of thyroid case-control data from various countries undertaken by the NCI.

Priority 3

Nutrients and cancer (RP 11-85); hormones and cancer (RP 10-85):

These two studies utilize stored sera for nutritional and hormonal assays. Preliminary analysis shows a relationship between total estradiol and breast cancer risk. Following the first paper on serum ferritin and stomach cancer risk (TR 14-89), the second paper on serum selenium and zinc in association with the subsequent development of lung and stomach cancer was published (*Cancer Epidemiology, Biomarkers & Prevention*). In this study of 208 cases with stomach cancer, and 77 cases with lung cancer and matched controls, a slightly increased risk of lung cancer was found to be associated with low serum levels of selenium but little association was found with either lung or stomach cancer across normal selenium or zinc ranges. A paper on breast and other cancers in relation to hormone assays is under preparation and is expected to be completed shortly.

C. New research activities anticipated in the next 5 years

As mentioned above, a number of important specific issues have been identified through the follow-up of the major cohorts. These are summarized below:

Cancer

Increased cancer risks have been clearly substantiated as a late effect of radiation exposure among the survivors. However, several issues regarding cancer risk remain to be clarified.

- Cancer risk among the young: The temporal pattern of cancer risk among the survivors exposed as children, that is before the age of 10, as they reach the ages at which background cancer risk is increased.

- Confounding and modifying effects of nonradiation factors: Because smoking and other life-style factors are important determinants of cancer, cardiovascular and other diseases, more research is needed to study the possible confounding and modifying of effects of nonradiation factors. This is an area which has received little attention in the past and will require collaboration with researchers in other RERF departments and outside RERF.

- Mechanistic models for radiation-induced cancer: Initial attempts by Donald Pierce and Mortimer Mendelsohn to develop a mechanistic model for radiation-induced cancer using the LSS data have provided some interesting and useful insights into how to interpret the age and time dependence seen in the solid cancer risks. There is also increasing interest in other biologically motivated models for radiation carcinogenesis. These models may provide useful insights into temporal patterns, sex differences and other aspects of the radiation-induced excess risk. While most of the developmental work will rely on the Statistics staff, RERF provides an environment for close interaction with radiation biologists. More effort at RERF along these lines of research seems warranted.

- Organ-specific cancer risks: Observed differences in site-specific cancer risks are difficult to interpret because of statistical variability and the relatively small excess number of cases involved. The joint analysis approach initiated by the Department of Statistics on this issue is promising and will be further pursued working with members of the Departments of Epidemiology.

- Incidence vs mortality: While mortality follow-up will continue to be the primary basis of risk assessment, cancer incidence patterns will play an increasingly important role, especially for breast, thyroid, and other less fatal cancers. The availability of both cancer mortality and incidence data now enables us to provide more comprehensive assessment of the radiation risk, starting from cancer onset to death. However, it has also become necessary to pay attention to how to interpret results from mortality and incidence data. It is important to develop methods to provide an integrated presentation of the mortality and incidence data. It will be useful too to develop measures of detriment using both results. While some work has already been done on mortality/incidence comparison and risk of second primary cancers, much more work is needed in this area.

Noncancer diseases

The evidence of an excess noncancer mortality risk in the LSS data is becoming more compelling. Thus, another outstanding issue is further characterization of the noncancer risks in the LSS.

- Working with the Department of Statistics, we will attempt to clarify essential characteristics of the noncancer excess including such issues as the shape of the dose response, patterns of risk by age, sex, and time, etc. Since the excess risk appears to be continuing, we can expect that further follow-up will make possible more detailed analyses and improve characterization of these risks.

- The AHS is the source of clinical data on diseases and laboratory measurements that are immensely useful for characterizing noncancer events. Therefore, it will be essential that we work with the Departments of Clinical Studies and Statistics to develop studies that integrate the LSS and AHS data on radiation effects on noncancer endpoints.

Some other important questions to be examined are as follows:

- Misclassification: We have already shown that the misclassification of cancer to noncancer

on death certificates contributes only a fraction of the observed excess noncancer mortality and that a noncancer excess exists even after the correction for such misclassification. More work is needed to learn how best to deal with misclassification between different noncancer diseases and how this misclassification affects the risk estimates.

- Confounding, biases and indirect effects: Whether the observed noncancer excess mortality results from confounding or indirect effects of other factors, selective or other biases, remains a central question. While all available data should be used to examine these issues, new ideas are also needed to initiate new research and analyses.

- Plausible disease mechanisms: A serious problem with the noncancer risk is the paucity of biological models for radiation induction of noncancer diseases at low dose levels. This is an area in which the development of new innovative research ideas requires close interaction with biologists and clinical investigators. Such collaborations should help us generate and test hypotheses regarding plausible mechanisms for the effects.

New research will be generated in the following areas. These topics are not covered under the existing platform or individual research protocols, but new specific RPs will be developed as needed.

Priority 1

Molecular epidemiology of cancer

As mentioned in the Blue Ribbon Panel recommendations, research on molecular oncology requires specific hypotheses or models that can be tested in this unique population of radiation exposed individuals. Contributions from the Departments of Epidemiology will be several-fold.

First, because of the involvement of the departments in the tumor and tissue registries and their long-standing relationships with the local medical communities, we must take a leading role in establishing collection and management procedures for tissues and other biological samples to ensure that appropriate samples are available for this research. It will be essential that we develop as the first step an efficient database management system, in collaboration with ITD and others, to catalogue all available tissues together with relevant information linked to the RERF cohorts. Second, the Departments of Epidemiology should provide intellectual input by identifying important research questions based on the ongoing analysis of cancer data and by being involved in study design, analysis, and interpretations of the results.

F_1 mail survey

As part of the planned clinical examination of the F_1 population, the Departments of Epidemiology will be involved in a mail survey on this cohort. It is anticipated that basic information obtained from this mail survey will provide data useful for assessing the feasibility of a full-scale investigation and the factors which may be considered as confounders in future analyses of the mortality and morbidity data and reproductive

performance among the F_1 cohort.

Site-specific cancer studies

Most of the currently active site-specific cancer incidence studies will be completed within the next few years. As they are completed, new studies will be initiated to update the case series or to investigate additional tumor sites of interest. These include such sites as colon, stomach, and bone and connective tissues (see table).

Priority 2

Family pedigree studies and genetic epidemiology

The setting in which the three RERF cohorts were established presents a unique opportunity for identifying family members within these cohorts and conducting a long-term prospective follow-up of the role of genetic and other familial factors in the occurrence of cancer and other common, chronic diseases. Some preliminary work has been undertaken in collaboration with the Departments of Statistics, Clinical Studies and Information Technology to set up a family pedigree database. In view of the evidence relating genetic predisposition for breast cancer, a pilot study is now underway to construct family pedigrees for young breast cancer patients as well as older breast cancer patients (as a comparison group). To obtain useful results, more formal research protocols will be developed in association with geneticists and statisticians. To implement this research may require the additional help of individuals who are familiar with Japanese kinship terms in establishing genealogical relationships and the use of the koseki records to verify the stated relationships.

Personnel requirements (Hiroshima)

In the last few years, the number of epidemiologists in the department's professional staff in Hiroshima has decreased from 6 (4 Japanese and 2 US) to 3 (Japanese only), while that in Nagasaki has remained at 2 (both Japanese). In view of the ongoing and anticipated research activities, the current size is woefully inadequate. The minimum staff requirement for Hiroshima is 6 professionals as it was in 1994. Because of the generally high level of epidemiologists trained in the US and some European countries, efforts are underway to recruit two epidemiologists through NAS. We also plan to recruit one Japanese epidemiologist. Finally, in anticipation of the retirement of the current Department Chief in 5 years, we should begin to consider the recruitment of another Japanese M.D. or Ph.D. level epidemiologist.

The Epidemiology support staff for Hiroshima has also decreased in size and currently consists of 35 full-time and 4 part-time employees. The support staff provides research assistance (data preparation, tabulation and analyses), technical assistance (the management of the Master-File and tumor registry database, the abstraction of medical records for the tumor registry operation, and histo-pathology work for specific cancer studies), clerical work (Master-File and tumor registry) and secretarial and administrative assistance. The current total size of 39 is adequate.

Hiroshima

Area	Current	1997	1998	1999	2000	2001
	Fiscal Year					
	Research scientists					
Epidemiology	1.5	4.5	4.5	4.5	4.5	4.5
Tumor registry	1.5	1.5	1.5	1.5	1.5	1.5
Total	3	6	6	6	6	6
	Support staff					
Research assistants	3	3	3	3	3	3
Master File	17 (1)[1]	18	18	18	18	18
Tumor registry	11 (2)	13	13	13	13	13
Pathology	2 (1)	3	3	3	3	3
Administration	2	2	2	2	2	2
Total	35 (4)	39	39	39	39	39

[1] Part-time employees shown in parentheses.

Space requirements (m^2) (Hiroshima)

Area	Current	1997	1998	1999	2000	2001
	Fiscal Year					
Research scientists	73	105	105	105	105	105
Administration	18	20	20	20	20	20
Research assistants	20	20	20	20	20	20
Master File	307	210	210	210	210	210
Tumor registry	112	210	210	210	210	210
Pathology	181	180	180	180	180	180
Other Support[1]	57	40	40	40	40	40
Total	768	785	785	785	785	785

[1] Includes half of the area of the conference, computer, and copier rooms which are shared with the Department of Statistics and of the visiting scientists office, which is also shared with Statistics.

Equipment budget (Hiroshima) (x ¥ 1,000)

Computer hardware and software are the primary equipment used by the Epidemiology staff. A three-year schedule for the replacement of computers and a continuing need to expand network storage capacity have been assumed. It also is assumed that replacing or upgrading hardware and software will occur on a regular basis. In addition, laboratory equipment for the Pathology Laboratory will be needed.

Hiroshima, Research and Administrative

Budget category	Fiscal Year 1997	1998	1999	2000	2001
Computer hardware replacement/upgrade[1]	6,060	6,000	6,200	6,140	6,140
New computer hardware and software[2]	660	780	640	760	760
Pathology lab	970+	150	150	150	150
Total	7,690	6,930	6,990	7,050	7,050

1. There are currently 26 PCS, of which 8 will be replaced each year.
2. There are currently 7 printers, one of which will be replaced each year. Also one new PC will be added each year.
+ Incubator, microtome, cleaner

Hiroshima, Research

Budget category	Fiscal Year 1997	1998	1999	2000	2001
Computer hardware replacement/upgrade[1]	4,292	4,200	4,390	4,298	4,348
New computer hardware and software[2]	549	617	536	608	608
Pathology lab[3]	970+	150	150	150	150
Total	5,811	4,967	5,076	5,056	5,106

1. 75% use for research assumed.
2. 75% use for research assumed.
3. 100% use for research assumed.

Personnel requirements (Nagasaki)

There are two Japanese professional staff in Nagasaki and the size is appropriate. However, we need one research assistant who has a sound knowledge of epidemiology, statistics and the computer sciences, and who will be expected to obtain a Ph.D. within 5 years.

The epidemiology support staff for Nagasaki has decreased in size and currently consists of 20 full-time employees. The support staff provides technical assistance (the maintenance of the computer system, the management of the Master-File and tumor registry database, the

abstraction of medical records for the tumor registry operation, the histopathology work for cancer studies, etc.), clerical work (Master-File and tumor registry) and secretarial and administrative assistance. The current total size of 20 should be increased to 21 through the employment of the one additional research assistant mentioned above.

Nagasaki

Area	Fiscal Year					
	Current	1997	1998	1999	2000	2001
	Research scientists					
Epidemiology	0.8	0.8	0.8	0.8	0.8	0.8
Statistics	0.2	0.2	0.2	0.2	0.2	0.2
Tumor registry	0.8	0.8	0.8	0.8	0.8	0.8
Clinics	0.2	0.2	0.2	0.2	0.2	0.2
Total	2	2	2	2	2	2
	Support staff					
Research assistant	0	1	1	1	1	1
Master File	9	9	9	9	9	9
Tumor registry	6	6	6	6	6	6
Pathology	3	3	3	3	3	3
Computer technicians	2	2	2	2	2	2
Total	20	21	21	21	21	21

Space requirements (m^2) (Nagasaki)

Area	Fiscal Year					
	Current	1997	1998	1999	2000	2001
Research scientists	28*	50	50	50	50	50
Research assistant	0	10	10	10	10	10
Master File	146	146	146	146	146	146
Tumor registry	61	70	70	70	70	70
Pathology	82	82	82	82	82	82
Computer technicians	18	22	22	22	22	22
Other Support[1]	96	96	96	96	96	96
Total	431	476	476	476	476	476

[1] Includes space for data and document storage ($52m^2$), network communication servers and equipment ($18m^2$) and underground storage of pathology samples ($26m^2$).

Equipment budget (Nagasaki) (x ¥ 1,000)

Budget category	Fiscal Year				
	1997	1998	1999	2000	2001
Computer hardware replacement/upgrade	2,570	2,500	1,000	0	3,000
additional	570				
Printer replacement/upgrade	1,900	700	1,500	700	1,900
Software upgrade	968	144	1,044	144	1,044
additional	190				
Pathology lab	1,618	30	30	30	30
Total	7,816	3,374	3,574	874	5,974

Survey Expenses (x ¥ 1,000)

				Projection					
	1993	1994	1995	1996	1997	1998	1999	2000	2001
Mortality surveillance									
Hiroshima	13,509	13,524	13,450	17,082	17,000	17,850	17,850	18,740	18,740
Nagasaki	7,489	7,337	7,423	11,294	11,000	11,550	11,550	12,130	12,130
Total	20,998	20,861	20,873	28,376	28,000	29,400	29,400	30,870	30,870
Tissue registry									
Hiroshima	12,000	12,000	12,000	12,000	12,000	12,000	12,000	12,000	12,000
Nagasaki	12,000	12,000	12,000	12,000	12,000	12,000	12,000	12,000	12,000
Total	24,000	24,000	24,000	24,000	24,000	24,000	24,000	24,000	24,000
F1 mail survey Hiroshima & Nagasaki					13,300	13,300	13,300	13,000	
Grand Total				52,376	65,300	66,700	66,700	68,170	54,870

1) Mortality surveillance: Projections based on a 5% biennial increase in fees for koseki request plus postage.
2) F1 mail survey: Estimates for 71,000 subjects currently alive, costs include survey form, envelope, labels and postage for residence check (¥6,350); fees for koseki (¥24,880); and postage for koseki and mailing (twice on the average)(¥22,050) for 71,000 subjects (alive)(Total: ¥53,280) equally distributed over the four year period 1997-2000.

Construction of LSS-based Family Pedigree Database

Hiroshima and Nagasaki Combined Estimates (x ¥ 1,000)

	Current	1997	1998	1999	2000	2001
Koseki check		19,450	19,450	19,400	19,400	19,400
Supplies		150	150	140	140	140
Total		19,600	19,600	19,540	19,540	19,540

Estimates for 120,000 subjects based on fees for original koseki and postage (¥97,100) and supplies (¥720) equally distributed over the 5-year period 1997-2001.

Department of Genetics

The current research activities of the Department of Genetics have two major thrusts, namely, a cytogenetics program that focuses on the occurrence of chromosomal abnormalities in the survivors as well as their offspring, and a biochemical genetics program that centers on the detection of gene-mutational events and the development of the requisite technology to achieve this end. These two programs have been carried out by the Cytogenetics Laboratory and the Laboratory of Biochemical Genetics, respectively.

In the past, screening for chromosomal abnormalities and gene mutations occurring in germ cells were carried out in the two laboratories by examining the children of the survivors selected from the same F_1 cohort. However, in the last 10 years, the cytogenetics program focused on screening for somatic chromosome abnormalities in the survivors in order to establish biological dosimetry as an alternative to physical dose estimation through the application of electron spin resonance (ESR) of tooth enamel obtained from the survivors. The efforts of the biochemical genetics program have been concentrated on developing technologies for the detection of germ cell DNA mutations in the children of the survivors and establishing cell lines from 1000 parent-child trios, with half of the trios including at least one proximally exposed parent.

In the next five years, in each program, on-going projects will be continued. In addition, the FISH (fluorescence in situ hybridization) technique will be utilized for the physical localization of unreported genes or new mutations in specific genes detected in the biochemical genetics program by using single probes of DNA fragments and a subsample of the 1000 trios whose lymphocytes and cell lines have been stored in our cell bank for the biochemical genetics program will be examined for the detection of chromosomal germline mutations.

The Cytogenetics Program

The research objectives of the Cytogenetics Laboratory are two fold. First, to collect cytogenetic information on the survivors and to use this information to strengthen the DS86 dose estimates, either by validating them or by indicating possible biases in them. Second, to determine by means of the F_1 cytogenetic studies whether parental exposure to A-bomb radiation caused an increased frequency of chromosomal abnormalities in their progeny. Since these aims entail

different studies, we describe them separately.

Cytogenetic studies of the survivors

Past experience has confirmed that the conventional Giemsa staining method can detect nearly two-thirds of all reciprocal translocations. However, even with the best technique and highly qualified investigators, the chromosome aberration data on each survivor scatter quite widely when regressed on the individual DS86 doses. This statistical "overdispersion" could be attributable to two possible sources of error, one physical and the other biological. The former includes errors in the physical estimation of the DS86 dose itself and in the interview information regarding location and shielding conditions ATB. The latter includes possible differences in radioresponse among individuals due to genetic factors, age ATB, sex, and life-style, including smoking habits, for example. To estimate the relative contributions of these possible confounding factors, it has long been considered desirable to estimate dose using another biodosimetric marker independent of the cytogenetic results.

The frequency of mutations in somatic cells was once considered a good candidate, and several assays were investigated by the Department of Radiobiology to see if they could serve as alternative biodosimetric tools. However, among some five different assays, only the glycophorin A (GPA) assay in erythrocytes can detect exposures to radiation that occurred several decades earlier. Furthermore, the overdispersion of mutant frequency is even greater than that seen in the chromosome data, most likely due to a "jackpot-type" event (an occasional large "payoff-type" event) stemming from the relatively small number of bone marrow stem cells (the target cells for mutation by radiation exposure revealed by the GPA assay) which are actively producing mature red blood cells. Thus, the erythrocyte-based GPA mutation assay does not seem capable of serving as an alternative tool for biodosimetry on individuals.

Electron spin resonance (ESR) to detect radicals in tooth enamel has been used by a number of laboratories as another indicator of past radiation exposure. Since installation of ESR equipment in the cytogenetics laboratory (January 1995), 100 teeth selected from over 300 samples donated during the past nearly 10 years have been examined. The results show a close association with the cytogenetic data from the tooth donors, and the ESR method appears to be a promising alternative means to estimate individual doses, which in turn supports the cytogenetic data on the survivors. Since ESR can be applied only to extracted teeth whereas chromosome tests require only 1 to 2 ml of blood that can be readily obtained from most of the survivors, ESR cannot supplant cytogenetic tests but serves to reemphasize the value of the latter.

Major research activities in the next five years

A. Core activities

Priority 1

A-1. FISH examination of Hiroshima and Nagasaki survivors (RP 8-93):

A recent summary of the cytogenetic data on over 2000 survivors revealed two important issues with respect to the accuracy of the dose estimates based on physical grounds.

First, the dose-response relationship for Nagasaki survivors exposed in factories was unusually shallow, only one-half as steep as that for the survivors exposed in Japanese houses. This implies that the DS86 system overestimated the doses of these workers. Second, among the survivors exposed in Japanese houses, the dose responses were similar in both cities, but the Hiroshima curve is consistently above the Nagasaki one, suggesting the possibility of a small systematic error in the calculation of the DS86 doses. However, because the conventional staining method used in cytogenetic studies is known to be affected by observer bias (the Hiroshima and Nagasaki survivors were examined separately in the two laboratories by different investigators), we need to confirm these findings using FISH, the most objective method of scoring stable-type chromosome aberrations. This will be undertaken in the Hiroshima laboratory exclusively.

In 1994, collection of blood samples began with the aim of applying the FISH technique to about 200 survivors a year for five years. In 1995, the sampling scheme was extended to include an additional 200 survivors of specific interest (for example, tooth donors for ESR, carriers of clonal chromosomal aberrations, and mothers of the in utero exposed). Further extension is planned in the near future to maximize sampling of those survivors who were below 20 years of age ATB and have DS86 doses of about 0.5 Gy or more. (The total number of subjects will be about 1,500.)

The motivation for this large scale survey comes from our recent finding, based on tooth enamel ESR and the cytogenetic data on the tooth donors, that the cytogenetic data are closely related to the real radiation dose. To document the apparently higher proclivity of the youngest cohort to develop excess cancers, evaluation of biases in DS86 dose estimates is critical and only cytogenetic data can provide the necessary information. For this purpose, information on middle to high dose survivors is important not only because they have the higher risks for cancer but also the fraction of LSS cohort members with such doses included in the AHS is larger (the fraction is 85% for those with DS86 doses of above 1 Gy).

B. Special research activities

Priority 1

B-1. Characterization of the ESR assay (RP 1-92):

Because the ESR assay is rather new, laboratory techniques differ in the various steps of the assay procedure. Creation of international guidelines for standardization of the assay is in progress, and we are eager to compare our technique with that of others to reduce possible laboratory-specific errors in estimating the dose. The major advantage of the ESR assay is that the measurement itself is not destructive and the same specimen can be repeatedly measured. ESR results for the first 100 tooth samples along with the cytogenetic data on the tooth donors will be published in 1997.

We propose to examine an additional 100 teeth in the future and to couple this examination with the FISH technique using lymphocytes from the tooth donors to strengthen the current results. At the same time, tooth collection will continue.

B-2. Clonal chromosome aberrations (RP 8-93):

In the past studies using conventional staining methods, some 20 survivors were identified who carry identical chromosome changes in 3 or more lymphocytes, defined as clonal aberrations. A priori, clonal expansion can occur in two ways. Either the stem cells proliferated extensively and produced a large number of progeny or the mature lymphocytes proliferated after being stimulated by certain antigen(s). In the former case, clonal aberrations are expected to be seen mainly in naive T cells ($CD45RA^+$), whereas in the latter case, mainly in memory T cells ($CD45RO^+$). Studies using separated lymphocytes ($CD45RA^+$ or $CD45RO^+$) are in progress and results will be obtained within 2 years.

Depending upon the findings, further detailed examinations (for example, $CD4^+$ vs $CD8^+$ lymphocytes) may be necessary. This research will be performed in collaboration with the Department of Radiobiology.

B-3. FISH examination of exposed parent(s) in the F_1 molecular genetics study sample (RP 8-93):

We now know that the DS86 dose estimates contain potentially systematic errors. Because the molecular genetics study sample is a small subsample of the AHS cohort, and a considerable fraction of the high dose survivors in Nagasaki consists of factory workers whose DS86 doses seem to be overestimated, it would be prudent to examine the exposed parent(s) with assigned DS86 doses above a certain level (say, 1 Gy) for the chromosome aberration frequency of lymphocytes to validate their gonadal doses. Because most of the exposed parents are in the AHS, they will be included in the routine FISH examination and the total number of parents examined will be about 200. This study will require at least one AHS examination cycle (two years) or possibly two (four years), and the participation of the Departments of Clinical Studies.

B-4. Detailed comparison of ESR dose with DS86 dose (RP 1-92):

The 100 tooth samples that have been examined by ESR were derived from 69 survivors. The ESR estimated tooth dose and DS86 kerma dose show a positive correlation, but considerable variation exists. In some cases, the chromosome data and the ESR data fit one another closely but deviate substantially from the DS86 estimates. As previously said, these discrepancies are likely to be due to errors in the information on survivor location ATB and are most likely unrelated to errors in the program designed to compute the DS86 dose. It would be useful to scrutinize the relationships among ESR dose, cytogenetic information, and DS86 dose in the remaining cases so that consistent deviations related to shielding conditions and other factors can be detected.

Priority 2

B-5. Scrutiny of ESR and DS86 doses for tooth donors (RP 1-92):

As mentioned in the previous section, ESR data are the first physical measurements of

gamma dose on individual survivors, and they should be carefully compared with the DS86 estimates. In 1995, Dean C. Kaul (SAIC) expressed an interest in the DS86 dose information on the tooth donors. A collaborative program with SAIC would be valuable if the necessary internal administrative agreements can be reached.

B-6. Domain structure of chromosomes in interphase nuclei (RP 8-93):

Brenner's hypothesis states that the ratio of interchromosomal versus intrachromosomal aberrations, termed the F-value, decreases from over 10 to nearly 5 as the LET of radiation increases. Current data, both in vivo and in vitro, obtained in the Cytogenetics Laboratory do not seem compatible with this hypothesis. There is no evidence that "the majority of the effective dose received by individuals in Hiroshima ... came from neutrons" as described by Brenner (1996), but the most recent tooth enamel ESR versus translocation data show that the majority of the cytogenetic effects are due to gamma-ray exposure.

Because the hypothesis is derived from the domain structure of chromosomes in interphase nuclei, several approaches from independent angles should be helpful to understand the issue. For example, do reciprocal translocations occur randomly among chromosomes? Do inactive X chromosomes in females undergo translocation less frequently? Are translocation breakpoints distributed homogeneously throughout a chromosome arm? Most of these questions can be answered by careful analysis of data presently available (both by G-band and FISH), and no extensive new experiments are required.

B-7. Research on genetic instability

Recent studies, both in vivo and in vitro, suggest that radiation exposure causes genetic instability in cells. We plan two approaches. One is to carefully examine previously collected G-band data to see if cells which have undergone a chromosomal change have an increased chance of having a second change. Second, if radiation exposure can cause instability which lasts for the lifetime of the individual, the frequency of unstable aberrations (dicentrics) would be expected to increase with dose. Scrutiny of the previously collected large set of cytogenetic data based on conventional staining procedures should provide an answer to this.

B-8. Assessment of errors in the DS86 system

As previously stated, recent ESR results on tooth enamel revealed that the ESR estimated dose more closely correlates with chromosome aberration data on the tooth donors than DS86 estimates. This finding along with in vitro studies indicate that chromosome data are good measures of the true dose. The extensive body of cytogenetic data collected in the past should be reviewed to estimate the distribution of true dose at different levels of DS86 dose.

Cytogenetic studies of the children of the survivors

Using conventional staining methods, an extensive cytogenetic survey was conducted in the past involving nearly 16,000 F_1 persons (8,000 born to exposed parent(s) and 8,000 to the unexposed). The results showed only one de novo autosomal mutation in each group, although not all of the parents of aberration-carrying individuals could be cytogenetically examined. Thus, no evidence of a radiation effect on the germ cells has been observed so far.

Major research activities in the next five years

Priority 1

C-1. Examination of EBV-transformed B-cell lines by the G-banding method

Because the previously used conventional staining method can detect only gross structural changes and is not suitable for detecting small deletions, it will be necessary to apply the G-banding method which can detect small changes.

EBV-transformed B-cell lines established from trios of families for molecular genetic studies in the Laboratory of Biochemical Genetics would be an appropriate source of materials, both in terms of sample size, estimated gonadal dose, and availability of cells from the parents. The work will require 3 to 4 years.

Priority 2

C-2. Development of FISH using a single probe

One application of the FISH technique is mapping using a single gene probe or a probe for a specific DNA segment. In the future, in the Laboratory of Biochemical Genetics, we anticipate that mutant genes will be detected using molecular analysis of the children born to the survivors. FISH mapping of the mutated gene would be useful in characterizing the mutation.

Project time lines (Cytogenetics)

Fiscal Year	1997	1998	1999	2000	2001
1. FISH examination of survivors	⇒	⇒	⇒	⇒	⇒
2. FISH by a single probe	⇒	⇒			
3. Chromosome domain structure	⇒	⇒			
4. Genetic instability	⇒	⇒			
5. Assessment of DS86 errors	⇒	⇒			

Biochemical Genetics Program

The primary objective of the biochemical genetics program is to determine whether an increase in mutations measurable at the molecular level has occurred in the children born to A-bomb exposed parents in Hiroshima and Nagasaki.

Past and recent accomplishments

Extensive studies of the children of the survivors of the atomic bombings of Hiroshima and Nagasaki, using various endpoints such as untoward pregnancy outcomes, mortality, chromosome aberrations, and gene mutations screened at the protein level, have thus far yielded no statistically significant increases in genetic effects compared to a control population.

Because it is important to determine the mutation rate induced by radiation in this unique population, detecting mutations at the DNA level has been explored in a feasibility study. Establishment of cell lines from parent-child trios was recommended by the Genetic Study Conference held in 1984. It is anticipated that immortalized B-lymphocyte cell lines from 1000 families, one-half of them from a proximally exposed parent(s), will be maintained at RERF. Cell lines from 800 families composed of 1600 parents having DS86 estimates and 1200 children are now in the cell bank. This is the largest properly selected population in the world for the detection of radiation effects on human germline mutations. The Human Germline Mutagenesis Workshop held in 1991 recommended starting a pilot study using 100 families (50 exposed and 50 control families), a subsample of the 800 families, to compare various types of DNA as potential targets for the detection of germinal mutations with various techniques, because there was no information about the genes sensitive to radiation-induced mutagenesis. In keeping with this recommendation, microsatellites, minisatellites and various functional single-copy sequences in 124 children and both parents of the 100 families have been examined to determine whether deletion/insertion/rearrangement (D/I/R) type mutations or mutations causing other types of quantitative changes, all commonly produced by radiation, as well as nucleotide substitutions, exist at higher frequency in the children of the exposed parents.

Preliminary studies have failed to reveal a significant difference between the children of the exposed and the control parents in the mutation rates at the microsatellite and the minisatellite loci, both of which are repetitive sequences dispersed through the human genome.

We have developed two techniques to screen for D/I/R type mutations in single-copy sequences. One is the quantitative measurement of intensities of chemiluminescent bands on Southern filters and the other is the two-dimensional electrophoresis (2-DE) of DNA digests followed by a quantitative image analysis of ^{32}P-labeled spots. Each technique can detect a 50% decrease or increase in band intensity or spot intensity that is derived from the D/I/R events on the totality of a single allele. Thus, these techniques are suitable to detect a fresh D/I/R type mutation because a fresh mutation would usually be detected in a heterozygote for a normal and a variant allele.

Major research activities in the next five years

A. Core activities

Priority 1

A-1. Pilot studies for the detection of D/I/R type mutations

In addition to the original 100 families, a new set of 100 families (50 exposed and 50

control families) will be selected and screened for mutations at the minisatellite loci during the first two years. It is important to use a larger body of data to confirm our preliminary results, which showed no effect of A-bomb radiation on genetic instability at the minisatellite loci in human germ cells obtained from the original 100 families, including children derived from 65 exposed gametes with a mean dose of 1.9 Sv. We have assumed that the 65 gametes received, on average, the doubling dose estimated by Neel et al. (1990)), namely, 1.7-2.2 Sv. For a locus with a spontaneous mutation rate of 0.02 per gamete, which is the mean mutation rate of the six minisatellite loci examined in the previous study, using standard power function statistics (a Type I error of 0.05 and a Type II error of 0.2), we calculate that we would need to survey two samples (exposed and unexposed) of 1,188 germ cells each to observe a significant difference at the 0.05 level.

By examining 60 children from an additional 50 exposed families, each one of them having one exposed parent and the mean gonadal dose of the parent being 1.9 Sv, it is anticipated that we can examine the required number of alleles for each sample. Dubrova et al. reported that mutation rates at minisatellite loci in 79 children of parents who lived in heavily polluted areas of Belarus after the Chernobyl accident were twice that of 105 control children from the United Kingdom although the estimated individual dose from external and internal chronic exposure to ^{137}Cs of inhabitants of those areas was less than 5 mSv per year. By comparing their data with our new data based on the projected additional sampling, it may be possible to determine whether there is a difference in the biological effects of radiation between acute external exposure and chronic internal exposure.

The pilot study for the screening of D/I/R mutations will be carried out with the quantitative measurement of intensities of chemiluminescent bands on Southern filters on two hundred families (the original 100 families and the new 100 families). Probes to be used are DNA fragments from the human counterparts of the seven mouse specific loci, other genes located nearby, and genes supposedly related to common chronic diseases such as hypertension, diabetes mellitus and hereditary nonpolyposis colorectal cancer (HNPCC).

The 2-DE technique will be used in the pilot study. DNA samples from the 200 families will be examined using this technique after digestion with three sets of restriction enzymes, that is, NotI/EcoRV-HinfI (NotI/EcoRV and HinfI being used before and after the first dimensional electrophoresis, respectively), NotI/EcoRV-PvuII and NotI/EcoRV/PvuII-HinfI, products of each set of enzymes being different from those produced with the other two sets of enzymes. These three kinds of DNA digests labeled with ^{32}P from one individual will be electrophoresed separately, and the resulting three gels will be quantitatively analyzed. A total of 2000 spots (fragments) will be suitable for the detection of the D/I/R type mutations among 6000 spots (fragments) visualized on the three autoradiograms from the three gels. With the current research design (2000 diploid fragments scored on three gels per individual), 5 mutations would be detected in 120 children from 100 control families, if we assume that the spontaneous mutation rate is 1×10^{-5}/fragment/generation.

Image analysis is an essential part of any 2-DE study of DNA fragments, and this will

require support of the Information Technology Department (ITD) in the rewriting of the 2-DE software developed at the University of Michigan and currently in use in the Department of Genetics. This software was developed for older computer operating systems and cannot be readily used with the system upgrades that have occurred and that are contemplated in future computer system upgrades at RERF. In addition, to organize the data from the various DNA examinations and perform analyses, support from the ITD and the Department of Statistics will be required.

Physical localization of mutant genes and their normal counterparts will be carried out using the FISH technique in collaboration with the Cytogenetics Laboratory. To understand the characteristics (physical nature and functional effects) of new mutations, not only molecular biological data but also physical data are essential.

In each of the 100 exposed families, at least one parent belongs to the most heavily exposed group among the approximately 400 exposed parents on whom permanent cell lines have been established. Therefore, if the mutation rate detected in the children of the exposed group is significantly higher than that in the children of the control group, and the efficiency of the technique we propose is sufficiently high to warrant screening a larger number of samples, the study will be expanded to determine the dose response relationship. However, if there is no significant difference in the mutation rates between the two groups or the efficiency of the technique is too low, the study will not be continued and new methods will be introduced or developed.

A-2. Culture of permanent lymphocyte cell lines as sources of biological samples for the study of germ cell mutations

Initially, families for this program were selected on the basis of T65DR doses since the DS86 system did not exist when the original selections were made. Some of the cell lines already established are from families including parents whose DS86 doses are unavailable. New families where parental DS86 doses exist will be selected and cell lines will be established keeping the original goal of 1000 families in mind. This means we shall try to add 200 families in Hiroshima and Nagasaki over the next two years.

In the beginning of the pilot study for the detection of mutations, DNA extracted from cell lines established from members of the 100 families, a subsample of the 1000 families of the cell-line project, was used. However, recently, in order not to exhaust the cell lines, portions of the cell lines have been proliferated and the resulting "re-cultured cell lines" have been used for routine purposes. For the additional new 100 families to be examined in the pilot study, "re-cultured cell lines" will be produced and they will be used as sources of DNA.

B. Special research activities

Priority 1

B-1. A feasibility study on the ascertainment of disease and disability among offspring of the survivors (Feasibility of F_1 health study)

The Blue Ribbon Panel urged that consideration be given to the feasibility of studying diseases and disabilities of late onset among the offspring (F_1 generation) of the survivors. A protocol for the feasibility study has been written. It includes a mail questionnaire survey for a total of 82,000 F_1 (F_1 Mortality Sample and the so-called BGS Extension Samples), physical examination of approximately 500 F_1 (F_1 reporting chronic illness and those not doing so) in the Departments of Clinical Studies, and analyses of genes related to common diseases such as hypertension and diabetes mellitus in approximately 50 F_1. It is anticipated that it will take two years to complete the study. As soon as the results of the feasibility study are obtained, a workshop will be held to determine whether a full-scale study is practical and warranted. This feasibility study will be carried out as a collaborative undertaking involving the Departments of Clinical Studies, Epidemiology, Statistics and Genetics.

B-2. Assessment of detectability of germ cell mutations by the 2-DE technique (Detectability of mutations by 2-DE: Approved by Chief of Research Donald Harkness on 14 March 1995)

A pilot study, which was begun in 1996 for the assessment of detectability of the 2-DE technique of radiation-induced germ cell mutations in mammals, will be continued for one more year. DNA samples from 100 control mice (BALB/c) and from two groups of 100 F_1 mice, one derived from spermatogonia irradiated with 3 Gy and the other from spermatogonia irradiated with 5 Gy, are being examined with the 2-DE technique after digestion with two sets of restriction enzymes (NotI/EcoRV-HinfI and NotI/EcoRV-PvuII). The search for D/I/R type mutations that result in spots with 50% decreased intensity at the normal positions among 1000 spots on a gel are being carried out using quantitative image analysis. Among DNA samples from 43 F_1 mice of 5 Gy irradiated male parents, examined in 1996, one mutation was detected. Results of the study will provide basic information for the estimation of the number of children of A-bomb survivors that should be examined in order to obtain statistically significant results.

B-3. Pilot study to evaluate various markers in potential candidate genes associated with hypertension. (Pilot study for the hypertension markers)

Suggestive radiation-related increases in cardiovascular disease incidence and the prevalence of aortic arch calcification and systolic hypertension have been reported. The Blue Ribbon Panel states that further studies are required to confirm a real association between radiation exposure and atherosclerosis. This indicates the importance of studying at the molecular level the hypertension observed in the AHS population. A protocol is being prepared for a pilot study to evaluate several markers in potential candidate genes associated with hypertension. Some 100 individuals each from the normal group and the hypertension group, defined by the 1993 WHO/ISH classification among the participants of the AHS, will be examined for their polymorphic markers in several candidate genes. DNA will be extracted from lymphocytes in the blood samples obtained in the biennial physical examination conducted at the Departments of Clinical Studies. Because some AHS participants with hypertension are parents of the cell line project for the germinal mutation study, family studies for the potential markers associated with hypertension can be carried out if the need arises.

Project time lines (Biochemical Genetics)

Project	1996	1997	1998	1999	2000	2001
Feasibility for F_1-health study		⇒	⇒			
Detectability of mutations by 2-DE	⇒	⇒				
Pilot study for the hypertension markers		⇒	⇒			

Personnel Requirements (Department of Genetics)

Fiscal Year	1996	1997	1998	1999	2000	2001
Research Scientists						
Cytogenetics	5	5	5	5	5	5
Biochem. Genet.	4+0.5[1]	5	5	5	5	5
Technicians						
Cytogenetics	5	6	6	6	6	6
Biochem. Genet.	11[2]	12	12	12	12	12
Clerks						
Cytogenetics	1	1	2	2	2	2
Biochem. Genet.	2.2[3]	3	3	3	3	3

[1] One visiting scientist (Dr. Murakami) is concurrently assigned to the Departments of Genetics (50%) and Clinical Studies (50%). Her employment as a permanent research scientist is required.
[2] One young technician retired at the end of FY95 and no replacement has been made.
[3] One clerk is assigned to the Department of Genetics (20%) and the Publication & Documentation Center (80%).

Space requirements (m^2) (Department of Genetics)

Fiscal Year	1996	1997	1998	1999	2000	2001
Bench Research						
Cytogenetics	146.2	146.2	146.2	146.2	146.2	146.2
Biochem. Genet.	402[1]	442	442	442	442	442
Support Space						
Offices cytogenetics	73.2	83.2[2]	83.2	83.2	83.2	83.2
Biochem. Genet.[3]	100	100	100	100	100	100
Slide Storage(Cytogenetics)	7.3	17.3[4,5]	17.3	17.3	17.3	17.3
Storage Space(Biochem Genet.)..	23	23	23	23	23	23
Total						
Cytogenetics	226.7	246.7	246	246.7	246.7	246.7
Biochem. Genetics.	525	565	565	565	565	565
Grand Total	751.7	811.7	811.7	811.7	811.7	811.7

[1] Some corridor space where various research equipment, refrigerators and incubators are installed for daily use is included.
[2] Computer space (+10 m^2).
[3] Space used for image analysis of the 2-DE gels and other types of gel analyses is included.
[4] Nagasaki slide storage (+10 m^2).
[5] Space for liquid nitrogen tanks, deep freezers and glassware for experiments.

Equipment Budget (× ¥ 1,000)

Fiscal Year			1997	1998	1999	2000	2001
Equipment							
	Routine	Laboratory[1]	2,149	3,695	4,789	0	0
	Replacement	Computer[1]	2,641	326	1,127	1,116	2,929
		Computer[2]	421	326	560	588	533
	Routine New	Computer[1]	2,200	850	890	930	490
		Computer[2,3]	600	150	155	160	50
	Major New Acquisitions/Repl.		13,000[4,5)]	5,000[6)]	22,880[7)]	0	0
	Total		21,011	10,347	30,381	2,794	4,002
Lab Supplies/Reagents[8)]			24,000	26,400	28,800	31,200	33,600

[1)] Laboratory and computer equipment for research purpose. For computer, 80% of the cost for hardware and 50% of that for software are included in this category.
[2)] Equipment for administrative/service-related. For computer, 20% of the cost for hardware and 50% of that for software are included in this category.
[3)] All new hard disks are for research purposes.
[4)] Software for 2-DE Analysis (¥10,000,000): For 2-DE analysis, the software developed at the University of Michigan has been used. It was developed for older computers and cannot be readily used with the upgrades that have occurred. If a computer scientist outside of the RERF rewrites the program, the estimated cost is about ¥10,000,000.
[5)] Pulsed Field Gel Electrophoresis Apparatus (¥3,000,000): DNA digests are electrophoresed by this apparatus for the detection of deletion mutations in DNA by quantitation of band-intensity on a Southern filter. One of the two apparatuses which we have been using for these 8 years is broken and cannot be repaired because the parts are unavailable. A new apparatus is essential to the continuation of our research.
[6)] Photon camera (¥5,000,000): For the quantification of the intensity of chemiluminescent bands on a Southern filter and for the detection of deletion mutations, images of the bands on the filter are taken by photon camera. The sensitivity to photons of the camera we have been using for the past 5 years is decreasing. The old camera should be replaced by a new one.
[7)] Bio-Imaging Analyzer with Imaging Plates and Cassettes (¥22,880,000): In the 2-DE analysis, the spot pattern on a gel is visualized by making an autoradiogram which requires at least two weeks or more. This will be a big problem in the screening for mutations using the 2-DE technique. By using this image analyzer, the problem will be solved and the accuracy of the measurement of spot intensity will be much improved because it has high sensitivity for radioactivity.
[8)] A 10% yearly increase is included.

Department of Radiobiology

The Department of Radiobiology came into existence in August 1985 at the time of the

reorganization of the Foundation's Department of Pathology. The primary objectives of the department are to determine the late effects of exposure to ionizing radiation on immune system function, on somatic cell mutation and altered gene expression; on cell survival and transformation; and to maintain serum and tissue resources for epidemiological, histo-pathological, and radiobiological investigations.

Recent achievements

The Department of Radiobiology has conducted research in three areas, namely, immunology, somatic mutation, and molecular oncology. Recent achievements in these areas can be summarized as follows:

a). The immunologic studies have revealed that among atomic-bomb survivors immune function, such as mitogen and alloantigen responsiveness of T-cells, lymphocyte subpopulation numbers, and anti-Epstein-Barr virus immunity, is still compromised fifty years after the atomic bombings.

b). The department has established various mutation assays, namely, the HPRT, HLA, Fcγ RIII, TCR, and GPA assays, and applied these to ascertain radiation doses among atomic bomb survivors and to estimate the risk of cancer development. These studies have shown that the somatic mutation frequency at the glycophorin A locus increases with increasing dose of A-bomb radiation, suggesting that various diseases among the A-bomb survivors, including cancer, develop in part from genetic alterations induced by radiation.

c). The molecular oncology/epidemiology study was initiated six years ago to elucidate possible unique molecular finger prints in cancers among A-bomb survivors. Technical problems in using formalin-fixed paraffin-embedded samples from the A-bomb survivors have been resolved. The molecular analyses of liver cancer and skin cancer are on going.

In addition to the above mentioned studies, new research areas have been opened up to understand the precise mechanisms of radiation-induced damage, which might be important in cancer development. It is now evident that alterations of cancer-specific genes, such as RET oncogene activation and BCR-ABL translocation, can be induced by radiation.

Program objectives

The survivors of the atomic bombings represent a population of individuals who have been exposed to a wide range of doses of ionizing radiation; therefore, the primary objective of RERF has been to ascertain the effects that might have been produced in the exposed individuals and their children as a result of exposure to A-bomb radiation, and to relate these changes to dose and to the subsequent health effects which may have occurred. Consequently, until recently, research at RERF has focused primarily on the long-term epidemiological studies of A-bomb survivors to ascertain morbidity and mortality of the exposed population, specific investigations on health-related effects that might be related to radiation exposure, and genetic studies to ascertain the mutation rate resulting from radiation exposure in the children of the survivors but clearly there is a need for molecular and cellular studies aimed at revealing the underlying bases of this morbidity and mortality. It is thus important to bear in mind that if the Foundation is to achieve

its goals it must necessarily maintain a balance between mechanistic studies aimed at understanding the biological bases of radiation-induced changes and the statistical description of risk. It behooves the Foundation, therefore, to establish a credible and strong program in molecular and cellular research if the biological origin of radiation-related damage is to be understood.

Accordingly, the mission of the Department of Radiobiology is to study the molecular mechanisms of radiation-induced carcinogenesis in A-bomb survivors. We also believe that it is our mission to clarify what the biological effects of radiation are on human health and why and how disease is induced as a consequent process.

Major projects in the next five years.

In the coming 5 years, as we explain in the next several pages, some current studies will be phased out, others will be continued, and new ones will be introduced. The determination of the fate of these studies will be based on their relevance to several factors. Simultaneously the department will concentrate its energy on three major core activities, namely, molecular epidemiology, molecular oncology, and immunology.

The studies will be prioritized by the direct impact they are projected to have on these three core fields. That is, the highest priority studies will be the ones that can potentially produce supportive evidence for the radiogenic etiology of diseases occurring in the A-bomb survivors via damage of key molecules and their pathways.

A. Molecular epidemiology

A major objective of the molecular epidemiological study is to identify radiation-induced gene alterations in cancer and normal tissues of A-bomb survivors, and thereby to provide significant insights into the molecular mechanisms of human radiation carcinogenesis and disease development. To accomplish this goal, we will analyze cancer-associated genes such as oncogenes and tumor suppressor genes in archival and surgical specimens of normal and tumor tissues obtained from A-bomb survivors.

Molecular epidemiology at RERF combines powerful data analysis methods for revealing trends in disease development among the A-bomb survivors with state-of-the-art techniques in molecular biology. Such a partnership of disciplines can produce the first line of attack for understanding the mechanisms behind the observed human diseases following exposure to the A-bomb radiation. There are now many epidemiological studies demonstrating an effect of the A-bomb on the survivors; and with these results are hypotheses that try to explain them. For example one belief is that cancer incidence is heightened among the exposed because the radiation inflicted damage to the DNA of cells led to the loss of function of some crucial genes that controlled growth. But what are these genes? In which tissues are they most affected? Why does sex, age ATB, dose of exposure make a difference? There are no clear answers to these and many other questions. Generation of some of these answers may help in the treatment and prevention of diseases in numerous groups such as other radiation exposed people, chemically exposed people, and cancer patients, as well as in the A-bomb population. But study of the A-bomb survivor population, because of its size and because it and its tissues have been so well catalogued

and followed up for nearly a lifetime, will provide the best opportunities for such analyses.

The large repository of archival tissues makes possible extensive retrospective molecular epidemiological studies. As indicated in the following table, high priority studies will include those cases showing the highest relative risk with sufficient number of high dose, histologically verified samples such as the female breast, thyroid, and skin. Because analysis of these cancers, given that 33 of 43, 12 of 17, and 15 of 22 breast, thyroid, and skin cancers, respectively, are due to radiation, have the highest probability of producing the most statistically significant difference between the exposed and control groups.

Estimation of the cancer cases due to radiation

Cancer site	ERR 1 Sv	0.01 - 0.99 Sv			1.0 Sv			
		mean dose	No. of cases	Fraction of cases due to radiation	mean dose	No. of cases	Fraction of cases due to radiation	HV (%)
Female Breast	1.6	0.18	252	0.22	2.01	43	0.76	96.7
Thyroid	1.2	0.17	115	0.16	1.83	17	0.69	93.3
Skin	1.0	0.18	76	0.15	2.22	22	0.69	96.4
Bladder	1.0	0.16	108	0.14	1.63	7	0.62	82.9
Ovary	0.99	0.16	60	0.14	1.65	6	0.62	84.2
Colon	0.72	0.16	201	0.10	1.63	22	0.54	80.7
Liver	0.49	0.16	262	0.07	1.72	22	0.46	38.8
Stomach	0.32	0.16	1227	0.05	1.71	80	0.35	72.8
Prostate	0.29	0.16	56	0.04	1.61	5	0.32	85.7

HV: Histological verifications; Mabuchi, et al., RERF CR3-91; Thompson, et al., RERF TR5-92

Core activities (Molecular epidemiology)

A-1. Oncogenes and tumor suppressor genes in A-bomb survivors with cancer (RP 7-92, 3-93, 7-93, 2-94):

Cancer development is believed to be a multi-step process. The steps are not known but major roles appear to be played by oncogenes and tumor suppressor genes. The former act to accelerate cell growth and the latter to suppress it. Radiation can potentially damage either or both which can lead to uncontrolled growth -- a hallmark of cancer. Such damage is presumed to be the key in the increased risk of various cancers in the survivors. One especially important gene to study is p53 because it is the most commonly mutated gene in human cancers suggesting that it is a major player in multi-step carcinogenesis. Differences in the frequencies of mutations or types of mutation between the exposed and unexposed are anticipated.

A-2. Tissue collection

The success of such studies depends heavily on our ability to obtain appropriate samples

from LSS cohort members who are diagnosed with cancer. It is possible to obtain archival material through the tissue registries in Hiroshima and Nagasaki; however better methods are needed to ensure the availability of the necessary materials from newly diagnosed cases. To achieve this end RERF is seeking support from the local medical community for the establishment of a community-wide tissue/DNA bank in Hiroshima. This bank would maintain tissue specimens or preserved DNA that could serve as a resource for all groups in Hiroshima engaged in studies of the molecular mechanisms of carcinogenesis.

Tissues to be collected will have to have an associated RP describing their use. Once the collected tissue samples are registered in the "tissue bank", they will be available for use internally or by outside collaborators. Registration will include entry of the tissues into a database that will catalogue and link them to relevant RERF cohorts.

A-3. Molecular analyses

The usefulness of preserved tissue specimens from A-bomb survivors has been demonstrated by means of the PCR method. PCR is a method for the amplification of DNA by over a million-fold. Thus PCR makes it possible to study the genes of A-bomb survivor using microscopic quantities of archival tissues from as far back as 1950.

A-3-1. *Skin cancer (RP3-93):*

We have already prepared DNA from 60 tissue samples of skin cancer and are currently analyzing the ras and p53 genes. We will continue this analysis and start an analysis of the patched gene, which has been cloned and found to be frequently mutated in skin cancer.

A-3-2. *Liver cancer (RP2-94):*

In addition to skin cancer, molecular analyses of liver cancer (total sample number is 800) are on going. Currently studies of mutation in the p53 tumor suppressor gene and genomic integration of the hepatitis B and C viruses are being carried out. It may take two more years to complete these analyses.

A-3-3. Thyroid cancer (RP7-93):

Thyroid cancer should also be analyzed at the molecular level since it is among the cancers with the highest risk seen in the A-bomb survivors, implying that this cancer may be one of the best candidates for the identification of an A-bomb radiation-induced unique fingerprint, if such exists. Thyroid samples will be analyzed for aberrations in RET by immunohistochemistry using monoclonal antibodies against the RET proteins, which is not expressed in normal thyroid tissues.

A-3-4. Female breast cancer (RP7-92):

Breast cancer has one of the highest increased risks in the survivors. The risk is even higher for those survivors exposed at a young age with an ERR at 1 Sv of 3.21 and 2.61

for age ATB of 0 - 9 years and 10 - 19 years, respectively. Moreover, breast cancer is a potential familial cancer that may predispose some women to radiogenic breast malignancies. These studies will be complemented by research on the genetic background of cancer patients among the A-bomb survivors (see special research activity B). BRCA1 and 2 have so far shown the best prospects as genes in the cause of the disease.

Breast samples will be screened for BRCA1 mutations by immunohistochemistry since antibodies to detect mutations are commercially available.

A-5-5. Others

Salivary cancer is another important candidate for analysis at the molecular level, since it has been revealed recently that the ERR is 3.47 at 1 Sv which makes it the highest risk cancer among the survivors. Specific salivary gland cancer related genes are currently unknown. At present p53 may be the best candidate.

Special research activities (Molecular epidemiology)

Priority 1

B. Genetic background of cancer patients among A-bomb survivors

It is suspected that certain genetic backgrounds may be involved in radiation carcinogenesis. The genes involved in some cancer prone diseases, such as those associated with the recessively inherited ataxia telangiectasia (AT) and the dominantly inherited hereditary non-polyposis colon cancer (HNPCC), in which individuals who possess abnormalities in these genes have high susceptibility to radiation damage and high genetic instability, will be surveyed to define the involvement of genetic background in cancer development among A-bomb survivors.

Individuals who were exposed at young ATB and developed early breast cancer will have priority in the survey of such gene mutations. A strong association has been reported between radiation-induced chromosomal damage and breast cancer in cells from AT heterozygotes, and thus peripheral lymphocytes would seem a logical starting point in this screening activity. Screening will be done using available antibodies for the ATM and BRCA1 gene products. Suspect cases will then be molecularly analyzed at the gene level by sequencing. The total number of cases to be initially screened will be 200 breast cancer patients among the survivors. If mutations are detected, family members will be tested. This study will be an interdepartmental collaboration with the Departments of Clinical Studies, Epidemiology and Statistics.

Priority 2

C. Molecular analyses of non-cancer diseases in A-bomb survivors

Epidemiological studies are beginning to reveal increased risks in various non-cancer diseases such as myoma uteri, atherosclerosis and hyperparathyroidism among the A-

bomb survivors. It is expected that this trend will increase with the aging of the survivor population. As the target genes become evident, molecular analyses will be required to illuminate the mechanisms.

C-1. Parathyroid disease

In parathyroid disease one candidate gene is PRAD1. PRAD1 is a mutant gene caused by a translocation of a gene associated with a cell growth regulating factor and the gene that regulates parathyroid stimulating hormone expression. This will be a cooperative study with the Department of Clinical Studies.

C-2. Atherosclerosis

In atherosclerosis one possibility is the ras oncogene. Screening will be conducted by immunohistochemistry. This study will be in collaboration with the Department of Clinical Studies.

B. Molecular Oncology

Molecular oncology is closely related to molecular epidemiology. Whereas the latter produces trends of molecular changes in radiogenic cancers, the former provides the explanation or mechanism for how these changes work to cause cancer. Such results will supply the direct evidence for the carcinogenic effect of A-bomb exposure on the survivors. Knowledge of the mechanism will allow improved management of exposure to ionizing radiation as well as provide information in the treatment and prevention of related diseases.

As stated earlier, molecular epidemiology will provide much of the basis for other molecular studies. To delve deeper into the mechanisms, more manipulative experiments will be necessary. Manipulations will include working with live human cells from the A-bomb survivors, other human populations, and with human tissues in animal models, in that order of priority. Live cells are necessary to recreate as accurately as possible the events and responses of the cells in the survivors after A-bomb exposure. In the light of recent advances and the relatively large radiation effects for breast and thyroid cancer, studies of tissues from breast and thyroid cancer cases among the high dose survivors have the potential to yield important results. It may also be useful to supplement the search for characteristic gene alterations in cancer cells with a search for evidence of specific mutations associated with cancer development in the blood of cancer-free survivors.

The Blue Ribbon panel emphasized the necessity to determine the shape of the dose-response curve for radiation carcinogenesis at low doses of radiation. The recommendation suggested initiation of a molecular oncological study to clarify the molecular mechanisms in human radiation carcinogenesis.

Core activities (Molecular oncology)

A. Alterations in cancer-associated genes among A-bomb survivors

It was observed in the recent somatic mutation study that the GPA mutation frequencies increased with increasing A-bomb radiation doses, and the dose-response curve is very similar to that for solid tumor incidence among the A-bomb survivors. We can expect that since radiation may cause DNA damage randomly in the cell, cancer-related gene alteration could have been induced and remained in the cells of the A-bomb survivors. Based on the multi-step carcinogenesis theory, it may be suspected that cells carrying cancer-related gene alterations and proteins exist in blood cells among the A-bomb survivors.

A-1. Detection of the cells carrying mutations

Recent advances in flow cytometry make it possible to analyze translocation of cancer-associated genes by in-cell PCR methods using fluorescent primers. BCR-ABL and Bcl2 translocations are both associated with blood malignancies and can be detected in peripheral blood lymphocytes by this method.

Newly developed antibodies against oncogenes and tumor suppressor gene products will be used to detect cells carrying cancer-associated gene alterations in the blood among A-bomb survivors. This technique can demonstrate the existence of mutant gene products or changes in levels of normal gene products which may be especially pertinent in cases of deletion of tumor suppressor genes like p53 and possibly the ataxia telangiectasia mutated (ATM) gene. The projected number of samples to be studied is a 300 (control and high risk group). These approaches could provide meaningful information for understanding the molecular mechanisms of human radiation carcinogenesis and cancer risk estimation.

Special research activities (Molecular oncology)

Priority 1

B. Human radiation carcinogenesis (RP 18-81):

Strategically, not only are studies directly looking at tissues from the A-bomb survivors important, but studies taking advantage of experimental models could be very helpful in interpreting effects on the survivors. In the experimental system we have developed, we can examine the first and consequent events occurring in the cell at the cellular and molecular levels which may have crucial roles in human carcinogenesis.

B-1. Models

The severe combined immunodeficient (SCID) mouse-human chimera makes it possible to study radiation effects on humans in vivo, and thereby provide more relevant and meaningful information than those obtained in vitro or from other non-human animal models. We have already established a transplantation system of normal human tissues (skin, intestine, thyroid and bone marrow) to SCID mice which preserves in situ histology, structure and function. These models will be improved so that they are as close to the human situation as possible and will be applied to the studies on radiation response (see

B-2) and radiation carcinogenesis (see B-3) described below.

B-2. Radiation Response

We will analyze cellular and molecular changes in human tissue/cell after radiation exposure, especially at low doses. This system will enable us to follow the various molecular changes in vivo in human tissues following irradiation. For example, this model demonstrated the dose-response and cellular mechanism of human radiation-induced epilation, which were not clear from the survivor study. Preliminary findings using the SCID-hu intestine model suggest that human crypt stem cells in the intestine are extremely resistant to radiation-induced apoptosis in comparison to mouse stem cells.

B-3. Radiation Carcinogenesis

The approach will make possible studying the process of carcinogenesis at the molecular level and to specify radiation specific gene alterations which induced cancers in the A-bomb survivors.

B-3-1. Thyroid cancer

We established a model of SCID-hu mice with human thyroid tissue, in which the normal histological features of the human thyroid can be maintained in the mammary fat pads of SCID mice for as long as 1 year. Using this model we will attempt to induce thyroid cancer by radiation. Preliminary data indicate that high-dose X-irradiation induces RET inversions in thyroid grafts, which have often been observed in the thyroid papillary cancers and the childhood thyroid cancer of Chernobyl victims. Furthermore, since the RET inversions were found to be sustained as long as 3 months in the grafts, we will follow-up the development of thyroid cancer in the SCID-hu mice.

B-3-2. Skin cancer

We have already established a SCID-hu mouse model for the analysis of human epilation by implanting human skin. This model will also be applied to human radiation-induced carcinogenesis. This project, unlike the thyroid study where no other laboratory has successfully maintained human tissues in SCID, can be a collaboration with outside researchers such as Professor Taisei Nomura of Osaka University, because his laboratory was the first to succeed with a SCID-hu skin model.

Priority 1

C. Radiation-susceptibility of somatic cells in radiation carcinogenesis (RP 7-87):

It is still unclear whether interindividual variation exists in the susceptibility to radiation, especially in radiation carcinogenesis. Individual variation in susceptibility to radiation carcinogenesis is believed to be partly due to a difference in cellular responses to ionizing radiation.

For analysis of interindividual variation in cellular responses, we will establish assay systems using molecular and flow cytometric techniques for the quantitative analysis of radiation-induced physiological and biochemical changes in key molecules responsible for cell apoptosis, signal transduction, and cell cycle regulation such as in ATP, oxygen radicals and protein phosphorylation.

These measurements will be used to evaluate interindividual variation in 100 non-cancer and 100 cancer patients among A-bomb survivors with the same exposure dose. This will be a collaborative effort with the Departments of Clinical Study, Epidemiology and Statistics.

C. Immunology

A major objective of the immunological study is to demonstrate the late effects of A-bomb radiation exposure and the combined effect of radiation exposure, age and sex on the hematolymphoid system and to identify the relationship between altered immune function and radiation-related disease, especially cancer. A-bomb radiation-induced alterations in the immune system may have caused the development of cancer. To achieve this objective we plan to continue our studies of the features and mechanisms of radiation-induced disorders in the hematolymphoid system at the cellular and molecular levels. These studies include radiation effects on the distribution of T-cell subsets in the survivors and of radiation effects on endocrine and hematopoietic growth factor levels. The survey of immune functions in A-bomb survivors will contribute to the health monitoring of the survivors.

Core activities (Immunology)

A. Disorders in the hematolymphoid system of A-bomb survivors (RP 3-87, 7-89, 2-90, 1-93):

The functionality of the hematolymphoid system is a key measure of the ability of A-bomb survivors to respond to infectious disease. Abnormalities in this system also lead to carcinogenesis and autoimmune disease. Aging, sex and radiation exposure affect immune competence, altering lymphocyte subsets in their number and in their differential responsiveness when challenged by various stimuli. Therefore, study of the hematolymphoid system is crucial to assessing the radiation-induced effects that may affect the long-term health of the survivors.

A-1. T-cell (RP 3-87, 1-93):

Since our previous studies demonstrated age-related dysfunctions of T cells in the high dose exposed, we should focus on the cellular and molecular mechanisms of disorders in T-cell differentiation and function. One of the approaches is the analysis of T-cell receptor (TCR) repertoire in A-bomb survivors, which is currently underway and will be finished within FY96. Another approach is to analyze helper T-cell differentiation into two functionally different subsets, Th1 and Th2, which are believed to have different roles in immunity to pathogens and malignant cells. Th1 helper T cells are mainly involved in cellular immunity; whereas Th2 cells are involved in humoral immunity. Our hypothesis

is that the balance between these two subsets is altered in the exposed. These subsets will be analyzed for about 1,000 Hiroshima survivors by flow cytometry using fluorescence-labeled antibodies to interferon gamma and Interleukin (IL)-4 which are specifically expressed in Th1 and Th2 cells, respectively. This study will take about 3 years. Expression of cytokines and other functional molecules in T-cells will be analyzed at the single cell level by using a combination of PCR and cell sorting techniques, which have been established in our department.

A-2. B-cell and stem cell (RP 3-87, 7-89):

As previously reported, white-blood cell production including B-lymphopoiesis is significantly increased with radiation dose, especially in female survivors. We have also observed a dose-dependent increase in hematopoietic stem cell functions in female A-bomb survivors. Based on these findings, we should focus on the analysis of the molecular mechanism of radiation-associated hyperfunctions of hematopoietic stem cells. We will measure some hematopoietic factors such as stem cell growth factor and IL-6, both associated with white-blood cell production and B-lymphopoiesis. It has been suggested by previous mouse studies that the endocrine system such as sex hormones (estrogen) is involved in the control mechanism of hematopoiesis. It was proposed that the decreased level of estrogen after menopause enhances the production of interleukin 6 and osteoclasts and thereby causes osteoporosis in female. Based on these findings, we will compare the onsets of menopause and these hematopoietic growth factors for about 500 female survivors. This will take about 2 years. This study will be in collaboration with the Department of Clinical Studies.

A-3. Blood cell preservation (RP 2-90):

To ensure that appropriate materials will be available for future studies of the late effects of exposure to A-bomb radiation, and to allow the exploitation of potential future technological advances and scientific discoveries, we are cryopreserving live blood cells from AHS participants in Hiroshima and Nagasaki. From 1990 to 1996, (3 AHS cycles), lymphocytes and granulocytes from 4,420 Hiroshima and 3,766 Nagasaki survivors were cryopreserved. We will continue this effort to complete all AHS participants. In the near future, retrospective study of immunological functions using these cryopreserved materials will be possible for the survivors who eventually develop cancer or other disease.

Special research activities (Immunology)

Priority 1

B. Clonal expansion (RP 3-87, 7-89, 1-93):

B-1. Mutant stem cells

After the atomic bombing, the number of hematopoietic stem cells decreased by cell killing and bone marrow death occurred in many survivors. Several months after the bombing the number of these cells should have returned to the normal level. Clonal expansion of

stem cells should have been involved in this recovery process in many survivors. We will focus our efforts on clonal expansion of hematopoietic stem cells carrying mutations and chromosome aberrations. So far two such cases have been documented by mutation and cytogenetic markers; further study is needed to illustrate that clonal expansion occurs as a result of A-bomb exposure. We will survey such cases using somatic mutations in blood cells (T-cells and granulocytes) as a marker. Stem cell expansion will also be analyzed at the molecular level for $CD34^+$ cells isolated from survivors' peripheral blood by a cell sorter. This work will be in collaboration with the Cytogenetics Laboratory.

B-2. Memory T cells

It has been reported that the frequency of abnormal expansion of memory T-cells increases with aging and this may be related to immunological aging and disease development. Abnormal expansion of memory T-cell clones in the periphery has also been observed in A-bomb survivors and this may be reflected in the radiation-induced T-cell dysfunctions mentioned above (see A-1). We have already screened about 1,000 survivors for their TCR repertoire and found about 50 who demonstrated abnormal expansion of T cells with a unique TCR V alpha or beta family. We will attempt to clarify the molecular mechanisms of clonal expansion of T-cells for these 50 survivors by using molecular biological methods such as single cell PCR.

Priority 1

C. Immunity to tumor-associated viruses in A-bomb survivors

Immunity to tumor-associated viruses in A-bomb survivors is one of the issues to be addressed for understanding interactive causality of radiation exposure and virus infections in cancer development. Radiation-induced alterations in tumor virus immunity might have induced some virus-related cancers in A-bomb survivors.

C-1. Hepatitis C virus (HCV)

Cell-mediated and humoral immune reactions to hepatitis C virus (HCV), which is believed to be directly involved in the development of hepatocellular carcinoma, might be altered in the exposed. In fact, our preliminary study on liver cancer of A-bomb survivors suggests that the integration rate of HCV increased with dose. Proliferative response and killer cell activity of T-cells against a mixture of virus-derived peptides or whole viral proteins will be measured for about 1,000 A-bomb survivors including about 20 HCV carriers in 4 years. This will be a collaborative effort with the Departments of Clinical Studies and Epidemiology and will be an extension of the molecular epidemiology based study of HCC (see core activity A-2-2) in the A-bomb survivors.

C-2. Epstein-Barr Virus (EBV)

The Epstein Barr virus (EBV) is another candidate to be studied because our previous study demonstrated a dose-dependent increase in the level of anti-EBV antibodies. Recent reports suggest the possible involvement of EBV infection in stomach cancer

development. Therefore, alteration of immunity against EBV in the survivors may be related to radiation-induced stomach carcinogenesis. We will measure lymphocyte response against whole EBV in culture for the same subjects as in the HCV studies. Recently developed PCR methods for measuring the frequency of EBV-infected B-lymphocytes in peripheral blood will also be applied in these 1,000 subjects.

Priority 2

D. Somatic mutations (RP 7-88):

As mentioned in the response to the recommendations of the Blue Ribbon Panel, the somatic mutation studies seem to have reached a logical end, because many of the somatic mutation assays are not particularly valuable dosimeters for A-bomb survivors. However, since many scientists still request RERF to measure mutation frequencies in exposed people, maintenance of the mutation assays, albeit at a much reduced level, is necessary for international collaborations. Also, these assays are useful in the assessment of various aspects of aging and cancer risk.

D-1. Follow up study (RP 7-88):

We will follow-up cancer incidence and life span for the survivors (n=2,000), whose GPA mutation frequencies have been measured to determine the relationship between somatic mutation and cancer risk or aging. This study will be carried out at a lesser effort than in the past.

Priority 3

E. Immunity to oncogene products in A-bomb survivors

Recent progress in tumor immunology allows us to assess lymphocyte reactivity to the products of cancer-associated genes such as p53 and ras. Such tumor specific immunity of T-cells may be disordered in the exposed. Proliferative response of T-cells against a mixture of peptide fragments of p53 gene products will be measured for about 1,000 A-bomb survivors, the same subjects as in HCV studies for 4 years. Furthermore, we will explore natural killer cell functions to autologous mutant cells lacking the expression of a single HLA class I allele as a model for natural immunity to transformed cells at an early stage of cancer development.

F. Somatic mutations among the in-utero exposed A-bomb survivors

As yet only a very limited amount of information on the occurrence of somatic mutations among the in utero exposed is available and it is not clear whether they will or will not exhibit a greater sensitivity to ionizing radiation as reflected in an increased frequency of mutation in comparison with the exposed A-bomb survivors. It should be emphasized that, although the fraction of the in-utero exposed to more than 0.1 Sv is 13.9 % of the 3,289 RERF cohort (*in utero* mortality, Clinical, and LSS), it is important to ascertain whether the mutation frequencies are different from those of the exposed. This project

is expected to be finished within four years.

Molecular and cellular biology is a rapidly moving field which requires constant upgrading of technique. For the department of Radiobiology to maintain pace with the rest of the scientific world, new methods of analysis have to be developed as well as introduced.

Establishment of in-cell PCR will allow careful scrutiny of individual cells for studying EBV integration frequency or Bcl2 and BCR-ABL translocation in blood samples, for example. Differential display is a potentially powerful technique that may reveal differences in transcription of various genes between tumor and normal cells. The tumor and normal parts of archival tissue sections can be separated and compared for changes that may have occurred in cancer related genes as a result of A-bomb exposure. A similar comparison technique is comparative genomic hybridization (CGH) which can scan the entire genome for possible changes, such as relatively large (10^7 bp) deletions, in cancer DNA versus normal DNA.

The introduction of new technologies is also important as new problems arise. After arrival of the new confocal microscope system, we will be able to study various new facets of radiation effects on cellular function and cellular structure. New studies that can be initiated are alterations of signal transduction in radiation induced tumors or molecular analysis of a single or a few cells from surgical and paraffin embedded archival tissues of the survivors. Such abilities will help to increase sensitivity and resolution for detection of changes in tissue samples.

Finally, it should be noted that most of the studies in the Department of Radiobiology cannot be performed without collaboration with the Departments of Clinical Studies, Genetics, Epidemiology, and Statistics. In view of RERF's limited resources it is important for us to develop a general research plan that defines specific projects that can be done at RERF and projects on which collaboration is important and establishes mechanisms for seeking this collaboration and, where necessary, support.

Project time lines

	1997	1998	1999	2000	2001
a) Genetic background	⇒	⇒	⇒	⇒	⇒
b) Non-cancer diseases			⇒	⇒	⇒
c) Human carcinogenesis	⇒	⇒	⇒	⇒	⇒
d) Susceptibility to radiation	⇒	⇒	⇒	⇒	⇒
e) Clonal expansion	⇒	⇒	⇒		
f) Viral immunity	⇒	⇒	⇒	⇒	
g) Somatic mutations	⇒	⇒	⇒	⇒	⇒
h) Immunity to oncogene products		⇒	⇒	⇒	⇒
I) Somatic mutation in-utero	⇒	⇒	⇒	⇒	

Personnel requirements

The present staff is barely adequate to conduct the studies in radiobiology outlined above.

In order to perform the studies, the following are needed;

1. a permanent researcher who can conduct molecular and pathological analysis of cancer is essential for molecular epidemiology because identification of tumors is the *sine qua non* of the study.

2. allocation of the proper support staff to the molecular epidemiology program for tissue collection.

Fiscal Year	Present	1997	1998	1999	2000	2001
Research Associates						
Immunology	5	5	4	4	4	4
Molecular epidemiology and oncology	5	6	7	7	8	8
Technicians						
Immunology	10	7	7	5	5	5
Molecular epidemiology and oncology	3	7	8	10	10	10
Technician helpers	2	2	2	2	1	1
Clerks	5	5	4	4	4	4
Total	30	32	32	32	32	32

Space requirements (m^2)

Fiscal Year	(1996)	1997	1998	1999	2000	2001
Bench Research						
Immunology	292	292	292	292	292	292
Molecular epidemiology and oncology	91	200	200	200	200	200
Support Space and Offices	97	157	157	157	157	157

Room G105 (temporarily used by the department of radiobiology; 53m^2) is not included.

Equipment budget

See Annex J.

Department of Statistics

The Department of Statistics provides expertise to all of the other research departments in the matter of study design, data analysis, and the construction of databases.

Program objectives

The Department of Statistics plays an important role in virtually all RERF research activities. Collaboration and the provision of guidance on statistical analyses and data management to researchers throughout RERF is a major function of the Department of Statistics. An equally important activity of RERF statisticians involves methodological research aimed at improved understanding of the statistical questions raised by the RERF data and the development and implementation of improved statistical methods for analyses of the broad range of data arising from RERF studies. The Department is also playing a leading role in the design of modern databases to make the RERF data more accessible to all RERF researchers. Finally, the Department of Statistics is responsible for management of the dosimetry data and the computation of individual dose estimates.

Major research activities in the next five years

A. Core activities

The core research and analysis activities carried out by the Department of Statistics focus largely on the need for continued analysis and improved presentation of the RERF epidemiological, clinical, and laboratory data. In addition to direct collaborations with other RERF researchers, RERF statisticians are actively involved in research that leads to the development and implementation of statistical methods applicable to the RERF data.

Preparation of the RERF reports on the epidemiologic follow-up of the survivors and their children require significant contributions from both the Departments of Epidemiology and Statistics. As a consequence of the need for more sophisticated statistical analyses and a shortage of epidemiologists, statisticians have taken increasingly central roles in work on LSS reports and other epidemiological studies at RERF. Because of staff reductions in the Department of Statistics we have had to devote an increased proportion of our resources to the epidemiological studies, which has made it difficult for us to address the statistical needs of RERF's clinical and laboratory programs. Over the next few years it will be necessary to maintain (or even slightly increase) our current level of support for the epidemiologic studies, but it is especially important for us to provide a greater level of support for the statistical needs of RERF's clinical and laboratory research programs.

It should be stressed that the work of the department is largely determined by the nature of statistical issues that arise in the course of RERF research. Thus, other than stating that RERF research will continue to be a source of interesting and challenging statistical problems it is difficult to make specific predictions about future statistical research at RERF.

Priority 1

A-1 *Assessment of mortality and cancer morbidity for the LSS, in-utero, and F_1 cohorts*

A significant portion of the work of RERF statisticians is concerned with ongoing analyses of the LSS follow-up data. This work is carried out in close collaboration with members of the Departments of Epidemiology. Over the next year we plan to complete the final

part of LSS Report 12 dealing with noncancer mortality for the period from 1950 through 1990. Within the next three years we intend to produce general summary reports extending mortality data through 1995 and tumor registry-based cancer incidence data through at least 1992. In preparing these updated reports we hope to develop methods for merging the mortality and incidence reports. Members of the in-utero and F_1 cohorts are now reaching ages at which mortality and cancer incidence rates increase markedly. A series of reports on mortality and cancer morbidity among the in-utero exposed will be completed in the coming year. Work on similar reports for the F_1 cohort is underway. It is likely that the in-utero findings will be updated during the coming five years since the number of deaths and cancer cases can be expected to increase rapidly with the lengthening follow-up.

RERF statisticians are also taking a leading role in the analysis and preparation of the reports on cancer risks based on the results of detailed site-specific pathology reviews, including those of the central nervous system (CNS tumors), liver cancer, and thyroid cancer. An important part of the department's work on these studies concerns the development of standards for the management of data arising from these site-specific studies in order to ensure that the findings are reflected in the tumor registry and are available for use in future analyses.

While RERF statisticians, together with members of the Departments of Epidemiology, plan, carry out and report the results of the analyses of these data, the statisticians' most important contributions concern the development and application of analytical methods and software needed to analyze and summarize these data and the development of procedures to address specific problems which arise in the course of work with the RERF data. These problems include: the development of a general class of statistical models that can be used for the description of and inference about patterns in the excess relative risks and excess absolute rates associated with radiation exposure; methods for the joint analysis of site-specific risk data; the development of procedures to adjust for biases in risk estimates caused by random errors in individual dose estimates; development of methods to determine the impact of death certificate misclassification on cancer and noncancer risk estimates; the development of methods to adjust for the impact of migration in analyses of the LSS cancer incidence data; statistical issues related to RBE estimation from the LSS data; and the development and application of "mechanistic" models for radiation carcinogenesis.

As noted below, an effort is now underway to incorporate the data obtained from the various mail surveys into the RERF research database. As this effort progresses it will become possible to make more effective use of these data in analyses of confounding and effect modification in RERF's epidemiological studies.

A-2 *Analysis of Clinical Studies Data*

The clinical data are an important and underutilized RERF resource. The Department of Statistics role in making more effective use of these data includes the application of recent developments in the analysis of complex longitudinal data sets to the RERF data and the development of more effective ways to store and access these data. While some progress

on analysis of these data has been made in recent years, there is a need to devote more of the departmental resources to the issues related to the clinical data. An area of particular importance over the next few years concerns studies that integrate the epidemiological and clinical data related to the finding of an association between radiation exposure and noncancer mortality. These analyses will undoubtedly lead to challenging statistical problems.

A-3 *Analyses of Laboratory Data*

The investigations carried out by the staff of the Departments of Genetics and Radiobiology often require statistical collaboration for planning and analysis. At the present time statisticians are actively involved in comprehensive final analyses of the conventional chromosome aberration data, assessment of the data on various somatic mutation assays, and the provision of advice and support for a broad range of fairly routine statistical analyses carried out by the researchers in the laboratories. Analyses of the laboratory data present a number of challenging statistical problems including issues related to over-dispersion (due to dosimetry error or unmeasured covariates) and correlated data. Over the next few years there will be a need for significant additional statistical support for the analyses of the 2-DE DNA study data (pattern recognition), for the planning and analysis of molecular epidemiological studies, and for work on the comparison of various potential biodosimeters.

A-4 *Database development*

The Department of Statistics has taken a leading role in the design and documentation of the new RERF research database. While the ITD is responsible for the actual implementation of the database, much of the design work involves issues of direct concern to the Department of Statistics. These issues include clarification of study population definitions, specification of contents of and relationships between individual database tables, and the identification of appropriate data sources, and, in some cases, the development of new coding schemes for specific items. At the present time the RERF research database includes most of the epidemiological follow-up data and basic dosimetry data for the major cohorts. Current efforts are focused primarily on the integration of the mail survey, clinical follow-up data, laboratory data and detailed dosimetric data (including shielding history and acute effects data), into the RERF research database.

A-5 *Dosimetry* (Work on dosimetry is covered by RP 18-59, *Shielding Survey and Dosimetry Study.*)

The Department of Statistics is responsible for management of the basic dosimetry data and for the computation of dose estimates for individual survivors. Current work includes the development of an expanded roster of persons whose exposure status is of interest to RERF (in addition to LSS cohort members, this roster includes mothers of in-utero cohort members and parents of F_1 cohort members) and the restructuring of the shielding history and acute effects data. As a part of this effort we are also working on an updated description of cohort definitions and dose estimation procedures. In the decade since the introduction of DS86 a number of questions have been raised about certain aspects of

current survivor dose estimates (including errors in Hiroshima neutron estimates, problems with gamma doses levels in both cities, and possible biases in estimated doses for Nagasaki factory workers). RERF has been asked to develop and maintain a database related to physical measurements as a part of the ongoing reassessment of DS86. It now appears likely that this reassessment will lead to the introduction of a new dosimetry system within the next five years. Even though current efforts to reorganize RERF's basic dosimetric data will make it easier to implement a new dosimetry system, the introduction of the new system will still require significant effort on the part of staff from the Department of Statistics and the ITD.

B. Special research activities

Most of the work of the Department of Statistics arises from projects undertaken in relationship to our core activities which revolve around collaborations with researchers from other departments. At this time there are only five time-limited special research projects and one outside contract for which the department has primary responsibility. While the department will continue to deal with new statistical problems that arise in the course of work related to our core activities, there is little likelihood that department members will initiate new research protocol-based projects in the coming years.

Priority 2

B-1 *Blood groups in Adult Health Study and in-utero ATB subjects, Hiroshima and Nagasaki (RP 63-63):*

The study is intended to examine blood group frequencies in the LSS and to investigate the relationship between serological type and mortality or morbidity for selected diseases. Following a long period of inactivity, a manuscript describing blood group frequencies for members of the AHS and F_1 cohorts has been prepared. Over the next two years we hope to work with members of the Departments of Clinical Studies to plan and conduct analyses of the relationship between blood group and cause-specific mortality.

B-2 *Cancer studies of occupational and environmental radiation exposure in the Mayak Nuclear Facility and the surrounding areas in the South Urals, Russia (NIH Contract N01-CP-51025, Principal Investigators: Preston DL, Mabuchi K, Koshurnkova NA, Kossenko MM).*

When the extent of radioactive contamination at the Mayak Nuclear Facility and the surrounding area became clear, the Foundation was approached to assist in the design and implementation of studies to determine the health consequences of exposure to this contamination. This contract supports joint work with the US National Cancer Institute and scientists at the Branch Laboratory 1 (Ozersk) and the Urals Research Center for Radiation Medicine (Chelyabinsk) in the Russian Federation on improvements to the epidemiological follow-up data risk estimation procedures for the Russian studies. It is hoped that by the end of this three year contract in September 1998 we will be able to complete some solid cancer and leukemia risk assessments for the Mayak worker and Techa River populations. During the first year of the contract, significant progress has

been made on improvements in the quality of the follow-up data for these cohorts. A paper describing the nature of the Techa River cohort just prior to the beginning of the NCI-RERF collaboration including comparison of the demographics of the LSS and Techa River cohorts has been completed.

Priority 3

B-3 *Radiation effects on the brain and central nervous system (RP 5-87 and RP 8-89).*

One of these studies is intended to search for physical evidence of radiation-related damage to the brain among in-utero survivors (RP 5-87) based on magnetic resonance imaging of a small number of in-utero survivors. The second (RP 8-89) was to make use of autopsy material to investigate the late effects of A-bomb exposure on aging of the central nervous system and to obtain basic data which would improve understanding of the anatomic and functional brain changes that may have resulted from atomic bomb exposure. There has been no significant activity associated with either of these projects for several years. Without the active involvement of physicians, pathologists and others responsible for obtaining the cooperation of the in-utero survivors for the first study or the specimens required for the second, these studies cannot continue. With the retirement of the Assistant Department Chief, Masanori Otake, earlier this year, no one at RERF is actively involved in either of these projects. It is unlikely that there will be any progress on either of these projects in the next five years. In view of the current level of support for these projects and the needs of other projects, it would probably be best to terminate them.

Personnel requirements

The number of research scientist positions has decreased from 10 to 7 as a result of retirements and the general cutbacks that have taken place over the past few years without any diminution in the workload. It is likely that we will lose another statistician within the next few months. These losses have seriously reduced our ability to meet RERF's needs for statistical support in all areas, but particularly with regard to analysis of the clinical and laboratory data. Recently we have been able to take some steps to deal with the impact of these losses. These steps include recruiting (through NAS) one or two additional statisticians, seeking approval of the Executive Committee to hire an experienced statistician to work part time under contract on problems related to analysis of the AHS clinical and laboratory data, and contacting statisticians at various Japanese institutions to solicit support (and candidates) for post-doctoral training in the Department of Statistics. Prior efforts to recruit qualified Japanese statisticians have been only moderately productive and as a consequence the Department has had and continues to have a need for a high proportion of non-Japanese statisticians, who tend to turnover frequently. This turnover gives us the flexibility to seek statisticians who can meet current needs, but it also means that we need to have the ability to employ qualified statisticians in anticipation of all upcoming losses.

In view of the nature of the department's work the table below is designed to reflect personnel needs associated with each of the core activities.

Area	Current	1997	1998	1999	2000	2001
	Fiscal Year					
		Research Associates				
Epidemiologic Studies	3	3.5	3.5	4	4	4
Clinical Studies	1	2	2.5	2.75	2.75	2.75
Laboratory Studies	1	1.5	2	2.5	2.5	2.5
Database design	1	1	0.5	0.25	0.25	0.25
Dosimetry	1	1	1.5	0.5	0.5	0.5
Total	*7*	*9*	*10*	*10*	*10*	*10*
		Research Assistants				
Epidemiologic Studies	0.75	0.75	0.75	0.75	0.75	0.75
Clinical Studies	0.5	0.5	0.5	1	1	1
Laboratory Studies	0.25	0.25	0.5	0.5	0.75	0.75
Database design	1	1	0.75	0.5	0.25	0.25
Dosimetry	0.5	0.5	0.5	0.25	0.25	0.25
Total	*3*	*3*	*3*	*3*	*3*	*3*
Clerical	2	2	2	2	2	2

Space requirements (m^2)

The space requirements for the Department of Statistics are summarized in the following table. The totals do not include hallways.

Area	Current	1997	1998	1999	2000	2001
	Fiscal Year					
Office	125†	142	142	142	142	142
Clerical Support	18	18	18	18	18	18
Other Support ‡	57	40	40	40	40	40
Total	*200*	*200*	*200*	*200*	*200*	*200*

† in square meters

‡ Includes half of the area of the conference, computer, and copier rooms which are shared with the Department of Epidemiology and of the visiting scientists office, which is also shared with Epidemiology.

Equipment budget (x ¥ 1,000)

Computer hardware and software are the primary equipment used by the staff of the Department of Statistics. Because of the size and complexity of many RERF data sets it is important for the statisticians to have access to versatile and powerful computers. In preparing these budget estimates a three year schedule for the replacement of computers and a continuing need to expand network storage capacity have been assumed. It has also been assumed that it will be necessary to replace or upgrade other hardware and software on a continuing basis. It should be noted that, as in recent years, Department of Statistics computers that are replaced can usually be used by other departments with less demanding computational needs for additional years. The following table presents estimates of the total costs for computer equipment and software for the Department for the next five years.

	Fiscal Year				
Budget Category	1997	1998	1999	2000	2001
Replacement hardware and software	4,000	4,500	4,215	4,715	4,400
New hardware and software	1,075	775	1,195	875	1,275
Total	5,075	5,275	5,410	5,590	5,675

Since this hardware and software is used for both and administrative purposes, it seems reasonable to assume that some fraction of these costs should be considered as administrative rather than research expenses. Based on the recommendations formulated by the ITD, the following table shows the research portions of the estimated equipment budget.

	Fiscal Year				
Budget Category	1997	1998	1999	2000	2001
Replacement hardware and software	2,700	3,050	2,850	3,220	2,970
New hardware and software	950	650	1,040	720	1,110
Total	3,650	3,700	3,890	3,940	4,080

SUPPORTING SERVICES

Department of Information Technology

Program objectives

The Information Technology Department (ITD) provides the necessary computing and data tools to all RERF departments to support the Foundation's research and administrative activities. Responsibilities are to maintain computer systems and software, manage the RERF research database, provide user support, and introduce new technology as appropriate to meet evolving needs. Although located in Hiroshima, planning, development, and support work extends to the Nagasaki Laboratory, and ITD coordinates activities with the two Nagasaki computer staff in the Department of Epidemiology. ITD also is responsible for operation of the library in Hiroshima, another information service at RERF. The Hiroshima library provides support to the library in Nagasaki as well.

To ensure that computing resources remain relevant and to play a leading role in ascertaining technology and user support needs, a key aspect of ITD activities is to maintain effective liaison with all RERF departments. ITD also must seek collaboration to utilize the technical skills of staff in other departments and that outside RERF to complement and supplement technical capabilities within the department. These are extremely important for making effective progress on multidisciplinary projects such as those involving database design, systems development, and support of laboratory research projects.

Because many of the activities undertaken by ITD reflect its technical support role in research activities, ITD project content within some of the core activity categories will change as research program emphasis evolves and changes. Project content listed below represents known major foci within the upcoming five-year period.

A. Core activities

- *Maintain and keep current the RERF computing environment*

ITD is responsible for the management and maintenance of all personal computers, Unix workstations, disk and tape data storage, printers, scanners, and other peripheral equipment. Network design and support responsibilities include the TCP/IP Ethernet network that links all computing resources within the Hiroshima and Nagasaki laboratories, the communications line linking the two laboratories, and the communications line linking RERF to the Internet. ITD provides maintenance and support of all operating systems, application software, and Internet services for these computer systems. With an increased awareness of the role that computers can play in the workplace, demand for resources and support continues to rise in all departments as they seek ways to automate work activities and increase staff productivity, partially in response to coping with personnel downsizing that has occurred (and continues) at the Foundation. It also is anticipated that the research demand for these resources and services will continue to increase as new research techniques increasingly rely on interfacing computers with laboratory equipment to process data.

ITD staff play an active role in assessing new technology and its relevance to RERF activities. The introduction of new tools to users ensures that the most recent and appropriate technologies are available to enable researchers to work competitively in their research fields and ensures that the RERF computing environment will remain compatible with future computer technology.

The RERF computing system has expanded greatly over the past few years, both within the two laboratories and in terms of outside linkage via connection to the Internet and dial-in lines to RERF. Because all RERF departments now rely quite heavily on computing resources to carry out their work, it is important that efforts be undertaken to review and strengthen system security. This includes additional measures to guard against unauthorized access to the RERF system by outsiders, to maintain confidentiality both within and outside RERF of personal identification data on study participants, and to ensure that appropriate disaster prevention/recovery plans and procedures are in place. These are necessary to protect the unique repository of data accumulated during the existence of ABCC/RERF, minimize system down time, and minimize user productivity loss resulting from damage to equipment, software, and data.

- *Engage in design and implementation efforts for the RERF research database*

As indicated in the Database Development section within The Structure of Research at the Foundation, the installed hardware and software that now comprise the RERF distributed computing system has resulted in great progress in building a new research database using

modern relational database technology. This technology has made it much easier for researchers to access data, link information from different sources, and extract the desired items for analysis. The new system has simplified data flow procedures for much of the mortality and incidence data follow-up activities. This, together with the elimination of redundant data storage, has contributed to improved data quality. The database system also supports direct links with certain analysis software packages, eliminating the need to create interim work files for analysis. However, much work remains to ensure that the database will serve the wide array of research needs at RERF.

Of utmost importance over the next several years is continued development of a comprehensive picture of study participants by clarifying study populations and incorporating more information into the database. As described earlier, more detailed data related to the major cohorts, such as clinical data, mail surveys, and dosimetry will be added. Biological materials collected over the years are a valuable resource for current and future studies. It is important to create a centralized registry of these materials and link it to other study participant data so that these samples are efficiently and effectively shared and used by the different RERF research programs. It also will be important to address both the volume of data and special data management issues that are expected to arise from data generated from the Department of Genetics DNA studies. All database work is being undertaken as a joint effort of the ITD and the departments responsible for collecting and using the data. These efforts involve major input on design issues from the Departments of Statistics and Epidemiology.

Together with developmental activities, it is important to provide information and training that will ensure that researchers are aware of the capability of the system and how to use it. In addition, researchers must have adequate information about the data in order to use it properly. Thus, it also is important to make suitable documentation available on paper and on-line to meet that need. Together with the Departments of Statistics and Epidemiology, ITD will be working toward that end.

- *Develop and maintain application systems*

Application systems are developed, as necessary, to meet specific needs at RERF, but, as much as possible, they are developed using commercial software packages to minimize time- and labor-intensive custom programming and maintenance efforts.

ITD has developed and supported the Adult Health Study (AHS) patient tracking and clinical management system. The hardware and software for this system are over ten years old, and efforts already are underway to develop a replacement system that will be compatible with the new network and software used for all other RERF activities.

ITD developed and currently maintains a name matching system used by the Departments of Epidemiology for its follow-up activities. With this system, individual follow-up information received from outside sources is matched with RERF database records so that mortality and incidence data can be updated accordingly.

ITD provides support to the Department of Statistic management and maintenance of

dosimetry-related data and the system used for computing dose estimates for individual survivors. Increased support for this activity is anticipated because of the likelihood that dosimetry reassessment activities will result in implementation of a new dosimetry system.

A significant increase in programming and data management support will be needed for the Department of Genetics' two-dimensional electrophoresis image analysis of DNA fragments. This work will involve a joint effort among the Departments of Genetics, and Statistics, and ITD.

The development of a new business system has enabled most day-to-day business computing activities to be carried out by staff in the Secretariat. ITD staff continue to play an integral role in troubleshooting, maintenance, and, as necessary, providing some of the more complex enhancements that users are not able to implement on their own.

- *Expand training and information outreach for users*

The distributed computing environment has provided users with direct access to many powerful hardware and software tools. An effective program of training and information dissemination is essential to enable users to make optimal use of these tools. While important initial progress has been made, many important subject areas still need to be covered or further supplemented. Thus, additional emphasis is being placed on organizing additional training courses and information seminars. Planning, preparation of materials, and actual instruction must involve those most familiar with software to ensure training and content is effective and relevant for RERF users. ITD has adopted a multi-departmental approach to this activity and has received collaborative support of departments who have staff expertise in pertinent areas. This has been a very effective way to meet educational needs. The user response to training courses conducted thus far has been overwhelming. Training could be conducted more efficiently and timely if room space and equipment could be expanded to better accommodate participant demand.

ITD also disseminates information to users outside a class or seminar setting. With the recent elimination of RERF's in-house publishing capabilities, ITD uses email and plans to expand its use of the Intranet as a means to providing a greater amount of reference information and announcements in a timely manner.

- *Support expansion of RERF information dissemination to outside communities*

ITD is providing technical support to the Publication and Documentation Center in its use of the Internet World Wide Web to widen accessibility and visibility of RERF's research activities to the outside. The RERF Web pages recently were reorganized and expanded, and information on those pages addresses issues of interest to both the scientific community and the general public. To widen accessibility and to provide a faster and less expensive method of distribution, ITD is working on enhancements that will allow Web users to download RERF public data and documentation files already available on floppy disk, such as those used in analyses conducted for Life Span Study Report 12.

- *Maintain the RERF library and archive*

Much of the institutional memory regarding ABCC and RERF has been and continues to be lost due to the many retirements occurring. Although efforts to establish a centralized archive have been initiated by various groups in the past, currently there exists no institutional archive documenting historical decisions, procedures, and materials that bear significance to the unique activities of the institution and that provide important background perspectives to current research efforts. If RERF is to retain its history, it is important to renew efforts in establishing the archive. The first step would require that RERF obtain outside expertise to obtain guidance in the planning, database cataloging, and management of archives for research institutions. As information services, the library and archive activities ideally should be coordinated and integrated with each other.

Due to staff losses, it has become difficult for the library to keep pace with the work needed to provide journals and books to researchers in a timely fashion. Together with the need to investigate and introduce new services that will give researchers wider access to research information, this provides a strong basis for reassessing library activities. The aim should be to identify the services that researchers find essential to their work and to determine how the library can provide those services effectively. With this information, the Foundation can ascertain what the appropriate resources are in terms of equipment, services, and personnel to meet those needs. This process should include streamlining and modernizing in-house library activities and establishing additional links to outside services for more effective and efficient operation. It will be extremely important to supplement or replace current on-line services with those that provide continuous update of publication and other research reference materials. It would be helpful to seek outside expertise in recent library technology to guide the efforts of library staff. Collaborative support from ITD computing staff will be needed for library and archive efforts.

Personnel requirements

Over approximately the last two years, ITD has lost a total of 5 computer professional/technical staff. This represents a 40% and 60% loss, respectively, among the two fastest growing areas of demand, database management and systems administration. During this period, ITD workload has increased dramatically. With the transition from a mainframe to a distributed computing environment, computing resources have become an integral part of the Foundation infrastructure upon which research, support, and business activities depend. The amount of equipment and software that must be maintained and the demand for support and services continues to grow out of the need to remain competitive on the research front and to automate activities to cope with personnel downsizing occurring throughout the Foundation. The introduction of modern database technology has renewed efforts by both computer and scientific staff to re-examine and reorganize data, and to expand and document the new research database to increase accessibility and usability of data, much of which has never been fully utilized. All these efforts to support research have been hindered because of staff shortages. In other cases, such as providing support for 2-DE image analysis, ITD currently has no personnel resources to undertake application development requirements. Without further action, the situation will worsen rapidly, and many of the core activity needs will go unmet. The department chief will depart at the beginning of 1997, and another two staff will leave within the coming 12 months. Anticipated attrition by 1999 will leave only one-third the original computing staff from two years ago.

To deal with the situation, recruitment is underway through NAS for a department chief and systems administrators. To seek additional personnel and expertise, steps have been taken to explore collaborative and post-graduate research/training relationships with regional Japanese universities. Additional recruitment of experienced database management personnel and qualified Japanese computer technical staff is essential.

Although reassessment of the library has not yet been undertaken, it is evident that establishment of the archive and proper operation and maintenance of the library will require one additional staff for the combined library/archive. During full-scale development and cataloging phases for the archive, additional staff will be required, most likely on a temporary basis.

	Fiscal Year					
Area	Current	1997	1998	1999	2000	2001
Computer	13	16	18	19	19	19
Professional/Technical						
Library/Archives	2	3	3	3	3	3
Clerical Administrative	3	2	2	2	2	2
Total	18	21	23	24	24	24

Space requirements (m^2)

Estimates reflect space for new staff and for the assortment of computers and peripheral equipment in their immediate work area for development, testing, and troubleshooting activities. A small increase in support space is needed to guarantee that all computer servers are installed in a temperature-controlled, restricted access area for security purposes, and to permit use of a projection panel in the training room to provide effective instruction on methods and procedures. Initial archives work most likely can be accommodated in the existing library space. The increase indicated in future years assumes that methods and resources can be introduced that would enable the library to reorganize and economize how it uses its current space, so that once the archive is in the full implementation phase, additional space required to house those materials is minimized.

	Fiscal Year					
Area	Current	1997	1998	1999	2000	2001
Office	180	228	228	228	228	228
Clerical Administrative	31	31	31	31	31	31
Library/Archives	337	337	337	357	357	357
Other Support[1]	166	183	183	183	183	183
Total	714	779	779	799	799	799

[1] includes server, user training, diagnostic workbench, and conference rooms

Equipment budget (x ¥ 1,000)

In the table below, computer hardware and software used by ITD staff to carry out development and support work are distinguished from resources used to provide RERF-wide services to users. In order to perform development, testing, and technical support, it is necessary for ITD to have within the department a variety of equipment and software used in other departments. Estimates are based on a three year schedule for replacement of computers. A faster turnaround is built in for systems administrators, who must troubleshoot problems on new systems installed in other departments. Functional equipment rotated out of service will be used to help keep the training room current, moved to meet needs in other departments, and serve as emergency replacements to minimize down time on critical work activities. Also accounted for is the ongoing need to expand network storage capacity. In the area of RERF-wide services and resources, the regular upgrading and replacement of hardware and software are an essential aspect of maintaining a modern computer environment, ensuring that it keeps pace with future technology developments and provides state-of-the-art tools for research.

	Fiscal Year				
Budget category	1997	1998	1999	2000	2001
ITD staff					
Replacement hardware and software	7800	8520	9095	9095	9550
New hardware and software	1100	900	1155	945	1210
ITD staff total	*8900*	*9420*	*10250*	*10040*	*10760*
RERF-wide services					
Computer and networking hardware/software replacement	36000	36000	37800	37800	39700
Grand Total	44,900	45,420	48,050	47,840	50,460

+ Support fees that cover Unix workstation hardware maintenance contracts, annual software license fees, and network line lease fees are included in the Secretariat operations budget.

Publication and Documentation Center

Dissemination of the findings of the Foundation's research to the scientific and lay communities, nationally and internationally, is centered in the Publication and Documentation Center. Broadly stated, the duties of the Center are the following: editing, production, preservation and management of publications; translation and interpretation services.

Specific roles

(1). Preparation of technical reports on the results of RERF research and studies, and distribution of them to interested organizations as well as to researchers worldwide.

a). Administrative procedures for the review of research manuscripts up to publication thereof in journals; administrative support for research scientists by documentation

of research results and by preserving and making available to them research protocols, abstracts for scientific meeting presentation, and reprints.

b). Publication of English and Japanese Newsletters, annual reports, and bibliographies of publications; management of RERF's World Wide Web site.

c). Proofreading and editing of English manuscripts; translation and interpreting services requested by departments; preparation of figures, diagrams, and slides using computers; photographic activities

Organization (see the following page)

Personnel strength at PDC for the past six years and projection of changes

	Fiscal Years					
	1990	1991	1992	1993	1994	1995
Research	1	2	4	2	2	1
Clerical	30	25	26	28	27	25
Technical	1	0	0	0	0	0

PDC's operational requirements cannot be fulfilled if replacements for retiring employees are not employed. Continued operation at current level requires at least maintenance of the current personnel strength.

Radioisotope Facility

The duties of the RI Facility are 1) management of the facility in accordance with Japanese laws, 2) maintenance of a safe working environment, and 3) summarization and realization of requests from facility users. It should be noted that until recently the Foundation maintained two radioisotope facilities, one in Hiroshima and one in Nagasaki. With the closure of the radiobiology program in Nagasaki, the facility there was no longer needed and was placed on inactive status. It has not, however, been formally closed. Whether it should be closed or merely maintained in an inactive status hinges on two considerations, namely, future use and cost. If this facility should be needed in the future for RERF research purposes, it would be cheaper in the long run to continue to maintain it. At present, the annual maintenance costs are between ¥ 700,000-800,000 but this will diminish in the future. If the facility is formally closed, the space and equipment must be decontaminated in accordance with Japanese regulations. This has been estimated to cost ¥ 8,000,000. Formal closure would, of course, free the space for other uses, and this is an important consideration given the size of the Nagasaki Laboratory. As yet no decision has been made about the fate of this facility.

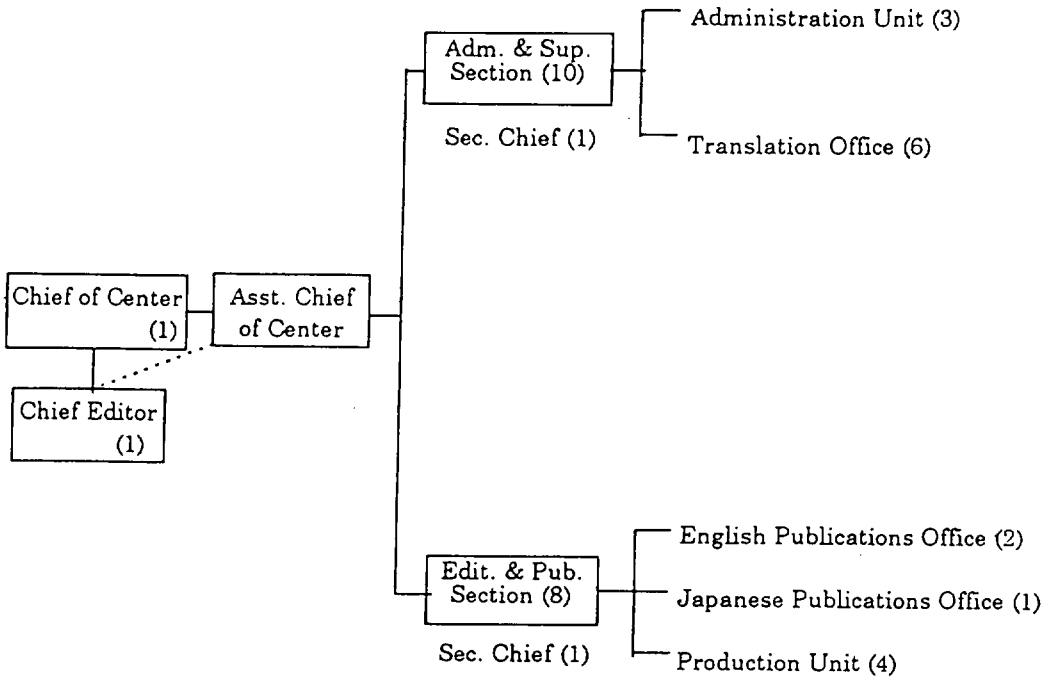
The remarks to follow pertain only to the Hiroshima facility.

Management of the RI facility

The RI Facility is being operated in accordance with various national laws. Detailed record-keeping on many aspects of the RI facility operation (e.g., measurements of air dose rate, concentration of RI in drainage, and the radiation dose to which the user is exposed) is mandated

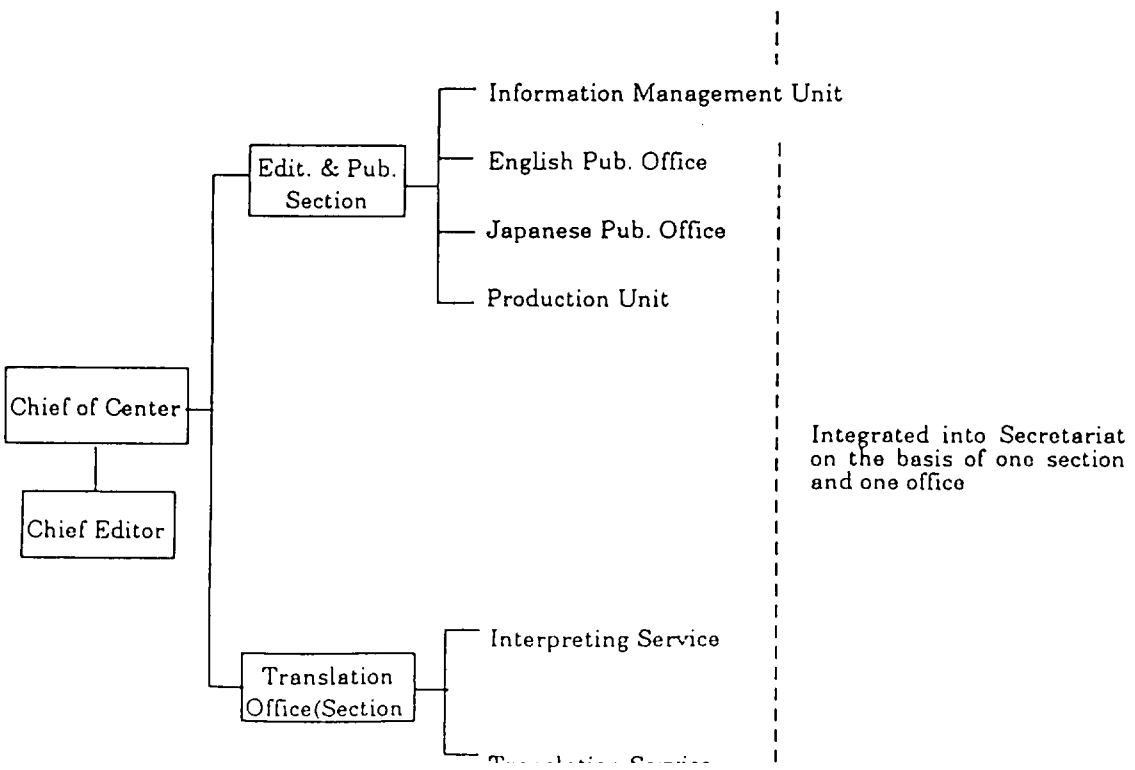
Present

Staff:		
	Professional	1
	Administrative	20
	Total	21



Revised Organizational Structure (draft)

1 January 1998 | 1 January 1999



by law for safe operation of the facility. It is obligatory to submit summary reports of these data to the Science and Technology Agency. Preparation of these documents has been completely computerized. However, the equipment being used to record and manage these data has exceeded its service life and should be replaced.

Maintenance of a safe working environment

The RI facility supports the activities of the Departments of Clinical Studies, Genetics, and Radiobiology. At present, 31 users are sharing a laboratory space of 75 m^2. Space per user at our laboratory is less than that at laboratories of other institutions. Furthermore, the equipment being used in our laboratory, such as the 2D-DNA electrophoretic apparatus, is larger than usual and occupies more space. In addition, studies being conducted at RERF are mainly conducted on a large scale, and many samples are simultaneously examined. Therefore, lots of different pieces of equipment are used simultaneously. It is dangerous to perform many experiments in such a small place. Expansion of the facility has been requested, but no action has been taken due to a shortage of funds.

Future of RI facility

The RI facility will be used for many aspects of the molecular studies newly proposed by the Blue Ribbon Panel. With future technical developments, it is likely that some of these studies will be less dependent on the RI facility than is present necessary (for example, DNA sequencing, use of the Southern blot method, and chemiluminescent procedures). However, it can be easily imagined that more new experiments will be performed at the RI facility, offsetting the number of experiments that require the use of radioisotopes and will cease due to using the above-mentioned new techniques. Expansion of laboratory space to accommodate these added needs is essential.

Replacement of equipment is also necessary. The current automatic developing machine for X-ray film and the γ-well counter may cease to function at any time. Repair is impossible because no spare parts are available for these old models. One possible option to replacement purchase is to relocate the γ-well counter from the Nagasaki Laboratory to Hiroshima. If this is feasible, measuring contamination on the surface of the equipment and transportation of the equipment to Hiroshima are the only two expenses that must be borne and neither should be unduly onerous.

Renovation of the facility is necessary to satisfy the need to change the type and amount of radioisotopes being used. Installation of a larger drainage tank is especially necessary.

Personnel requirements

Fiscal Year	1996	1997	1998	1999	2000	2001
Research Scientists	0.1[1]	0.1	0.1	0.1	0.1	0.1
Technicians	0.7[2]	1	1	1	1	1

[1] One scientist is concurrently assigned to the Department of Genetics (90%) and the RI Facility (10%).

[2] One technician is concurrently assigned in the RI Facility (70%) and the Department of Clinical Studies (30%).

Space requirements (m^2)

Fiscal Year	1996	1997	1998	1999	2000	2001
Bench Research	75	120*	120	120	120	120
Support Space						
Darkroom	12.5	12.5	12.5	12.5	12.5	12.5
Contamination inspection room	7.7	7.7	7.7	7.7	7.7	7.7
RI depository	5.5	5.5	5.5	5.5	5.5	5.5
Storage disposal room	9.1	9.1	9.1	9.1	9.1	9.1
Waste disposal room	6.8	6.8	6.8	6.8	6.8	6.8
Exhaust facility	9.9	9.9	9.9	9.9	9.9	9.9
Stock room	6.0	6.0	6.0	6.0	6.0	6.0
Office	12.5	12.5	12.5	12.5	12.5	12.5
Total	145	190	190	190	190	190

*: Space for stairs and corridor is included.

Equipment budget (× ¥ 1,000)

Fiscal Year	New/ Repl	Item	Q'ty	Unit Cost	Total
1997	N	PC	1	570	570
	R	Printer	1	220	220
	R	Software version up	1	50	50
1998	R	PC	1	500	500
1999	R	Software version up	2	50	100
2001	R	PC	1	500	500
	R	Printer	1	220	220
	R	Software version up	2	50	100

* Other equipment items requested for each fiscal year are shown in Annex J.

Secretariat

The Secretariat, as the administrative department for the Foundation's operations, is responsible for the procurement of human and material resources required for the smooth conduct of research activities. As of 1 April 1996, the Hiroshima Secretariat was composed of 48

employees in four sections (General Affairs, Personnel, Accounting, and Supply and Property), and the Nagasaki Secretariat of 17 employees in two sections (General Affairs and Accounting).

Organization and personnel strength (as of April 1, 1996)

The numbers in parentheses indicate personnel strength, and "+" indicates section chiefs or other managerial positions.

	[Hiroshima]	
	Assistant Chiefs and others (3)	
		Director's Office (5) +2
	General Affairs Sec. (18)	General Affairs Unit (7)
		Document and Archive Unit (2)
		External Affairs Unit (2)
	Personnel Sec. (6)	Personnel Unit (3) +1
		Payroll Unit (2)
	Accounting Sec. (7)	Accounting Unit (3) +1
Secretariat (65)		Receipts & Disbursement Unit (3)
		Supply Unit (4) +1
	Supply & Property Sec. (14)	Physical Plant Unit (5)
		Welfare Unit (4)
	[Nagasaki]	
	Assistant Chief (1)	
		Public Relations Office (2) +2
	General Affairs Sec. (11)	General Affairs Unit (4)
		Employees Unit (3)
	Accounting Sec. (5)	Accounting Unit (2) +1
		Supply Unit (2)

Duties

Hiroshima Laboratory

1. General Affairs Section

Administrative duties in support of the Directors' Offices; administrative support for meetings and official functions of the Foundation; management of administrative documents; labor safety and health, security and safety; and external affairs and public relations activities.

2. Personnel Section

Duties concerning employment and dismissal, payroll, social and labor insurance, and administrative procedures for appointment of consultants, etc.

3. Accounting Section

Duties concerning preparation and execution of budget, settlement of accounts, management of cash and special accounts, and management of assets.

4. Supply and Property Section

Duties concerning purchase and management of supplies and equipment, maintenance of the facilities, heat control and energy conservation, employee welfare, and management of lodging facilities of the Foundation.

Nagasaki Laboratory

1. General Affairs Section

Duties corresponding to those discharged by the Hiroshima General Affairs Section and Personnel Section; administrative duties concerning functions of the Foundation; payroll and labor insurance, labor safety and health; and employee welfare.

2. Accounting Section

Duties correspond to those discharged by the Hiroshima Accounting Section and Supply and Property Section; purchase and management of goods; maintenance of facilities; security and safety.

Personnel of Secretariat, Hiroshima and Nagasaki laboratories

(1) Changes of personnel strength (actual) (1990 - 1996)

		1990	1991	1992	1993	1994	1995	1996
Total		93	99	93	90	84	71	65
Total (Hiroshima)		70	76	67	66	62	50	48
Attached to the Secretariat		5	6	4	4	4	3	3
General Affairs Section	Total	24	25	24	22	21	17	18
Personnel Section		6	8	9	8	7	7	6
Accounting Section		6	5	6	7	7	7	7
Supply and Property Section	Total	29	29	24	25	23	16	14
Total (Nagasaki)		23	23	26	24	22	21	17
Attached to the Secretariat		1	1	2	1	2	1	1

General Affairs Section	Total	14	15	16	15	13	13	11
Accounting Section	Total	8	7	8	8	7	7	5

2) Personnel strength required for the next five years

a) Secretariat

The Secretariat will support continued improvement of work procedures to cope with personnel reduction. However, considering the workload of the present organization, a staff of 46 and 14, respectively, for Hiroshima and Nagasaki, 60 in total, is necessary. In the event of relocation to new facilities, personnel strength can be reduced by 7 in the area of security and maintenance of the facilities.

b) Necessary personnel strength by section and projection of change in personnel number (1996 - 2001)

		Necessary personnel	1996			1997			1998			1999			2000			2001			02
			Apr. 1	Ret.	Rep	Apr. 1	Ret.	Rep	Apr. 1	Ret.	Rep	Apr. 1	Ret.	Rep	Apr. 1	Ret.	Rep	Apr. 1	Ret.	Rep	Apr.
Total		60	65	6	0	59	2	0	57	6	0	51	2	0	49	4	0	45	3	0	42
Total (Hiroshima)		46	48	3	0	45	1	0	44	4	0	40	2	0	38	4	0	34	2	0	32
Attached to the Secretariat		1	3	1		2			2			2			2			2			2
General Affairs Sec.	Clerical	15	14			14	1		13			13	1		12	1		11	1		10
	Technical	3	4	1		3			3	1		2	1		1			1			1
	Total	18	18	1	0	17	1	0	16	1	0	15	2	0	13	1	0	12	1	0	11
Personnel Sec.		6	6			6			6	1		5			5	1		4			4
Accounting Sec.		7	7	1		6			6	1		5			5			5			5
Supply & Property Sec.	Clerical	9	9			9			9			9			9	2		7	1		6
	Technical	5	5			5			5	1		4			4			4			4
	Total	14	14	0	0	14	0	0	14	1	0	13	0	0	13	2	0	11	1	0	10
Total (Nagasaki)		14	17	3	0	14	1	0	13	2	0	11	0	0	11	0	0	11	1	0	10
Attached to the Secretariat		1	1			1			1	1		0			0			0			0
General Affairs Sec.	Clerical	7	10	3		7	1		6			6			6			6	1		5
	Technical	1	1			1			1			1			1			1			1
	Total	8	11	3	0	8	1	0	7	0	0	7	0	0	7	0	0	7	1	0	6
Accounting Sec.		5	5			5			5	1		4			4			4			4

Note: "Retirement" in 1996 includes employments, transfers and retirements up to July 1.
Ret. = Retirement; Rep. = Replacement

c) Relationship with duties of the Publication and Documentation Center

Despite the research support aspects of PDC, better results can be expected by removing the division between the duties of the Secretariat and those of PDC. Therefore, in the future, translation which is done at PDC at present and the public relations activities will be put under the charge of the Secretariat together with the Document and Archive Unit and the External Affairs Unit for better utilization of talent. The duties relating to research protocols and technical reports will be placed under the direct charge of the Chief of Research for better coordination of activities. These arrangements should be further discussed. However, they are not considered in the estimation of personnel strength required.

Changes in the Foundation's overall personnel strength

1. Actual changes (1990 - 1996)

Personnel no. as of April 1	Total	Directors	Chief of Secretariat	Research Scientists	General Employees
1990	427	6		57	364
1991	433	6		61	366
1992	437	5		64	368
1993	435	6		62	367
1994	412	6		57	339
1995	373	4	1	48	320
1996	335	4	1	47	283

MAINTENANCE OF AN ADEQUATE INFRASTRUCTURE

Three needs are paramount if the Foundation is to fulfill its mission as set out in the preceding pages. First, there must be adequate staff and these individuals must have the appropriate skills to meet an evolving research program. Second, there must be the requisite equipment to support the research activities of that staff. Finally, there must be sufficient, suitable space in which to house the staff and equipment. Given the recent pace of technological developments it is difficult to project these needs over the next five years with the assurance that is desirable. Nonetheless, some projection is obviously necessary and to make that projection assumptions must be made. We now set out the assumptions that underlie the projections to follow.

Personnel

First, some further reduction in staff from that presently obtaining is possible. However, this assertion tacitly assumes that the future, through increasing use of computer technology, automated laboratory equipment, and better, faster means of communication, will make some current positions that are labor intensive redundant and others less time-consuming. But, it is our view that this reduction should be an orderly one and not so precipitous as to jeopardize the Foundation's research

and capacity to fulfill its charge either in the short or the long run. Accordingly, we have projected staff needs on the assumption that to maintain a viable staff size it will be necessary to replace two out of every three retirements over the next five years. This will amount to a further reduction in staff of about 10% over this period of time; however, the impact of this further loss in personnel must be seen in the context of the 25% reduction that has occurred in the past five years and to which we are still adjusting.

These replacements will be recruited on the basis of demonstrated need and will not be automatically made to the department or unit from which the retiree(s) came. Emphasis will be placed upon technical staff, such X-ray technicians, clinical and research laboratory personnel, and clinical and public health nurses with due allowance for changing workloads with time. However, it is clear that an adequate cadre of support staff is also essential and replacements will be made in the Secretariat, the Information Technology Department, and the Publication and Documentation Center to ensure this end.

Second, there are staff inequities between Hiroshima and Nagasaki that need to be resolved. For example, with the closure of the Radiobiology Department in Nagasaki, all of the technicians employed in this laboratory were transferred to the Clinical Laboratory there. This has resulted in a staff that is actually larger than the one in the Clinical Laboratory in Hiroshima despite the much heavier workload of the latter. These technicians should be offered transfer to Hiroshima or to other positions as retirements occur in lieu of a replacement. Other instances of inequity can be cited.

Third, particularly detrimental to the Foundation's research activities has been the loss of professional employees. Over the past five years, when no replacements of any sort occurred, their number has fallen from 64 to 47. Since it is precisely these employees that are essential to the Foundation's mission we propose increasing this number to 50.

Projected yearly staff changes by broad work categories are given in the tables at the end of this section. These tables should be seen as guides, and not as firm commitments which will, as previously said, be determined by need.

Equipment

Contemporary science rests on increasingly complex and sophisticated equipment both in the laboratory and as a means of communication, data management and analysis. Much of this equipment has, unfortunately, a relatively short useful life, arguably three to five years in most instances. This implies, in turn, that replacements will be necessary periodically. Again, it is our intent to make these replacements on the basis of need and relevance to the current research program. Wherever equipment is outdated for use in one department, if circumstances permit, it will be transferred to another department with less demanding needs.

Clearly high on the list of priorities will be the maintenance of a strong computing capability including the continued cost of transition from a mainframe environment to a distributed system. This is essential not only to research but to the proper administration of that research. As the body of information available at the Foundation grows, which is inevitable, the need for efficient data management grows too. Moreover, significant staff reduction appears possible only if some of the current routine work can be automated, and delegated to computers.

Budget projections for the next quinquennium will be found at the end of this section. These projections set forth personnel and operating costs as well as equipment needs. However, in departure from previous budget projections, equipment expenditures have been divided into those supporting research and those supporting administrative needs. In the past, administrative equipment needs, primarily computing capability, have generally been funded out of operating costs and therefore, not reflected in the overall equipment forecasts. This accounts for much of the seemingly larger equipment projections seen in these tables. It should also be noted that the bulk of the equipment expenditures predicted are for the replacement of outdated apparatus and not new devices, new in the sense of not previously in use at the Foundation.

Space

Although planning for the relocation of the Foundation's facilities in Hiroshima continues, there is as yet no firm date for this to occur. Accordingly, for the purposes of this document, we have assumed that the relocation will not occur in the next five years. However, if this should prove to be incorrect, clearly additional costs over those here projected would occur. It is important to note that the Hiroshima facilities are old, and barely adequate; however, we continue to review space allocations and strive for the most efficient use of the space that is available. This process of review will continue.

Changes of personnel strength
(2/3 replacement of retirements)

		Total	Director	Research Scientist	Clerk	Computer Specialist	B	C	D
FY1996	As of Apr. 1	335	5	47	178	12	16	57	20
	Retirement	10			4		2	3	1
	Replacement	6		3	1		1	1	
FY1997	As of Apr. 1	331	5	50	175	12	15	55	19
	Retirement	30	4	1	18	1		3	3
	Replacement	22	4	1	12	1		2	2
FY1998	As of Apr. 1	323	5	50	169	12	15	54	18
	Retirement	14			10	1	2	1	
	Replacement	9			6	1	1	1	
FY1999	As of Apr. 1	318	5	50	165	12	14	54	18
	Retirement	14	4	1	7	1	1		
	Replacement	11	4	1	5	1			
FY2000	As of Apr. 1	315	5	50	163	12	13	54	18
	Retirement	12			11				1
	Replacement	9			8				1
FY2001	As of Apr. 1	312	5	50	160	12	13	54	18
	Retirement	10		2	7				1
	Replacement	8		2	5				1
FY2002	As of Apr. 1	310	5	50	158	12	13	54	18

1) The expiration of directors' terms of office is considered as mandatory retirements, and replacements for all of the retiring directors will be employed.
2) Number of research scientists is 50 and the replacements for all terminating will be employed.
3) 2/3 of replacement of retirements of general employees will be employed as of 1 April of the next year.
4) B: Technical staff C: Clinical radiology technicians and medical technicians
D: Nurses and public health nurses

Comparison of personnel strength between actual and requested (Total)
(2/3 replacement of retirements)

		Total	Director	Research	General	A	B	C	D
FY1996	as of Apr. 1	335	5	47	283	190	16	57	20
	Retirement	10			10	4	2	3	1
	Sub-total	325	5	47	273	186	14	54	19
	Requested	**331**	**5**	**46.5**	**279.5**	**188**	**11**	**60.5**	**20**
FY1997	Replacement	6		3	3	1	1	1	
	as of Apr. 1	331	5	50	276	187	15	55	19
	Retirement	30	4	1	25	19	0	3	3
	Sub-total	301	1	49	251	168	15	52	16
	Requested	**342.5**	**5**	**50.5**	**287**	**195**	**11**	**62**	**19**
FY1998	Replacement	22	4	1	17	13		2	2
	as of Apr. 1	323	5	50	268	181	15	54	18
	Retirement	14			14	11	2	1	0
	Sub-total	309	5	50	254	170	13	53	18
	Requested	**346.5**	**5**	**51.5**	**290**	**198**	**11**	**63**	**18**
FY1999	Replacement	9			9	7	1	1	
	as of Apr. 1	318	5	50	263	177	14	54	18
	Retirement	14	4	1	9	8	1	0	0
	Sub-total	304	1	49	254	169	13	54	18
	Requested	**348.5**	**5**	**52.5**	**291**	**199**	**11**	**63**	**18**
FY2000	Replacement	11	4	1	6	6			
	as of Apr. 1	315	5	50	260	175	13	54	18
	Retirement	12			12	11	0	0	1
	Sub-total	303	5	50	248	164	13	54	17
	Requested	**347.5**	**5**	**52.5**	**290**	**199**	**10**	**63**	**18**
FY2001	Replacement	9			9	8			1
	as of Apr. 1	312	5	50	257	172	13	54	18
	Retirement	10		2	8	7	0	0	1
	Sub-total	302	5	48	249	165	13	54	17
	Requested	**347.5**	**5**	**52.5**	**290**	**199**	**10**	**63**	**18**

SUMMARY

Investigations have been in progress for 50 years to ascertain the health effects produced by radiation in the survivors of the atomic bombings of Hiroshima and Nagasaki. It is appropriate to ask (1) what the results of these studies have been, (2) what more is to be done, and (3) what changes, if any, are anticipated in the future for RERF. One purpose of this document is to address these issues.

The long-term follow-up of this unique population has provided results of considerable value to the medical as well as the radiobiological community. Significant associations between radiation dose and cancer have been seen among the survivors for most types of cancer, including leukemia, multiple myeloma and cancers of the thyroid, lung, breast, stomach, skin, colon, esophagus, liver, urinary tract, and ovaries. The RERF data provide unique, quantitative information on how these risks are affected by sex, age-at-exposure, and time. The excess relative risks for most solid cancers are found to be higher for men than women and to increase with decreasing age at exposure. There is weak evidence that the high relative risks seen for those exposed as children have decreased with time while the relative risks for those exposed as adults have remained constant. Recent analyses of the LSS data indicate that excess rates increase throughout life and that these rates do not vary much with sex and age-at-exposure. The RERF data also provide evidence of a positive association between radiation dose and noncancer disease mortality. While this effect is small, it does not appear to be an artifact of misclassification of cause of death on death certificates. Clinical studies of cardiovascular disease morbidity and related endpoints have been carried out using the RERF clinical data. The results of these studies also support the notion of a radiation effect on some noncancer diseases. Over the next few years we must develop a more unified approach for combining the epidemiological and clinical data on radiation and noncancer disease morbidity. The presence of dose-dependent developmental effects on survivors who were exposed in-utero is well-documented and it is now becoming clear that radiation exposure is associated with elevated risks of cancer later in life for this group of survivors. If, as seems likely, these risks continue throughout life the coming decades will provide further information on the extent and nature of these risks. It is also important to follow-up earlier findings that the developing human brain is extremely sensitive to teratogenic effects of relatively low doses of ionizing radiation since this vulnerability might manifest itself in earlier onset of cognitive disorders and an increased frequency of senile dementia.

Evidence is still lacking that radiation induces heritable genetic damage in humans. Research with experimental animals, however, has clearly demonstrated that heritable changes are positively associated with radiation exposure. In general, RERF's findings in various genetic studies are as expected if the atomic-bomb radiation exposure has produced mutations. But, to date, the differences between the children of proximally and distally exposed survivors are far from significant. However, none of the strategies to assess mutation risk used thus far has addressed the full gamut of possible genetic damage. For example, the program of clinical examinations of the newborn was designed to identify congenital abnormalities demonstrable soon after birth but could not identify those abnormalities that are not readily detectable until later in life, nor those simply or complexly inherited disabilities that do not manifest themselves until adolescence or later. The latter represent by far the largest proportion of all inherited handicaps, and there has been no systematic program of health examinations of the F_1 after the first year of life which might

detect an increase in these diseases and disorders.

Developments in molecular biology have identified a number of new approaches that will permit mutations at the level of nucleotide bases in DNA to be detected in human populations in the foreseeable future. Although these techniques are not available for use at the present time to monitor human mutation rates, cells from exposed and unexposed parents and their children are being collected now. Some of these cells are being immortalized using the Epstein-Barr virus, cultured, and stored for use when the new molecular approaches to mutation detection can be used cost-effectively.

Continuation of the investigations at RERF will (1) strengthen evidence about the cancer dose-response, (2) clarify the impact of exposure on cancer risks for the survivors exposed as children in-utero, (3) provide additional information on the nature of radiation effects on cardiovascular and other noncancer diseases, and (4) offer new insights into the role of biological and environmental factors on radiation risks.

Initial efforts to develop a database that contains information on family relationships among members of the LSS and other RERF cohorts suggest that these data can be useful for studies of the interaction between hereditary factors and radiation- or nonradiation-related cancer risks. This work will continue during the next five years provided that adequate computing and personnel resources are available.

Public concern over the potential risks of exposure to ionizing radiation shows no sign of abating; indeed it is possibly even greater now than in the past largely due to a series of accidents at nuclear power generating facilities, and increased medical usage. To allay this concern will require greater knowledge of how radiation affects somatic and genetic diseases in human beings. While there are experts in most disciplines related to understanding radiation effects on humans at many institutions all over the world, the Foundation is the only one with many of these experts in one place, and with access to the largest, well-defined and studied population of radiation-exposed individuals. To not maintain this "critical mass" of interested scientists focused on this important human problem would create a serious setback to the Foundation and the successful prosecution of its mission. In addition, with the increasing concern of the effects of environmental chemicals on human health, RERF scientists have the potential to use the information from this unique population to determine how chemical and radiation effects might interact.

With the decrease in the numbers of the A-bomb survivors occurring, and the current lack of sensitive and fully validated techniques to measure mutational effects in both somatic and germ cells, emphasis has been and should continue to be placed on the long-term storage of biological material until appropriate techniques to measure important parameters can be developed. In addition, research should be directed towards the incorporation of new molecular biological approaches in the study of the F_1 generation and the incorporation of new concepts and techniques from molecular and cell biology to study the non-mutagenic mechanisms that may modify radiation effects, aspects that are not, at present, part of the Foundation's current research base.

The development of such new molecular biological techniques; of new conceptual understanding of chronic diseases, including cancer; of the deeper insights into the role of

oncogenes and tumor suppressor genes; and an understanding of chemicals which enhance or suppress tumor growth can be expected to stimulate new laboratory approaches and new epidemiological studies.

研究部門備品要求表 (1996年 ~ 2001年)
Equipment Requests by Research Departments

(単位：千円) (UNIT:¥1,000)

部・局	DEPARTMENT	FY1996	FY1997	FY1998	FY1999	FY2000	FY2001	合計
疫学部	EPIDEMIOLOGY	0	7,690	6,930	6,990	7,050	7,050	35,710
臨床研究部	CLINICAL STUDIES	0	8,372	4,485	16,210	712	11,565	41,344
遺伝学部	GENETICS	0	21,011	10,347	30,381	2,794	4,002	68,535
放生部	RADIOBIOLOGY	0	49,412	83,652	20,682	13,572	6,882	174,200
統計部	STATISTICS	0	5,075	5,275	5,410	5,590	5,675	27,025
広島合計	HIROSHIMA TOTAL	0	91,560	110,689	79,673	29,718	35,174	346,814
臨床研究部	CLINICAL STUDIES	0	20,117	1,052	2,252	3,452	852	27,725
疫学部	EPIDEMIOLOGY	0	6,198	3,344	3,544	844	5,944	19,874
長崎合計	NAGASAKI TOTAL	0	26,315	4,396	5,796	4,296	6,796	47,599
① 両市合計	BOTH TOTAL	0	117,875	115,085	85,469	34,014	41,970	394,413

サポート部門備品要求表 (1996年 ~ 2001年)
Equipment Requests by Supporting Departments

部・局	DEPARTMENT	FY1996	FY1997	FY1998	FY1999	FY2000	FY2001	合計
出版資料センター	PDC	0	8,860	3,640	4,960	2,540	3,200	23,200
研究情報センター	ITD	0	44,900	45,420	48,050	47,840	50,460	236,670
放射線同位 RI	RI FACILITIES	0	2,500	0	450	360	700	4,010
事務局	SECRETARIAT	1,770	6,240	8,320	4,690	2,950	1,420	25,390
広島合計	HIROSHIMA TOTAL	1,770	62,500	57,380	58,150	53,690	55,780	289,270
事務局	SECRETARIAT	2,720	2,620	440	2,220	1,040	0	9,040
長崎合計	NAGASAKI TOTAL	2,720	2,620	440	2,220	1,040	0	9,040
② 両市合計	BOTH TOTAL	4,490	65,120	57,820	60,370	54,730	55,780	298,310
①+② 合計		4,490	182,995	172,905	145,839	88,744	97,750	692,723

現金購入	PURCHASE COST	4,490	110,655	86,872	86,021	73,344	87,967	449,349
リース支払い	LEASE CHARGE	0	16,754	36,680	50,533	54,100	56,365	214,431
従来のリース支払	CURRENT LEASE CHARGE	17,095	5,082	5,082	5,082	4,598	2,177	39,116
合計	TOTAL	21,585	132,491	128,634	141,636	132,042	146,509	702,896

コンピューター関係分	For Computer	4,490	94,381	80,017	82,462	73,314	86,797	421,461

ANNEX A

THE PROJECTED SIZE OF THE LIFE SPAN STUDY COHORT, 1995-2020.

	Year					
	1995	2000	2005	2010	2015	2020
Age at exposure (y)						
0-9	16,450	15,990	15,290	14,280	12,710	10,390
10-19	14,500	13,540	12,040	9,800	6,780	3,620
≥ 20	12,800	8,910	5,430	2,710	970	100
Total	43,750	38,440	32,760	26,790	20,460	14,110
Average attained age (y)						
	64.7	67.9	71.3	74.7	78.0	81.3
Average age at time of bombing (y)						
	14.7	12.9	11.3	9.7	8.0	6.3

ANNEX B

WORKSHOPS SINCE 1988

• Radiation susceptibility workshop, 18-20 March 1988	RERF Hiroshima
• Immunology workshop, 28-29 November 1988	RERF Hiroshima
• Radiation carcinogenesis workshop, 16-18 March 1989	RERF Hiroshima
• Aging workshop, 29-31 March 1990	RERF Hiroshima
• Human germline mutagenesis workshop, 12-14 November 1991	RERF Hiroshima
• Health monitoring workshop, 25-27 January 1993	RERF Hiroshima
• US Department of Energy and RERF scientific research activity exchange workshop, 14-16 April 1993	Beckman Center, Irvine, California, USA

ANNEX C

SELECTED REFERENCES

Pierce, D. A., Shimizu, Y., Preston, D. L., Vaeth, M., and Mabuchi, K.: Studies of the Mortality of Atomic Bomb Survivors. Report 12, Part I. Cancer: 1950-1990. Radiat. Res. 146: 1-27, 1996.

Preston, D. L., Kusumi, S., Tomonaga, M., Izumi, S., Ron, E., Kuramoto, A., Kamada, N., Dohy, H., Matsuo, T., Nonaka, H., Thompson, D. E., Soda, M. and Mabuchi, K.: Cancer incidence in atomic bomb survivors. Part III. Leukemia, lymphoma and multiple myeloma, 1950-1987. Radiat. Res. 137: S68-S97, 1994.

Schull, W. J.: Effects of Atomic Radiation: A Half Century of Studies from Hiroshima and Nagasaki. New York: John Wiley and Sons, Inc., 1995.

Shigematsu, I., Ito, C., Kamada, N., Akiyama, M., and Sasaki, H. (Eds.): Effects of A-Bomb Radiation on the Human Body. Tokyo: Bunkodo Co., Ltd., 1995.

Thompson, D. E., Mabuchi, K., Ron, E., Soda, M., Tokunaga, M., Ochikubo, S., Sugimoto, S., Ikeda, T., Terasaki, M., Izumi, S. and Preston, D. L.: Cancer incidence in atomic bomb survivors. Part II. Solid tumors, 1958-1987. Radiat. Res. 1327: S17-S67, 1994.

ANNEX D

MASTER SAMPLE, PROPER AND RESERVE
BY EXPOSURE CATEGORY AND CITY

Exposure Group (M)	Proper Part	Reserve Part	Total
HIROSHIMA	90,697	30,403	121,100
0-1999	21,329	4,845	26,174
2000-2499	11,524	3,019	14,543
2500-9999*	36,023	8,455	44,478
10000 or NIC*	21,821	14,084	35,905
NAGASAKI	35,495	7,125	42,620
0-1999	6,801	858	7,659
2000-2499	5,144	805	5,949
2500-9999*	15,642	2,510	18,152
10000 or NIC*	7,908	2,952	10,860
TOTAL	126,192	37,528	163,720
0-1999	28,130	5,703	33,833
2000-2499	16,668	3,824	20,492
2500-9999*	51,665	10,965	62,630
10000 or NIC*	29,729	17,036	46,765

* Matched by sex and age to those exposed between 0 and 1999 meters

ANNEX E

LIFE SPAN STUDY SAMPLE, ORIGINAL AND EXTENDED

City	Original (LSS)	Extended (LSS-E85)
Hiroshima	74,356	82,220
Nagasaki	25,037	37,912
Total	99,393	120,132

ANNEX F

ADULT HEALTH STUDY SAMPLE BY CITY, SEX, AND EXPOSURE GROUP

City and sex	Exposure Group				Total
	With symptoms	Without symptoms	Distal	Not exposed	
HIROSHIMA	3,431	3,417	3,429	3,441	13,718
Male	1,315	1,307	1,309	1,319	5,250
Female	2,116	2,110	2,120	2,122	8,468
NAGASAKI	1,567	1,558	1,559	1,559	6,243
Male	682	676	673	675	2,706
Female	885	882	886	884	3,537
TOTAL	4,998	4,975	4,988	5,000	19,961
Male	1,997	1,983	1,982	1,994	7,956
Female	3,001	2,992	3,006	3,006	12,005

ANNEX G

IN UTERO SAMPLE BY CITY, IDENTIFICATION SOURCE, AND STUDY COHORT MEMBERSHIP

Cohort membership	Source	Hiroshima	Nagasaki	Total
In utero mortality	Birth records	1,104	247	1,351
(only)	ABCC records	183	34	217
	1960 Census	416	62	478
In utero clinical	Birth records	0	0	0
(only)	ABCC records	578	259	837
	1960 Census	0	0	0
In both cohorts	Birth records	515	83	598
	ABCC records	167	6	173
	1960 Census	0	0	0
Total	Birth records	1,619	330	1,949
	ABCC records	928	299	1,227
	1960 Census	416	62	478
Grand total	All sources	2,963	691	3,654

ANNEX H

F_1 MORTALITY SAMPLE, ORIGINAL AND EXTENDED

Sample	City		Total
	Hiroshima	Nagasaki	
Original	34,790	18,731	53,521
Extended	13,225	10,074	23,299
Total	48,015	28,805	76,820

ANNEX I

ACTIVE RESEARCH PROJECTS BY RERF PROGRAM

As of 31 August 1996

LIFE SPAN STUDY

RP	2-61	Study of mortality in children exposed in utero
	1-75	Research plan for RERF study of Life-Span of A-bomb survivors, Hiroshima and Nagasaki
	6-88	Comparative analysis of the LSS population and a cohort of 265,000 Japanese men and women
(Inactive)	4-91	Mail survey on epidemiologic factors in the Extended Life Span Study sample, 1991

ADULT HEALTH STUDY

	2-75	Research plan for RERF Adult Health Study, Hiroshima and Nagasaki

IMMUNOLOGY

	36-63	Blood groups in Adult Health Study and in utero ATB subjects Hiroshima and Nagasaki
(Inactive)	16-81	Establishment of specific reagents for detection of human cancers through in vitro immunologic and biochemical assays
	3-87	Cellular immune function and its relationship to in vitro T-lymphocyte radiosensitivity and MN blood group locus mutation frequency in A-bomb survivors: Precursor frequency analysis of mitogen- and antigen-responsive blood lymphocytes
	7-87	X-ray radiosensitivity of lymphocytes in vitro from A-bomb survivors. Part 3: Transformation of B-cells by Epstein-Barr virus and their cryopreservation (addendum to RP 3-86)
	7-88	Study of somatic mutations at the glycophorin A locus in erythrocytes of atomic bomb survivors
	7-89	Screening of stem cell mutation in lymphoid lineage among A-bomb survivors and its characterization
	9-89	Detecting erthrocyte mutations at the glycophorin A locus in Nagasaki A-

bomb survivors and in Hiroshima area poison gas workers (addendum to RP 7-88)

11-89 A pilot study for detection of somatic mutations at the HLA-A locus in lymphocytes

2-90 Cryopreservation of blood cells from Hiroshima and Nagasaki Adult Health Study participants

4-90 Establishment of a method for HLA-DQ and DP gene typing using the polymerase chain reaction (Inactive)

1-93 Study on T-cell antigen receptor repertoire and hematopoietic progenitor cell activity in peripheral blood of atomic bomb survivors (addendum to RPs 3-87, 4-87 and 7-89)

2-93 Development of assay for somatic mutation at the locus of the neutrophil Fcγ receptor III gene and preliminary study on atomic-bomb survivors

SPECIAL CLINICAL STUDIES

4-85 Incidence and risk factors of coronary heart disease (CHD) in Japanese men living in Japan and Hawaii, 1966-78 (addendum to Research Plan TR 12-71)

6-85 Study of M-proteinemia in the Adult Health Study sample (addendum to RP 9-79)

4-86 Evaluation of index of physiological measurements: A predictor of mortality or morbidity associated with aging

5-86 Dietary habit survey using a simple and computerized diet survey system (addendum to RP 8-83)

11-86 Prevalence of hyperparathyroidism in atomic bomb survivors during AHS cycle 15, Hiroshima and Nagasaki

5-87 Radiation-related damage to the developing human brain

(Inactive) 9-87 The effect of pulmonary function on the subsequent risk of coronary heart disease in Japanese men living in Hiroshima and Nagasaki, Japan and Hawaii, 1966-78 (addendum to RP 4-85)

1-89 Prevalence of radiation-related skin lesions in the Adult Health Study population, Hiroshima and Nagasaki

2-89 Hypercalcemia in A-bomb survivors, Hiroshima and Nagasaki

(addendum to RP 11-86)

3-89 Osteoporosis in Hiroshima atomic bomb survivors

(Inactive) 6-89 Incidence of radiation-related skin lesions in the Adult Health Study populations of Hiroshima and Nagasaki, 1958-89

3-90 The association of serum cholesterol with noncardiovascular mortality and morbidity in the Adult Health Study population

3-91 A comparative study of vertebral fracture prevalence among Japanese, Japanese-Americans in Hawaii, and Caucasians in Minnesota

5-92 Study on senile dementia among the Adult Health Study subjects in Hiroshima and Nagasaki

6-92 Establishment and operation of a system for collecting and storing leukemia cells

9-92 Study of liver diseases in the Adult Health Study sample. Relationship between radiation dose and infection by B and C hepatitis virus

5-93 A longitudinal study of hormone indicators of menopause in female A-bomb survivors of perimenopausal age

1-95 Effects of menopause on risk factors for ischemic heart disease - a longitudinal study of the Nagasaki Adult Health Study sample (addendum to RP 5-93)

2-95 Pilot study: characterization of monoclonal gammopathy by studying the role of BSAP gene in CD19 antigen expression

HISTO-PATHOLOGY

5-89 Pathology studies in Hiroshima and Nagasaki, revised research plan (Formerly RP 3-75)

8-89 Senile changes of the brain in Hiroshima and Nagasaki A-bomb survivors

CELL BIOLOGY

18-81 Pathophysiology and radiation response of human thyroid cells in culture and in grafts in athymic nu/nu mice

7-92 Molecular analysis of the p53 tumor-suppressor gene in breast cancers of

atomic bomb survivors (with addendum)

3-93 Molecular analysis of skin cancers in atomic bomb survivors

7-93 Molecular analysis of thyroid cancers among atomic bomb survivors

2-94 Molecular analysis of hepatocellular carcinoma among atomic-bomb survivors

BIOCHEMICAL GENETICS

5-85 Culture of permanent lymphocyte cell lines as sources of biological samples for investigation of genetic effects of radiation on children of atomic bomb survivors

7-85 Study to develop methods of DNA analysis for detection of mutations in children of atomic bomb survivors

CYTOGENETICS

8-93 Cytogenetic study in the Adult Health Study population by fluorescence in situ hybridization (FISH)

F1 STUDIES

4-75 Research plan for RERF studies of the potential genetic effects of atomic radiation; Hiroshima and Nagasaki. Part 1. Mortality study of children of atomic bomb survivors

SPECIAL CANCER STUDIES

29-60 Detection of leukemia and related disorders

7-76 The value of Adult Health Study family history records in the determination of genetic influences on the development of cancer and other disorders

14-79 Interaction between radiation dose and host factors. An epidemiological case-control study of female breast cancer in atomic bomb survivors

(Inactive) 15-81 Case-control study of lung cancer among atomic bomb survivors

8-85 Incidence study on malignant and benign genital tumors among females,

Hiroshima and Nagasaki, 1950-80

(Inactive) 11-85 Hormone status in relation to cancer: A prospective epidemiologic study using stored sera

2-86 Collection of surgically removed cancer tissues from A-bomb survivors: Special reference to thyroid and breast cancers

6-86 Ultrasonographic screening of Adult Health Study participants to detect cancer and other diseases

9-88 Guidelines for the conduct of site-specific cancer incidence studies among A-bomb survivors, Hiroshima and Nagasaki

5-90 Primary liver cancer incidence study among atomic bomb survivors, 1958-87

1-91 Studies of salivary gland tumors among the RERF Extended Life Span Study cohort, Hiroshima and Nagasaki, 1950-87

2-91 Studies of skin cancer incidence among the RERF Extended Life Span Study cohort, Hiroshima and Nagasaki, 1950-87

6-91 Studies on thyroid tumor incidence among the RERF Extended Life Span Study cohort, 1950-87

2-92 Studies on ovarian tumor incidence among the RERF Extended Life Span Study cohort, 1950-87

4-92 Incidence study of tumors of the central nervous system among atomic-bomb survivors

6-93 Breast cancer incidence study among atomic bomb survivors, 1950-90

1-94 Studies on lung cancer incidence among A-bomb survivors, 1950-90

3-94 Incidence of lymphoid malignancies among A-bomb survivors, 1950-90

A-BOMB DOSIMETRY STUDIES

18-59 Shielding survey and dosimetry study

10-86 Radiation dose estimates using tooth samples. Part 1. Collection of tooth samples from A-bomb exposed people in Hiroshima and Nagasaki

1-92 Radiation dose estimates using tooth samples. Part 2. Use of electron spin resonance on tooth enamel from Hiroshima atomic bomb survivors

MEDICAL DOSIMETRY STUDIES

(Inactive) 7-81 Radiation therapy among Life Span Study subjects

7-86 Doses to Adult Health Study participants from RERF radiological examinations, Hiroshima and Nagasaki

8-86 Ionizing radiation for medical reasons reported by Adult Health Study participants, Hiroshima and Nagasaki

8-87 Organ doses from medical x-ray exposures (addendum to RP 8-84)

5-91 Radiation-therapy-related cancer among Life Span Study subjects (addendum to RP 7-81)

TUMOR REGISTRY AND TISSUE REGISTRY

18-61 Tumor registry study in Hiroshima and Nagasaki [Editor's note: See ABCC Technical Report 2-61 for the full text.]

Following are tissue registry-related protocols that are also listed under the category Special Cancer Studies.

29-60 Detection of leukemia and related disorders

9-88 Guidelines for the conduct of site-specific cancer incidence studies among A-bomb survivors, Hiroshima and Nagasaki

5-90 Primary liver cancer incidence study among atomic bomb survivors, 1958–87

1-91 Studies of salivary gland tumors among the RERF Extended Life Span Study cohort, Hiroshima and Nagasaki, 1950–87

2-91 Studies on skin cancer incidence among the RERF Extended Life Span Study cohort, Hiroshima and Nagasaki, 1950–87

6-91 Studies on thyroid tumor incidence among the RERF Extended Life Span Study cohort, 1950–87

2-92 Studies on ovarian tumor incidence among the RERF Extended Life Span

Study cohort, 1950–87

4-92 Incidence study of tumors of the central nervous system among atomic-bomb survivors

6-93 Breast-cancer incidence among atomic-bomb survivors, 1950–90 (supersedes RP 1-90)

1-94 Studies on lung-cancer incidence among the atomic-bomb survivors, 1950–90

3-94 Incidence of lymphoid malignancies among the atomic-bomb survivors, 1950–90

ANNEX J

ITEMIZED EQUIPMENT LISTS

Department of Clinical Studies

Hiroshima

Fiscal year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
1997	R	Autoclave	1	3,360	3,360
	N	Laser printer	1	400	400
1998	R	Deep freezer	1	2,533	2,533
1999	R	High pressure sterilizer	1	3,358	3,358
	R	Dryer	1	770	770
	R	Ultrasonography	1	9,400	9,400
2001	R	Freeze dryer	1	4,750	4,750
	R	Deep freezer	1	2,533	2,533
			Total		27,104

1. Autoclave (for Departments of Clinical Studies):

   The autoclave currently in use was purchased in 1980 and being used beyond its expected life-span. The early replacement is requested.

2. Personal computer and laser printer (for Departments of Clinical Studies):

   At present, there is no IBM PCs available for research scientists in the department._@ Since there are many research projects to be studied, an early distribution of PCs to some of the key investigators is one of the items with higher priority in the department.

3. Deep freezers (for Departments of Clinical Studies):

   Two of the deep freezers currently in use for storage of biological materials, such as serum and plasma, were purchased in 1972 and 1973. These two freezers have been used beyond their life-span and it is expected to break down in the near future.

4. High pressure sterilizer (for Departments of Clinical Studies, Genetics and Radiobiology):

expected life-span. The early replacement is requested.

5. Dryer (for Departments of Clinical Studies, Genetics and Radiobiology):

   The dryer for glassware and other laboratory equipments currently in use was purchased in 1977 and being used beyond its life-span. The early replacement is requested.

6. Ultrasonography (for Departments of Clinical Studies):

   The ultrasonography currently in use was purchased in 1989. Since this is one of the equipments which have been providing direct benefits to the AHS participants, it is requested to replace before it breaks down.

6. Freeze dryer (for Departments of Clinical Studies):

   The freeze dryer of serum currently in use was purchased in 1988. Since storage of serum is one of the most important activities in the department, the replacement is requested.

Nagasaki

Fiscal year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
1997	R	Portable ECG	1	1,350	1,350
	R	Autoclave	1	650	650
	R	X-Ray Camera Ident.	1	302	302
	R	X-Ray Microreader	1	550	550
	R	Ultrasonography (Abdomen)	1	8,000	8,000
	R	Magazine for Imaging Camera	1	564	564
	R	Freezer (-40°C)	1	785	785
	R	Freezer (-80°C)	1	1,845	1,845
	R	Refrigerator	2	200	400
	R	Autodiluter	1	1,055	1,055
	R	Oven Drying	1	520	520
	R	Freeze Dryer	1	1,550	1,550
	R	Ampoule Seare	1	314	314
	R	Multi Tube, Ampoule	1	230	230
	R	Centrifuge Refrig	1	930	930
2000	R	ECG	1	3,000	3,000
			Total		22,045

Department of Genetics

Fiscal year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
1997	N	Software for 2-DE Analysis	1	10,000	10,000
	R	Pulsed Field Gel Electrophoresis Apparatus	1	3,000	3,000
	R	Refrigerated Centrifuge	1	1,270	1,270
	R	Refrigerator (with freezer)	1	94	94
	R	Centrifuge (for microtubes)	2	45	90
	R	Spectrophotometer	1	695	695
1998	R	Refrigerator (with freezer)	1	869	869
	R	Autoclave	2	580	1,160
	R	Water bath (with cooling system)	1	379	379
	R	Water bath (with cooling system)	1	447	447
	R	Power supply	4	150	600
	R	Centrifuge	1	240	240
	R	Photon camera	1	5,000	5,000
1999	N	Bio-Imaging Analyzer with Imaging Plates and Cassettes	1	22,880	22,880
	R	PCR equipment	1	4,000	4,000
	R	Water bath (with cooling system)	1	675	675
	R	Refrigerator (with freezer)	1	94	94
			Total		51,493

Department of Radiobiology

Fiscal year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
1997	R	Deep Freezer	1	2,200	2,200
	R	Thermal Cycler	2	850	1,700
	R	Clean Lack for Animal Facility	2	2,650	5,300

1998	R	Thermal Cycler	2	850	1,700
	R	Autoclave	1	700	700
	R	Laser for FACScan	1	1,300	1,300
	R	Laser for FACStar	1	3,500	3,500
	R	Cell Sorter (FACSvantage)(2)	1	75,000	75,000
1999	R	Deep Freezer	1	2,200	2,200
	R	Thermal Cycler	2	850	1,700
	R	Power Supply	2	550	1,100
	R	FACScan(2)	1	15,000	15,000
2000	R	Refrigerated Microcentrifuge	1	900	900
	R	Clean Bench	2	2,200	4,400
	N	Image Analyzer	1	8,000	8,000
2001	R	Fluorescence Microscope	1	2,500	2,500
	R	Thermal Cycler	2	850	1,700
			Total		164,600

Note: (1) The X-ray generator is for interdepartmental use. These items are not included in the total cost. (2) The FACSvantage and FACScan will be obtained on a lease-purchase basis to reduce annual equipment costs. The FACSvantage is basically a replacement for an earlier model flow cytometer that is now 13 years old.

A. Deep freezer (-80_‹)

Long term preservation of DNA, RNA and serum of the atomic-bomb survivors are necessary for the molecular epidemiology/oncology and immunology studies. The current equipment (15 years old) should be replaced before it breaks down to assure that the samples are safe.

B. Thermal cycler

Thermal cyclers (program cell cycler) are essential machines for molecular epidemiology/oncology and immunology in the department of radiobiology. These machines can amplify DNA and RNA from very small amounts of materials obtained from A-bomb survivors. Eight machines are currently working in the department of radiobiology. Four of the 8 have been used longer than 5 years. The life span of this machine is 5 years because the cyclic raising and lowering of the temperature causes metal exhaustion.

C. Clean rack for mouse cages

Since the present mouse racks are very old (15 years) and severely deteriorated, they should be

replaced to maintain clean conditions in the cages.

D. Autoclave

The autoclave currently used in the immunology laboratory is seriously deteriorated and should be replaced.

E. X-ray generator

The 250 KV X-ray generator is for interdepartmental use; the current machine is badly in need of repair and cannot be expected to last more than a few years in its present condition, but this model is no longer being manufactured and parts are unavailable to effect the needed repair.

F. Laser tube for the FACScan

A laser tube unit for one of two FACScan flow cytometer should be replaced in FY98, because its expected life will be up within two years.

G. Laser tube for FACStar cell sorter

The laser tube unit for the FACStar should be replaced in FY98, because its expected life will be up within two years. If we can purchase FACS vantage through a lease in FY98, this replacement laser will not be needed.

H. FACS Vantage (dual laser model) cell sorting system

The present cell sorter, FACStar installed in the Radiobiology Department was purchased more than 10 years ago. Because this apparatus often breaks down, it should be replaced as soon as possible. This cell sorter is essential for conducting immunology and molecular oncological studies of A-bomb survivors. Also, it can be used to analyze somatic mutations in exposed people for international collaboration.

I. Power supply

Electrophoresis for detection of point mutation and identification of HLA alleles requires a stable electric power supply. Because, currently, we are using outdated power supplies, some replacements may be needed in a few years.

J. FACScan

The FACScan machine currently used in the Radiobiology Department was installed 8 years ago. Since this apparatus is essential for conducting immunological analyses of lymphocytes from A-bomb survivors, it should be replaced.

K. Refrigerated Microcentrifuge

For studies of molecular oncology/epidemiology, extraction of DNA, RNA and proteins from micro-samples is necessary. Considering the frequency of use, it is expected at least one refrigerated microcentrifuge will break down within a few years, because two of five centrifuges currently used in the Department of Radiobiology is older than 10 years.

L. Clean bench

The clean bench in use in the Immunology Laboratory is used for multiple purposes such as separation, culture and manipulation of the biological materials of A-bomb survivors. This was purchased more than ten years ago and needs to be replaced to assure safety of the staff from biohazardous agents.

M. Image analyzer and video system for microscope

This system is required for precise analysis of cellular functions of lymphocytes and stem cells from the survivors blood. Also, this system is needed for quantitative immunohistochemical analysis of the expression of tumor associated genes in survivors' tumor specimens.

N. Fluorescence Microscope

The microscope in use for 14 years is deteriorated and should be replaced. The fluorescence microscope is essential for cytological and histological examination in the immunological laboratory.

O. Personal Computer

In the Department of Radiobiology, we are currently using 7 PCs in total. Since 6 of them were purchased prior to last year, they should be replaced by new models during the next 5 years. Furthermore, 4 new computers for data analysis, manuscript preparation, literature search and e-mail need to be installed in 4 offices used by research scientists.

Radioisotope Laboratory

Fiscal year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
1997	R	Automatic X-ray Film Processor	1	2,500	2,500
1999	R	GM-Survey Meter	1	450	450
2000	R	Survey Meter with Ionization Chamber	1	360	360
2001	R	Scintillation Survey Meter	1	700	700
			Total		4,010

Publications and Documentation Center

Fiscal Year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
1997	R	PC DX-33	1	500	500
	R	PC DX/66	3	500	1,500
	R	PC P5-90	2	500	1,000
	R	PC P5-166	1	570	570
	R	Printer NEC PR-3000ps/4	1	400	400
	R	Printer JBCC PW5036	1	400	400
		Printer Brother HL-8PSJ	1	400	400
	R	Scanner set	1	410	410
	R	Software	14	50	700
	R	Canon EZPS	1	2,980	2,980
1998	R	Color copier, A Color 635	1	1,500	1,500
	R	Software	7	20	140
	R	PC P5-90	4	500	2,000
1999	R	PC P5-90	2	500	1,000
	R	Printer QMS825PS	1	480	480
	R	Software	10	50	500
	R	Canon EZPS	1	2,980	2,980
2000	R	PC P5-90	3	500	1,500
	R	PC P5-100	1	500	500
	R	Printer Xerox 4150	1	400	400
	R	Software	7	20	140
2001	R	PC P5-133	2	500	1,000
	R	Printer Zerox 4150	1	400	400
	R	Printer Canon LBP-203PS	1	1,300	1,300
	R	Software	10	50	500
			Total		23,200

Secretariat, Hiroshima

Fiscal Year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
Director's Office					
1996	N	Printer	3	400	1,200
1997	N	PC	2	570	1,140
	R	Software	12	50	600
1998	R	PC	2	500	1,000
1999	R	PC	4	500	2,000
2000	R	Printer	2	400	800
	R	Software	14	50	700
2001	R	Printer	3	400	1,200
General Affairs Section					
1997	R	PC	2	500	1,000
	R	Software	8	50	400
1998	R	PC	2	500	1,000
	R	Printer	2	220	440
2000	R	Software	8	50	400
Personnel Section					
1996	N	PC	1	570	570
1997	N	PC	1	570	570
1998	R	PC	2	500	1,000
	R	Printer	2	220	440
2000	R	Printer	1	750	750
	R	Software	6	50	300
Accounting Section					
1997	R	Printer	1	220	220
	R	Software	7	50	350
1998	R	PC	4	500	2,000
	R	Printer	1	220	220
1999	R	PC	3	500	1,500
	R	Printer	1	220	220
	R	Software	7	50	350
2001	R	Printer	1	220	220
Supply & Property Section					
1997	N	PC	3	570	1,710
	R	Software	5	50	250
1998	R	PC	4	500	2,000
	R	Printer	1	220	220
1999	R	Printer	1	220	220
	R	Software	8	50	400
			Total		25,390

Secretariat, Nagasaki

Fiscal Year	New/ Repl	Item	Q'ty	Unit Cost (x¥1000)	Total (x¥1000)
General Affairs Section					
1996	N	PC	2	570	1,140
	N	Printer	1	220	220
1997	R	PC	2	500	1,000
	R	Printer	1	220	220
	R	Software	6	50	300
1998	R	Printer	2	220	440
1999	R	PC	4	500	2,000
2000	R	Printer	1	220	220
	R	Software	8	50	400
Accounting Section					
1996	N	PC	2	570	1,140
	N	Printer	1	220	220
1997	R	PC	2	500	1,000
	R	Software	2	50	100
1999	R	Printer	1	220	220
2000	R	Printer	1	220	220
	R	Software	4	50	200
			Total		9,040

Department of Clinical Studies (Hiroshima)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC DX2-66 (Replace)	3	500	-	1,500
	PC P5-166 (Add)	4	570	1,824	456
	Laser printer (Add)	1	400	320	80
	Basic Software version up	1	50	25	25
	Basic Software version up	5	50	-	250
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Corel Draw Soft. version up	2	40	80	-
	Total			**2,301**	**2,311**
1998	PC P5-90 (Replace)	3	500	-	1,500
	Laser printer (Replace)	1	400	-	400
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**52**	**1,900**
1999	PC P5-133 (Replace)	1	500	400	100
	PC P5-133 (Replace)	2	500	-	1,000
	Laser printer old Xerox	1	400	-	400
	Basic Software version up	5	50	125	125
	Basic Software version up	8	50	-	400
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Corel Draw Soft. version up	2	40	80	-
	Total			**657**	**2,025**
2000	Laser printer (Replace)	1	400	-	400
	Software version up (OS)	5	20	50	50
	Software version up (OS)	8	20	-	160
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**102**	**610**
2001	PC P5-166 (Replace)	4	500	1,600	400
	PC P5-166 (Replace)	3	500	-	1,500
	Basic Software version up	5	50	125	125
	Basic Software version up	8	50	-	400
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-

	Corel Draw Soft. version up	2	40	80	-
	Total			**1,857**	**2,425**
	Grand Total			**4,969**	**9,271**

Department of Clinical Studies (Nagasaki)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC DX-33 (Replace)	1	500	-	500
	Laser printer (Replace)	1	220	-	220
	Basic Software version up	3	50	75	75
	Basic Software version up	3	50	-	150
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**127**	**945**
1998	PC P5-90 (Replace)	1	500	400	100
	PC P5-90 (Replace)	1	500	-	500
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**452**	**600**
1999	PC P5-133 (Replace)	1	500	400	100
	PC P5-133 (Replace)	2	500	-	1,000
	Laser printer (Replace)	1	400	-	400
	Basic Software version up	3	50	75	75
	Basic Software version up	3	50	-	150
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**527**	**1,725**
2000	Laser printer (Replace)	1	400	-	400
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**52**	**400**
2001	PC P5-166 (Replace)	1	500	400	100
	Basic Software version up	3	50	75	75
	Basic Software version up	3	50	-	150
	Exceed Software version up	2	6	12	-
	Origin Software version up	2	20	40	-
	Total			**527**	**325**
	Grand Total			**1,685**	**3,995**

Department of Epidemiology (Hiroshima)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC replacement	8	500	2,800	1,200
	Printer replacement	1	500	400	100
	New Hardware	1	500	421	79
	Software upgrades	26	60	1,092	468
	New software	4	40	128	32
	Mocrotome (Path)	1	600	600	-
	Incubator (Path)	1	240	240	-
	Paraffin cleaner (Path)	1	130	130	-
	Total			**5,811**	**1,879**
1998	PC replacement	8	500	2,800	1,200
	Printer Replacement	1	500	350	150
	New Hardware	1	500	421	79
	Sofware upgrades	25	60	1,050	450
	New software	7	40	196	84
	Path equipment replacement	1	150	150	-
	Total			**4,967**	**1,963**
1999	PC replacement	8	525	2,940	1,260
	Printer Replacement	1	500	400	100
	New Hardware	1	520	440	80
	Sofware upgrades	25	60	1,050	450
	New software	3	40	96	24
	Path equipment replacement	1	150	150	-
	Total			**5,076**	**1,914**
2000	PC replacement	8	525	2,940	1,260
	Printer Replacement	1	500	350	150
	New Hardware	1	520	440	80
	Sofware upgrades	16	90	1,008	432
	New software	6	40	168	72
	Path equipment replacement	1	150	150	-
	Total			**5,056**	**1,994**
2001	PC replacement	8	525	2,940	1,260
	Printer Replacement	1	500	400	100
	New Hardware	1	520	416	104
	Sofware upgrades	16	90	1,008	432
	New software	6	40	192	48

	Exceed software version up	9	6	43	11
	Origin software version up	3	20	60	-
	Total			**2,791**	**753**
2000	Laser printer (4-year lease)	1	700	560	140
	Exceed software version up	3	6	18	-
	Exceed software version up	2	6	-	12
	Exceed software version up	9	6	43	11
	Origin software version up	3	20	60	-
	Total			**681**	**163**
2001	PC P5-166 (Replace)	6	500	2,400	600
	Laser printer (4-year lease)	1	700	560	140
	Laser printer (Replace)	3	400	960	240
	Basic software version up	3	50	150	-
	Basic software version up	2	50	-	100
	Basic software version up	13	50	520	130
	Exceed software version up	3	6	18	-
	Exceed software version up	2	6	-	12
	Exceed software version up	9	6	43	11
	Origin software version up	3	20	60	-
	Total			**4,711**	**1,233**
	Grand Total			**15,482**	**4,392**

Department of Genetics (Hiroshima)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC (Add)	4	500	1,600	400
	PC hontai (Replace)	4	300	960	240
	Workstation (Replace)	1	1,500	1,500	-
	Hard disk (New)	2	200	400	-
	Software version up	18	20	181	181
	Software (New)	4	100	200	200
	Total			**4,841**	**1,021**
1998	PC (Add)	1	500	400	100
	Hard disk (New)	2	200	400	-
	Software version up	19	34	326	326
	Software (New)	1	100	50	50
	Total			**1,176**	**476**
1999	PC (Add)	1	525	420	105
	PC hontai (Replace)	3	315	756	189
	Hard disk (New)	2	210	420	-

	Path equipment replacement	1	150	150	-
	Total			**5,106**	**1,944**
	Grand Total			**26,016**	**9,694**

Department of Epidemiology (Nagasaki)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC withfull set of standard software	1	570	456	114
	PC 486DX/66 (Replace)	2	500	800	200
	PC 486DX/33 (Replace)	2	500	800	200
	PC 386/33 (Replace with full set of	1	570	456	114
	Laser printer (Replace by 4-year lease)	1	700	560	140
	Laser printer (Replace)	3	400	960	240
	Exceed software (New)	1	40	40	-
	Origin software (New)	1	50	50	-
	Basic software version up	2	50	100	-
	Basic software version up	2	50	-	100
	Basic software version up	13	50	520	130
	Exceed software version up	2	6	12	-
	Exceed software version up	2	6	-	12
	Exceed software version up	9	6	43	11
	Origin software version up	2	20	40	-
	Chameleon software (New)	1	100	80	20
	Total			**4,917**	**1,281**
1998	PC P5-130 (Replace)	1	500	500	-
	PC P5-90 (Replace)	1	500	-	500
	PC P5-90 (Replace)	3	500	1,200	300
	Laser printer (4-year lease)	1	700	560	140
	Exceed software version up	3	6	18	-
	Exceed software version up	2	6	-	12
	Exceed software version up	9	6	43	11
	Origin software version up	3	20	60	-
	Total			**2,381**	**963**
1999	PC P5-130 (Replace)	2	500	800	200
	Laser printer (4-year lease)	1	700	560	140
	Laser printer (Replace)	2	400	640	160
	Basic software version up	3	50	150	-
	Basic software version up	2	50	-	100
	Basic software version up	13	50	520	130
	Exceed software version up	3	6	18	-
	Exceed software version up	2	6	-	12

	Software version up	20	37	371	371
	Software (New)	1	100	50	50
	Total			**2,017**	**715**
2000	PC (Add)	1	550	440	110
	Printer (Replace)	2	440	704	176
	Hard disk (New)	2	220	440	-
	Software version up	21	39	412	412
	Software (New)	1	100	50	50
	Total			**2,046**	**748**
2001	PC hontai (Replace)	2	330	528	132
	Workstation (Replace)	1	2,000	2,000	-
	Hard disk (New)	2	220	440	-
	Software version up	21	38	401	401
	Software (New)	1	100	50	50
	Total			**3,419**	**583**
	Grand Total			**13,499**	**3,543**

Department of Radiobiology (Hiroshima)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC DX-66 (Replace)	3	500	-	1,500
	PCP5-166(Add)	4	570	1,824	456
	Laserprinter(Replace)	1	400	-	400
	BasicSoftwareversionup	2	50	50	50
	BasicSoftwareversionup	2	50	-	100
	ExceedSoftwareversionup	2	6	12	-
	OriginSoftwareversionup	2	20	40	-
	CorelDrawSoft.versionup	2	40	80	-
	Total			**2,006**	**2,506**
1998	PCP5-90(Replace)	2	500	-	1,000
	Laserprinter(Replace)	1	400	-	400
	ExceedSoftwareversionup	2	6	12	-
	OriginSoftwareversionup	2	20	40	-
	Total			**52**	**1,400**
1999	BasicSoftwareversionup	6	50	150	150
	BasicSoftwareversionup	5	50	-	250
	ExceedSoftwareversionup	2	6	12	-

	OriginSoftwareversionup	2	20	40	-
	CorelDrawSoft.versionup	2	40	80	-
	Total			**282**	**400**
2000	Softwareversionup(OS)	6	20	60	60
	Softwareversionup(OS)	5	20	-	100
	ExceedSoftwareversionup	2	6	12	-
	OriginSoftwareversionup	2	20	40	-
	Total			**112**	**160**
2001	PCP5-90(Replace)	4	500	1,600	400
	BasicSoftwareversionup	6	50	150	150
	BasicSoftwareversionup	5	50	-	250
	ExceedSoftwareversionup	2	6	12	-
	OriginSoftwareversionup	2	20	40	-
	CorelDrawSoft.versionup	2	40	80	-
	Total			**1,882**	**800**
	GrandTotal			**4,334**	**5,266**

Department of Statistics (Hiroshima)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC replacement	6	500	2,000	1,000
	Network Disk Storage	1	300	300	-
	New Hardware	1	475	400	75
	Sofware upgrades	12	83	700	300
	New software	6	50	250	50
	Total			**3,650**	**1,425**
1998	PC replacement	6	500	2,000	1,000
	Printer Replacement	1	500	350	150
	New Hardware	1	475	400	75
	Sofware upgrades	12	83	700	300
	New software	6	50	250	50
	Total			**3,700**	**1,575**
1999	PC replacement	6	525	2,100	1,050
	Network Disk Storage	1	320	320	-
	New Hardware	1	520	440	80
	Sofware upgrades	12	89	750	315
	New software	6	59	280	75

	Total			**3,890**	**1,520**
2000	PC replacement	6	525	2,100	1,050
	Printer Replacement	1	500	370	130
	New Hardware	1	520	440	80
	Sofware upgrades	12	89	750	315
	New software	6	59	280	75
	Total			**3,940**	**1,650**
2001	PC replacement	6	550	2,200	1,100
	Network Disk Storage	1	330	330	-
	New Hardware	1	565	480	85
	Sofware upgrades	12	92	770	330
	New software	6	63	300	80
	Total			**4,080**	**1,595**
	Grand Total			**19,260**	**7,765**

Department of Information Technology (Hiroshima)
5-Year Computer Equipment Summary

Year	Item	Qty	Unit Cost	Research Use Total	Admin and Service Use Total
1997	PC (Add)	3	520	-	1,560
	PC(Replace)	7	520	-	3,640
	Network disk storage	1	200	-	200
	Printer (Replace)	1	500	-	500
	New hardware	1	500	-	500
	Software (New)	21	19	-	400
	Software version up	21	100	-	2,100
	ITD Staff Total			-	*8,900*
	RERF-wide services: computer and network hardware/software replacement	1	36,000	-	36,000
	Grand Total			-	**44,900**
1998	PC (Add)	2	520	-	1,040
	PC(Replace)	9	520	-	4,680
	Printer (Replace)	1	500	-	500
	New hardware	1	500	-	500
	Software (New)	23	17	-	400
	Software version up	23	100	-	2,300
	ITD Staff Total			-	*9,420*

	RERF-wide services: computer and network hardware/software replacement	1	36,000	-	36,000
	Grand Total			-	**45,420**
1999	PC (Add)	1	550	-	550
	PC(Replace)	10	550	-	5,500
	Network disk storage	1	210	-	210
	Printer (Replace)	1	525	-	525
	New hardware	1	525	-	525
	Software (New)	24	18	-	420
	Software version up	24	105	-	2,520
	ITD Staff Total			-	***10,250***
	RERF-wide services: computer and network hardware/software replacement	1	37,800	-	37,800
	Grand Total			-	**48,050**
2000	PC(Replace)	11	550	-	6,050
	Printer (Replace)	1	525	-	525
	New hardware	1	525	-	525
	Software (New)	24	18	-	420
	Software version up	24	105	-	2,520
	ITD Staff Total			-	***10,040***
	RERF-wide services: computer and network hardware/software replacement	1	37,800	-	37,800
	Grand Total			-	**47,840**
2001	PC(Replace)	11	577	-	6,350
	Network disk storage	1	220	-	220
	Printer (Replace)	1	550	-	550
	New hardware	1	550	-	550
	Software (New)	24	18	-	440
	Software version up	24	110	-	2,650
	ITD Staff Total			-	***10,760***
	RERF-wide services: computer and network hardware/software replacement	1	39,700	-	39,700
	Grand Total			-	**50,460**
	Five-Year Total			-	**236,670**

Actual Personnel Strength and Projected Changes

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Grand Total	427	433	437	435	412	373	335	331	323	318	315	312
Director & Other	6	6	5	6	6	5	5	5	5	5	5	5
Professional Staff	57	61	64	62	57	48	47	50	50	50	50	50
General Staff	364	366	368	367	349	320	283	276	268	263	260	257

Actual Personnel and Operating Costs and Budget Estimates (Unit:¥1,000)

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
onnel costs m. allowance)	3,227,676 (208,852)	3,304,603 (163,105)	3,742,938 (391,230)	3,635,153 (274,021)	3,559,650 (405,884)	3,881,353 (947,102)	2,781,100 (27,137)	3,692,476 (789,902)	3,296,604 (446,993)	3,170,297 (314,997)	3,301,463 (427,976)	3,252,828 (335,835)
rating costs	802,336	858,687	871,424	851,988	799,292	851,549	725,385	819,419	825,866	849,327	850,348	875,590
l	4,030,012	4,163,290	4,614,362	4,487,141	4,358,942	4,732,902	3,506,485	4,511,895	4,122,470	4,019,624	4,151,811	4,128,418

Actual Costs of Equipment and Supplies and Budget Estimates (Unit:¥1,000)

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
pment	98,262	110,204	81,072	96,180	125,014	95,965	51,808	132,491	128,634	141,636	132,042	146,509
lies(Reagent)	67,587	61,305	70,879	70,154	55,953	49,908	49,908	50,656	51,416	52,187	52,970	53,765
lies(Lab)	82,770	71,923	77,649	93,165	83,247	58,413	66,129	67,121	68,128	69,150	70,187	71,240

Personnel and operating costs are actual up to FY95, estimate from FY96 and after. For calculation of personnel costs, 1% base up is assumed for FY96, 2% for FY97 and after. Operating costs in FY96 were estimated to be ¥725,385,000 and a 1.5% yearly increase in FY97 and after. The number of employees as of 1 January 2002 is 310.

FY96 research activities report and audit report, etc.

CHIEF OF RESEARCH REPORT

Several changes have occurred in the Office of Chief of Research in the year since Dr. Abrahamson made the last report to you. After successfully marshalling the RERF through the Blue Ribbon Panel's Review, he returned to the University of Wisconsin. Dr. Schull then took over and was responsible for producing the 5-year plan recommended by the Blue Ribbon Panel, and also for framing the response to the recommendations made by the Science Council in November of 1996. In the middle of January 1997 I then succeeded him as Chief of Research and Vice-Chairman. Three people have thus held the office in the past year, and consequently, the perspective presented in this report comes from someone who had been in the job only three months as it was being written in April.

It is quite clear that the turmoil brought about by the budgetary uncertainties of 1995-1996 and the proposed changes in management on the American side has subsided. As a result the morale of the professional staff has improved markedly, and they are now able to rededicate their time to scientific pursuits, as opposed to being heavily involved in battles to save the Foundation and its relation with the National Academy of Sciences.

The uncertainties engendered by the problems of that era, however, have left scars that still disfigure and weaken the organization. For instance a large number of the American staff lost confidence in RERF's stability. This, directly or indirectly, led to the departure of one Department Chief and three other Americans, which, when coupled with the nominal reduction of American permanent directors to one, diminished the American presence here to only six people, a number inappropriately low for a binational organization. At the time of this Board meeting the number will have risen to 8 Americans with the appointment of a new editor and a new member of the statistics department. This number, however, is still too low for the optimal staffing of the research departments. In fact there is an urgent need to fill a large number of both Japanese and American vacancies at RERF.

Although the cohort of A-bomb survivors is diminishing as people have aged in the 52 years that have passed since the bombings, approximately 50% are still alive. As people in this group near the ends of their lives, more health effects, both spontaneous and radiation induced, are being found. This has increased the burdens on the Epidemiology and Statistics Departments, and also on the Information Technology Department that provides the informatics backdrop for them. The Epidemiology Departments at Hiroshima and Nagasaki have only a minimal number of professional epidemiologists. There is a need to recruit at least two more people. Our attitude is that we should recruit the best possible people irrespective of their country of origin. It is apparent, however, that as strong as Japanese universities are in most of the research areas represented at RERF, as yet they do not universally have strength in epidemiology. This means that recruitment in this area will still most likely come from the US. Within the Department of Statistics, there is a need to recruit statisticians knowledgeable about genetic and analysis of longitudinal clinical data. These people logically could come from either Japan or the U.S. In addition, in line with the Blue Ribbon Panel's recommendation that we strengthen ties with universities, we would like to institute a postdoctoral program in statistics.

Of particular concern is the attrition that has occurred in the Information Technology Department (ITD). As the work of the research departments have become more data intensive there has become an increased need for, and reliance on, computerization. The ITD has lost

6 people in the last 2-1/2 years. Furthermore, two retirements are scheduled for this year. This decrease in 8 people at a time when not only the research departments but also the financial, personnel, and support services are evermore dependent upon computing could lead to a potentially disastrous situation. There is a need for knowledgeable people in both primary and backup positions. For instance RERF has gone to a very efficient distributed computing environment centered on UNIX workstation servers. There is only one person who handles the UNIX side, which is central to all the computing being carried out. Recruitment of a backup person is crucial to forestall a calamity. There is also a pressing need to strengthen the database design and management groups. A committee composed mainly of department chiefs plus members from other areas dependent upon computing, such as the Secretariat, has been constituted. The charge to the committee is first to determine the RERF-wide ITD needs, and second, after making this determination to the search for an appropriate new department chief as well as for those people necessary to fill other positions. It is anticipated that the wide representation on this committee will allow it to reach a consensus regarding the selection of an appropriate chief.

To prepare this research activities report I noted that you have already been given descriptions of the research program in the 5-year plan. I, therefore, have taken the statements of purpose, which you have already seen, and asked the department chiefs to enhance them by updating the progress on each research protocol (RP), and to list the papers published in 1996.

Sheldon Wolff
Vice Chairman and Chief of Research

RESEARCH PLANS BY DEPARTMENT

Research at the Foundation centers on two broad fronts, namely, those programs that will presumably continue well into the future, such as the periodic reports on mortality and cancer incidence in the LSS sample, and are commonly designated as the "core activities," and those programs, the "specific research activities," that are initiated within a single department and are generally time-limited. As previously noted, the core activities are set forth in the so-called "platform protocols" whereas the specific research activities are described in individual research protocols. Largely for convenience, we describe departmental research activities on an individual departmental basis.

Department of Clinical Studies, Hiroshima

The AHS biennial examinations initiated in 1958 continue. The primary purposes of these examinations have been to determine the types of diseases and abnormalities in physiologically or biochemically determined values that may have occurred as a consequence of previous exposure to ionizing radiation and to collate this information with other life experiences and death. The AHS clinical examination is the only point of direct contact with the survivors and functions as a source of biological materials for various special studies.

The AHS has greatly increased in importance in recent years as a result of the accumulation of an enormous body of data on serial medical examinations, with and without the superimposed radiation aspects. Particularly noteworthy is the accumulating evidence that cardiovascular mortality may have a positive radiation-dose response. This potentially important and largely unexpected relationship could never be properly studied using death certificate data alone. Similarly intriguing and potentially important relationships arise from the clinical studies on hyperparathyroidism and serum levels of parahormone, calcium, and alkaline phosphatase. These results suggest that significant deviation in calcium metabolism may be a direct radiation effect and raise further questions about bone density and osteoporosis among the survivors. Still another unexpected finding is the retrospective evidence that radiation is associated with premature menopause and this, in turn, may result in earlier onset of other physiologic conditions such as an increase in cholesterol levels and cardiovascular disease. However, given the age of the survivors, the window of time for such studies is growing shorter, and it is imperative that these opportunities be exploited soon.

AHS Platform Protocol

RP 2-75 Research plan for the RERF Adult Health Study, Hiroshima and Nagasaki.
Kodama K, Fujiwara S, Neriishi K, Yamada M. Nobuyoshi M, Shimizu M (Hiroshima), Akahoshi M, Soda M, Tominaga T, (Nagasaki):

The primary purpose of this study has been to determine the types of diseases and abnormalities in physiologically or biochemically determined values occurring as a consequence of A-bomb exposure, and to correlate this information with other life experiences and death. Providing information on non-fatal events as well as fatal ones has long been one of the purposes of the Adult Health Study. The major research elements of the Adult Health Study can be categorized as follows: (1) characterization of cancer types in relation

to various confounders of radiation effects, (2) radiation related non-cancer diseases (thyroid disease, cataract, etc.), (3) benign tumors, (4) cardiovascular disease, (5) aging, (6) medical dosimetry, (7) psychosocial changes associated with exposure, and (8) radiation or age related changes in other physiological endpoints.

Since the information on disease morbidity has been mainly dependent on the findings obtained at the time of examination, the maintenance of the participation rate has been an essential factor in the quality control of the AHS program. However, because of natural aging processes, it is anticipated that the participation rate will fall significantly in the near future, resulting in less complete data collection on morbidity. To improve health information retrieval a mail survey followed by telephone contact of non-responders was introduced in August, 1995 in Hiroshima, and in March, 1996 in Nagasaki. In both cities, the response rate to the new surveillance system over the past three surveys was around 85%, which is extremely good. The response rates were 70% and 80% for those AHS members who refused to participate in the biennial medical examination and those who migrated out of the contact area, respectively. (Table 1 and 2) Moreover, the response rate of those who were above 70 years old, in which age group the participation rate in medical examinations has been poor, was 86.8%. (Table 2) In addition, a substantial amount of information on newly developed diseases was obtained from this surveillance program. (Table 3) The above results indicate that the data collection on morbidity has become more complete upon the introduction of the new system, and future analysis of data on morbidity of various diseases may give answers regarding the association between morbidity and previous exposure to ionizing radiation.

Table 1. **Number of Replies and Response Rate**
(August 1995 - January 1996, Hiroshima)

		No. of Replies		
No. of Mail Surveys		Mail	Phone	Total
Examined	2,995	2,304 (76.9)	546 (18.2)	2,850 (95.1)
Refusal	1,409	498 (35.3)	490 (34.8)	988 (70.1)
Migrants	741	484 (65.3)	119 (16.1)	603 (81.4)
Total	5,145	3,286 (63.9)	1,155 (22.4)	4,441 (86.3)

(): Response Rate (%)

Table 2. **Response Rate**
(August 1995 - January 1997, Hiroshima)

1st Survey (1995.8 - 96.1)	
Total	**86.3%**
Examined	95.1%
Refusal	70.1%
Migrants	81.4%
Age 70+	86.8%
Examined	94.3%
Refusal	70.1%
Migrants	81.3%
2nd Survey (1996.2 - 96.7)	
Total	**83.0%**
3rd Survey (1996.8 - 97.1)	
Total	**84.2%**

Table 3. **Number of Newly Identified Cases**
(August 1995 - January 1996, Hiroshima)

Respondents	No. of Mailings	No. of Replies	Cancer	Myocardial Infarction	Cerebral Infarction	Liver Cirrhosis
Participants	2,995	2,850	35	4	15	1
Nonparticipants (Refusal & Migrants)	2,150	1,591	17	9	10	2
Total	5,145	4,441	52	13	25	3

Special emphasis has been placed on screening for skin, breast, and thyroid cancers, which are often not fatal. Although the Adult Health Study sample is limited, exposures to other carcinogens through personal interviews and through measurements using serum can be obtained. A case-control study will be conducted on various cancers related to nutrients and potential carcinogen and/or promoter substances using serum that had been stored for future analysis.

Detection of various benign tumors such as uterine myoma, ovarian tumor, prostatic tumor and liver hemangioma are being undertaken in Hiroshima with abdominal ultrasonographic techniques.

The storage of serum and other biological materials has been a high priority of the AHS. Routine collection and storage of lymphocytes from AHS participants was initiated in June 1990 in collaboration with the Department of Radiation Biology.

A study of accumulated data to assess the frequency and nature of the social and psychological problems experienced by the survivors has been in progress. It is not known whether psychological problems themselves ultimately influence the magnitude of the risk through the adoption of life style changes.

In order to elucidate pathogenic mechanisms of radiation induced diseases, molecular epidemiological studies on the AHS population will be initiated with interdepartmental collaboration. For this study, in addition to the preservation of lymphocytes of the AHS subjects, which is being conducted, the collection of fresh biological materials from surgery, such as tissues of cancers, benign tumors, blood vessels and skin, is desirable through a more intensive morbidity surveillance.

There have been many special clinical studies conducted in the Adult Health Study population. The summary of the ongoing studies will follow.

1) RP 2-95 Pilot Study: Characterization of monoclonal gammopathy by studying the role of the BSAP gene in CD 19 antigen expression.
Nobuyoshi M, Neriishi K, Kusumi S, Seyama T, Kawano M, Nakashima E, Kodama K, Akiyama M, Kuramoto A:

The objective of this pilot study is to develop sensitive cellular and molecular methods for the characterization of benign monoclonal gammopathy (BMG) by studying the role of B-cell lineage-specific activator protein (BSAP) for CD19 antigen expression. This is being done to enable the identification in the near future of those A-bomb survivors who are most probably in transition to multiple myeloma.

2) RP 9-92 Study of liver diseases in the Adult Health Study sample -Relationship between radiation dose and infection by B and C hepatitis virus-.
Fujiwara S, Kusumi S, Kodama K, Neriishi K, Nonaka H, Akahoshi M, Akiyama M, Akiba S, Mabuchi K, Cologne JB, Hasegawa Y:

The most recent incidence study of non-cancer diseases in the AHS has demonstrated a significant dose response in the incidence of chronic hepatitis and cirrhosis. To elucidate whether infection of hepatitis C virus (HCV) or hepatitis B virus (HBV) contribute to an increased incidence of chronic liver diseases with radiation dose, HCV, HBs antigen and antibody, and HBe antigen were measured among all AHS participants in Hiroshima and Nagasaki. The statistical analysis is currently under way.

3) RP 6-92 Establishment and operation of a system for collecting and storing leukemia cells.
Nobuyoshi M, Kusumi S, Kodama K, Mabuchi K, Akiyama M, Dohi H, Kamada N, Kuramoto A:

Through this system, leukemia cells derived from bone marrow and peripheral blood from leukemia cases occurring among Life Span Study participants are being collected and stored to perform molecular biological studies of the developmental mechanism of leukemia due to Atomic bomb radiation.

4) RP 5-92 Study on senile dementia among the Adult Health Study subjects in Hiroshima and Nagasaki.
Kodama K, Yamada M, Akahoshi M, Nakamura S, Nagataki S, Kasagi F, Shibata Y, White LR, Oishi K, Sasaki H, Tsujihata M, Seto M, Shimizu Y, Ohara JL, Schull WJ:

The objective of the senile dementia study is to determine if there is an association between exposure to ionizing radiation and subsequent impairment of cognitive function and the occurrence of senile dementia. This study will also provide cross-cultural comparisons of the prevalence of senile dementia, since the same neuropsychological test batteries and the same criteria for diagnosis are used in ongoing cohort studies in Honolulu and Seattle.

5) RP 5-91 Radiation therapy among Life Span Study subjects; Addendum to RP 7-81.
Kato K, Antoku S, Sawada S, Kodama K, Kawamura S, Mabuchi K:

RP 7-86 Doses to Adult Health Study participants from RERF radiological examinations, Hiroshima and Nagasaki.
Yamada M, Fujita S, Kato K, Kodama K:

RP 8-86 Ionizing radiation exposure for medical reasons reported by Adult Health Study participants, Hiroshima and Nagasaki.
Yamada M, Sawada S, Fujita S, Kodama K:

RP 8-87 Organ doses from medical X-ray exposures; Addendum to RP 8-84.
Kato K, Sawada S, Antoku S, Russell WJ, Fujita S, Kodama K, Yamada M:

In any assessment of A-bomb radiation effects, the contribution of medical radiation exposures must be considered. Information concerning therapeutic and diagnostic radiation exposures has been obtained by interviewing the AHS participants. To determine the organ doses, some of the medical radiation exposures have been experimentally reproduced using technical exposure factors obtained from hospital and clinic surveys. Information on medical radiation exposure is useful for determining the relative amounts of medical and A-bomb radiation doses to the A-bomb survivors.
(RP 5-91, 7-86, 8-86, and 8-87)

6) RP 3-91 A comparative study of vertebral fracture prevalence in Japan, Hawaii, and the U.S. mainland.
Fujiwara S, Ross PD, Melton III LJ, Huang C, Davis JW, Epstein RS, Wasnich RD, Kodama K:

RP 3-89 Osteoporosis in Hiroshima atomic bomb survivors.
Fujiwara S, Pawel D, Kodama K, Fukunaga M, Orimo H:

The objective of the osteoporosis study is to determine if previous exposure to radiation influences the occurrence of aging-related disorders. Osteoporosis is a common consequence of aging, and bone loss is influenced by menopause and parathyroid hormone levels, which are radiation-related. Bone mineral density is being measured with dual X-ray absorptiometry among the AHS participants. Measurements of an individuals bone mass and its temporal changes provide the relation between radiation and aging. (RP 3-91 and 3-89)

7) RP 3-90 Study on the association of serum cholesterol with non-cardiovascular mortality and morbidity in the Adult Health Study population.
Yamada M, Kasagi F, Kodama K, Fujiwara S, Soda M, Sasaki H:

The previous analysis showed that the serum cholesterol level in exposed people was significantly elevated compared to that in nonexposed people. Since January 1997, the analyses for estimating the total cholesterol growth models to determine whether radiation effects exist on the levels of total cholesterol have been conducted by Dr. Wong et al. The major objectives of this study are to assess the association of serum cholesterol with subsequent mortality and morbidity and to evaluate the effects of ionizing radiation on such an association.

8) RP 2-89 Hypercalcemia in A-bomb survivors, Hiroshima and Nagasaki.
Fujiwara S, Nakashima E, Delongchamp RR, Ezaki H, Kodama K, Tsuruta M, Shiraki M:

RP 11-86 A Study of hyperparathyroidism (HPT) in atomic bomb survivors in Hiroshima and Nagasaki.
Fujiwara S, Nakashima E, Delongchamp RR, Ezaki H, Kodama K, Tsuruta M:

A radiation-related increase in occurrence of hyperparathyroidism is one of the most recent findings found in a prevalence study. Continuation of this study should provide not only incidence data of hyperparathyroidism but also a clue to the cause of slight elevated levels of serum calcium, parathyroid hormone, and calcitonin among those exposed to higher doses. In addition, a molecular biological study of parathyroid adenoma to elucidate its pathogenic mechanism has been initiated with cooperation of the Department of Radiobiology. (RP 2-89 and 11-86)

9) RP 1-89 The prevalence of radiation-related skin lesions in the Adult Health Study population, Hiroshima-Nagasaki.
Yamada M, Yamamoto S, Yoshida H, Kodama K:

Studies of skin cancer induced among persons exposed to radiation due to occupational or medical therapeutic exposures showed that skin was vulnerable to radiation carcinogenesis. In this study, dermatological examinations are carried out during the biennial AHS health examinations to detect not only skin cancer but also precancerous lesions such as senile keratosis. Information concerning UV radiation and burn and trauma scars will be taken into consideration in the analysis.

10) RP 6-86 Ultrasonographic screening of Adult Health Study participants to detect cancer and other diseases.
Kodama K, Kawamura S, Fujiwara S, Akahoshi M:

The increased incidence of uterine myoma among heavily exposed subjects was reported in AHS report 7. To avoid any potential bias in diagnosis, abdominal ultrasonographic examinations were conducted in Hiroshima between 1992 and 1993. The prevalence of uterine nodules increased

significantly with radiation dose, with an odds ratio of 1.6 for those exposed to 1 Gy. This result suggested that benign tumors such as uterine myomas may be induced by exposure to radiation, although the pathogenesis remains unclear. Further studies are needed to clarify whether the association is the result of radiation or not.

11) RP 5-86 Dietary habit survey using a simple and computerized diet survey system.
Yamada M, Hayabuchi H, Kodama K, Sasaki H, Fujita Y:

Dietary factors are considered to be one of the confounding factors of radiation effects in the A-bomb survivors. However, in the past, only old fashioned dietary habit surveys including a 24-hour recall survey have been conducted. Recently, simple and accurate methods comprised of a computerized diet survey system have become available and the nutritional factors obtained by this system will be used for the analysis of risk factors on the prevalence or incidence of certain diseases in the A-bomb survivors.

12) RP 6-85 Follow up study of M-proteinemia in the Adult Health Study sample (Addendum to RP 9-79).
Neriishi K, Yoshimoto Y, Carter R, Kawamura S, Iwato K, Kawano M, Fujimura K, Kuramoto A:

Uncertainties exist regarding the apparent dose-related increase of multiple myeloma. Clinical studies to detect a precursor state of multiple myeloma by protein electrophoresis have been employed in the AHS biennial examinations since 1985. A previous study suggested a marginal increase in the prevalence of benign monoclonal gammmopathy in the exposed. A longitudinal study during 1985-1995 revealed an increased incidence in exposed persons, but only among those who were less than 80 years old at the time of examination. The incidence study is continuing for aging subjects who are at high risk of monoclonal gammopathy.

13) RP 4-85 Incidence and risk factors of coronary heart disease (CHD) in Japanese men living in Japan and Hawaii.
Kodama K, Shimizu Y, Kasagi F, Ueda H, Yamada M, Sasaki H (RERF), Curb D, Rodoriguez B, Yano K (Honolulu Heart Program):

There are two major objectives in this research protocol. The first objective is to study the morbidity, mortality and the risk factors of cardiovascular diseases (CVD) in the NI-HON-SAN (Nihon-Honolulu-San Francisco) cohort of the AHS and compare the findings with those in the cohort of the Honolulu Heart Program in Hawaii.

The second objective, which is more important for RERF, is to study the association between radiation exposure and CVD in the entire AHS cohort. The epidemiological methodology developed by this project has been effectively utilized to elucidate radiation effects on CVD in the A-bomb survivors.

The most recent findings on radiation and CVD is that weak, but very consistent, association between radiation dose and various endpoints of atherosclerosis have been observed. These endpoints include myocardial infarction, thromboembolic stroke, calcification of the aortic arch, retinal arteriosclerosis, isolated systolic hypertension, and abnormality of pulse wave velocity.

A study on the ankle-arm blood pressure ratio is currently underway in Hiroshima. A new study on titers of Chlamydia pneumoniae and serum levels of homocysteine as a confounder of radiation effects on CVD will be initiated in the near future.

Publications (1996-1997)

RP 2-75 KODAMA K, MABUCHI K, SHIGEMATSU I: A long-term cohort study of the atomic-bomb survivors. J Epidemiol, 6 (supple): 95-105, 1996.

YAMADA M: Psychical and Psychological effects of A-bomb radiation. (in Japanese) Hiroshima Med J, 49(3): 294-6, 1996.

KODAMA K, FUJIWARA S, YAMADA M, KASAGI F, SHIMIZU Y, SHIGEMATSU I: Profiles of non-cancer diseases in the atomic bomb survivors. Wld Hlth Statist Quart, 49: 7-16, 1996.

YAMADA M, WONG LF, KODAMA K, SASAKI H, SHIMAOKA K: Longitudinal trends in total cholesterol levels in a Japanese cohort, 1958-1986. J Clin Epidemiol, 1997. (in press)

RP 3-91
RP 3-89 FUJIWARA S, HUANG C, ROSS PD, YAMADA M, KODAMA K, DAVIS JW, WASNICH RD: Differences in health characteristics between Japanese and Japanese-Americans. J Cross-Cultural Gerontology, 1997. (in press)

FUJIWARA S: Quality of life: Risk factors of Osteoporosis. Metabolic Bone Disease. (in Japanese) ed by FUJITA T, Iyaku Journal Co, Tokyo, p112-21, 1996.

HUANG C, ROSS PD, FUJIWARA S, DAVIS JW, EPSTEIN RS, KODAMA K, WASNICH RD: Determinants of vertebral fracture prevalence among native Japanese women and women of Japanese descent living in Hawaii. Bone, 18: 437-42, 1996.

FUJIWARA S: Epidemiological study of osteoporosis. (in Japanese) Obstetrical and Gynecological Therapy, 72: 279-283,1996.

FUJIWARA S: Frequency and distribution of vertebral fracture. (in Japanese) Clinical Calcium, 6: 19-22, 1996.

FUJIWARA S: Epidemiology of osteoporosis-associated fracture.(in Japanese) Laboratory Animal Technology and Science, 8: 295-9, 1996.

FUJIWARA S: Epidemiological study of osteoporosis in a Japanese polulations. Hong Kong J Gerontoloty, 10: 300-2, 1996.

FUJIWARA S, ROSS PD: Epidemiological study of osteoporosis in Japan. Osteoporosis in Asia. ed by LAU EMC, World Scientific Publishing Co, 1997. (in press)

FUJIWARA S, KODAMA K, ROSS PD: Osteoporosis in a Japanese population. J Epidemiol, 6(supple), 1997. (in press)

FUJIWARA S, KASAGI F, YAMADA M, KODAMA K: Risk factors for hip fracture in a Japanese cohort. J Bone Mineral Res, 1997. (in press)

RP 1-89 YAMADA M, KODAMA K, FUJITA S, AKAHOSHI M: Prevalence of skin neoplasm in the atomic bomb survivors. Radiat Res, 146:223-6, 1996.

RP 4-85 KODAMA K, KASAGI F, FUJITA S, FUJITA Y: Epidemiological study on physical activity and index of aging. (in Japanese) Saishin Igaku 51(3):78-86, 1996.

CURB JD, KODAMA K: The NI-HON-SAN Study. J Epidemiol, 6(supple), 1997. (in press)

Department of Clinical Studies, Nagasaki

RP 5-92 Study of senile dementia among the Adult Health Study subjects
Kodama K, Oishi K, Yamada M, Sasaki H, Akahoshi M, Shimaoka K, Kasagi F, Shimizu Y, Shibata Y, Ohara J, Nakamura S, Tsujihata M, Nagataki S, Seto M, White LR, Schull WJ.

This study is being conducted for four years from 1 December 1993 to 30 November 1997. A total of 1155 cases have been examined to date, leaving approximately 200 cases to be investigated.

RP 1-95 Effects of menopause on risk factors for ischemic heart disease - a longitudinal study of the Nagasaki Adult Health Study sample
Akahoshi M, Soda M, Tsuruta M, Rose TP, Nakashima E, Saimei M, Seto S, Yano K.

This study was initiated in January 1995 on 79 subjects. At present the sixth and seventh collection of blood samples is underway. The study will be continued until one year after all subjects experience menopause. Menopause has not been confirmed in approximately 60 subjects.

Publication (1996)

RP 4-93 OISHI K, SHIBATA Y, NAKAMURA T, TSUJIHATA M, AKAHOSHI M, MATSUO T, TOMONAGA M, NAGATAKI S, SHIMAOKA K:

Autoantibodies and immunoglobulins in atomic bomb survivors with human T-lymphocyte virus Type I. Internal Medicine 35:624-628, 1996

Departments of Epidemiology

Until the mid-1980s, epidemiology, statistics, and computing were combined in a single Department of Epidemiology and Statistics at the Foundation. It became clear, however, that this was neither an efficient nor cost-effective organization of resources and skills. During 1984-85, these disciplines were established as independent research or support departments. In 1994, the Departments of Epidemiologic Pathology, responsible for the conduct of pathology studies and the tumor and tissue registries, were merged with the Departments of Epidemiology.

Program objectives

The Departments of Epidemiology play a central role in the conduct of the long-term follow-up of the three cohorts, LSS, in-utero, and F_1. The follow-up of these cohorts has long relied on mortality surveillance through the use of the nationwide family registration system, the *koseki*. Recently, cancer incidence data from improved tumor registries in Hiroshima and Nagasaki have become available on these cohorts, adding new dimensions to our studies of radiation cancer risks. Continued follow-up of these cohorts is essential in clarifying the temporal patterns of cancer risk as young subjects reach ages when background cancer risk is increased. In addition, the emerging excess noncancer mortality risk is of particular concern as the nature of the risk is still unclear. Although the numerous mail surveys conducted in the LSS provide potentially valuable data on the role of nonradiation risk factors, little effort has been made to incorporate these data into RERF analyses. We must place increased emphasis on the studies of nonradiation risk factors in relation to cancer and noncancer disease risks.

Because of the nature of the RERF research, the Departments of Epidemiology should and will play a key role in the design and conduct of various interdepartmental research activities. As indicated in the Blue Ribbon Panel report, one of the most important multidisciplinary programs at the present time is the molecular epidemiology of cancer, which will require close interdepartmental and interdisciplinary communication. In addition, the Departments of Epidemiology must also play a more active role in generating new ideas for studies to answer questions arising from the ongoing epidemiological studies, which are being conducted in collaboration with other RERF departments or outside research groups.

The epidemiological research activities in Hiroshima and Nagasaki are carried out following common research protocols and procedures. The professional staff in the Department of Epidemiology in Hiroshima currently consists of three epidemiologists supplemented by one pathology consultant and one visiting pathology investigator. The professional staff in the Nagasaki Department of Epidemiology consists of one epidemiologist and one physician. The epidemiology staff work closely with the staff in the Department of Statistics in study design, data analysis, and preparation of major reports; they also work with the Departments of Statistics and Information Technology in database design and development.

RP 3-94 Incidence of lymphoid malignancies among the atomic bomb survivors, 1950-90

Nanba K, Matsuo T, Tokunaga M, Jubashi T, Fujita Y, Soda M, Dohy H, Kamada N, Tomonaga M, Travis LB, Preston DL, Mabuchi K, Land CE, Tokuoka S

The relationship between lymphopoietic malignancies and radiation exposure is complicated because of variability of diagnostic categories and uncertainty about the potential for radiation carcinogenesis for certain important categories. For instance, the risk for acute lymphocytic leukemia was markedly elevated among the atomic bomb survivors, particularly children during the early years, while there is no convincing evidence of a radiation-induced excess of chronic lymphocytic leukemia. Multiple myeloma, derived from terminally differentiated B-cells, has been identified as a radiation-induced cancer in the analysis of the LSS mortality data, but recently published incidence data demonstrated only a weak association with radiation exposure. Studies of non-Hodgkin's lymphoma in the LSS have also demonstrated variable and inconsistent results, at least in part because of different sources of diagnostic data and diagnostic variability. On the other hand, recent advances in immunological studies of malignant lymphoma are remarkable. Surface markers to tumor cells can be used to distinguish B and T-cells involved in malignant lymphomas, and a new classification has replaced the conventional classification of lymphomas. The objective of the present study is to investigate all lymphopoietic tumors (lymphomas, multiple myeloma, lympocytic leukemias) that occurred between 1950 and 1990 in the LSS. Emphasis is on confirmation and classification of cases with modern techniques, and classification applied to cases ascertained from all sources. The study will involve both hematologists and pathologists engaged in lymphoid tumor research. Non-Hodgkin's lymphomas will be classified by immunohistochemical studies into T- or B-cell lymphomas, and diagnosis of adult T-cell leukemia will be based on detection of proviral DNA of HTLV-I in archived tissues. This study is in the first phase of investigation, i.e., screening of several thousands of potential cases with a wide range of diagnoses to which lymphoid tumors may be misclassified. It is expected to take at least another year to complete the first phase and a pathology review. Data analyses will begin in 2 or 3 years.

RP 1-94 Studies of lung cancer incidence among the atomic bomb survivors, 1950-90

Egawa H, Matsuo T, Yenehara S, Fujita Y, Nakashima E, Soda M, Tokunaga M, Tokuoka S, Akiba S, Mabuchi K, Preston DL, Land CE

Lung cancer is a well established late effect of radiation exposure in various irradiated populations including the atomic bomb survivors. However, there remain several specific issues and questions. These include the specificity of various cell types involved in radiation- versus smoking-related cancers, confounding and joint effects of smoking in the relation to radiation exposure, delineation of temporal trends with allowance given to the age-at-exposure, and attained-age effects. ICRP also has recently published a new report on the risk of lung cancer from inhaled radionuclides modeled on anatomical basis in

terms of lung "compartments." New information on the anatomical distribution of lung cancers resulting from uniformly distributed radiations may be useful for evaluating the ICRP model. This RP was developed to address these questions and issues. The study will evaluate lung cancer incidence in the Life Span Study for the period of 1950-1990. Pathology reviews will continue during the next 6 months. Data analyses will begin next year and first draft papers will be prepared in the following year. The study will be completed in the next 3-4 years.

RP 5-93 Longitudinal study of hormone indicators of menopause in premenopausal female atomic bomb survivors
Rose T, Soda M, Yamada M, Sasaki H, Akahoshi M, Cologne JB, Kodama K

An analysis of self-reported menopause in the Nagasaki portion of the Adult Health Study sample demonstrated early onset of menopause associated with radiation exposure from the atomic bombs and was presented at the 8th International Congress on the Menopause. This RP was developed to measure biochemical indicators to estimate the incidence of early menopause in pre-menopausal AHS participants in Hiroshima and Nagasaki. Occurrence of menopause is monitored with two perimenopausal hormones, follicular stimulating hormone (FSH) and estradiol (E2), at 6-month intervals. A total of 211 women were enrolled into this study in early 1994. Information on drinking habits and changes in menopausal symptoms are documented. A quality control study was undertaken on 20 women to evaluate the sources of variability in hormone assays. As of this writing, the subjects are in the 6th follow-up examination cycle. This study is expected to continue till 1998.

RP 6-93 Breast cancer incidence study among atomic bomb survivors, 1950-90
Tokunaga M, Land CE, Tokuoka S, Ikeda T, Soda M, Mabuchi K

This is the latest of a series of breast cancer incidence surveys conducted by Tokunaga and Land. A previously completed fourth survey (RP 1-90) included 807 primary breast cancer cases and 20 second breast cancer cases diagnosed during the period 1950-1985. A strong linear radiation-dose response was found, with the highest excess relative risk averaged over the entire observation period occurring among women who were <20 years of age at the time of exposure to radiation from the bombings. A much lower, marginally significant dose response was seen among women exposed at >40 years. A strikingly high risk per unit of radiation for early-onset breast cancer cases led the authors to suspect the possible presence of a genetically susceptible subgroup. A new research protocol expands the breast cancer series through 1990. Data collection for this series has been completed, adding 261 newly accessed cases (250 for the period of 1986-1990 and 11 prior to 1986). Of these, 58 cases were exposed at <10 years, and this should strengthen risk estimates for this age-at-exposure group. Data analysis is under way. It is expected that the analyses will be completed within the next 12 months, resulting in publication of the new incidence data. Upon completion of this RP, a new RP will be proposed within 2-3 years to further update the series, possibly adding another 5 years of follow-up.

RP 4-92 Incidence of tumors of the central nervous system among A-bomb survivors
Yenehara S, Fujii H, Kishikawa M, Kobuke T, Thompson D, Soda M, Tokunaga M, Tokuoka S, Mabuchi K, Ron E, Preston DL, Land CE

Tumors of the nervous system have been associated with late effects of medical radiation at all ages, although detailed risk assessment has been difficult primarily due to the small number of cases. Until recently, there has been very limited information on brain and other tumors of the nervous system in the LSS cohort. In the recent solid cancer incidence report, a suggestive dose response was found for tumors of the nervous system except for the brain among those exposed at ages <20 years. These findings prompted the present study. The objective is to ascertain malignant and benign tumors of the central nervous system in the LSS during the period 1950-91 under the guidelines established for the conduct of site-specific studies. All the work related to case finding and histological review has been completed, and a total of 374 tumors, benign and malignant, has been identified. Of these 282 (75%) are histologically confirmed. Menigioma is most frequent (41%), followed by schwannoma (or neurilemmoma) of the cranial and spinal nerves (25%), cerebrospinal glioma (19%) and pituitary adenoma (11%). Preliminary analysis shows a significant dose response for neurilemmoma. All analyses will be completed within the next 12 months, and the writing of papers will begin. It is expected that the study will be completed within a year or two.

RP 2-92 Studies of ovarian tumor incidence among the RERF extended Life Span Study cohort, 1948–89
Tokuoka S, Kawai K, Inai K, Shimizu Y, Nakashima E, Tokunaga M, Soda M, Mabuchi K, Land CE

An increased risk of ovarian cancer among the atomic bomb survivors has been reported from an earlier site-specific study of ovarian cancer as well as from the analyses of LSS mortality and incidence. No clear evidence exists for any specific histologic type being particularly associated with radiation exposure. In the previous study, the frequency of benign tumors of the ovary detected at autopsy was also found to increase with radiation dose. The present study extends the previous ovarian cancer series by 9 years (1948–89) and also includes a systematic ascertainment of benign tumors. All work related to the identification of cases and histological verification was completed. A total of 727 primary ovarian tumors(Hiroshima 503/Nagasaki 224) have been identified, of which 605 cases (83.2%) were histologically confirmed and were composed of 185 cases of malignant tumors (including 46 cases of borderline malignancy) and 420 cases of benign tumors. In malignant tumors, the most preponderant type was the common epithelial tumor (Group I; 168/185 cases, 90.8%). Cases of the sex-cord stromal tumors (Group II; 12 cases, 6.5%) and of the germ cell tumors (Group IV; 5 cases, 2.7%) were rare. In benign tumors, cases of Group I tumors were predominant (251/420 cases, 59.8%), followed by cases of Group IV tumors (117 cases, 27.9%), Group II (50 cases, 11.9%), and others (2 cases, 0.5%) in a descending order. There were 146 multiple ovarian tumors encountered in 71 persons. Among the 28 malignant tumor cases, tumors of Group I were predominant (26 cases, 92.9%) and

among the 118 benign tumor cases, tumors of Group I (77 cases, 65.3%) and Group IV (35 cases, 29.7%) were preponderant. In the 573 exposed cases, malignant as well as benign tumors showed a dose-response relationship, and this tendency was especially remarkable in the serious tumors of Group I. Data analysis will continue during the next 12 months. It is expected that the study will be completed in 1-2 years with the publication of papers.

RP 6-91 Studies of thyroid tumor incidence among the RERF extended Life Span Study cohort, Hiroshima and Nagasaki, 1950–90
Hayashi Y, Tsuda B, Akiba S, Fujita S, Tokunaga M, Tokuoka S, Ron E, Land CE, Mabuchi K

Thyroid cancer was one of earliest solid cancers found to be increased in atomic bomb survivors, and several thyroid cancer studies have been conducted among the survivors over the last 40 years. The aim of the present investigation is to update and expand the earlier thyroid cancer incidence series (through 1979), including both benign and malignant tumor cases diagnosed between 1950 and 1990. An increased number of cases over an extended study period should allow more detailed risk analyses. All the work related to case ascertainment and histological grouping has been completed. A total of 2,637 potential cases were reviewed, resulting in the identification of a total of 915 thyroid tumor cases. Histological verification was possible for 851 (93%) of these cases: 558 with malignant tumors, 293 benign tumors. The majority of malignant thyroid carcinomas are of the papillary type (96%), followed by the follicular type (1%), malignant lymphoma (<1%), medullary (<1%), and undifferentiated carcinoma (<1%). The 537 papillary carcinomas include 297 micro-carcinomas detected mostly at autopsy. Data analysis is expected to begin shortly. Papers will be written and submitted for publication in the next 2-3 years.

RP 2-91 Studies of skin cancer incidence among the RERF extended Life Span cohort, Hiroshima and Nagasaki, 1950-87
Kishikawa M, Kobuke T, Iseki M, Sadamori N, Yamamoto S, Soda M, Tokunaga M, Tokuoka S, Mabuchi K, Ron E, Preston DL, Land CE

An elevated risk of skin cancer, mostly basal cell carcinoma, has been reported from the follow-up of children treated with radiation for tinea capitis, enlarged thymus, and various head and neck diseases. The LSS solid cancer incidence report demonstrated, for the first time, an increased risk of skin cancer in the atomic bomb survivors. Because the completeness of the ascertainment of skin cancer from tumor registries is questionable, and also because diagnoses of skin cancer are highly variable among physicians and pathologists, the present study is designed to provide extended case-finding and a standardized pathology review for diagnosis and histological typing of skin tumors. All work related to case ascertainment has been completed and analyses have almost been completed. A total number of skin cancer cases obtained for the study period 1950-87 is 343, of which 301 (88%) were histologically verified by a panel of pathologists. Basal cell carcinomas comprise 37% of the cases; squamous cell carcinomas, 33%; Bowen's disease, 14%; malignant melanomas,

5%; and other various types, 11%. A significant dose response is demonstrated for non-melanoma skin cancers as a group, and especially for basal cell carcinomas and other epithelial skin cancers (non-basal, non-squamous cell). There is no evidence of a dose response for squamous cell carcinoma. Noteworthy is the absence of a suspected combined effect of UV and ionizing radiation exposure, and a strong effect of age at exposure on basal cell carcinoma. Two draft papers have been written. The first paper presents histological characteristics of skin cancer, and the second paper discusses risk estimates. The second paper has been submitted for RERF internal review and will be submitted for journal publication shortly.

RP 1-91 Studies of salivary gland tumors among the RERF extended Life Span Study cohort, Hiroshima and Nagasaki, 1959-87
Saku T, Hayashi Y, Takahara O, Tokunaga M, Tokuoka S, Mabuchi K, Soda M, Ron E, Preston DL, Land CE

Despite much evidence in the literature linking increased risk of benign and malignant tumors of the salivary glands to ionizing radiation exposure, little detail is known about the risk beyond a linear dose-response. This is because these tumors are rare. Also, minor salivary gland tumors are not identifiable under the conventional coding scheme (International Classification of Diseases) used by tumor registries. The present study is designed to include both benign and malignant tumors of the major and minor salivary glands diagnosed between 1950 and 1987. A large number of potential cases are screened including those diagnoses under which salivary gland tumors are likely to be misclassified and coded. Pathology reviews are conducted in a standardized manner. This study has been almost completed. The total number of cases identified for the above period is 135 (41 malignant and 94 benign tumor cases). Analysis shows a significant dose response for both benign and malignant tumors. Most of the dose response for malignant tumors is provided by an exceptionally strong dose response for a particular type, mucoepidermoid carcinoma, and most or all of the dose response is attributable to that for Warthin's tumor. Two papers have been published. The first paper (published in *Cancer,* 1997) presents methods used for case-ascertainment and histo-pathological features of salivary tumors. The second paper (published in *Radiation Research,* 1996) presents the results of risk assessment. This RP has been terminated.

RP 5-90 Primary liver cancer incidence study among atomic bomb survivors, Hiroshima and Nagasaki, 1958-1987
Fukuhara T, Itakura E, Yamamoto M, Tokuoka S, Mabuchi K, Seyama T, Nakamura N, Akiyama M, Cologne JB, Soda M, Tokunaga M, Beebe GW

Liver cancer among the atomic bomb survivors is of special interest because: (1) it is a major site of cancer in Japan and has been shown to respond not only to radiation by alpha particles but also to low-LET radiation in the recently published LSS cancer incidence data; (2) roles of hepatitis virus infection in liver cancer are rapidly being understood; and (3) an earlier RERF study showed an increased prevalence of hepatitis-B surface antigen (HBsAg)

positively in exposed individuals. Since diagnostic misclassification is a major concern for liver cancer, the primary objective of this study is to assess the relationship between atomic bomb radiation and liver cancer based on data confirmed by a panel of pathologists. The pathology review will include not only tissue slides but pathology, clinical, and other diagnostic information. Another objective is to investigate, in a nested case-control study, the possible role of HBV, and possibly HCV, infection in radiation-related liver cancer. In the case-control study, for each autopsied liver cancer case, two matched controls are selected. The pathology review extends from histologic classification of liver cancer in the incidence series to diagnosis of any accompanying liver cirrhosis and testing for HBV markers in the case-control study. In the companion study conducted in the Department of Radiobiology (RP 5-90), molecular techniques are also used to characterize the HB and HC viruses. Case-ascertainment and diagnostic confirmation has been completed, resulting in the identification of 830 cases of primary liver cancer for the study period 1958-1987. Of these, 43% were histologically verified. A majority (85%) of liver cancers are hepatocellular carcinomas, 63% of which are accompanied by liver cirrhosis. The Radiobiology Department has developed techniques for assaying HCVs using tissue samples, and work is underway to study HCVs in the case-control study. The analysis of the incidence data and the HBV data is almost completed and draft papers have been written. The study will be completed within the next two years.

RP 5-89 Pathology studies in Hiroshima and Nagasaki, revised research plan
(Former 3-75) Tokuoka S, Tokunaga M, Mabuchi K

A Pathology Program, which was started at the inception of the ABCC, has undergone several major revisions. At the beginning, it consisted almost entirely of an autopsy program in the cities of Hiroshima and Nagasaki with emphasis on the procurement of "exposed" individuals. In 1961, the pathology population was defined as a subset of the LSS sample in order to include adequate controls. An active and aggressive autopsy procurement effort was introduced, which resulted in increased autopsy rates. The autopsy rates reached a peak in the range of 40-45% in the early 1960s, but declined subsequently. In 1979, active solicitation of autopsies was terminated in favor of a completely voluntary cooperation of local physicians. In 1987, the program was redesigned to place major emphasis on patho-epidemiological follow-up studies of the atomic bomb survivors in search for specific histologic, cytologic, or other tissue changes directly or indirectly attributable to irradiation. The present RP reflects the latest change. Under newly developed guidelines, "Guidelines for the site-specific cancer incidence studies" (RP9-88), a number of site-specific studies have been initiated and are currently in progress. The autopsy program at RERF was completely terminated in 1988. However, through the ABCC/RERF Pathology Program, a large number of LSS autopsy (about 7,500 cases) and surgical tissue samples (about 13,000 cases) have been collected over the years. These archived tissues have been found to be useful for molecular studies. However, for recently diagnosed cases, we must seek tissue samples from outside hospitals. Tissues used for a series of site-specific studies and molecular studies at RERF

are obtained under an agreement signed for the Pathology Program. For future research in this field, it is essential that we establish a mechanism to identify and secure important tissue samples, especially located outside RERF. Within the next 12 months, a concentrated effort should be made to develop a community-wide agreement to create such a tissue storage program. Detailed plans of each site-specific and molecular study underway are described under specific RPs.

RP 9-88 Guidelines for the conduct of site-specific cancer incidence studies among A-bomb survivors, Hiroshima and Nagasaki
Tokunaga M, Mabuchi K, Tokuoka S, Land CE

The intent of the guidelines described in this RP is to simplify the preparation of research plans for site-specific cancer incidence studies and also to provide uniformity in basic design and operation of studies. The guidelines state that case-ascertainment be undertaken through the Hiroshima and Nagasaki tumor registries supplemented by an extended case-finding search. Histopathological verification should be achieved by a panel of collaborating pathologists specializing in respective areas. Tumor types are to be classified using internationally accepted tumor classification systems. Analyses of data should be performed by RERF and/or other participating epidemiologists and statisticians. Under these guidelines, the following site-specific cancer incidence studies are currently undertaken: liver (RP 5-90); salivary glands (RP 1-91); skin (RP 2-91); thyroid (RP 6-91); ovary (RP 2-92); central nervous system (RP 4-92), breast (RP 6-93), lung (RP 1-94) and lymphoid tissues (RP 3-94). Work on case-ascertainment and pathology review has been completed for breast cancer, ovary cancer, liver cancer, and central nervous system tumors; data analyses for these sites are under way.

Two papers on salivary gland tumors have been published. The salivary tumor study has been terminated. Two draft papers on skin cancer will be submitted for journal publication. In addition, draft papers on central nervous system tumors and liver cancer will be prepared and possibly be submitted for internal review. It is expected that most of the site-specific studies now in progress will be completed within the next 3 or 4 years. New studies will be started on cancers of the colon/rectum and stomach. Other sites of interest will likely be identified.

RP 6-88 Comparative analysis of the LSS population and a cohort of 265,000 Japanese men and women
Mabuchi K, Akiba S, Hirayama T
A large prospective cohort study conducted by Hirayama consists of 265,000 people selected from among residents of 6 prefectures in Japan, with a follow-up covering 16 years. The purpose of this RP is to undertake comparative analyses of data from the LSS and Hirayama cohorts with respect to smoking and other life-style factors related to cancer and other diseases. Knowledge gained from the analyses will lead to better understanding on the role of non-radiation risk factors which may be operative as confounding factors in the LSS risk assessment. Several papers on cigarette smoking and cancer have

been published as a result of analyses conducted under this RP. Following the death of Dr. Hirayama, future collaborative arrangement needs to be established.

RP 8-85 Incidence study on malignant and benign genital tumors among females, Hiroshima and Nagasaki, 1950-80
Tokuoka S., Kawai K., Shimizu Y., Inai K., Ohe K., and Mabuchi K.

Several reports suggest genital cancer as a late effect of local irradiation, but evidence on genital cancers induced by whole body irradiation is limited. This RP intends to determine the incidence of tumors of various female genital organs in the LSS. A study of ovarian tumors has been superseded by RP 2-92, as reported elsewhere. It is planned that a separate RP be prepared for uterine tumors.

RP 14-79 Interaction between radiation dose and host factors. An epidemiological case-control study of female breast cancer in atomic bomb survivors
Mabuchi K, Cologne J, Shibata Y, Tokunaga M, Land CE

This ongoing case-control study nested in the LSS cohort is intended to evaluate the effects, if any, of host factors other than age on radiation carcinogenesis in women. Host factors of interest have included traditional risk factors such as reproductive histories, ovarian activity, and use of exogenous hormones. In a recently published case-control study of 196 breast cancer cases and 566 controls, the risk was found to be positively associated with age at first full-term pregnancy, while negative associations were observed with number of births and total cumulative period of breast feeding. Significant positive associations were also found with histories of treatment for dysmenorrhea, and uterine or ovarian surgery. Neither age at menarche nor age at menopause was significantly associated with breast cancer. Radiation exposure (from the atomic bombs) was associated in a multiplicative manner with age at first full-term pregnancy, number of children, and cumulative total period of lactation. More recently, special attention has been given to family predisposition because of the rapidly increasing knowledge on BRCA-1, -2 and ATM, possibly other genes which may play an important role in heritable forms of breast cancer. Preparations are currently underway for conducting a new study of early-onset versus late-onset breast cancer cases to investigate family pedigrees and inherited mutations in the genes mentioned above using tissues and blood samples. A research protocol for this study will be presented within the next 12 months, and the study will be carried out over a 3- to 4-year period.

RP 7-76 The value of Adult Health Study family history records in the determination of genetic influences on the development of cancer and other disorders
Cologne JB, Yamada M, Mabuchi K

This project was originally undertaken to ascertain the feasibility of using AHS family-history information for studying genetic influences on cancer and other

diseases. For many years there was little or no activity on this project and the data that were collected in the earlier years were not stored in computer databases. Recent advances in the understanding of genetic effects on disease, particularly cancer, together with the development of improved methods for genetic epidemiology and statistical genetics have lead to specific hypotheses concerning genetic epidemiology and radiation carcinogenesis. By combining data in familial relationships with information in the tumor and tissue registries and taking advantage of our molecular genetics capabilities, RERF is in a unique position to investigate some of these hypotheses. Over the last few years efforts have been made to revive and modernize this project with a short-term goal of developing a family-relationship database for the RERF cohorts based on information from a variety of sources. Once established this database will serve as the basis for specific research projects such as case-control studies, or family history studies with possible sampling of blood for molecular-genetic analysis. At this time a family study of breast cancer incidence is being designed and we are considering participation in an international thyroid cancer consortium. With the aging of the RERF study population it is becoming increasingly difficult to obtain the information needed for genetic studies, thus rapid progress in database development and study design is essential. Unfortunately, progress has been hampered by the loss, without replacement, of an epidemiologist and a database specialist interested in, and knowledgeable of, genetic studies and data management issues. Given current trends in radiation research, the development of the family relationship data base and the design and conduct of studies based on these data should receive high priority. While outside collaboration and support will be essential for the success of this effort, it is also critical that RERF be able to employ personnel with the appropriate epidemiologic and database skills to design and conduct family studies. Despite personnel shortages progress has been made and we anticipate further significant progress on the creation of a family pedigree database in the coming year. Family data obtained from questionnaires from approximately 7,000 AHS members have been checked against the Master Sample Questionnaire and 1950 Census data. The Master File Section is currently adding these data to the family database.

RP 4-75 Research plan for RERF studies of the potential genetic effects of atomic radiation: Hiroshima and Nagasaki Part 1. Mortality study of children born to atomic bomb survivors
Mabuchi K, Schull WJ, Neel VJ

This is a long-term mortality follow-up of a cohort of 77,000 children born to parents, either one or both of whom were exposed to radiation from the atomic bombs, and to control parents. As with the LSS, the mortality follow-up is based on the ascertainment of deaths through the nation-wide family registration; the Hiroshima and Nagasaki tumor registries also provide cancer incidence data for a subset of the cohort. Previously published 1945-85 mortality data for diseases excluding external causes showed no significant increase associated with parental radiation exposure. An apparent increase in non-cancer mortality at attained ages < 20 years in the >2.5 Sv dose category was considered to be caused by the worsened socioeconomic conditions in

which many survivors lived in the aftermath of the bombings. Tumor registry cancer incidence (through 1982) showed no excess cancer risk during the first two decades of life associated with parental radiation. Through 1990, 4,130 deaths have occurred including 203 cancer deaths in about 67,500 with DS86 dose estimates. Through the tumor registries, 448 cancer cases have been identified, including 60 leukemia and 28 lymphoma cases. Preliminary analyses show no significant relationship between parental exposure and the risk of leukemia or lymphoma. We plan to complete the analysis of the latest mortality and cancer data within in the next 12 months. A possibility of mail or other surveys will be explored in order to determine the whereabouts of each subject and also to obtain information on socioeconomic and life-style characteristics as well as the health status of each subject. Mortality and morbidity follow-up will continue so that potential effects of parental exposure on adult-type cancers and diseases will be studied.

RP 1-75 Research plan for RERF studies of Life Span of A-bomb survivors, Hiroshima and Nagasaki

Shimizu Y, Mabuchi K, Preston DL, Shibata Y, Pierce DA

This is a long-term follow-up of a fixed cohort consisting of 93,000 atomic bomb survivors and 27,000 non-exposed individuals, known as the Life Span Study (LSS) cohort. The follow-up began in 1950 using the family registration system, *Koseki*, which assures virtually complete ascertainment of mortality. It also serves as the sampling frame for a clinical subcohort, the Adult Health Study sample. Periodical analyses of the LSS mortality data have resulted in a series of reports. LSS Report 12 on cancer mortality updated through 1990 has been published in 1996. Recently, through the tumor registries in Hiroshima and Nagasaki, it has also become possible to study cancer incidence in a subset of the LSS. The first comprehensive LSS cancer incidence data were published in 1995. As of 1995, about 50% of the subjects in the LSS sample are alive, and about 85% of those exposed at ages less than 30 years are alive. Because of the uncertainty of the current risk estimates based on the incomplete follow-up of those exposed early in life, continuation of the follow-up, in terms of both mortality and cancer incidence, is essential. The latest published LSS mortality data also demonstrated an excess risk of death from non-cancer causes, largely from cardiovascular and digestive diseases, associated with radiation exposure. Further research is needed to elucidate the nature and magnitude of the excess non-cancer risk. Analyses of LSS non-cancer mortality data through 1990 are in the final stage. We plan to submit Report 12 on non-cancer mortality report in the coming year. Within the next three years, work will begin in preparation for the next LSS report which will include updated (possibly through 1995) incidence and mortality data.

RP 18-61 Tumor registry study in Hiroshima and Nagasaki

Mabuchi K, Soda M, Fujita Y

This RP provides the framework for the operation of the Hiroshima and Nagasaki tumor registries. The objective of these registries is to provide a systematic collection and management of tumor cases in the populations of the

cities of Hiroshima and Nagasaki. These registries are undertaken under the auspices of the medical association of each city, with technical support provided by RERF. The registries are linked with the Master-File for the major RERF cohort samples (LSS, In-utero, and F1) and thus serve as the source of RERF cancer incidence studies in each cohort. The Hiroshima and Nagasaki tumor registries are the first population-based registries in Japan. Case ascertainment and data collection is based on abstraction of medical records conducted by trained personnel at regularly scheduled hospital visitations. This active approach is reflected in a high quality of incidence data not typically seen for other tumor registries in Japan, most of which rely on passive case notifications by physicians. The Hiroshima and Nagasaki tumor registry data have regularly been included in recent volumes of "Cancer Incidence of Five Continents" compiled by the International Association of Cancer Registries (IACR) at the International Agency for Research on Cancer (IARC) in Lyon, France. The latest cancer incidence from the two cities will be included in the next volume, Volume VII, of this monograph, which is expected to be published within the next two years. The latest childhood cancer incidence data in Hiroshima and Nagasaki will be included in an upcoming edition of "International Incidence of Childhood Cancer", also compiled by IARC.

RP 29-60 Detection of leukemia and related disorders

Mabuchi K, Kuramoto A, Tomonaga M, Kusumi S, Nonaka H, Kamada N, Dohy H, Soda M, Fujita Y, Preston DL

This case-finding program, known as the Leukemia Registry, was started in 1948, with collaborations of hematologists and physicians involved in the treatment and care of leukemia patients in Hiroshima and Nagasaki. It is designed to detect, document, evaluate, and diagnose cases of leukemia and certain closely related hematological disorders occurring among the LSS and other RERF cohorts. In the early years, case-finding was based on a wide variety of sources including reports from the participating physicians, clinical examination as carried out at ABCC, death certificates, obituaries, etc. With the recent improvement in the Hiroshima and Nagasaki tumor registries, the ascertainment of leukemia cases currently relies primarily on the tumor registry's activities. In the mid-1980s, over 60% of leukemia cases in the Leukemia Registry were reclassified using modern diagnostic criteria and nomenclature, including the French-American-British (FAB) classification for acute leukemias. The latest published report results from comprehensive analyses of LSS incidence data for 1950-1987, involving analyses of a dose response and modifying effects for major leukemia types (acute lymphocytic leukemia, acute myelogenous leukemia, chronic myelocytic leukemia, adult T-cell leukemia) and lymphoma and multiple myeloma. An important question remaining at the present time relates to the risk for multiple myeloma (see RP 3-94). A new site specific RP, which is to be undertaken jointly by hematologists and pathologists, has been developed to investigate all lymphoid tumors including multiple myeloma so that more definitive data can be obtained on the risk of these tumors. This new lymphoid study will be a major focus of this RP in the next few years (see detailed plan under RP 3-94).

Tissue registry
Mabuchi K, Soda M, Fujita Y

Tissue registries, started in 1973, are undertaken under the auspices of the prefecture medical association in Hiroshima and the city medical association in Nagasaki. Pathology slides are collected for each tumor, malignant and benign, together with pathology reports. Tissue registry data are processed at RERF together with the tumor registry data from each city and entered into a common data base. These registries provide a supplemental source for ascertainment of tumor cases for the tumor registries, and were especially valuable in the early years when there was difficulty in seeking collaboration from certain hospitals Hiroshima. A large number of pathology slides collected and stored at one location greatly facilitate the conduct of a large number of site-specific studies involving pathology reviews of cases diagnosed over many years.

Publications (1996)

RP 1-91 SAKU T, HAYASHI Y, TAKAHARA O, MATSUURA H, TOKUNAGA M, TOKUOKA S, SODA M, MABUCHI K, LAND CE
Salivary gland tumors among atomic bomb survivors 1950-87. Cancer (In press)

RP 1-91 LAND CE, SAKU T, HAYASHI Y, TAKAHARA O, MATSUURA H, TOKUOKA S, TOKUNAGA M, MABUCHI K
Salivary gland tumor incidence among atomic Bomb survivors, 1950-87: Evaluation of radiation-related risk. Radiation Research 146:28-36, 1996

RP 5-89 IWAMOTO KS, MIZUNO T, ITO T, AKIYAMA M, TAKEICHI N,MABUCHI K, SEYAMA T
Feasibility of using decades-old archival tissues in molecular oncology/epidemiology. American Journal of Pathology 149:399-406, 1996

RP 6-82 SODA M, OTAKE M, IZUMI S, OCHI Y, MORIYAMA, SCHULL WJ
The effect of radiation exposure and physical measurements on menarche among the prenatally exposed A-bomb survivors. Submitted to Radiation Research

RP 1-75 PIERCE DA, SHIMIZU Y, PRESTON DL, VAETH M, MABUCHI K
Studies of the mortality of A-bomb survivors. Report 12, Part 1. Cancer:1950-1990. Radiation Research 146:1-27, 1996

RP 2-75 KODAMA K, MABUCHI K, SHIGEMATSU I
A long-term cohort study of the atomic-bomb survivors. Journal of Epidemiology 6:S95-S105, 1996

RP18-61 MABUCHI K, FUJITA Y
Childhood cancer incidence in Hiroshima, 1980-1989. Submitted to "International Incidence of Childhood Cancer" Vol.II, IARC, Lyon, France

RP18-61 IKEDA T, SODA M
Childhood cancer incidence in Nagasaki, 1985-1992. Submitted to "International Incidence of Childhood Cancer" Vol. II, IARC, Lyon, France

RP18-61 MABUCHI K, FUJITA Y
Cancer incidence in Hiroshima, 1986-1992. Submitted to "Cancer Incidence in Five Continents" Vol. VII, IACR/IARC, Lyon, France

RP18-61 IKEDA T, SODA M
Cancer incidence in Nagasaki, 1988-1992. Submitted to "Cancer Incidence in Five Continents" Vol. VII, IACR/IARC, Lyon, France

Department of Statistics

The Department of Statistics provides expertise to all of the other research departments in the matter of study design, data analysis, and the construction of databases.

Program objectives

The Department of Statistics plays an important role in virtually all RERF research activities. Collaboration and the provision of guidance on statistical analyses and data management to researchers throughout RERF is a major function of the Department of Statistics. An equally important activity of RERF statisticians involves methodological research aimed at improved understanding of the statistical questions raised by the RERF data and the development and implementation of improved statistical methods for analyses of the broad range of data arising from RERF studies. The Department is also playing a leading role in the design of modern databases to make the RERF data more accessible to all RERF researchers. Finally, the Department of Statistics is responsible for management of the dosimetry data and the computation of individual dose estimates.

RP 5-87 Radiation-related damage to the developing human brain
Schull WJ, Otake M, Masuda M, Nishitani H, Hasuo K, Goto I, Kobayashi T

A pilot project involving brain imaging of five severely mentally retarded people who were exposed in utero suggested that radiation exposure between the 8th and 15th week of gestation can lead to specific neuronal migration errors in the developing brain. The principal objective of this protocol was to obtain brain scans from additional mentally retarded individuals who were exposed in utero and from some low IQ in utero exposed subjects who are not mentally retarded. There has been virtually no progress on these primary objectives over the past decade. This is largely due to concerns about the nature of the procedures involved and the lack of any clear benefit to those who would participate in the project. The primary work related to this RP during the past year concerns summarization and reanalysis of related data on mental and physical development of children exposed in utero, with a particular emphasis on assessment of effect modification associated with gestational age at the time of exposure. Drs Otake and Schull have completed a draft review paper summarizing the full range of RERF data related to this

issue. This paper is now undergoing internal review and will be submitted for publication. There is a need to decide if the original goals of this project can be met. With the retirement of Dr. Otake and the departure of Dr. Schull there are no active RERF staff members involved in this project . It is not appropriate for the Department of Statistics to have primary responsibility for this work. Unless the Department of Clinical Studies is willing to take the leading role in this project it should be discontinued. Discontinuation will not prevent further analyses of previously collected data.

RP 4-86 Evaluation of physiological measurements: A predictor of mortality or morbidity associated with aging
Fujita S, Sasaki H, Kodama K, Kasagi F

This is an ongoing follow-up study of the relationship between physiological measurements taken between 1970 and 1972 and subsequent morbidity or mortality in a cohort of 8,000 people in the Adult Health Study. The measurements were used to develop an index of physiological age. Cohort members have been classified into three relative age groups according to whether their physiological age index was less than, similar to, or greater than their chronological age. Recently completed analyses have revealed an association between relative age and subsequent mortality, especially cardiovascular disease mortality, after allowance for other risk factors. A manuscript on these analyses is being prepared and will be submitted for internal review and publication within the next six months. Over the next three years additional analyses will be carried out, and new data on grip strength collected in recent AHS examinations will be used to assess the stability of the relative age index.

RP 36-63 Blood groups in Adult Health Study and in utero ATB subjects, Hiroshima and Nagasaki
Izumi S, Ohara J, Preston DL

Current work on this protocol involves the assessment of phenotype and genotype frequencies in 16,600 members of the LSS who participate in the AHS, about 1000 in utero subjects, and almost 26,000 F1 subjects examined at ABCC or RERF. A paper on genotype frequencies for the major blood groups was completed during the past year. The analyses in the paper are concerned with the assessment of allele and genotype frequencies, departures from Hardy-Weinberg equilibrium, comparison of the genotype distributions in the two cities and for the two generations, together with some assessment of typing error rates based on repeated measurements and inconsistencies within families. This paper has gone through internal review and will be submitted for publication within three months. Future analyses will investigate the relationship between blood group and morbidity or mortality. An analysis of the relationship between the ABO group and digestive diseases or cancer of the digestive organs is being planned. In its 1996 meeting, the Science Council suggested that this protocol be discontinued. Since serological data have been obtained for virtually all AHS participants and since there is no ongoing program for the clinical examination of F_1 cohort members there is

little need for a formal protocol dealing with blood groups. The additional analyses noted above can be carried out in conjunction with other projects, therefore there is no compelling reason to continue this protocol.

RP 2-61 Study of mortality in children exposed in utero
Preston DL, Mabuchi K

This research is aimed at characterization of the relationship between mortality or cancer incidence and radiation dose in people who were in utero at the time of the bombs. Earlier analyses have focused on the 2700 members of the in utero mortality cohort. During the past few years we worked to clarify the nature of the in utero populations studied by RERF. On the basis of this work it was decided that analyses of mortality and morbidity should be based on data from the combined in-utero mortality and clinical cohorts. This increases the number of in-utero subjects considered in analyses of mortality and morbidity by about 30%. Analyses of cancer mortality through the end of 1992 in the in-utero and childhood exposure cohorts have been published. The results presented in the paper indicate that despite the small number of cancer deaths among exposed in-utero cohort members there is, especially for women, evidence of radiation-related excess risks of solid cancer after the age of 17. These risks are similar to those seen for LSS cohort members who were six years of age or less at the time of exposure. A draft paper on cancer incidence in the in-utero and childhood exposure cohorts is nearing completion and should be submitted for publication by fall. Analyses of general mortality in the in-utero cohort are also being carried out. As the members of this cohort are approaching 50 years of age death and cancer incidence rates are increasing rapidly. Therefore it will be important to reconsider risks in this population in three to five years.

RP 18-59 Shielding survey and dosimetry study
Fujita S, Funamoto S, Katagami K, Kerr GD, Kohda M, Ohara JL, Preston DL, Watanabe T

The DS86 dosimetry system provides the dose estimates that are used as the basis of all current RERF analyses of radiation effects. The computation of individual DS86 doses requires computer programs and data bases developed for the US-Japan Joint Committee for Reassessment of Atomic Bomb Dosimetry, additional computer programs developed at RERF, and extensive data on location and shielding at the time of the bomb for individual survivors. In early 1995 the DS86 computer programs and data bases were moved to the new workstation-based RERF computer system. Fundamental work on the installation and validation of the DS86 system on the new computers has been completed. However, a major effort to review and restructure all data related to the dose estimation at RERF is continuing. This review has included the development of an expanded comprehensive roster of persons alive at the time of the bombs whose dose estimates and exposure status are relevant to RERF studies. This roster, which includes members of the LSS cohort, mothers of members of the in-utero cohort, and parents of F_1 cohort members, contains more than 192,000 people (roughly 50,000 people more than the current DS86

master list). Shielding and acute effects data have been reviewed and placed in relational database tables. A major goal in designing the new tables has been the development of documented and consistent data on the nature of the shielding and acute injuries for all cohort members. The new tables should be incorporated into the main REFF database during the coming year. Documentation of the implementation and use of the DS86 system at RERF is incomplete. We hope to complete an updated version of this documentation within the next year. During the past two years we have worked with scientists from Hiroshima University on the comparison of DS86 dose estimates with DS86-like dose estimates computed by Hiroshima University. This project has made it clear that we should publish a short note describing a simple scheme for the computation of approximate DS86 shielded kerma and organ doses. We hope to produce such a paper within the next year.

In the decade since the introduction of DS86 it has become apparent that there are problems with both the DS86 neutron and gamma dose estimates in Hiroshima. In addition, a reassessment of the chromosome aberration data for Nagasaki survivors suggests that DS86 estimates for Nagasaki factory workers are too large. In response to a letter in Radiation Research we published an assessment of the potential impact of changes in the Hiroshima neutron doses on cancer risk estimates. A short note about the chromosome aberration data for Nagasaki survivors is currently being prepared for publication. The US-Japan Joint Committee met in May 1996 to discuss the neutron issue. Data on the factory worker dose estimates problem was brought to the attention of the committee at that time. Hopefully a revised dosimetry system that addresses all of the problems with DS86 will be developed and made available to RERF sometime during the next two or three years. The implementation of a new dosimetry system is likely to require a considerable effort on the part of the RERF staff.

Publications* (1996-1997)

RP 02-61 Delongchamp RD, Mabuchi M, Yoshimoto Y, Preston DL. Cancer mortality among Atomic Bomb survivors exposed *in-utero* or as young children, October 1950 - May 1992. *Radiation Research* **147**:385–895 (197)

RP 18-59 Kerr GD; Development of A-bomb Survivor Dosimetry in *Proceedings of the First Schull International Symposium* Schull WJ, Abrahamson SA eds. 1997(in press).

RP 01-75 Pierce DA, Shimizu Y, Preston DL, Væeth M, Mabuchi K. Response to the Letter of Drs. Rossi and Zaider. *Radiation Research* **146**:591-593, 1997.

* This list includes only publications related to Research Protocols that list a member of the Department of Statistics as the first current investigator. Most papers that involve statisticians, including many in which a member of the department is first author, are related to Research Protocols associated with other departments.

Department of Genetics

The current research activities of the Department of Genetics have two major thrusts, namely, a cytogenetics program that focuses on the occurrence of chromosomal abnormalities in the survivors as well as their offspring, and a biochemical genetics program that centers on the detection of gene-mutational events and the development of the requisite technology to achieve this end. These two programs have been carried out by the Cytogenetics Laboratory and the Laboratory of Biochemical Genetics, respectively.

In the past, screening for chromosomal abnormalities and gene mutations occurring in germ cells were carried out in the two laboratories by examining the children of the survivors selected from the same F_1 cohort. However, in the last 10 years, the cytogenetics program focused on screening for somatic chromosome abnormalities in the survivors in order to establish biological dosimetry as an alternative to physical dose estimation through the application of electron spin resonance (ESR) of tooth enamel obtained from the survivors. The efforts of the biochemical genetics program have been concentrated on developing technologies for the detection of germ cell DNA mutations in the children of the survivors and establishing cell lines from 1000 parent-child trios, with half of the trios including at least one proximally exposed parent.

In the next five years, in each program, on-going projects will be continued. In addition, the FISH (fluorescence in situ hybridization) technique will be utilized for the physical localization of unreported genes or new mutations in specific genes detected in the biochemical genetics program by using single probes of DNA fragments and a subsample of the 1000 trios whose lymphocytes and cell lines have been stored in our cell bank for the biochemical genetics program will be examined for the detection of chromosomal germline mutations.

The Cytogenetics Program

The research objectives of the Cytogenetics Laboratory are two fold. First, to collect cytogenetic information on the survivors and to use this information to strengthen the DS86 dose estimates, either by validating them or by indicating possible biases in them. Second, to determine by means of the F_1 cytogenetic studies whether parental exposure to A-bomb radiation caused an increased frequency of chromosomal abnormalities in their progeny.

Cytogenetics Lab

RP 8-93 Cytogenetic study in the Adult Health Study population by fluorescence in situ hybridization (FISH).
Kodama Y, Nakano M, Ohtaki K, Itoh M, Awa AA, Pawel DJ, Nakamura N

This study using FISH is expected to provide answers to several questions raised by the past cytogenetic studies using conventional staining method. Mainly, these questions include city difference among those who were exposed in Japanese houses, different dose responses by different shielding categories primarily in Nagasaki, and possible bias in cytogenetic dose estimation due to clonal expansion of aberration-bearing cells. Because previous studies were

not free from laboratory bias, a whole FISH study must be achieved in Hiroshima laboratory. Initially, it was planned to test 200 survivors (120 Hiroshima + 80 Nagasaki survivors) a year. We will initiate sampling Nagasaki cases on May 1997. Within 3 years, nearly 500 Hiroshima survivors and 150 to 200 Nagasaki survivors will be examined. High dose parents of progeny in the DNA study will also be introduced into this study. Further, nearly 150 survivors who donated their teeth extracted by medical reasons will be FISH examined to compared with tooth enamel ESR data.

RP 10-86 Radiation dose estimates using tooth samples. Part 1. Collection of tooth samples from A-bomb exposed people in Hiroshima and Nagasaki.
Nakamura N

The purpose of this research protocol is to collect A-bomb survivors' teeth extracted by medical reasons. RERF has not been involved in Nagasaki collection because Nagasaki University group had already sent letters to proximally exposed individual before this protocol was approved in 1986. On the average, over 30 teeth have been continuously received every year from Hiroshima survivors, giving rise to over 600 specimens. About 30 to 50 % of the collected materials are suitable for subsequent study.

RP 1-92 Radiation dose estimates using tooth samples. Part 2. Use of electron spin resonance on tooth enamel from Hiroshima atomic bomb survivors.
Nakamura N, Miyazawa C, Awa AA

Electron spin resonance (ESR) measurements were conducted for 100 samples of teeth collected from Hiroshima survivors. To estimate the effects of dental X-ray exposures, each tooth was divided into two halves, lingual and facial ones, followed by independent enamel isolation and ESR measurements. Because most of the conventional dental X-ray exposure comes from outside of the mouth, facial halves may possibly produce a larger ESR signal compared with lingual ones. Indeed, this was the case for about 20 samples out of the 100. These discrepant teeth were mostly incisors and canines, which are known to be affected by exposure to solar light (UV light). Chromosome translocation data from the donors of the teeth showed a close correlation with the dose estimated from the ESR signal from both halves of molars and the lingual halved of the front teeth. The dose estimated from ESR is based on a calibration curve of standard enamel samples exposed to 0 to 4 Gy. Further, the dose response relation was very close to what would be expected from the in vitro dose response of dicentric yield assuming that the detection rate of translocations by conventional staining is 70% compared with that of dicentric chromosomes. The relation of translocations with the signal from the buccal halves of front teeth showed a translocation frequency considerably lower than expected, which is attributable to overestimation of the ESR dose caused by UV light exposure. A manuscript is currently under internal review process for subsequent journal publication.

Another topic relates to development of a new simple method to isolate enamel. Treatment of teeth with a high concentration of sodium hydroxide was

found to denature dentine, whereas enamel could remain intact even after 4 weeks of treatment. Radiation effects recorded in the enamel before its isolation was found to be unaffected by the treatment. The method is especially useful for teeth that have been stored for over 2 years, which are prone to a loss of enamel integrity and thus break apart into small pieces. Whereas the previous method of mechanical isolation is tedious, the new method is quick and easy because the dentine is softened and a simple rubbing of small pieces is sufficient to separate the enamel.

Publications (1996-1997)

RP 8-93 NAKANO M, KODAMA Y, OHTAKI K, NAKAMURA N, AWA AA: Detection of stable chromosome aberrations in A-bomb survivors - comparison of conventional staining and FISH methods. Hiroshima Igaku 49:322-323, 1996 (in Japanese)

RP 8-93 KODAMA Y, PAWEL DJ, NAKANO M, OHTAKI K, NAKAMURA N, AWA AA: Frequencies of stable chromosome aberrations in A-bomb survivors - variation in dose-response relationship by shielding categories. Hiroshima Igaku 49:319-321, 1996 (in Japanese)

RP 8-93
RP 10-86
RP 1-92
NAKAMURA N, PAWEL DJ, KODAMA Y, NAKANO M, OHTAKI K, MIYAZAWA C, AWA AA: Biodosimetry of atomic bomb survivors by karyotyping, chromosome painting and electron spin resonance. Proc. of the 1995 Schull International Symposium (in press)

RP 8-93
RP 10-86
RP 1-92
NAKAMURA N, IWASAKI M, MIYAZAWA C, NIWA K, SAWADA S, AKIYAMA M, AWA AA: Radiation dose estimation by ESR for teeth donated by A-bomb survivors. Hiroshima Igaku 49:314-318, 1996 (in Japanese)

RP8-93 KODAMA Y, NAKANO M, OHTAKI K, DELONGCHAMP R, AWA AA, NAKAMURA N: Estimation of minimal size of translocated chromosome segments detectable by fluorescence in situ hybridization. Int J Radiat Biol 71:35-37, 1997

Biochemical Genetics Program

The primary objective of the biochemical genetics program is to determine whether an increase in mutations measurable at the molecular level has occurred in the children born to A-bomb exposed parents in Hiroshima and Nagasaki. Extensive studies of the children of the survivors of the atomic bombings of Hiroshima and Nagasaki, using various endpoints such as untoward pregnancy outcomes, mortality, chromosome aberrations, and gene mutations screened at the protein level, have thus far yielded no statistically significant increases in genetic effects compared to a control population.

Because it is important to determine the mutation rate induced by radiation in this unique population, detecting mutations at the DNA level has been explored in a feasibility

study. Establishment of cell lines from parent-child trios was recommended by the Genetic Study Conference held in 1984. It is anticipated that immortalized B-lymphocyte cell lines from 1000 families, one-half of them from a proximally exposed parent(s), will be maintained at RERF. Cell lines from 800 families composed of 1600 parents having DS86 estimates and 1200 children are now in the cell bank. This is the largest properly selected population in the world for the detection of radiation effects on human germline mutations. The Human Germline Mutagenesis Workshop held in 1991 recommended starting a pilot study using 100 families (50 exposed and 50 control families), a subsample of the 800 families, to compare various types of DNA as potential targets for the detection of germinal mutations with various techniques, because there was no information about the genes sensitive to radiation-induced mutagenesis. In keeping with this recommendation, microsatellites, minisatellites and various functional single-copy sequences in 124 children and both parents of the 100 families have been examined to determine whether deletion/insertion/rearrangement (D/I/R) type mutations or mutations causing other types of quantitative changes, all commonly produced by radiation, as well as nucleotide substitutions, exist at higher frequency in the children of the exposed parents.

Preliminary studies have failed to reveal a significant difference between the children of the exposed and the control parents in the mutation rates at the microsatellite and the minisatellite loci, both of which are repetitive sequences dispersed through the human genome.

We have developed two techniques to screen for D/I/R type mutations in single-copy sequences. One is the quantitative measurement of intensities of chemiluminescent bands on Southern filters and the other is the two-dimensional electrophoresis (2-DE) of DNA digests followed by a quantitative image analysis of ^{32}P-labeled spots. Each technique can detect a 50% decrease or increase in band intensity or spot intensity that is derived from the D/I/R events on the totality of a single allele. Thus, these techniques are suitable to detect a fresh D/I/R type mutation because a fresh mutation would usually be detected in a heterozygote for a normal and a variant allele.

Biochemical Genetics Lab

RP 5-85 Culture of permanent lymphocyte cell lines as sources of biological samples for investigation of genetic effects of radiation on children of atomic bomb survivors.
Satoh C, Takahashi N, Hiyama K, Otake M, Akahoshi M

Our goal is to establish cell lines from B-lymphocytes from 1000 families composed of father-mother-child trio using Epstein-Barr virus transformation. In half of the families, one or both parents were exposed to A-bomb radiation of more than 0.01 Sv gonadal dose calculated with the relative biological effectiveness (RBE) of 20; the remaining half will be the controls. Intact lymphocytes and granulocytes are also stored in liquid nitrogen for confirmation of mutations. In 1985, we selected 1525 families using the T65 dose revised (T65DR). We have established cell lines from 963 families. Among the 963 families, 835 families are usable for our future study because DS86 is available for both parents or DS86 is available for one parent and the

other parent was either NIC or the other parent was 3000 m or more from the hypocenter ATB. New families for which parental DS86 doses are available will be selected and cell lines will be established keeping the original goal of 1000 families in mind. However, success of this additional work depends on the availability of help mainly from the Nagasaki Department of Clinical Studies, who are short staffed.

RP 7-85 Study to develop methods of DNA analysis for detection of mutations in children of atomic bomb survivors.
Satoh C, Takahashi N, Kodaira M, Asakawa J

To examine efficiencies of techniques and to compare various types of DNA as potential targets for the detection of mutations, we have been carrying out pilot studies in which we are examining 50 exposed families with 64 children and 50 control families with 60 children which are a subsample study. Techniques for screening for nucleotide substitution mutations were too inefficient compared for the required number of nucleotides to detect a significant difference between two groups. For the detection of deletion/insertion/rearrangement (D/I/R) type mutations believed to predominate among radiation induced mutations, we are examining repetitive sequences and single-copy sequences. No significant differences were detected in the mutation rates at the repetitive sequences including six minisatellites and six microsatellites between the two groups of children. DNA fingerprints composed of multiple minisatellites are being examined by multilocus probes to increase the power of our study. For D/I/R mutations in single-copy sequences, we have developed two techniques. One is a new two-dimensional gel electrophoresis (2-DE) technique and the other is the quantitative searching for a 50% decrease or increase in intensity of chemiluminescent bands on a Southern filter.

We have started a pilot study for the assessment of detectability of germ cell mutations in mice using the 2-DE method. From a mouse (BALB/c) DNA sample digested with a set of three restriction enzymes, approximately 1000 spots are detected on a single gel. Quantitative image analysis showed that 700 spots among them are usable for the detection of D/I/R mutations. Each of the DNA samples from 36 offspring of the control mice and from 43 offspring derived from spermatogonia irradiated by 5 Gy of X rays, was digested separately with two different sets of restriction enzymes, and the resulting two digests were independently electrophoresed 2-dimensionally. Two mutations were detected among a total of 45,264 spots from the exposed group and no mutations were detected among 31,859 spots from the control group. The offspring of male mice irradiated by 3-Gy X rays are being examined by 2-DE. Results will be obtained in one year. At the same time, we are preparing to examine 100 families with this technique. In regard to the quantitative analysis of Southern bands, the best conditions to detect a 50% change in the band intensity have been determined for 40 probes that can detect loci that are human counterparts of the mouse seven specific loci or of

other loci located nearby. A total of 8.9×10^8 bp of DNA from 124 children from the 100 families have been screened for D/I/R mutations with 16 probes, but, as yet, no mutations have been detected. Screening for mutations will be continued on children of a new 100 families. For the quantitative analysis of data that will be obtained from these studies, we require the assistance of the Departments of Information Technology and Statistics.

RP01-97 Pilot study of the genetic background of the AHS population: Identification of markers in potential candidate genes associated with hypertension.
Takahashi N, Murakami H, Yamada M, Kasagi F, Kodama K, Satoh C

This protocol was approved on 24 March 1997. The association between hypertension and polymorphic markers of the human *SA* gene and three genes encoding proteins in the renin-angiotensin (RA) system will be examined in 250 individuals from the AHS population (125 from a hypertensive group and 125 from a normotensive group). The *SA* gene was originally obtained by positional cloning from spontaneous hypertensive rats, and a polymorphism on the human gene homologous to the *SA* gene was reported to be associated with hypertension in a Japanese population. The three genes in the RA system are those encoding angiotensinogen, angiotensin I converting enzyme, and angiotensin II type 1 receptor. The results of reported studies on these four genes are still controversial and the association with hypertension has not yet been established. If markers constituting an inherited predisposition to essential hypertension are identified, a larger study will be designed to determine whether there is any difference in genotype distribution between the exposed and the control group. If such a difference exists, the association between radiation exposure and hypertension that was detected in the Adult Health Study could be attributable to a difference in genotype distribution.

Publications (1997)

RP 7-85 HAYASHIZAKI Y, HIROTSUNE S, OKAZAKI Y, MURAMATSU M, ASAKAWA J: Restriction Landmark Genomic Scanning (RLGS). In *Encyclopedia of Molecular Biology*. Fundamentals and applications. Editor-in-chief: Meyers R.A. VCH publisher Weinheim. New York, Basel, Cambridge, in press

RP 7-85 SATOH C, TAKAHASHI N, ASAKAWA J, KODIARA M, KUICK R, HANASH SM, NEEL JV: Studies on germline mutations in the children of atomic bomb survivors. World Health Stat. Quart., in press

RP 7-85 TAKAHASHI N: Denaturing gradient gel electrophoresis (DGGE). In *Molecular Biology Protocols.*, 2nd Edition. Ed by Koike K, Sekiya T, Kondo H. Nanko-do Inc., in press (in Japanese)

Publications (1996)

RP 7-85 ASAKAWA J: High resolutional two-dimension electrophoresis of DNA: A refinement of RLGS method. Protein, Nucleic Acid and Enzyme 41: 170-177, 1996 (in Japanese)

RP 7-85 ASAKAWA J, KODAIRA M, KANEOKA S, SATOH C: A new method for the mutation study on the children of the Atomic bomb survivors: Two-dimensional electrophoresis of DNA. J. Hiroshima Med. Assoc. 49: 431-433, 1996 (in Japanese)

RP 7-85 KUICK R, ASAKAWA J, NEEL JV, KODAIRA M, SATOH C, THORAVAL D, GONZALEZ IL, HANASH SM: Studies of the inheritance of human ribosomal DNA variants detected in two-dimensional separations of genomic restriction fragments. Genetics 144: 307-316, 1996

RP 4-75 NEEL JV, MAJOR EO, AWA AA, GLOVER T, BURGESS A, TRAUB R, CURFMAN B, SATOH C: Hypothesis: "Rogue cell"-type chromosomal damage in lymphocytes is associated with infection with the JC human polyoma virus and has implications for oncogenesis. Proc. Natl. Acad. Sci. USA 93: 2690-2695, 1996

RP 7-85 SATOH C, KODAIRA M: Effects of radiation on children. Nature 383: 226, 1996

RP 7-85 SATOH C, TAKAHASHI N: Denaturing gradient gel electrophroesis of DNA fragments attached with a GC-clamp. In *The Frontier in the PCR.* Special issue of Protein, Nucleic Acid and Enzyme 41 (Suppl.), 556-560, 1996 (in Japanese)

RP 7-85 SATOH C, TAKAHASHI N, ASAKAWA J, KODIARA M, KUICK R, HANASH SM, NEEL JV: Genetic analysis of children of atomic bomb survivors. Environ. Health Perspect. 104 (Suppl. 3), 511-519, 1996

RP 7-85 SATOH C, YASUNAGA K, MIURA A: Effects of atomic bomb radiation on genetic instability of microsatellites in human germ cells. J. Hiroshima Med. Assoc. 49: 423-426, 1996 (in Japanese)

RP 7-85 TAKAHASHI N, KANEKO J, SATOH C: Quantitative analysis of bands on a Southern filter using nonradioisotope (digoxigenin)-labeled probes. J. Hiroshima Med. Assoc. 49: 448-450, 1996 (in Japanese)

RP 7-85 TAKAHASHI N, SATOH C, ASAKAWA J, KODAIRA M: Monitoring of germ line mutations in A-bomb survivors by DNA-level examination of their children. Environ. Mut. Res. Commun., 17: 301-306, 1996 (in Japanese)

RP 7-85 THORAVAL D, ASAKAWA J, KODAIRA M, CHANG C, RADANY E, KUICK R, LAMB B, RICHARDSON B, NEEL JV, GLOVER T, HANASH SM: A methylated human 9-kb repetitive sequence on acrocentric

chromosomes is homologous to a subtelomeric repeat in chimpanzees. Proc. Natl. Acad. Sci. USA 93: 4442-4447, 1996

RP 7-85 THORAVAL D, ASAKAWA J, WIMMER K, KUICK R, LAMB B, RICHARDSON B, AMBROS P, GLOVER T, HANASH S: Demethylation of repetitive DNA sequences in neuroblastoma. Genes Chromosomes Cancer 17: 234-244, 1996

RP 7-85 WIMMER K, THORAVAL D, ASAKAWA J, KUICK R, KODAIRA M, LAMB B, FAWCETT J, GLOVER T, CRAM S, HANASH S: Two-dimensional separation and cloning of chromosome 1 *Not*I-*Eco*RV-derived genomic fragments. Genomics 38: 124-132, 1996

Department of Radiobiology

The Department of Radiobiology came into existence in August 1985 at the time of the reorganization of the Foundation's Department of Pathology. The primary objectives of the department are to determine the late effects of exposure to ionizing radiation on immune system function, on somatic cell mutation and altered gene expression; on cell survival and transformation; and to maintain serum and tissue resources for epidemiological, histo-pathological, and radiobiological investigations.

Program objectives

The survivors of the atomic bombings represent a population of individuals who have been exposed to a wide range of doses of ionizing radiation; therefore, the primary objective of RERF has been to ascertain the effects that might have been produced in the exposed individuals and their children as a result of exposure to A-bomb radiation, and to relate these changes to dose and to the subsequent health effects which may have occurred. Consequently, until recently, research at RERF has focused primarily on the long-term epidemiological studies of A-bomb survivors to ascertain morbidity and mortality of the exposed population, specific investigations on health-related effects that might be related to radiation exposure, and genetic studies to ascertain the mutation rate resulting from radiation exposure in the children of the survivors but clearly there is a need for molecular and cellular studies aimed at revealing the underlying bases of this morbidity and mortality. It is thus important to bear in mind that if the Foundation is to achieve its goals it must necessarily maintain a balance between mechanistic studies aimed at understanding the biological bases of radiation-induced changes and the statistical description of risk. It behooves the Foundation, therefore, to establish a credible and strong program in molecular and cellular research if the biological origin of radiation-related damage is to be understood.

Accordingly, the mission of the Department of Radiobiology is to study the molecular mechanisms of radiation-induced carcinogenesis in A-bomb survivors. We also believe that it is our mission to clarify what the biological effects of radiation are on human health and why and how disease is induced as a consequent process.

RP 7-93 Molecular analysis of thyroid cancers among atomic bomb survivors
Hamatani K, Seyama T, Mizuno T, Iwamoto KS, Suzuki T, Nobuyoshi M, Shimizu Y, Tokuoka S, Mabuchi K

Recent studies have shown that a fraction of thyroid cancer contains a dominantly acting RET oncogene. We have found and published, that rearrangement to the activated form of the RET oncogene is possible in cell lines X-irradiated in vitro. The present study tests a hypothesis that the increased risk of thyroid cancer among the atomic bomb (A-bomb) survivors is at least partly due to the induction of mutational changes, such as the D10S170-RET rearrangement. In addition, 19 tissue blocks of thyroid cancers of children from areas contaminated by the Chernobyl accident were obtained. The activated RET oncogene was detected in 4 of 7 cases from which RNAs were successfully extracted; a high rate compared with published data. This suggests that some of the thyroid cancers in children from contaminated areas developed as a result of their radiation exposure. About one year is still needed to complete the collection of thyroid cancers for molecular analysis among survivors of the atomic bomb. After preparation of the samples, we will start molecular analyses in the next two years because we have already established the techniques.

RP 3-93 Molecular analysis of skin cancers in atomic bomb survivors
Mizuno T, Iwamoto KS, Kyoizumi S, Seyama T, Fujita Y, Shimizu Y, Tokunaga M, Kishikawa M, Tokuoka S, Mabuchi K

The purpose of this study is to investigate the roles of the ras oncogenes and p53 tumor suppressor gene in skin cancer in atomic bomb survivors. In reports regarding solid tumor incidence in A-bomb survivors, an elevated risk of non-melanoma skin cancer has been noted among the survivors. Furthermore, analysis of histological types suggests that basal cell carcinoma is associated more commonly with radiation than squamous cell carcinoma. It is also well known that skin tumors generally arise in areas of the body exposed to sunlight. However, all areas of the skin of A-bomb survivors should have had an equal chance of being targets for molecular lesions of ionizing radiation. Our general objectives are to identify the mutational changes caused by the A- bomb radiation and differences in the spectra of mutations induced by ionizing radiation and UV-light. All samples to be analyzed in this study have been collected. Several tumors had multiple mutations within exons 5 to 8 of the p53 gene. There appears to be a difference in the mutation spectrum between control and highly-exposed groups. Within the next several months, we project the completion of the mutation analyses of p53 in these cases. And within the forth coming two years, we hope to complete molecular analysis of the ras oncogenes and the entire p53 tumor suppressor gene. In addition to these genes, we will analyze the patched gene.

RP 2-93 Development of an assay for somatic mutation at the locus of the neutrophil Fcγ receptor III gene and preliminary study of atomic-bomb survivors.
Hirai Y, Kusunoki Y, Kyoizumi S, Suzuki T, Seyama T, Fujita S, Kodama K

For the purpose of establishing a new somatic mutation assay system, with molecular analysis capabilities, we developed the neutrophil Fcγ RIII locus

assay, and began to evaluate its suitability for biological dosimetry in A-bomb survivors. The frequency of mutant neutrophils (Mf) lacking expression of the NA1 antigen was measured in appropriately 500 A-bomb survivors. Furthermore, we measured the Mf at the MA 2 locus in about 120 survivors. A technical report will be prepared within FY97.

RP 1-93 Repertoire of T-cell antigen receptors and activity of hematopoietic progenitor cells in peripheral blood of Atomic-bomb survivors
Kusunoki Y, Suzuki T, Hirai Y, Seyama, Kyoizumi S, T, Fujita S, Kodama K

The repertoire of T-cell-receptor (TCR) variable-region (V) genes of mature T cells in the peripheral blood of 1280 A-bomb survivors is being studied by flow cytometry using antibodies against the products of TCR V genes and by T-cell responsiveness to the superantigen staphylococcal enterotoxin. Peripheral-blood progenitor cells are also being measured with flow cytometry and the hematopoietic colony assay. These studies address the late effects of radiation on the generation of T-cell diversity and the production of hematopoietic cells. Approximately 1000 AHS subjects have been examined so far, and statistical analyses are being performed of the stem cell data. Briefly, the number of peripheral blood stem cells is significantly higher in males than in females, and their number decreases with age. Only in females was there a significant increase of the granulocyte stem cells with exposure dose. This finding is consistent with the AHS report that the number of leukocytes increases with dose in females, suggesting that myelopoiesis is promoted in women in the high-dose group. We will prepare several manuscripts in FY97.

RP 7-92 Molecular analysis of the p53 tumor suppressor gene in breast cancers of atomic bomb survivors (with Addendum)
Addendum to RP 7-92: Molecular analysis of Rb, PHB, and other tumor-suppressor genes in breast cancers among atomic-bomb survivors
Seyama T, Hayashi T, Mizuno T, Iwamoto KS, Kyoizuimi S, Tokunaga M , Tokuoka S, Fujita Y, Mabuchi K

There is an increased risk of breast cancer among the A-bomb survivors, especially among those younger than nineteen at the time of the bomb. But to date there is no knowledge about the mutational events that are directly involved in radiation carcinogenesis. The p53 gene and other genes, which include, but are not limited to, Rb, PHB, and BRCA1 will be examined regarding development of breast cancer. We established methods to investigate p53 gene alterations, and as soon as the samples become available for these studies we will start the molecular analyses. Currently, arrangements for collection of tissue materials are ongoing. Because many of the breast cancer tissues are preserved at outside hospitals and institutes in Hiroshima and Nagasaki, agreements for the use of materials were concluded between the outside institutes and hospitals and the RERF. After collection of the materials, we will start the molecular analyses.

RP 5-90 Primary liver cancer incidence study among atomic bomb survivors, 1958-87 - molecular analysis of HBV and HCV
Iwamoto KS, Mizuno T, Seyama T, Fujita S, Tokunaga M, Tokuoka S, Fujita Y, Mabuchi K

RP 2-94 Molecular analysis of hepatocellular carcinoma among atomic bomb survivors
Iwamoto KS, Mizuno T, Seyama T, Tokunaga M, Tokuoka S, Fukuhara T, Yamamoto M, Itakura H, Ikeda T, Fujita Y, Mabuchi K

RP's 5-90, 2-92, and 2-94 are parts of the liver cancer study series being conducted on the atomic bomb survivors at the foundation. The particular role of the Dept. of Radiobiology (RP's 5-90 and 2-94) is the molecular analysis of the liver tissue with relation to hepatitis viruses B and C, and various tumor suppressor genes, especially p53. We have almost completed the extraction and isolation of DNA and RNA from some 800 paraffin-embedded tissues. Loss of heterozygosity analyses of the p53, RB, APC, and Mcc tumor supressor genes are completed. Sequencing of the four hot-spot exons of p53 is nearly complete. Our objectives for the next two years are the completion of analysis for HCV infection and the sequencing of the remaining six exons of p53. In addition we will continue our efforts to collect more samples. Hopefully some trends in p53 mutations (the existence of and the spectra of) and HBV (with HVC by the next two years) with regard to exposure status, sex, city, ATB, HCC grade, etc. will become evident within the next year.

RP 4-90 Establishment of a method for HLA-DQ and DP gene typing using the polymerase chain reaction.
Hayashi T, Kusunoki Y, Hirai Y, Kyoizumi S, Seyama T, Kodama K
The objectives of this study are to establish a method of human leukocyte antigen (HLA) genotyping at RERF, and to test for a possible population bias among the A-bomb survivors on the assumption that some people's ability to survive might have differed from that of others during the period of reduced immune function after the A-bombing. HLA-DQA1 and DRB1 genotyping methods have been established. DNA samples of 1018 A-bomb survivors in Hiroshima were analyzed by these genotyping methods. The statistical analyses of the results have been finished. A manuscript describing a possible population bias among high-dose A-bomb survivors in the frequency of the HLA type is currently in press. (Health Physics)

RP 2-90 Cryopreservation of blood cells from Hiroshima and Nagasaki AHS participants.
Hirai Y, Kusunoki Y, Hamatani K, Ban S, Kyoizumi S, Seyama T, Kodama K, Akahoshi M

The present total number of survivors whose lymphocytes were preserved is approximately 15,000. The effects of A-bomb radiation have been studied in these cells for various endpoints. The analytic techniques have continuously improved over time. We expect that studies of hithero unmeasurable effects will become possible in the future. Because, A-bomb survivors are reaching advanced ages we proposed to cryopreserve live blood cells from all AHS participants in order to have an available source of material for future studies.

We will continue to cryopreserve blood cells from 411 AHS participants from whom less than two vials have been stored. The blood from about 4000 AHS participants has not yet been collected due to various reasons. It is desirable to establish some way to resolve this problem.

RP 11-89 A pilot study for detection of somatic mutations at the HLA-A locus in lymphocytes .
Kusunoki Y, Hayashi T, Hirai Y, Suzuki T, Kyoizumi S, Seyama T

We have studied human somatic mutations using, as markers, five different gene loci: GPA in erythrocytes, HPRT, TCR, and HLA-A in lymphocytes, and Fcγ RIII in neutrophils. However, we have not yet carried out simultaneous comparative studies of various cells using a single marker. In healthy adults, no difference was detected in the frequencies of mutant HLA T lymphocytes, B lymphocytes, and neutrophils. No general trends were noted over the time period sampled and the reproducibility was good. We determined the mutant frequencies of various blood cells from 120 A-bomb survivors. The statistical analysis of the data regarding the late effects of A-bomb radiation on various blood cells with differing cell kinetics will be performed, and a manuscript describing the results will be prepared.

RP 7-89 Screening of stem cell mutation in lymphoid lineage among A-bomb survivors.
Suzuki T, Kusunoki Y, Hirai Y,Seyama T, Kyoizumi S, Kodama K

The purpose of this study is to identify individuals in whom mutations have occurred in hematopoietic stem cells due to the atomic bomb radiation and to elucidate the in vivo kinetics of the mutant stem cells by estimating frequencies of their progenies in different cell lineages. This study was strongly recommended by the Blue Ribbon Panel. Two survivors have so far been identified as such individuals. In one case, mutants bearing the same alteration of the HPRT gene were observed in both T and B cells at a high frequency (10^{-3} - 10^{-4}) and each mutant had a unique pattern of TCR or Ig gene rearrangement. In the other case, the same chromosome aberration was observed in 10% of in vitro colonies from peripheral $CD34^+$ cells as well as T and B cell colonies. This is the first evidence for a chromosome aberration occurring in a multipotent hematopoietic stem cell of an A-bomb survivor. In the next year, we will investigate whether T cells with this chromosome aberration are also observed more frequently in the $CD45RA^+$ naive T cell population than in the memory T cell population. Over the next two years, we will continue the attempt to identify additional persons showing mutations or chromosome aberrations in stem cells and estimate the number of stem cells participating in hematopoiesis and lymphopoiesis in humans.

RP 7-88 Study of somatic mutations at the glycophorin A locus in erythrocytes of atomic bomb survivors.
Kyoizumi S, Hirai Y, Kusunoki Y, Suzuki T, Seyama T, Kodama K

RP 9-89 Detection of erythrocyte mutations at the glycophorin-A locus in Nagasaki survivors and in Hiroshima area poison gas workers
Kyoizumi S, Umeki S, Matsusaka S, Yamakido M

The glycophorin A (GPA) mutation assay does not directly measure the mutations in cancer-associated genes, this assay reflects the probability of mutations of these genes. Recently our findings on about 1200 survivors in Hiroshima and Nagasaki show that the dose response of the deletion type GPA Mf is very similar to that of solid tumor incidence. This indirectly supports the involvement of radiation-induced mutations in human carcinogenesis. (Kyoizumi et al, Radiat. Res, 1996) The molecular analyses of mutant reticulocytes by RT-PCR demonstrated that A-bomb radiation mainly induces non-productive-type mutations in the GPA gene, most probably gene deletion. We will prepare a manuscript describing the molecular analysis and the direct relationship between GPA Mf and cancer risks for about 2000 AHS participants within FY97. The measurements of nearly all MN heterozygotes among Nagasaki AHS participants have been completed. Measurements in a series of poison gas workers who worked at the Ohkunoshima poison gas factory during World War II were finished several years ago. Long-term follow-up of cancer development in survivors whose Mf has already been measured may demonstrate the relationship between radiation-induced somatic mutations and cancer risks.

RP 7-87 X-ray radiosensitivity of lymphocytes in vitro from A-bomb survivors. Part 3: Transformation of B cells by Epstein-Barr virus and their cryopreservation. (Addendum to RP 3.-86).
Hirai Y, Kusunoki Y, Suzuki T, Kyoizumi S, Seyama T

We have begun cryopreservation of lymphocytes and granulocytes as per RP 2-90. For this study, initially, it was proposed to cryopreserve EB virus transformed B cell lines from high dose and control survivors for future studies in cell biology such those dealing with radiosensitivity. But the usefulness of these B cell lines in many other fields including immunological studies has become apparent. To date, cell lines from a total of 807 AHS participants have been cryopreserved for future studies. We will continue EBV-transformation of B cells from the same subjects of RP 2-90.

RP 3-87 Cellular immune function and its relationship to in vitro T-lymphocyte radiosensitivity and MN blood group locus mutation frequency in A-bomb survivors: Precursor frequency analysis of mitogen- and antigen- responsive blood lymphocytes
Kusunoki Y, Kyoizumi S, Hirai Y, Iwamoto KS, Seyama T

The measurements for almost all subjects have been completed. Manuscripts describing the results of the statistical analyses are being prepared. During the course of this study, we found mature T cells with rare phenotypes such as $CD4^-8^-$ and $CD3^-4^+$ T cells. Three articles describing $CD4^-8^-$ T cells in A-bomb survivors have been published. $CD3^-4^+$ cells were found to be mutant T cells lacking T-cell receptor α or_β chains (TCR mutants). Extensive studies have been conducted on radiation-induced in vivo and in vitro TCR mutations, and demonstrated that the TCR mutation assay using flow cytometry is a sensitive indicator of recent radiation exposure and the TCR mutant frequency is highly correlated to the frequency of unstable type

chromosome aberrations, which have been generally used for biodosimetry. Recently, we have improved the TCR mutation assay in order to apply this biodosimeter to victims immediately after radiation exposure accidents (Mutat. Res. in press). The TCR mutation assay has already been applied to a group of individuals in the Chelyabinsk contaminated area, and a significant increase of TCR Mf with estimated cumulative exposure dose was found.

RP 2-86 Collection of surgically removed cancer tissues from A-bomb survivors: Special reference to thyroid and breast cancers
Ban S, Hamatani K, Hirai Y, Mizuno T, Iwamoto KS, Kyoizumi S, Seyama T

This research protocol proposes the collection and cryopreservation in liquid nitrogen of possibly radiation-induced thyroid and breast cancer tissues to be used as a resource for future studies on oncogene and tumor suppression genes. These tissues will also be useful for the preparation of DNA and possibly mRNA for studies of oncogenes and other molecular biological aspects of cancer. The current status of the collection of surgical samples of thyroid and breast cancers in Hiroshima is 41 cases of thyroid cancer (A-bomb (+) = 12, A-bomb (-) = 12, exposure status unknown = 17) and 78 cases of breast cancer (A-bomb (+) = 36, A-bomb (-) = 24, early entrant = 7, exposure status unknown = 7), respectively. The collection of only a small number of specimens does not satisfy the requirements of any study that requires matching of cases and controls. RERF may create a platform research plan for molecular epidemiology through close collaboration with City and Prefectural Medical Associations to call attention to pathologists that the survivors' specimens are a common heritage of Hiroshima and Nagasaki. We should emphasize that such a collaboration will be essential to garner financial support as is done for the Tumor and Tissue Registry.

RP 18-81 Pathophysiology and radiation response of human thyroid cells in culture and in grafts in athymic Nu/Nu mice
Kyoizumi S, Nobuyoshi M, Suzuki T, Kusunoki Y, Mizuno T, Seyama T.

The radiobiological study of humans has been hampered by a lack of suitable in vivo experimental models. To overcome this limitation, we have attempted to create models using small animals that maintain human normal tissues with their active functions. This project originally sought to implant human thyroid tissues into athymic nude mice, but recently severe combined immunodeficient mice (SCID mice) were found to be better recipients, i.e., the success rate of human tissue implantation is much higher in SCID mice than nude mice. Thus, SCID mouse-human chimeras (SCID-hu mice) can be used not only for human thyroid tissue but also various human epithelial and hematolymphoid tissues. We demonstrated the usefulness of a SCID-hu skin model for the study of radiation-induced human epilation and a SCID-hu cord blood model for human hematopoiesis. Furthermore, for the thyroid model we showed radiation-induced mutagenesis in cancer-associated genes such as RET oncogene activation, which is believed to be one of the gene alterations specific for thyroid carcinogenesis. These approaches will clarify the

molecular mechanisms of human radiation carcinogenesis, which have not been clear from studies on the survivors.

Publications (1997)

RP 4-90 HAYASHI T, DELONGCHAMP RR, KUSUNOKI Y, SEYAMA T, KYOIZUMI S, HIRAI Y, ITO T, FUJITA S, NAKAMURA N, AKIYAMA M: Evaluation of population bias among high-dose atomic-bomb survivors in the frequencies of HLA-DQA1 allele and DR antigen types. Health Physics in press

RP 3-87 ISHIOKA N, KYOIZUMI S, UMEKI S, HIRAI Y, AKIYAMA M, KODAMA T, OHAMA K: Early detection of in vivo T-cell receptor mutations induced by radiation exposure. Mutat. Res. in press

RP 3-87 UMEKI S, SUZUKI T, KUSUNOKI Y, SEYAMA T, FUJITA S, KYOIZUMI S: Development of a mouse model for studying in vivo T-cell receptor gene mutations. Mutat. Res. in press

RP 2-94 IWAMOTO KS, MIZUNO T, KURAT A, MASUZAWA M, MORI T, SEYAMA T: Molecular analysis of the p53 gene in four primary cancers from a man who received thorotrast. New England Journal of Medicine submitted

RP 3-93
RP 2-94 SUYAMA N, IDE T, NODA A, IWAMOTO KS, MIZUNO T, KYOIZUMI S, SEYAMA T: X-rays induce dose-dependent and cell cycle-independent accumulation of $p21^{sdel/WAF1}$. Cancer Res. submitted

RP 7-93 MIZUNO T, KYOIZUMI S, SUZUKI T, IWAMOTO KS, SEYAMA T: Continued expression of a tissue specific activated oncogene in the early steps of radiation-induced human thyroid carcinogenesis. Oncogene submitted

RP 18-81 KYOIZUMI S, SUZUKI T, TERAOKA S, SEYAMA T: Radiation sensitivity of human hair follicle in SCID-hu mice. MS approved

RP 3-87
RP 1-93 UMEKI S, KUSUNOKI Y, COLOGNE JB, IWAMOTO KS, HIRAI Y, SEYAMA T, OHAMA K, KYOIZUMI S: Lifespan of human memory T-cells in the absence of antigenic stimuli mediated by T-cell receptor. MS approved

RP 7-88 VICKERS M, KYOIZUMI S: Determination of human hemopoietic stem cell number and mutation rate from single locus mutant frequencies. Submitted to SRRC

RP 3-87 KUSUNOKI Y, MORISHITA Y, MAKI M, KYOIZUI S, HIRAI Y, AKIYAMA M, KODAMA K: Effects of atomic-bomb radiation on human immune responses (12) Analysis of T cell function using the limiting dilution analysis. Nagasaki Igakkai Zassi [Nagasaki Med J] 71:218-223, 1997 (Japanese)

RP 3-92
RP 3-93
RP 7-93

IWAMOTO KS, MIZUNO T, ITO T, AKIYAMA M, TAKEICHI N, MABUCHI K, SEYAMA T: The feasibility of using decades-old archival tissues in molecular oncology/epidemiology. Nagasaki Igakkai Zassi [Nagasaki Med J] 71:224-229, 1997 (Japanese)

RP 7-89
RP 1-93

SUZUKI T, KYOIZUMI S, SAITO M, YAMAOKA M, HIRAI Y, KUSUNOKI Y, KODAMA K: Analysis of hematopoietic stem cells in peripheral blood of Atomic -bomb survivors. Nagasaki Igakkai Zassi [Nagasaki Med J] 71:200-204, 1997 (Japanese)

Publications (1996)

RP 7-88
RP 9-89

KYOIZUMI S, AKIYAMA M, COLOGNE JB, TANABE K, NAKAMURA N, AWA AA, HIRAI Y, KUSUNOKI Y, UMEKI S: Somatic cell mutations at the glycophorin A locus in erythrocytes of atomic-bomb survivors: Implications for radiation carcinogenesis. Radiat. Res. 146:43-52, 1996

RP 2-94
RP 3-93

IWAMOTO KS, MIZUNO T, ITO T, AKIYAMA M, TAKEICHI N, MABUCHI K, SEYAMA T: The feasibility of using decades-old archival tissues in molecular oncology/epidemiology. American J. of Pathology 149:399-406, 1996

RP 7-88
RP 9-89

AKIYAMA M, KYOIZUMI S, KUSUNOKI Y, HIRAI Y, TANABE K, COLOGNE JB: Monitoring exposure to atomic bomb radiation by somatic mutation. Environmental Health Perspectives 104:493-496, 1996

RP 7-91

ARAKI R, ITOH M, HAMATANI K, ABE M: Normal D-J_H rearranged products of the IgH gene in SCID mouse bone marrow. International Immunology 8:1045-1053, 1996

RP 3-87

IWAMOTO KS, MIZUNO T, ITO T, TSUYAMA N, KYOIZUMI S, SEYAMA T: Gain-of-function p53 mutations enhance alteration of the T-cell receptor following X-irradiation, independently of the cell cycle and cell survival. Cancer Res. 56:3862-3865, 1996

RP 7-91

ARAKI R, KAKU M, ITOH M, HAMATANI K, USUI T, ABE M: Recombination activating gene (RAG)-1 and 2 encoding proteins expressed by the baculovirus system. Acta Med. Nagasaki 41:43-47, 1996

RP 3-87

KYOIZUMI S: Characteristics and kinetics of mutant T cells lacking T-cell receptor expression. Inflamation and Immunology 4:33-41, 1996 (Japanese)

RP 3-87

SUZUKI T, KYOIZUMI S, UMEKI S, AKIYAMA M, AIZAWA S: T-cell receptor gene mutations in p53 gene deficient mice. Hiroshima Igaku 49:468-470, 1996 (Japanese)

RP 2-93 TAKAHASHI K, HIRAI Y, KITAHIRA M, ISHIOKA N, KUSUNOKI Y, KYOIZUMI S, AKIYAMA M: Development of a novel assay system to detect somatic mutations using neutrophils and a study of atomic bomb survivors. Hiroshima Igaku 49:434-436, 1996 (Japanese)

RP 2-94 TSUYAMA N, SEYAMA T, IWAMOTO KS, MIZUNO T, AKIYAMA M: Mechanism of sdi1/WAF1 gene induction by ionizing radiation. Hiroshima Igaku 49:451-454, 1996 (Japanese)

RP 3-87 ISHIOKA N, KYOIZUMI S, UMEKI S, HIRAI Y, SUZUKI T, KODAMA T, OHAMA K, AKIYAMA M: Early detection of in vivo T-cell receptor mutations induced by radiation exposure. Hiroshima Igaku 49:437-440, 1996 (Japanese)

Information Technology Department

For about two years since the transition to the distributed processing system centering workstations, the Department of Information Technology (ITD) has worked on various tasks such as the addition and updating of computer resources, application of the Internet and Intranet, expansion and improvement of the network environment, database development and management, upgrading and improvement of research and business software packages, shifting to a new AHS Examination Control System, supporting DS-86 computing, user training, and computerization of library information.

ITD's goal in FY96 was to provide more advanced computer service to users. The task of shifting from the previous host-computer environment to the distributed computer environment centered on workstations has almost been completed, and now specific environments have to be upgraded to meet the needs of users. What first needed to be done to establish computer use at RERF and to make more profitable and timely use of information was to improve as much as possible the environment for use by users, that is, to increase the number of personal computers (PCs) connected to the network. Further, to minimize application errors related to the management of memory on Windows 3.1, it was also necessary to shift to Windows 95, to upgrade the hardware and software resources necessary for this, and to convert the application software developed on Windows 3.1. Fortunately the budget enabling us to upgrade the hardware and software resources to Windows 95 has been secured in FY96, and all PCs at RERF will be upgraded to Windows 95 by May 1997.

ITD has also worked on dividing the network built at RERF into subnetworks to accommodate the network environment to the increasing number of PCs. The number of users who access RERF's network from places they visit on official business and from their homes has been steadily increasing. To deal with this, the lines for simultaneous access from outside have been increased from four to eight. At the same time, analogue lines were replaced with digital lines to improve the reliability of data communication. By supporting the point to point protocol (PPP), the connection to the RERF network through telephone lines made the same environment available at RERF also available at home or at places visited on official business. Furthermore, we plan to make possible higher-speed access (64-128 Kbps) next fiscal year (possible in part already). However, the above are about the network within RERF. As regards the connection with the outside, troubles in access to and from other

organizations are emerging because the WIDE (academic) line has only one connection point with a commercial line. This is because the academic organizations nationwide, including universities, are concentrated at one connection point. As no dramatic improvement of the situation can be expected in the future, RERF will need to think of a method to directly connect to a commercial line other than the WIDE line.

As the number of the PCs available for users has increased, in addition to the conventional media of hard copies for circulation or transmission of information, a new type of service has been made available for internal use using the World Wide Web (WWW) server. The WWW server is used not only to transmit information but also to download various application formats to PCs, for entering necessary items, and printing documents. Therefore, it is no longer necessary to prepare conventional pre-printed forms, which has eliminated the necessity to stock such pre-printed forms and made it possible to change the contents freely.

The safety of the data should be secured against recently increasing unauthorized access from outside, particularly because RERF keeps valuable data. Because ITD thus far has had to focus on the transition to the new distributed computing system from the host computer, we have not been able to lay stress on, and take actions for, security. However, we intend to give priority to installing firewalls as early as possible next fiscal year. Installation of firewalls will necessitate changing the settings of various servers including the name server as well as installing a proxy server for access from RERF to the outside. All PCs (presently 250) will need to be set up to be connected to the proxy server.

ITD recommends users to use network drives to keep their files safe and when they share a file by section or office. Using a network drive means to using the Unix file system, which stores user files on a hard disk connected to a Unix workstation and automatically backs them up on 8 mm tapes every night. Each of these tapes is used in a cycle of six months, which means that users can retrieve files for the past six months. Recommending users to use the network drives has led to increased use of Unix hard disks and increased the amount of data to be backed up each night. To cope with this, one large-capacity-high-speed hard disk unit will be installed for the Departments of Epidemiology and Statistics and another for users in other departments. ITD also is seeking an efficient means of automating back-up of data.

Although the performance of the workstations used at RERF is only as good as that of a desk top workstation, the features of each have been clearly defined and adjusted to suit their purpose so that a consummate distributed processing system has been established. In the future, RERF should utilize workstations with multi CPU's for further improvement of computing ability and have a network feature that enables high-speed transfer of data between workstations. The present data transfer speed is 10 Mbps, which is not very fast, and ITD plans to construct another network that connects workstations to each other to allow data transfer speed of 100 Mbps. Considerable efforts will be required to construct this new network; however, once it is completed, it will provide us with a remarkably improved data processing ability.

The number of PCs installed at RERF by the end of FY96 reached nearly 200, and the types of software are various. As many other types of hardware as PC are also used and presently debugging software has to be obtained on-line through WWW, Nifty-Serve, etc. This means we have to be alert to gain the latest information on driver and software debugging. That is, even after installation of hardware and software, the time ITD has to spend on user training,

obtaining such information, notifying users of such information, and installation continues to increase. The actual management of PCs/Unix and network is done by only two members of the Systems Administration Unit, and support to users regarding their troubles is mainly provided by these members also. Therefore, some of the system administrators' maintenance duties and duties to introduce the latest technology are performed after closing time. The cumulative intensification of labor caused by shortage of manpower cannot be left unattended any longer. With the removal of the host computer, we need to review our working conditions for system management under the present distributed computer environment centered on workstations, which requires 24-hour operation of machines.

In regard to database management and development, the Index, Master File, and Tumor Registry systems have more or less been established as RERF's main databases, and currently ITD is working on incorporation of autopsy data and Hiroshima therapy data into the Tumor Registry system. As the International Classification for Diseases (ICD) was revised from the 9th to the 10th edition and the Oncology Code from the 1st to the 2nd edition, ITD has started to revise the related systems, such as the tumor, tissue, and mortality information systems.

ITD, in cooperation with the Departments of Statistics and Epidemiology, is working to develop shadow tables for storing records concerning additions, corrections, and deletions of data, which occur in the databases and tables during operation, and for allowing retrieval of the past data. As for the data on in-utero A-bomb survivors, a definition table and database tables have been completed, and construction of a database is proceeding. A database is also being constructed for individuals who have undergone intelligence tests (IQ tests). Definition of the cohorts of the Life Span Study (LSS), F_1, and in-utero survivors has been completed and reflected in their databases. In cooperation with the Departments of Statistics, Epidemiology and Clinical Studies, ITD also is working to develop a definition table and database tables for various examination data and clinical diagnoses (ICD) of the Adult Health Study (AHS). The number of accesses to the main database has vastly increased with the increase in the number of database users, and the load has become too great for one database server. Therefore, a second database server has been installed. One server is used for management work and the other by employees involved in research studies.

The definition table of major RERF databases is loaded on RERF WWW internal home page in an MS-Excel format for users' convenience, and, to make it easier for users to use the databases, ITD is preparing database dictionaries and manuals in cooperation with the Departments of Statistics and Epidemiology. ITD is considering the means for allowing the users to use them.

Recently, a review committee was established to construct databases for each department, and this has made it definite that ITD will have to work on developing databases. However, due to the shortage of staff for preparing specifications, etc. for developing and constructing a system that suits the various activities using databases, implementation of the plan tends to be behind schedule, and complaints are frequently heard from the departments concerned. In addition, daily trouble-shooting takes much time, and this has made the shortage of staff more serious.

The first stage of switching from the old processing method to a new method in the accounting, supply and property, and personnel and pay-roll systems of the Secretariat has

been completed, and computerization in the Secretariat has progressed further.

The AHS Examination Control System has been operating for over 10 years and the machinery used has become markedly decrepit. In addition, the system needed to be adjusted to the system centered on the Unix workstations after the mainframe computer was removed. Construction of a new AHS Examination Control System has begun for operation from July 1 1997.

A Sybase database system will be adopted for the new system, and Windows NT, with which construction of the system is the least expensive, was chosen as the platform. In FY1996, ITD introduced a server personal computer for testing, designed database tables, developed test tables, constructed a system for selecting and testing client software, and introduced personal computers to be used as clients and for laser printers.

Prior to the above, ITD had investigated the operating status of the present system, made an overall design of the new system, and established the standards of design. Other than these, following the replacement of a part of the examination data collection system used under the present AHS Examination Control System with HILAS-CS, which has been introduced at the Division of Clinical Laboratories this year, ITD developed software for connecting the new system with the old one for smoother operation until the new system begins functioning.

Work is proceeding in conjunction with the Department of Statistics to calculate if necessary data are available, new doses as much as possible for those cases that have no DS86 doses calculated for them. ITD is providing support by developing expanded database tables that include F_1 and in-utero survivors data and archive data. ITD has also begun to work on revision of procedures for estimating doses. At present, DS86 doses are calculated through two steps, one using the direct computing program developed at the Science Applications International Corporation (SAIC) and the other using the indirect computing program developed at RERF. The possibility of unifying these programs for automatic retrieval of a series of processes necessary for estimation of doses, and making the system easily adjustable to partial changes, is under consideration.

ITD has continued to provide training courses on the use of PCs which are open to all users in Hiroshima. The training covered the basics of Windows 3.1, courses on the MS-Word from introduction to advanced level, email (Winbiff), introduction to making WWW home pages (HTML), an introductory course on the network, Netscape (WWW browser), intensive courses for managers, etc. About 250 users attended those courses. The operating system for PCs is already shifting to Windows 95, and ITD plans to provide training courses on Windows 95 this fiscal year and next.

As a part of computerization of library information, ITD has introduced a library management system to enable retrieval of information on books and magazines through PCs which has been a pending problem for many years, and is entering library card data so that RERF employees can retrieve data through WWW from the beginning of next fiscal year.

The shortage of technical staff at ITD has become more serious than last year. The situation is worse than ever, with the loss of two Japanese technicians during the past two and a half years, and the resignation of four NAS staff members, including the department chief, by the end of 1996. Furthermore, one employee each is due to retire in June and December, 1997.

If no replacement is employed now or in the future, ITD's capability will substantially deteriorate. The system administrators and database managers will have to spend many hours of their off-duty time to meet research and research-support needs. The situation cannot be left as is.

Audit report, etc.

(This material will be distributed at the meeting)

FY96 settlement of accounts and audit report

Supervisor's Report on Scientific Activities Report

This is to report that as one of the supervisors I have examined the scientific activities of FY1996.

To inspect the scientific activities of the Radiation Effects Research Foundation in FY1996, I visited the Hiroshima Laboratory from 1st to 2nd of May 1997 and reviewed in detail the status of the research activities of both Hiroshima and Nagasaki and also examined related papers.

As a result, I deem the contents of the Scientific Activities Report for FY1996 to be true and correct.

2 May 1997

Radiation Effects Research Foundation

Supervisor Shudo Yamazaki

Shudo Yamazaki

Dr. Itsuzo Shigematsu
Chairman
Radiation Effects Research Foundation

Radiation Effects Research foundation

Settlement of Account (Summary Sheet)

1 April 1996 - 31 March 1997

1. Income

(in yen)

Category	Total	Regular Accoount	Cancer Case LSS SP. A/C	Termination Trust Fund SP. A/C	NAS Housing SP. A/C
Subsidy	3,862,637,941	3,862,637,941	0	0	0
Operational Income (Interest etc.)	71,030,342	65,408,028	4,720	3,907,057	569,013
Transferred from Special Account	0	0	0	0	0
Entrustment fund	205,298,031	0	35,539,000	0	1,224,540
Carried over from Previous year	547,203,272	0	△651,435	542,987,431	1,362,227
Total	4,686,169,586	3,928,045,969	34,892,285	546,894,488	3,155,780

2. Expenditure

Category	Total	Regular Accoount	Cancer Case LSS SP. A/C	Termination Trust Fund SP. A/C	NAS Housing SP. A/C
Personnel Expenses	3,186,147,886	3,076,362,855	9,903,545	72,254,468	0
Operational Expenses	1,043,886,268	850,780,028	25,980,066	0	2,207,731
Total	4,230,034,154	3,927,142,883	35,883,611	72,254,468	2,207,731
Balance, Income Less Expenditure	456,135,432	903,086	△991,326	474,640,020	948,049

Radiation Effects Research foundation

Settlement of Account (Summary Sheet)

1 April 1996 - 31 March 1997

1. Income

(in yen)

Category	Nagasaki Pref. Cancer Regist. SP. A/C	A - Bomb Memorial SP. A/C	Non - Subsidy Expenses SP. A/C	Epi. Study Mayak & Techa riv. SP. A/C	Bias Study EP. Radiation Date SP. A/C
Subsidy	0	0	0	0	0
Operational Income (Interest etc.)	0	9,059	1,122,179	9,653	0
Transferred from Special Account	0	0	0	0	0
Entrustment fund	7,500,000	110,278,000	0	21,855,491	0
Carried over from Previous year	0	0	0	3,505,049	0
Total	7,500,000	110,287,059	1,122,179	25,370,193	0

2. Expenditure

Category	Nagasaki Pref. Cancer Regist. SP. A/C	A - Bomb Memorial SP. A/C	Non - Subsidy Expenses SP. A/C	Epi. Study Mayak & Techa riv. SP. A/C	Bias Study EP. Radiation Date SP. A/C
Personnel Expenses	6,162,345	10,507,380	0	0	0
Operational Expenses	1,337,655	99,779,679	1,122,179	25,152,590	4,000,000
Total	7,500,000	110,287,059	1,122,179	25,152,590	4,000,000
Balance, Income Less Expenditure	0	0	0	217,603	△4,000,000

Radiation Effects Research foundation

Settlement of Account (Summary Sheet)

1 April 1996 - 31 March 1997

1. Income (in yen)

Category	International Exchange Program SP. A/C	Epi. Method for TR System SP. A/C			
Subsidy	0	0			
Operational Income (Interest etc.)	633	0			
Transferred from Special Account	0	0			
Entrustment fund	28,901,000	0			
Carried over from Previous year	0	0			
Total	28,901,633	0			

2. Expenditure

Category	International Exchange Program SP. A/C	Epi. Method for TR System SP. A/C			
Personnel Expenses	0	10,957,293			
Operational Expenses	28,901,633	4,624,707			
Total	28,901,633	15,582,000			
Balance, Income Less Expenditure	0	△15,582,000			

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

I. Regular Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Subsidy Income	(3,470,648,000)	(3,862,637,941)	(△391,989,941)	△ indicates income in excess of budget.
GOJ Treasury	1,735,324,000	2,329,571,000	△594,247,000	
GUS Treasury	1,735,324,000	1,533,066,941*	202,257,059	
Independent Income	(35,838,000)	(65,408,028)	(△29,570,028)	
Medical Exam.	24,200,000	25,226,738	△1,026,738	
Miscellaneous	11,638,000	40,181,290	△28,543,290	
Total, Income (A)	3,506,486,000	3,928,045,969	△421,559,969	

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Personnel Expenses	(2,781,101,000)	(3,076,362,855)	(△295,261,855)	△ indicates expenditure in excess of budget.
Salary	2,753,964,000	2,739,468,925*	14,495,075	
Termination Allw.	27,137,000	336,893,930	△309,756,930	
Operational Expenses	(725,385,000)	(850,780,028)	(△125,395,028)	
Fees & Honorarium	32,626,000	31,322,470	1,303,530	
Trav. Dir. & Staff	19,472,000	14,308,055	5,163,945	
Travel, Committee	7,185,000	7,187,123	△2,123	
Travel, Relocation	14,485,000	11,392,946	3,092,054	
Travel, Overseas	6,452,000	4,799,820	1,652,180	
Office & Lab. Exp.	575,419,000	694,676,399*	△119,257,399	
Rent. Land & Bldgs	52,846,000	52,843,388	2,612	
Maint. & Repair	16,000,000	31,612,800	△15,612,800	
Taxes	900,000	2,637,027	△1,737,027	
Total, Expenditure(B)	3,506,486,000	3,927,142,883	△420,656,883	
Balance, (A) - (B)	0	903,086		FY-1996 Expenses (surplus)

* The subsidy from the GUS Treasury (¥1,533,066,941) includes NAS expenses (¥201,384,941), ¥25,489,710 of which was classified as personnel expenses and ¥175,895,231 as operational expenses.

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

II. Special Account

1. Cancer Case-LSS, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(35,539,000)		
Interest on Deposit		(4,720)		
Carried over from previous year		(△651,435)		
Toatal, Income (A)		34,892,285		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Personnel Expenses		(9,903,545)		
Operational Expenses		(25,980,066)		
Fees & Honorarium		2,202,000		
Trav. Dir. & Staff		558,520		
Travel, Overseas		216,300		
Office & Lab. Exp.		23,003,246		
Total, Expenditure(B)		35,883,611		
Balance, (A) - (B)		△991,326		(Receivale Entrust. Fund)

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

3. Termination Trust Fund, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Interest on Investment		(3,907,057)		
Carried over from previous year		(542,987,431)		
Trust Fund Principal		163,276,218		
Interest on Investment		379,711,213		
Total, Income (A)		546,894,488		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Termination Payouts from Principal		(21,657,684)		
Termination Payouts from Interest		(50,596,784)		
Total, Expenditure(B)		72,254,468		
Balance, (A) - (B)		474,640,020		(to The Next Year)

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

4. NAS Housing Fund, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
NAS Housing Fund		(1,224,540)		
Payment for Utilities by Occupants		(567,609)		
Interest on Deposit		(1,404)		
Carried over from Previous year		(1,362,227)		
Total, Income (A)		3,155,780		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Utilities		(2,207,731)		
Total, Expenditure(B)		2,207,731		
Balance, (A) - (B)		948,049		(Prereceived Entrust. Fund)

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

5. Nagasaki Prefecture Cancer Registration, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(7,500,000)		
Total, Income (A)		7,500,000		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Personnel Expenses		(6,162,345)		
Operational Expenses		(1,337,655)		
Office & Lab. Exp.		1,337,655		
Supply & Materials		370,748		
Print & bindings		228,895		
Freight & Communi.		197,220		
Contract Services		540,792		
Total, Expenditure(B)		7,500,000		
Balance, (A) - (B)		0		

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

6. A-Bomb Memorial, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(110,278,000)		
Interest on Deposit		(9,059)		
Total, Income (A)		110,287,059		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Personnel Expenses		(10,507,380)		
Operational Expenses		(99,779,679)		
Fees & Honorarium		4,706,000		
Traveling Expense		5,167,015		
Lab. & Expenses		89,906,664		
Supply & Materials		5,788,807		
Printing & Binding		1,222,529		
Freight & Communi.		236,833		
Meeting Expenses		839,022		
Contract Service		81,819,473		
Total, Expenditure(B)		110,287,059		
Balance, (A) - (B)		0		

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

7. Non-Subsidy Expenses, Special Account

(in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Interest on Deposit		(1,122,179)		
Total, Income (A)		1,122,179		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Operational Expenses		(1,122,179)		
Fees & Honorarium		82,091		
Supply & Materials		40,750		
Meeting Expenses		489,278		
Employee Welfare		510,060		
Total, Expenditure(B)		1,122,179		
Balance, (A) - (B)		0		

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

8. Epidemiological Studies in Mayak & Techa River, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(21,855,491)		
Interest on Deposit		(9,653)		
Carried over from Previous year		(3,505,049)		
Total, Income (A)		25,370,193		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Operational Expenses		(25,152,590)		
Trav. Dir. & Staff		570,000		
Freight & Communi.		48,252		
Contract Services		24,534,338		
Total, Expenditure(B)		25,152,590		
Balance, (A) - (B)		217,603		(Prereceived Entrust. Fund)

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

9. Bias Study EP. Radiation Data, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(0)		
Total, Income (A)		0		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Operational Expenses		(4,000,000)		
Fees & Honorarium		29,000		
Traveling Expenses		152,800		
Lab. & Expenses		3,818,200		
Supply & Materials		374,332		
Contract service		3,443,868		
Total, Expenditure(B)		4,000,000		
Balance, (A) - (B)		△4,000,000		(Receivale Entrust. Fund)

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

10. International Exchange Program, Special Account (in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(28,901,000)		
Interest on Deposit		(633)		
Total, Income (A)		28,901,633		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Operational Expenses		(28,901,633)		
Fees & Honorraium		673,000		
Trav. Dir. & Staff		22,881,907		
Lab. & Expenses		5,346,726		
Supply & Materials		1,696,892		
Printing & Binding		412,500		
Freight 6 Communi.		680,405		
Meeting Expenses		986,775		
Contract Services		1,570,154		
Total, Expenditure(B)		28,901,633		
Balance, (A) - (B)		0		

Radiation Effects Research Foundation

FY-1996 Statement of Income & Expenditure

1 April 1996 - 31 March 1997

11. EPI Method for TR System, Special Account

(in yen)

Income

Category	Budget a	Settlement b	Balance a - b	Remarks
Entrustment Fund		(0)		
Total, Income (A)		0		

Expenditure

Category	Budget a	Settlement b	Balance a - b	Remarks
Personnel Expenses		(10,957,293)		
Operational Expenses		(4,624,707)		
Trav. Dir. & Staff		1,623,480		
Lab. & Expenses		3,001,227		
Supply & Materials		748,173		
Printing & Binding		120,400		
Contract Services		2,132,654		
Total, Expenditure(B)		15,582,000		
Balance, (A) - (B)		△15,582,000		(Receivable Entrust. Fund)

Radiation Effects Research foundation

Settlement of Account (Summary Sheet)

As of 31 March 1997

1. Assets

(in yen)

Category	Total	Regular Accoount	Cancer Case LSS SP. A/C	Termination Trust Fund SP. A/C	NAS Housing SP. A/C
Current Assets	889,515,048	424,290,156	6,262,154	437,685,781	1,079,022
Fixed Assets	689,182,279	652,228,040	0	36,954,239	0
Total, Assets	1,578,697,327	1,076,518,196	6,262,154	474,640,020	1,079,022

2. Liabilities

Category	Total	Regular Accoount	Cancer Case LSS SP. A/C	Termination Trust Fund SP. A/C	NAS Housing SP. A/C
Current Liabilities	83,613,984	56,074,873	6,262,154	0	1,079,022
Fixed Liabilities	842,855,303	368,215,283	0	474,640,020	0
Total, Liabilities	926,469,287	424,290,156	6,262,154	474,640,020	1,079,022

3. Net Assets

Category	Total	Regular Accoount	Cancer Case LSS SP. A/C	Termination Trust Fund SP. A/C	NAS Housing SP. A/C
Property Funds	652,228,040	652,228,040	0	0	0
Basic fund	0	0	0	0	0
Surplus	0	0	0	0	0
Net Value of property	652,228,040	652,228,040	0	0	0
Total of Liabilities & Net Value of Property	1,578,697,327	1,076,518,196	6,262,154	474,640,020	1,079,022

Radiation Effects Research foundation

Settlement of Account (Summary Sheet)

As of 31 March 1997

1. Assets

(in yen)

Category	Nagasaki Pref. Cancer Regist. SP. A/C	A - Bomb Memorial SP. A/C	Non - Subsidy Expenses SP. A/C	Epi. Study Mayak & Techa riv. SP. A/C	Bias Study EP. Radiation Data SP. A/C
Current Assets	0	0	0	615,935	4,000,000
Fixed Assets	0	0	0	0	0
Total. Assets	0	0	0	615,935	4,000,000

2. Liabilities

Category	Nagasaki Pref. Cancer Regist. SP. A/C	A - Bomb Memorial SP. A/C	Non - Subsidy Expenses SP. A/C	Epi. Study Mayak & Techa riv. SP. A/C	Bias Study EP. Radiation Data SP. A/C
Current Liabilities	0	0	0	615,935	4,000,000
Fixed Liabilities	0	0	0	0	0
Total. Liabilities	0	0	0	615,935	4,000,000

3. Net Assets

Category	Nagasaki Pref. Cancer Regist. SP. A/C	A - Bomb Memorial SP. A/C	Non - Subsidy Expenses SP. A/C	Epi. Study Mayak & Techa riv. SP. A/C	Bias Study EP. Radiation Data SP. A/C
Property Funds	0	0	0	0	0
Basic fund	0	0	0	0	0
Surplus	0	0	0	0	0
Net Value of property	0	0	0	0	0
Total of Liabilities & Net Value of Property	0	0	0	615,935	4,000,000

Radiation Effects Research foundation

Settlement of Account (Summary Sheet)

As of 31 March 1997

1. Assets

(in yen)

Category	International Exchange Program SP. A/C	EPI Method for TR System SP. A/C			
Current Assets	0	15,582,000			
Fixed Assets	0	0			
Total, Assets	0	15,582,000			

2. Liabilities

Category	International Exchange Program SP. A/C	EPI Method for TR System SP. A/C			
Current Liabilities	0	15,582,000			
Fixed Liabilities	0	0			
Total, Liabilities	0	15,582,000			

3. Net Assets

Category	International Exchange Program SP. A/C	EPI Method for TR System SP. A/C			
Property Funds	0	0			
Basic fund	0	0			
Surplus	0	0			
Net Value of property	0	0			
Total of Liabilities & Net Value of Property	0	15,582,000			

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

I. Regular Account

(in yen)

I. Assets		
1. Current Assets		
(1) Cash, Deposit	391,240,958	
(2) Accounts Receivable	3,224,417	
(3) Accounts Prepaid	2,451,322	
(4) Interfund Receivable	26,373,459	
(5) Prepayments	1,000,000	
Total, Current Assets		424,290,156
2. Fixed Assets		
(1) Buildings	212,913,445	
(2) Equipments	439,314,595	
Total, Fixed Assets		652,228,040
Total, Assets		1,076,518,196
II. Liabilities		
1. Current Liabilities		
(1) Account Payable (Regular A/C)	32,702,473	
(2) Salary deductions on Hand	22,469,314	
(3) Balance of Susidy to be returned to GOJ	903,086	
(4) Balance of Susidy to be returned to GUS	0	
Total, Current Liabilities		56,074,873
2. Fixed Liabilities		
(1) Termination Allowance Reserve Fund	368,215,283	
Total, Fixed Liabilities		368,215,283
Total, Liabilities		424,290,156

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

I. Regular Account (in yen)

III. Property Funds		
1. Basic Property (Buildings)	212,913,445	
2. Operating Property (Equipment)	439,314,595	
Total, Property Funds		652,228,040
Total, Liabilities and Property Funds		1,076,518,196

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

II. Special Account

1. Cancer Case-LSS, Special Account

(in yen)

I. Assets		
1. Current Assets		
(1) Cach, Deposit	5,270,828	
(2) Entrust Fund Receivable	991,326	
Total, Current Assets		6,262,154
Total, Assets		6,262,154
II. Liabilities		
1. Current Liabilities		
(1) Interfunds Payable	6,262,154	
Total, Current Liabilities		6,262,154
Total, Liabilities		6,262,154

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

2. Termination Trust Fund, Special Account (in yen)

I. Assets		
1. Current Assets		
(1) Cach, Deposit	437,685,781	
Total, Current Assets		437,685,781
2. Fixed Assets		
(1) Employee Loan Fund	36,954,239	
Total, Fixed Assets		36,954,239
Total, Assets		474,640,020
II. Liabilities		
1. Fixed Liabilities (Termination Allowance Reserve Fund)		
(1) Termination Trust Fund	141,618,534	
(2) Interest on Investment	333,021,486	
Total, Fixed Liabilities		474,640,020
Total, Liabilities		474,640,020

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

3. NAS Housing Fund, Special Account

(in yen)

I. Assets		
1. Current Assets		
(1) Cach, Deposit	1,079,022	
Total, Current Assets		1,079,022
Total, Assets		1,079,022
II. Liabilities		
1. Current Liabilities		
(1) Entrustment Fund Advanced	948,049	
(2) Interfund Payable	130,973	
Total, Current Liabilities		1,079,022
Total, Liabilities		1,079,022

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

4. Nagasaki Pref. Cancer Registration, Special Account (in yen)

I. Assets	
1. Current Assets	
Total, Current Assets	0
Total, Assets	0
II. Liabilities	
1. Current Liabilities	
Total, Current Liabilities	0
Total, Liabilities	0

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

5. A-Bomb Memorial, Special Account (in yen)

I. Assets	
1. Current Assets	
Total, Current Assets	0
Total, Assets	0
II. Liabilities	
1. Current Liabilities	
Total, Current Liabilities	0
Total, Liabilities	0

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

6. Non-Subsidy Expenses, Special Account (in yen)

I. Assets	
1. Current Assets	
Total, Current Assets	0
Total, Assets	0
II. Liabilities	
1. Current Liabilities	
Total, Current Liabilities	0
Total, Liabilities	0

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

7. Epidemiological Studies in Mayak & Techa River, Special Account (in yen)

I. Assets		
1. Current Assets		
(1) Cach, Deposit	615,935	
Total, Current Assets		615,935
Total, Assets		615,935
II. Liabilities		
1. Current Liabilities		
(1) Entrustment Fund Advanced	217,603	
(2) Interfund Payable	398,332	
Total, Current Liabilities		615,935
Total, Liabilities		615,935

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

8. Bias Study EP. Radiation Data, Special Account (in yen)

I. Assets		
1. Current Assets		
(1) Entrust Fund Receivable	4,000,000	
Total, Current Assets		4,000,000
Total, Assets		4,000,000
II. Liabilities		
1. Current Liabilities		
(2) Interfund Payable	4,000,000	
Total, Current Liabilities		4,000,000
Total, Liabilities		4,000,000

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

9. Intenational Exchange Program, Special Account (in yen)

I. Assets	
1. Current Assets	
Total, Current Assets	0
Total, Assets	0
II. Liabilities	
1. Current Liabilities	
Total, Current Liabilities	0
Total, Liabilities	0

Radiation Effects Research Foundation

Balance Sheet as of 31 March 1997

10. EPI Method for TR System, Special Account (in yen)

I. Assets		
1. Current Assets		
(1) Entrust Fund Receivable	15,582,000	
Total, Current Assets		15,582,000
Total, Assets		15,582,000
II. Liabilities		
1. Current Liabilities		
(1) Interfund Payable	15,582,000	
Total, Current Liabilities		15,582,000
Total, Liabilities		15,582,000

Radiation Effects Research Foundation

Inventory of Assets as of 31 March 1997

I. Regular Account (1) (in yen)

I. Assets			
1. Current Assets			
(1) Cash			
Petty Cash - Hiroshima	1,000,000		
Petty cash - Nagasaki	700,000	1,700,000	
(2) Checking Account			
Bank of Tokyo Mitsubishi, Hiroshima-chuou	35,155,684		
18th.Bank, Nagasaki	1,393,274	36,548,958	
(3) Notice Account			
Bank of Tokyo Mitsubishi, Hiroshima-chuou	352,992,000	352,992,000	
(4) Account Receivable			
ABSMTL Income Due, Hirohsima	2,299,292		
ABSMTL Income Due, Nagasaki	708,102		
Advance, Telephone Charges	59,023		
Vending Machine, Coca-Cola	8,000		
Nagasaki Association for Hibakusha Medical Care	150,000	3,224,417	
(5) Prepaid Insurance			
Employment & Labor Accident Ins.	2,451,322	2,451,322	
(6) Interfund Receivable			
Cancer case - LSS SP. A/C	6,262,154		
NAS Housing SP. A/C	130,973		
Bias Study EP. Radiation Data SP. A/C	4,000,000		
EPI Method for TR System SP. A/C	15,582,000		
Epidemiological Studies in Mayak & Techa River SP. A/C	398,332	26,373,459	
(7) Prepayments			
Postage Meter, Hiroshima	800,000		
Postage Prepayment, Nagasaki	200,000	1,000,000	
Total, Current Assets			424,290,156

Radiation Effects Research Foundation

Inventory of Assets as of 31 March 1997

I. Regular Account (2) (in yen)

2. Fixed Assets			
(1) Buildings Structures			
Hiroshima			
Acquisition cost at the beginnig of FY-96 period (At cost)	257,309,074		
Depreciation for the period prior to FY-96	△193,731,960		
Depreciation for FY-96 period	△9,264,039		
Net book value at the end of FY-96 period		54,313,075	
Nagasaki			
Acquisition cost at the beginnig of FY-96 period (At cost)	219,080,593		
Depreciation for the period prior to FY-96	△56,285,063		
Depreciation for the FY-96 period	△4,195,160		
Net book value at the end of FY-96 period		158,600,370	
Total, Hiroshima & Nagasaki		212,913,445	
(2) Equipment			
Acquisition cost at the beginning of FY-96 period (At cost)	1,524,426,558		
Additions during the FY-96 period	107,503,920		
Acquisition by donations during the FY-96 period	2,226,900		
Disposal during the FY-96 period (at cost)	△81,270,232	1,552,887,146	
Depreciation for the period prior to FY-96	△1,085,850,673		
Depreciation for the FY-96 period	△100,643,786		
Accumulated depreciation of disposed items during the FY-96 period	72,921,908	△1,113,572,551	
Net book value at the end of the FY-96 period		439,314,595	
Total, Fixed Assets			652,228,040
Total Assets			1,076,518,196

Radiation Effects Research Foundation

Inventory of Assets as of 31 March 1997

I. Regular Account (3)

(in yen)

II. Liabilities			
1. Current Liabilities			
(Details as per Attached)			
(1) Account Payable			
Regular Account	32,702,473	32,702,473	
(2) Salary Deductions on Hand			
Hiroshima Employees	19,325,087		
Nagasaki Employees	3,144,227	22,469,314	
(3) Balance of Subsidy			
Personnel Fund to be Returned			
Japan	903,086		
U.S.	0	903,086	
Total, Current Liabilities			56,074,873
2. Fixed Liabilities			
(1) Termination Allowance Reserve Fund	368,215,283	368,215,283	
Total, Fixed Liabilities			368,215,283
Total, Liabilities			424,290,156
Property Fund (Buildings & Equipment)			652,228,040

Radiation Effects Research Foundation

Details of Account Payable

As of 31 March 1997

Regular Accout (in yen)

Accout	Amount	Payable to	Remarks
Personnel Expenses			
Part-Time Doctors (Hiro.)	464,000	Hiroshima Employees	March 1997
Health Insurance (Hiro.)	4,449,320	Social Insurance Office	〃
〃 (Naga.)	1,239,594	〃	〃
Welfare Insurance (Hiro.)	8,633,402	〃	〃
〃 (Naga.)	2,556,009	〃	〃
Child Allowance (Hiro.)	109,472	〃	〃
〃 (Naga.)	32,410	〃	〃
Labor Acc. Ins. (Hiro.)	1,856	Hiroshima Employees	〃
Overtime Allowance(Hiro.)	2,654,228	Hiroshima Employees	〃
〃 (Naga.)	272,473	Nagasaki Employees	〃
Salary Career Staff	510,777	Career Staff Office	〃
Oprational Costs			
Fees & Honorarium (Hiro.)	4,520,948	Hiro. Consultants, Others	March 1997
〃 (Naga.)	874,000	Naga. Consultants, Others	〃
Salary (Hiro.)	827,805	Hiro. Temp. Employees	〃
〃 (Naga.)	203,630	Naga. Temp. Employees	〃
〃 (Hiro.)	511,923	Career Staff Office	〃
Consumption Taxes	4,840,626	Regular Account & 7 Special Accounts	FY-96
	32,702,473		

Radiation Effects Research Foundation

Details of Account Payable

As of 31 March 1997

Special Account

(in yen)

Account	Amount	Payable to	Remarks
Bias Study EP. Rad. Data	4,000,000	Regular Account	FY-96
NAS Housing	130,973	〃	〃
Cancer Case - LSS	6,262,154	〃	〃
EPI Method for TR System	15,582,000	〃	〃
Epidemiological Studies in Mayak & Techa River	398,332	〃	〃
	26,373,459		

Radiation Effects Research Foundation

Inventory of Assets as of 31 March 1997

II. Termination Allowance Trust Fund Account (1) (in yen)

I. Assets			
1. Current Assets			
(1) Savings Account			
Bank of Tokyo Mitsubishi, Hiroshima-chuou	11,450,197	11,450,197	
(2) Fixed Account			
Bank of Tokyo Mitsubisi, Hiroshiama-chuou	105,000,000		
Labor Bank, Hiroshima	60,000,000		
Daiwa Security, Hiroshima	11,235,584		
18th Bank, Nagasaki	10,000,000		
Mitsubishi Trust Bank	80,000,000		
Mitsui Trust Bank	80,000,000		
Yasuda Trust Bank	80,000,000	426,235,584	
Total, Current Assets			437,685,781
2. Fixed Assets			
(1) Employee Loan Fund			
Hiroshima Employees	24,650,333		
Nagasaki Employees	12,303,906	36,954,239	
Total, Fixed Assets			36,954,239
Total, Assets			474,640,020
II. Liabilities			
1. Fixed Liabilities			
(1) Termination Allowance Reserve Fund			
Termination Trust Fund	141,618,534		
Interest on Investments	333,021,486		
Total, Fixed Liabilities		474,640,020	
Total, Liabilities			474,640,020

Explanatory Notes on Statements

1. Important accounting policy

(1) Standard and method for appraisal of securities

Cost standard is adopted by the individual method.

(2) Depreciation of fixed assets

Building. fixtures and equipment are depreciated by fixed installment method.

(3) Coverage of funds

Funds include cash, deposits, accounts receivable, accouts payable, prepaid expenses, prepayments, loans to employees, loan fund, securities, salary deductions on hand, repayments of subsidies, and profit from use of retirement allowance trust fund.

(4) The exchange rate in foreign money

Adopt the exchange rate on the settling day.

And current terms are shown in attached table 1 and table 2.

Balance carried forward to the next term Table 1

Regular Account

	FY-95	FY-96
	Balance End of FY-94	Balance End of FY-95
Cash, Deposits	348,689,572	391,240,958
Accounts Receivable	4,061,687	3,224,417
Accounts Prepaid	3,533,689	2,451,322
Interfund Receivable	5,376,084	26,373,459
Prepayments	1,149,940	1,000,000
Total	362,810,972	424,290,156
Accounts payable	25,160,419	32,702,473
Salary Deductions on hand	19,254,319	22,469,314
Termination Allowance Reserve Fund	309,441,686	368,215,283
Subsidy to be returned (Japan) (U.S.A.)	8,954,548 (8,954,548) (0)	903,086 (903,086) (0)
Total	362,810,972	424,290,156

Table 2

Termination Trust fund Special Account

	FY-95	FY-96
	Balance End of FY-94	Balance End of FY-95
(Currne Assets) Cash. Deposits	503, 645, 740	437, 685, 781
(Fixed Assets) Employee Loan Fund Loan Trust	39, 341, 691 0	36, 954, 239 0
Total	542, 987, 431	474, 640, 020
Fixed Liabilities		
Termination Trust Fune	163, 276, 218	141, 618, 534
Interest on Investment	379, 711, 213	333, 021, 486
Total	542, 987, 431	474, 640, 020

2. Increase and decrease in the value of fundamental property and the balance are as follows :

Explanatory notes on fundamental property

Item	Carried over from FY-95	Current Increase	Current Decrease	Carried over to next year
Buildings	226, 372, 644	0	△13, 459, 199	212, 913, 445
Total (Foundation Fund)	226, 372, 644	0	△13, 459, 199	212, 913, 445

3. Explanatory notes on increase and decrease in assets and liabilities

Account of Net Changes in Assets (FY-96)

1 April 1996 - 31 March 1997

(in yen)

Item		Amount	
I. Increase			
1. Increase of assets			
Balance Between Income and Expenditure for the Present Term	903,086		
Equipment purchases (Includes donation)	109,730,820		
Total, Increase		110,633,906	110,633,906
II. Decrease			
1. Decrease of assets			
Depreciation of Buildings	13,459,199		
Depreciation of Equipment	100,643,786		
Removal of Equipment	8,348,324	122,451,309	
2. Increase of Liabilities			
Unused Subsidy to be returned	903,086	903,086	
Total, Decrease			123,354,395
Decrease of Net Assets during the present term			12,720,489
Net Assets brought forward from last term			664,948,529
Total Net Assets at the end of the Term			652,228,040

June 1997

Radiation Effects Research Foundation
Supervisor's Report

The Financial Statements of the Radiation Effects Research Foundation, represented by the Settlement of Accounts, fairly state the financial position and the results of operations for the fiscal year ended 31 March 1997. I have reviewed the monthly financial reports prepared throughout the year by the Foundation's accounting staff. Price Waterhouse, independent public accountants, also conducted an audit of the Foundation's accounts as of 31 March 1997 and have provided me with a draft of their report indicating that the accounts are in good order. A copy of the final Price Waterhouse audit report will be provided to any of the Foundation's Directors upon request.

In addition to reporting on the direct research activities of the Foundation covered by the Act of Endowment, the auditors provided a summary report on other related activities whose financial accounting is performed by the staff of the Foundation.

Accrual Basis Adjustments and Reclassification

The Foundation's financial records are maintained on a cash basis in accordance with Accounting and reporting conventions generally accepted in Japan. The financial report prepared by Price Waterhouse is stated on an accrual basis in accordance with Accounting and reporting conventions general accepted in the United States. Three significant items of accrued income or expense, i.e. activities for which liabilities have been incurred or income that has been earned but which are not yet reflected on the Foundation's books, are contained in the auditor's report:

1. Unfunded portion of the Termination Allowance Liability (Net after reduction accrued interest, #3 below)	¥2,926,799,000
2. Seasonal allowances payable in June, 1997 which were earned during the period December 1, 1996 to March 31, 1997	¥232,000,000
3. Accrued interest income from investments of the Termination Trust Fund (See #1 above)	¥1,698,000

Of these three items, #2 and #3 will be recorded on the Foundation's accounts in the normal course of events during the current fiscal year. However, the unfunded termination liability continues to be calculated each year but does not appear on the Foundation's accounts. The current unfunded liability (#1 above) represents a ¥25,000,000 increase (1%) compared to the liability one year earlier.

Both governments need to be fully cognizant of this liability to pay Termination Allowance that has already been earned by the employees but for which no funds are currently set aside.

One major reclassification has been made between the Foundation's records and the accrual basis statements. The Foundation recorded the expenditures of the Academy in support of RERF in its records and reports as Personnel and Operational Expenses. Price Waterhouse has reclassified these costs as Contributed Services in accordance with reporting standards generally accepted in the United States.

Termination Liability

The Secretariat staff regularly makes a five-year projection of the termination liability and the most recent projection in graph form is attached. The liability increases that were the pattern in many previous year has now been broken and it appears that after a significant decline in fiscal year 1997 the Foundation can look forward to stable or even a declining liability for unfunded Termination Allowance expenses.

Looking back five years the unfunded liability has decreased from over ¥3.2 billion at the end of FY93 to about ¥2.9 billion a the end of 1997. Looking ahead five years, the latest projection indicates the liability will eventually decline to about ¥2.5 billion at the end of FY 2001.

The projection estimates only take into account known terminations due to compulsory age retirement. Since there are always some additional voluntary retirements, and if these positions are only partially replaced the liability may be expected to decline to a somewhat lower level than now projected. However, these voluntary retirements will result in an increase to personnel costs at the time Termination Allowance payments are made.

The current unfunded liability in U.S. dollars for termination payments totals about $23,400,000 using 31 March 1997 exchange rates (¥125 per $1.00), a decrease of about $4,000,000 (15%) during the past year.

A-122 Audit

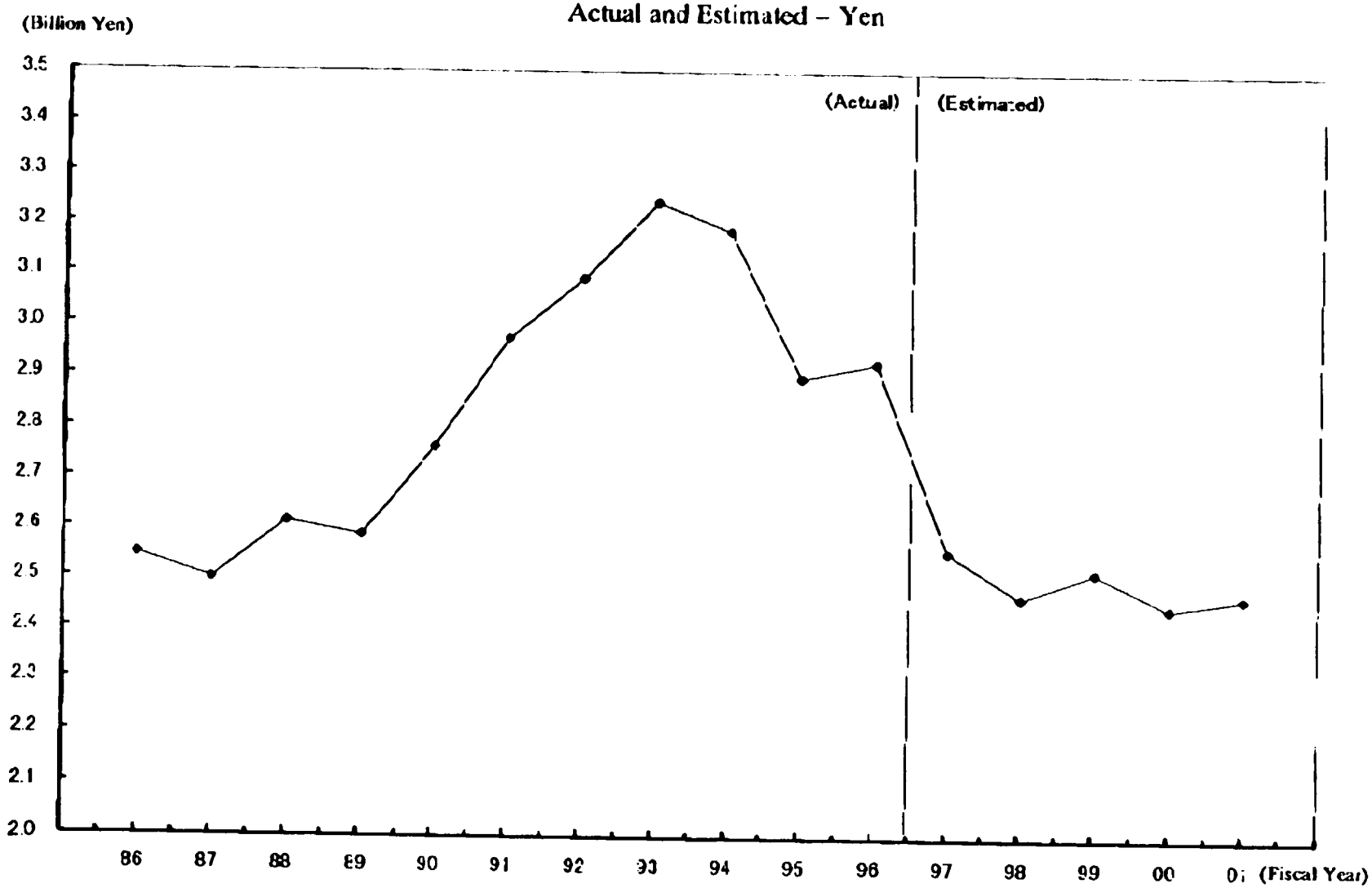
This audit is made to comply with U.S. government regulations concerning "allowable" costs. This was accomplished by the Secretariat conducting an internal audit for the nine months April through December, 1996 using U.S. government regulations as a guide that involved close cooperation with the Office of Internal Audit of the NAS. This internal audit indicated that no unallowable costs were incurred during this period using subsidy funds provided by the Japanese and U.S. governments.

I would like to thank the staff of the Secretariat for their assistance to representatives of Price Waterhouse and to me during the audit of the Foundation's financial records.

David Williams
Supervisor

RERF SHARE – TERMINATION LIABILITY

Actual and Estimated – Yen



Supervisor's Report

This is to certify that we have reviewed the Scientific Activities Report and Settlement of Accounts Report for FY1996 and have found them to be fairly stated.

11 June 1997

Radiation Effects Research Foundation

Supervisor _____
David Williams

Supervisor _____
Syudo Yamazaki

Dr. Itsuzo Shigematsu
Chairman
Radiation Effects Research Foundation

Audit report

(This material will be distributed at the meeting)

FY97 working budget

Revised Format

FY-97's Working Budget (draft)

(UNIT: ¥1,000)

ITEM	FY-96 WORKING BUDGET	FY-96 SETTLEMENT EXPENSES	FY-97 BOARD APPROVED BUDGET (1)	FY-97 WORKING BUDGET (DRAFT) (2)	FY-97 DIFFERENCE (2) minus (1)
(INCOME)					
I. INDEPENDENT INCOME	35,838	65,408	35,838	34,382	-1,456
HEALTH EXAMINATION INCOME	24,200	25,227	24,200	22,744	-1,456
MISCELLANEOUS INCOME	11,638	40,181	11,638	11,638	0
II. SUBSIDY INCOME	3,470,648	3,861,735	4,242,826	4,040,207	-202,619
1.FUND FROM JP GOV'T	1,735,324	2,328,668	2,121,413	2,519,255	397,842
2.FUND FROM US GOV'T	1,735,324	1,533,067	2,121,413	1,520,952	-600,461
TOTAL INCOME (I + II)	3,506,486	3,927,143	4,278,664	4,074,589	-204,075
(EXPENDITURES)					0
I. PERSONNEL COST	2,781,101	3,076,363	3,460,592	3,271,083	-189,509
1.SALARIES	2,753,964	2,739,469	2,669,651	2,871,035	201,384
2.TERMINATION ALLOWANCE	27,137	336,894	790,941	400,048	-390,893
II. OPERATIONAL COST	725,385	850,780	818,072	803,507	-14,565
1.FEES & HONORARIAM	32,626	31,322	32,626	32,626	0
2.TRAVEL,DIR. & STAFF	19,472	14,308	19,472	19,472	0
3.TRAVEL,COMMITTEES	7,185	7,187	7,185	10,198	3,013
4.TRAVEL,RELOCATION	14,485	11,393	14,485	12,500	-1,985
5.TRAVEL,OVERSEAS	6,452	4,800	6,452	14,146	7,694
6.LABORATORY EXPENSE	575,419	694,676	644,106	615,372	-28,734
(1)EQUIPMENT	51,808	108,716	116,000	116,000	0
(2)LAB. & OFFICE SUPPLIES	142,803	129,576	165,000	115,349	-49,651
(3)PRINTING & BOOKBINDING	16,682	13,458	16,682	16,682	0
(4)COMMUNICATION	26,117	24,456	26,117	26,117	0
(5)UTILITIES	53,570	48,739	53,570	53,570	0
(6)RENTALS	70,039	65,792	70,039	62,963	-7,076
(7)MEETING EXPENSES	1,588	1,170	1,588	1,588	0
(8)SALARY (TEMP.EMP.)	10,500	11,521	10,500	12,000	1,500
(9)INSURANCE	2,438	2,426	2,438	2,508	70
(10)CONTRACT SERVICES	193,874	284,046	176,172	202,285	26,113
(11)EMPLOYEE WELFARE	6,000	4,776	6,000	6,310	310
7.RENT LAND/BUILDINGS	52,846	52,844	52,846	57,693	4,847
8.PLANT MAINTENANCE	16,000	31,613	40,000	40,000	0
9.TAXES	900	2,637	900	1,500	600
TOTAL EXPENDITURES (I + II)	3,506,486	3,927,143	4,278,664	4,074,590	-204,074

* NAS expenditure of ¥201,384 is included into the personnel expenses.

FY-97 WORKING BUDGET PLAN (DRAFT)

(UNIT:¥1,000)

ITEM	(1) FY-96 SETTLEMENT EXPENSES	(2) FY-97 BOARD MEETING APPROVED BUDGET	FY-97 WORKING BUDGET	DETAILS		
I . PERSONNEL COSTS	3,076,363	3,460,592	3,271,083	BUDGETED POSITIONS		
1. SALARIES	2,739,469	2,669,651	2,871,035		(97/4/1)	
(1)BASE PAY	1,545,339	1,518,893	1,750,277	DIRECTORS	3	
(2)ALLOWANCES	912,731	871,743	871,743	CHIEF OF SECRETARIAT	1	
(3)OVERTIME	21,464	20,274	20,274	PROFESSIONAL STAFF	48	
(4)SOCIAL INSURANCE	259,935	258,741	228,741	GENERAL STAFF	260	
				GRAND TOTAL	312	
2. TERM. ALLOWANCE	336,894	790,941	400,048			
II . OPERATIONAL COSTS	850,780	818,072	803,506			
1 . FEES & HONORARIUM	31,322	32,626	32,626			
(1)COMMITTEE FEES	1,609	1,728	1,798			
				A.BOARD OF DIRECTORS MEETING (AT HIROSHIM/		1,798
				1.VISITING DIRECTORS		
				¥ 32,000 X 3 DAYS X 6 PRS=	576	
				2.SUPERVISORS		
				¥ 32,000 X 3 DAYS X 2 PRS=	192	
				¥ 32,000 X 5 DAYS X 1 PRS=	160	
				3.SCIENTIFIC COUNCILORS' MEETING		
				¥ 29,000 X 3 DAYS X 10 PRS=	870	
(2)FEES FOR PART-TIME	24,515	25,296	25,296			
PHYSICIANS AND						25,296
COUSULTANTS				A.PART-TIME PHYSICIANS		
				¥29,000	23,318	
				B.CONSULTANTS		
				¥26,000	1,978	
(3)GRATUITIES FOR	5,198	5,532	5,532			
PARTICIPANTS						5,5
				A.GRATUITIES TO STUDY PARTICIPANTS	4,882	
				B.TISSUE REGISTRY PROGRAM		
					150	
				C.AUTOPSY		
				50 SPECIMENS/YEAR	500	

FY-97 WORKING BUDGET PLAN (DRAFT)

(UNIT:¥1,000)

ITEM	(1) FY-96 SETTLEMENT EXPENSES	(2) FY-97 BOARD MEETING APPROVED BUDGET	FY-97 WORKING BUDGET	DETAILS		
2. TRAVEL. DIRECTORS & STAFF (DOMESTIC)	14,308	19,472	19,472			
(1)SCIENTIFIC MEETINGS	4,893	6,831	6,831			
						6,831
				A.PROFESSIONAL STAFF	5,044	
				B.TECHNICAL STAFF	1,787	
(2)TRAINING	2,007	2,000	2,000			
						2,000
(3)RESEARCH COORDINATION	4,830	7,000	7,000			
						7,000
(4)ADMINISTRATIVE CONTACT	2,578	3,641	3,641			
						3,641
3. TRAVEL, COMMITTEE	7,187	7,185	10,197			
						10,197
				A. BOARD OF DIRECTORS MEETING (AT HIROSHIMA)		
					3,834	
				JAPAN		
				¥ 692,400 X 4 PRS= 2,770		
				USA		
				¥ 266,000 X 4 PRS= 1,064		
				B. SCIENTIFIC COUNCILORS' MEETING (AT HIROSHIMA)		
					3,266	
				JAPAN		
				¥ 105,900 X 5 PRS= 530		
				USA		
				¥ 547,200 X 5 PRS= 2,736		
				C.SUPERVISORS		
					1,200	
				JAPAN		
				¥ 105,800 X 1 TIMES X 1 PRS= 106		
				USA		
				¥ 547,200 X 2 TIMES X 1 PRS= 1,094		
				D.OBSERVERS FOR 50TH ANNIV. ABCC/RERF EVENTS		
					1,898	
				¥ 632,880 X 3 PRS= 1,898		
4. RELOCATION EXPENSES	11,393	14,485	12,500			
				RELOCATION EXPENSES		12,500
				DOMESTIC TRAVEL		
				11 ADULTS AND 2 CHILDREN	9,000	
				HOMELEAVE	1,000	
				OVERSEAS TRAVEL		
				2 ADULTS	385	
				C.OTHERS	2,115	
5. TRAVEL, OVERSEAS	4,800	6,452	14,146			
						14,146
				INTERNATIONAL SCIENTIFIC MEETINGS	6,452	
				THE 50TH ANNIV. OF ABCC/RERF EVENTS		
				¥164,120 × 30 人 =	4,924	
				BOARD MEETING		
				¥307,800 × 9 人 =	2,770	

FY-97 WORKING BUDGET PLAN (DRAFT)

(UNIT:¥1,000)

ITEM	(1) FY-96 SETTLEMENT EXPENSES	(2) FY-97 BOARD MEETING APPROVED BUDGET	FY-97 WORKING BUDGET	DETAILS			
6. LAB.EXPENSES	694,676	644,106	615,372				
(1)EQUIPMENT	108,716	116,000	116,000				
				LABORATORY EQUIPMENT			116,000
				A.RESEARCH EQUIPMENT		48,437	
				B.COMPUTER HARDWARE AND SOFTWA		64,363	
				C.MEDICAL BOOKS		1,200	
				D.OFFICE EQUIPMENT		2,000	
(2)SUPPLIES & MATERIALS	129,576	165,000	115,349				115,349
				A.LABORATORY SUPPLIES		61,985	
				(A)LIQUID NITROGEN	8,554		
				(B)MEDICINES	1,230		
				(C)REAGENT	22,468		
				(D)MISC. RESEARCH SUPPLIES	22,733		
				(E)MAINTENANCE MATERIALS	4,000		
				(F)PRINTING MATERIALS	3,000		
				B.OFFICE SUPPLIES		5,250	
				(A)OFFICE SUPPLIES	2,000		
				(B)MISCELLANEOUS ITEMS	3,250		
				C.JOURNALS & PERIODICALS		11,886	
				(A)ENGLISH AND JAPANESE MEDICAL JOURNALS	9,325		
				(B)OFFICIAL GAZETTE, STATUTE BOOKS,ETC.	1,308		
				(C)NEWSPAPERS & MAGAZINE	1,253		
				D.FUEL OIL		4,400	
				(A) GASOLINE	400		
				(B) FUEL	4,000		
				E.RESERVE		31,828	
(3)PRINTING & BOOKBINDING	13,458	16,682	16,682				16,682
				A.JOURNAL PAGE CHARGES		1,960	
				(A)TECHNICAL REPORTS			
				(B)PAGE CHARGES			
				B.NEWSLETTERS AND ANNUAL REPORT		2,005	
				C.COPY CHARGES		6,917	
				D.PRINTING OF BOOKBINDING INCLUDI PRINTING OF VARIOUS FORMS		5,800	
(4)COMMUNICATION & FREIGHT	24,456	26,117	28,117				28,117
				A.TELEPHONE & TELEGRAM		17,637	
				(A)DOMESTIC	16,168		
				(B)OVERSEAS	1,469		

FY-97 WORKING BUDGET PLAN (DRAFT)

(UNIT:¥1,000)

ITEM	(1) FY-96 SETTLEMENT EXPENSES	(2) FY-97 BOARD MEETING APPROVED BUDGET	FY-97 WORKING BUDGET	DETAILS			
				B.POSTAGE		8,930	
				C.FREIGHT AND PUBLIC TRANSPORTATION		1,550	
(5)UTILITIES	48,739	53,570	53,570				
							53,570
				A.ELECTRICITY		46,000	
				B.WATER		7,000	
				C.GAS		570	
(6)RENTAL & LEASE	65,792	70,039	62,963				
							62,963
				A.TAXI CHARGES		25,555	
				(A)PATIENT TRANSPORTATION	14,355		
				AHS STUDY	13,770		
				BGS STUDY	585		
				(B)PATIENT CONTACTING AND OTHER BUSINESS	11,200		
				B.COPY MACHINE LEASE CHARGES		2,192	
				HIROSHIMA	1,524		
				NAGASAKI	668		
				C.COMPUTEI		694	
				¥ 57,855 X 12 months=	694,260		
				D.TELEPHON AUTO - EXCHANGE SYSTEM AND TERMINAI		3,963	
				¥ 278,460 X 12 months=	3,341,520		
				¥ 51,765 X 12 months=	621,180		
				E.OTHER RENTALS(ALARM EXT.)		1,058	
				CALMIC AIR UNIT			
				CLEAN-MAT			
				PLANT			
				F.RENTED HOUSES FOR NAS PERSONNEL		16,360	
				¥ 170,414 X 8 HOUSES 12 months=	16,359,744		
				G.RENTED HOUSES FOR DIRECTORS		2,400	
				¥ 200,000 X 1 HOUSE X 12 months=	2,400,000		
				H.DIGITAL TELEPHONE		69	
				¥ 5,775 X 12 MONTHS=	69,300		
				I.FREE RADICAL DETECTOR		2,247	
				¥ 187,254 X 12 MONTHS=	2,247,048		

FY-97 WORKING BUDGET PLAN (DRAFT)

(UNIT:¥1,000)

ITEM	(1) FY-96 SETTLEMENT EXPENSES	(2) FY-97 BOARD MEETING APPROVED BUDGET	FY-97 WORKING BUDGET	DETAILS			
				J.PRINTER (EPIDEMIOLOGY)		658	
				¥ 54,796 X 12 MONTHS =	657,552		
				K. DIGITAL MULTIPLE DEVICE		850	
				¥ 70,864 X 12 MONTHS =	850,368		
				L.MULTI SCAN SYSTEM		5,531	
				¥ 460,950 X 12 MONTHS =	5,531,400		
				M.PRINTER (PDC)		715	
				¥ 59,619 X 12 MONTHS =	715,428		
				N.PRINTER (NAGASAKI)		671	
				¥ 55,891 X 12 MONTHS =	670,692		
(7)MEETING EXPENSES	1,170	1,588	1,588				1,588
				A.BOARD OF DIRECTOR'S MEETING		253	
				B.OTHER MEETING		1,335	
(8)SALARY	11,521	10,500	12,000				
							12,000
(9)INSURANCE	2,426	2,438	2,508				
							2,508
				A.AUTOMOBILE INSURANCE		160	
				B.FIRE INSURANCE		2,210	
				C.COMPOSITE CASH INSURANCE		34	
				D.MALPRACTICE RELIABLE INSURANCE		104	
(10)CONTRACT SERVICES	284,046	176,172	200,285				
							200,285
				A.JANITORIAL SERVICE		21,739	
				HIROSHIMA	16,666		
				NAGASAKI	5,073		
				B.KOSEKI CHECK FEES		37,511	
				HIROSHIMA	16,404		
				NAGASAKI	9,065		
				HIROSHIMA (F1)	6,816		
				NAGASAKI (F1)	5,226		
				C.CONTRACT [		3,439	
				HIROSHIMA	2,339		
				NAGASAKI	1,100		
				D.TUMOR AND TISSUE REGISTRY CONTRACT		24,000	
				E.PLANT MAINTENANCE SERVICE		9,000	
				F.MACHINE MAINTENANCE SERVICE		8,500	
				HIROSHIMA	6,000		
				NAGASAKI	2,500		
				G.REPAIR OF EQUIPMENT		9,000	
				H.AUTOMOBILE INSPECTION		300	
				I.VARIOUS HANDLING CHARGES		12,000	
				J.MENBERSHIP AND REGISTRATION FEES		3,200	
				K.CONTRACT TESTS AND EXAMINATIONS		6,103	

FY-97 WORKING BUDGET PLAN (DRAFT)

(UNIT:¥1,000)

ITEM	(1) FY-96 SETTLEMENT EXPENSES	(2) FY-97 BOARD MEETING APPROVED BUDGET	FY-97 WORKING BUDGET	DETAILS		
				L.CONTRACT OPERATE COM.	3,000	
				M.CAREER STAFF	12,000	
				N.OTHERS	1,000	
				O.ANALYZE	5,500	
				P.RESERVE	43,993	
(11)EMPLOYEE WELFARE	4,776	6,000	6,310			6,310
				A.HEALTH CARE FEE	1,600	
				B.WELFARE FEE	1,500	
				C.EVENTS FOR RETIREMENTS AND AWARDI	3,160	
				D.EMPLOYEE'S DINING ROOM EXPENSES	50	
7. RENTAL LAND & BUILDINGS	52,844	52,846	57,693			57,693
				A.RENTAL,HIJIYAMA LAND	20,153	
				B.NAGASAKI LAND(RERF)	5,130	
				C.NAGASAKI BLDG (EDUC ASSOC.)	28,300	
				D.NAGASAKI LAND (EDUC ASSOC)	4,110	
8. PLANT BUILDINGS	31,613	40,000	40,000	PLANT MAINTENANCE & REPAIR		40,000
9. TAXES	2,637	900	1,500			1,500
				A.HIJIYAMA HALL PROPERTY TAX	686	
				B.AUTOMOBILE AND CONSUMPTION TAXES	214	
				C.CONSUMPTION TAXES	600	

Outline of FY98 budget request

This material will be distributed at the meeting

平成10年度 収支予算書
FY-98 BUDGET PLAN

（収入 INCOME）

科目 INCOME ITEM	(1) 平成9年度 予算 FY-97 BUDGET	(2) 平成10年度 予算 FY-98 BUDGET	増△減 INCREASE OR △ DECREASE
1. 財団収入 INDEPENDENT INCOME	34,382	34,382	0
健康診断検診事業収入 HEALTH EXAMINATION FEE	22,744	22,744	0
雑収入 MISCELLANEOUS INCOME	11,638	11,638	0
2. 補助金収入 SUBSIDY INCOM	4,040,208	4,148,124	107,916
日本政府国庫補助金収入 FUNDS FROM JAPANESE GOV'T	2,519,256	2,573,214	53,958
米国政府国庫補助金収入 FUNDS FROM USA GOV'T	1,520,952	1,574,910	53,958
総収入 TOTAL INCOME	4,074,590	4,182,506	107,916

（支出 EXPENDITURES）

（単位：円, Y1,000'S）

科目 EXPENSE ITEM	(1) 平成9年度 予算 FY-97 BUDGET	(2) 平成10年度 予算 FY-98 BUDGET	増△減 INCREASE OR △ DECREASE
1. 人件費 PERSONNEL COSTS	3,271,083	3,356,640	85,557
(1) 役職員給 SALARY	2,871,035	2,913,189	42,154
(2) 退職金 TERMINATION ALLOW.	400,048	443,451	43,403
2. 事業費 OPERATING COSTS	803,507	825,866	22,359
(1) 諸謝金 FEES & GRATITUDE	32,626	32,626	0
(2) 役職員旅費 TRAVEL EXPENSE, DIRECTORS & STAFF	19,472	19,472	0
(3) 委員等旅費 TRAVEL EXPENSE, COMMITTEES	10,198	7,185	△3,013
(4) 赴任旅費 TRAVEL EXPENSE FOR ACCEPTING EMPLOYEES	12,500	14,485	1,985
(5) 外国旅費 OVERSEAS TRAVEL EXPENSE	14,146	6,452	△7,694
(6) 庁費 LABORATORY EXPENSE	615,372	643,452	28,080
(7) 土地建物借料 RENT FOR LAND & BUILDINGS	57,693	60,694	3,001
(8) 各所修繕 PLANT MAINTENANCE	40,000	40,000	0
(9) 税金 TAX	1,500	1,500	0
(10) 国際協力事業費 INTERNAT. COLLAB. PROG.	0	0	0
総支出 TOTAL EXPENDITURES	4,074,590	4,182,506	107,916

平成10年度　予算概算要求書総括表
FY-1998 BUDGET REQUEST

（単価：千円）
(UNIT:¥1,000)

		(1) 平成9年度 実行予算額 FY-97 BUDGET	(2) 平成10年度 既定経費分 FY-98 BUDGET REQUEST	(3) (2)-(1) 増減 INCR. △DECR.	
Ⅰ．人件費	PERSONNEL COSTS	3,271,083	3,356,640	85,557	2.5%
1．役職員給	SALARIES	2,871,035	2,913,189	42,154	1.4%
2．退職金	TERMINATION ALLOWANCE	400,048	443,451	43,403	9.8%
Ⅱ．事業費	OPERATIONAL COSTS	803,507	825,866	22,359	2.7%
1．諸謝金	FEES & HONORARIA	32,626	32,626	0	
委員等謝金	COMMITTEE FEES	1,798	1,798	0	
非常勤医師謝金	PART-TIME DOCTORS	25,296	25,296	0	
研究協力者謝金	GRATUITY TO COOPERATOR	5,532	5,532	0	
2．役職員旅費	TRAVEL, DIR.& STAFF	19,472	19,472	0	
学会旅費	SCIENTIFIC MEETING	6,831	6,831	0	
研究研修旅費	LECTURE AND TRAINING	2,000	2,000	0	
研究連絡旅費	RESEARCH CONTACT	7,000	7,000	0	
事務連絡旅費	ADM. CONTACT	3,641	3,641	0	
3．委員等旅費	COMMITTEE TRAVEL	10,198	7,185	-3,013	
4．赴任旅費	RELOCATION TRAVEL	12,500	14,485	1,985	
5．外国旅費	OVERSEAS TRAVEL	14,146	6,452	-7,694	
6．庁　費	LABORATORY EXPENSES	615,372	643,452	28,080	4.4%
備品費	EQUIPMENT	116,000	71,679	-44,321	△61.8%
消耗品費	LAB. & OFFICE SUPPLIES	115,349	185,000	69,651	37.6%
印刷製本費	PRINTING & BOOKBINDING	16,682	16,682	0	
通信運搬費	COMMUNICATION & FREIGHT	26,117	26,117	0	
光熱水料	UTILITIES	53,570	53,570	0	
借料及び損料	RENTALS & LEASE	62,963	65,963	3,000	
会議費	MEETING EXPENSES	1,588	1,588	0	
賃金	SALARIES	12,000	12,000	0	
保険料	INSURANCE	2,508	2,438	-70	
雑役務費	CONTRACT SERVICES	202,285	202,285	0	0.0%
厚生経費	EMPLOYEE WELFARE	6,310	6,130	-180	
7．土地建物借料	RENT, LAND/BUILDINGS	57,693	60,694	3,001	
8．各所修繕	PLANT MAINTENANCE	40,000	40,000	0	0.0%
9．税金	TAXES	1,500	1,500	0	
(Ⅰ・Ⅱ)合　計	TOTAL EXPENDITURES	4,074,590	4,182,506	107,916	2.6%

Summary of FY98 Budget Request

The FY98 Budget request totals ¥4,182,506,000. A comparison of the FY97 budget and FY98 budget request is shown below.

Classification	(1) FY97 Budget (¥1000)	(2) FY98 Budget Request (¥1000)	(2) - (1) (¥1000)	(2)/(1) X 100 (%)
Personnel Expenses	3,271,083	3,356,640	85,557	102.62%
(1)Salaries of Directors and Staff	2,669,651	2,711,805	42,154	101.58%
(2)Termination Allowance	400,048	443,451	43,403	110.85%
(3)NAS Expenses	201,384	201,384	0	
Operating Expenses	803,507	825,866	22,359	102.78%
Total	4,074,590	4,182,506	107,916	102.65%

The major increases and decreases compared to the FY97 budget are as follows:

I. Personnel expenses

(1) Personnel expenses are budgeted allowing for a 3.8% increase of salaries in total to cover the FY98 salary revision (2%) and anniversary salary increases(1.8%). The actual number of directors and staff at the beginning of the fiscal year was a total of 298 directors 4, chief of secretariat 1, professional staff 48, and general staff 245.

II. Operating expenses

The FY98 request was calculated by adding 1.5% to the original FY97 budget (¥813,661,000). The following items are not included in the budget:

(1) Fluctuation in expenses due to temporary fluctuation in prices

(2) Unexpected expenses (for example, costs for relocation and major emergency repair works)

(3) Increase or decrease of expenses due to drastic redirection of research projects

Revision of Act of Endowment

Revision of Act of Endowment

Summary of revision

1. RERF Act of Endowment will be partially revised to implement the recommendations of the Blue Ribbon Panel and Scientific Council, advising that the Scientific Council takes a more active role with a close involvement in the assessment and guidance of RERF.

2. Effective date:
   This Act of Endowment will be effected from 1 July 1997.

Table of comparison

New	Old
'erm of Office of Scientific Councillors) rticle 31 - The term of office of the Scientific Councillors shall be five (5) years. The Scientific Councillors may be re-appointed to their posts only when the Board of Directors expressly deems it necessary. The tenure of the Scientific Councillors reelected under the provision of the preceding clause above shall be one term only. The provisions of paragraphs 5 and 6 of Article 16 shall apply to the Scientific Councillors.	(Term of Office of Scientific Councillors) Article 31 - The term of office of the Scientific Councillors shall be four (4) years. 2 The Scientific Councillors may be re-appointed to their posts. 3. The provisions of paragraphs 5 and 6 of Article 16 shall apply to the Scientific Councillors.
Supplementary Provisions :ctive Date) cle 1 - This Act of Endowment will be effected from 1 July 1997. :rim Measures) cle 2 - Those who are in the position of scientific councillor at the time this Act of ɔwment becomes effective will be considered to have resigned as of the effective of the Act of Endowment. cle 3 - Of the scientific councillors to be appointed by the Board of Directors for the time after the Act of Endowment becomes effective, the term of office of four of the nese councillors and four of the American councillors will be one, two, three, and years, irrespective of the provision in Paragraph 1, Article 31.	

Revision of rules and regulations

Revision of Rules of Employment

Summary of Revision

1. Establishment of special leaves

   (1) Special leave will be granted to female employees when they undergo health examinations during pregnancy or after childbirth as a health management measure for the protection of mothers.

   (2) Special leave will be granted to employees when they undergo comprehensive health examinations.

2. Disciplinary provision against sexual harasser has been established for the purpose of maintaining and improving the working environment by preventing sexual harassment and others.

3. Effective date : These rules were effected from 1 January 1997.

Table of comparison

New

ial Leave)

le 17 - Special leave will be granted for any one of the circumstances described in the following:

(1) When transportation is blocked or the area in which employee lives is quarantined according to the requirements of the Communicable Disease Prevention Law, period as authorized by the Foundation upon receipt of a report

(2) When transportation is disrupted due to typhoon, flood, earthquake, fire or like disasters, period as authorized by the Foundation upon receipt of a report

(3) When the house in which employee lives is destroyed or damaged by typhoon, flood, earthquake, fire or like disaster, period as authorized by the Foundation upon receipt of a report

(4) When there are traffic accidents or other unavoidable accidents other than those described in (1)-(3) above, period as authorized by the Foundation upon receipt of a report

(5) When employee is required to appear in governmental or public offices as a witness or reference person, period as authorized by the Foundation upon receipt of a report

(6) When employee exercises the right of suffrage or other civic rights, period as authorized by the Foundation upon receipt of a report.

(7) Periods authorized immediately preceding and following childbirth are as follows:

1) Female employees who request leave within 6 weeks including the delivery day (in case of multiple pregnancy; 10 weeks) will not be placed on duty.

2) Female employees who give birth to a child will not be placed on duty within 8 weeks after delivery date. However, female employees who request permission to resume duty 6 weeks after delivery date may be placed on duty if such duty, in the opinion of a physician, is not harmful to health.

(8) Female employees who have infants under one year old will, in addition to prescribed recess time, be granted nursing time of 30 minutes each twice a day at request.

(9) Leave of up to one day will be granted for attending a memorial service held for spouse, parents or children within one year of death in conformity with common practice. Where travel of four (4) hours or more but less than eight (8) hours one way is involved, leave up to one day for a round trip may be added; where travel of eight (8) hours or more one way or a distance of 300 kilometers one way by train is involved, leave up to two (2) calendar days may be added.

(10) Obituary leave will be granted as shown below to employees for mourning. Additional days of leave for travelling to remote areas will be as it is in the preceding item above

1)	For mourning for spouse (includes common law marriage)	up to 10 calendar days		
2)	For mourning for parents(includes foster parents) or children (includes adopted children)	up to 7	"	"
3)	For mourning for grandparents, brothers, or sisters (sib) who lived with employee	up to 5	"	"
	who lived separately	up to 3	"	"
4)	For mourning for great grandparents, uncle or aunt who lived with employee	up to 3	"	"
	who lived separately	up to 1	"	"
5)	For mourning for grandchildren	up to 3	"	"

Old

(Special Leave)

Article 17 - Special leave will be granted for any one of the circumstances described in the following:

(1) When transportation is blocked or the area in which employee lives is quarantined according to the requirements of the Communicable Disease Prevention Law, period as authorized by the Foundation upon receipt of a report

(2) When transportation is disrupted due to typhoon, flood, earthquake, fire or like disasters, period as authorized by the Foundation upon receipt of a report

(3) When the house in which employee lives is destroyed or damaged by typhoon, flood, earthquake, fire or like disaster, period as authorized by the Foundation upon receipt of a report

(4) When there are traffic accidents or other unavoidable accidents other than those described in (1)-(3) above, period as authorized by the Foundation upon receipt of a report

(5) When employee is required to appear in governmental or public offices as a witness or reference person, period as authorized by the Foundation upon receipt of a report

(6) When employee exercises the right of suffrage or other civic rights, period as authorized by the Foundation upon receipt of a report.

(7) Periods authorized immediately preceding and following childbirth are as follows:

1) Female employees who request leave within 6 weeks including the delivery day (in case of multiple pregnancy; 10 weeks) will not be placed on duty.

2) Female employees who give birth to a child will not be placed on duty within 8 weeks after delivery date. However, female employees who request permission to resume duty 6 weeks after delivery date may be placed on duty if such duty, in the opinion of a physician, is not harmful to health.

(8) Female employees who have infants under one year old will, in addition to prescribed recess time, be granted nursing time of 30 minutes each twice a day at request.

(9) Leave of up to one day will be granted for attending a memorial service held for spouse, parents or children within one year of death in conformity with common practice. Where travel of four (4) hours or more but less than eight (8) hours one way is involved, leave up to one day for a round trip may be added; where travel of eight (8) hours or more one way or a distance of 300 kilometers one way by train is involved, leave up to two (2) calendar days may be added.

(10) Obituary leave will be granted as shown below to employees for mourning. Additional days of leave for travelling to remote areas will be as it is in the preceding item above

1)	For mourning for spouse (includes common law marriage)	up to 10 calendar days		
2)	For mourning for parents(includes foster parents) or children (includes adopted children)	up to 7	"	"
3)	For mourning for grandparents, brothers, or sisters (sib) who lived with employee	up to 5	"	"
	who lived separately	up to 3	"	"
4)	For mourning for great grandparents, uncle or aunt who lived with employee	up to 3	"	"
	who lived separately	up to 1	"	"
5)	For mourning for grandchildren	up to 3	"	"

New

6)	For mourning for parents in law who lived with employee	up to 7	"	"
	who lived separately	up to 3	"	"
7)	For mourning for son or daughter in law who lived with employee	up to 5	"	"
	who lived separately	up to 3	"	"
8)	For mourning for spouse of brother or sister (sib) who lived with employee	up to 3	"	"
	who lived separately	up to 2	"	"
9)	For mourning for brothers or sisters of spouse who lived with employee	up to 3	"	"
	who lived separately	up to 1	"	"
10)	For mourning for spouse of brother or sister in law, grandparents in law or other relatives who lived with employee	up to 1	"	"

(11) When it is deemed appropriate that employees upon marriage do not report for duty to attend the functions and the like considered necessary with marriage, period within 5 days

(12) When it is deemed appropriate that employees upon childbirth of their wife (including common law wife) not report for duty to attend on their wife in hospital following childbirth, period within 2 days

(13) When it is deemed appropriate that employees not report to work in summer-time for the maintenance and enhancement of their mental and physical health and the pursuance of a rich family life, in principle period within 3 consecutive days during July to September annually, excluding the days on which reporting to work is not required and rest days.

(14) When employee registers at an organization which operates a bone marrow registry as a donor of bone marrow for bone marrow transplant, or offers bone marrow to recipients other than spouse, parents, children and brothers and sisters, and it is deemed that the employee is unable to report for duty for reasons such as examinations and hospitalization required for registration or for donation of bone marrow, period as authorized by the Foundation.

(15) Hours of leave will be granted during the regular working hours to women during the period of pregnancy or within one year after childbirth as shown below as required for undergoing health examinations; However, if a doctor finds it necessary, the frequency of leave granted will be as indicated by the doctor for each of the periods given.

1) Up to and through the 27th week(7 months) of pregnancy
Once every 4 weeks

2) From the 28th week(8 months) through the 35th week(9 months)
Once every 2 weeks

3) From the 36th(10 months) to the time of delivery(childbirth)
Once a week

4) Once within one year after childbirth

(16) When an employee undergoes a comprehensive health examination, time necessary for the examination up to one day will be authorized.

2. Special leave is to be taken upon approval by the Chairman of a leave request which will have been submitted in advance (or at the earliest possible time if a request cannot be submitted in advance for compelling reasons) in prescribed form.

3. Special leave is subject to payment of salary.

Old

6)	For mourning for parents in law who lived with employee	up to 7	"	"
	who lived separately	up to 3	"	"
7)	For mourning for son or daughter in law who lived with employee	up to 5	"	"
	who lived separately	up to 3	"	"
8)	For mourning for spouse of brother or sister (sib) who lived with employee	up to 3	"	"
	who lived separately	up to 2	"	"
9)	For mourning for brothers or sisters of spouse who lived with employee	up to 3	"	"
	who lived separately	up to 1	"	"
10)	For mourning for spouse of brother or sister in law, grandparents in law or other relatives who lived with employee	up to 1	"	"

(11) When it is deemed appropriate that employees upon marriage do not report for duty to attend the functions and the like considered necessary with marriage, period within 5 days

(12) When it is deemed appropriate that employees upon childbirth of their wife (including common law wife) not report for duty to attend on their wife in hospital following childbirth, period within 2 days

(13) When it is deemed appropriate that employees not report to work in summer-time for the maintenance and enhancement of their mental and physical health and the pursuance of a rich family life, in principle period within 3 consecutive days during July to September annually, excluding the days on which reporting to work is not required and rest days.

(14) When employee registers at an organization which operates a bone marrow registry as a donor of bone marrow for bone marrow transplant, or offers bone marrow to recipients other than spouse, parents, children and brothers and sisters, and it is deemed that the employee is unable to report for duty for reasons such as examinations and hospitalization required for registration or for donation of bone marrow, period as authorized by the Foundation.

2. Special leave is to be taken upon approval by the Chairman of a leave request which will have been submitted in advance (or at the earliest possible time if a request cannot be submitted in advance for compelling reasons) in prescribed form.

3. Special leave is subject to payment of salary.

Table of comparison

No. 3

New	Old
(Discharge by Official Prompt, Disciplinary Discharge) Article 41 - Employees who come under any one of the circumstances described below may be discharged for disciplinary reasons. However, where there are extenuating circumstances, discharge by official prompt may be effected. (1) Employees who, willfully or unwillfully, inflict heavy damages upon the Foundation (2) Employees who refuse to observe the instructions of their superiors and disturb the order of the place of work (3) Employees who resort to violence (includes sexual harassment caused by taking advantage of the higher position or the job), threaten other people or interfere with work (4) Employees who accept money or goods illicitly in connection with duty (5) Employees who are convicted of criminal offense (6) Employees who are absent without leave for 20 consecutive days or more (7) Employees who commit offenses similar to those described above	(Discharge by Official Prompt, Disciplinary Discharge) Article 41 - Employees who come under any one of the circumstances described below may be discharged for disciplinary reasons. However, where there are extenuating circumstances, discharge by official prompt may be effected. (1) Employees who, willfully or unwillfully, inflict heavy damages upon the Foundation (2) Employees who refuse to observe the instructions of their superiors and disturb the order of the place of work (3) Employees who resort to violence, threaten other people or interfere with work (4) Employees who accept money or goods illicitly in connection with duty (5) Employees who are convicted of criminal offense (6) Employees who are absent without leave for 20 consecutive days or more (7) Employees who commit offenses similar to those described above
Supplementary Provision (Effective Date) These rules will be effected from 1 January 1997.	

Revision of Regulations Governing Salaries of Directors and Chief of Secretariat.

Summary of revision

1. The base pay of the directors and chief of secretariat was increased by 0.45% on average using as a guide the revision of the National Government Payscale for Designated positions.

2. If it is not practicable to determine the monthly amount of the salary of the chief of secretariat under these regulations, it will be determined by the chairman each time.

3. Effective date: These regulations were promulgated on 24 December 1996 and effected from 1 April 1997.

Table of comparison

Radiation Effects Research Foundation

Regulations Governing Salaries of Directors and Chief of Secretariat

New	Old
(Base Pay) Article 3 - The monthly rates of the base pay of the directors and staff will be as follows: (1) Chairman ¥ 1,253,000 (2) Vice Chairman ¥ 1,129,000 (3) Permanent Directors ¥ 974,000 (4) Chief of Secretariat ¥ 839,000	(Base Pay) Article 3 - The monthly rates of the base pay of the directors and staff will be as follows: (1) Chairman ¥ 1,249,000 (2) Vice Chairman ¥ 1,125,000 (3) Permanent Directors ¥ 970,000 (4) Chief of Secretariat ¥ 836,000
Supplementary Provisions These regulations will be promulgated on 24 Descembre 1996 and be effected retroactively to 1 April 1997. 2. If it is not practicable to determine the monthly amount of the salary of the chief of Secretariat under those regulations, it will be determined by the Chairman each time.	

Revision of Employee Wage Regulations

Summary of revision

1. The payment amounts and payment rates of base pay, dependents allowance, and transportation allowance were revised using as a guide the revisions effected for national government employees in fiscal 1996.

   (1)Base pay:

   Base pay for general employees was increased by 0.97% on average and that for research scientists by 0.71% on average.

   (2)Dependents allowance:

   When there are among the children who are employee's dependents children who have attained 15 years of age and the first 1st April after their date of birth has passed, a sum of ¥3,000(currently ¥2,500)will be added for each of those children to the monthly amount of the dependents allowance payable to employee.

   (3)Transportation allowance:

   Full cost of transportation up to ¥45,000(currently ¥40,000) will be paid to employees who use public transportation,

2. Schedule of Standard Jobs for Pay Scale Grades

   As full-scale improvement of the method to decide payscale grades and steps at the time of promotion is implemented from this year, an upper grade has been newly established in medical technical positions (I) which has less grades in the base payscale compared to medical technical positions (I) of government officials.

3. Effective date: These regulations were effected from 1 April 1996.

Table of comparison

New

)ependents Allowance)

rticle 22 - Dependents allowance will be paid to employees who have dependents.

Dependents eligible for dependents allowance are those who come under the following categories and who have no source of income and are supported primarily by employee. However, those for whom dependents allowance or a corresponding allowance of another business establishment are paid to employee's spouse or siblings and those who are expected to have a regular yearly income of ¥1,300,000 or more will not be eligible as dependents.

(1) spouse (including common law spouse though not officially registered as married)
(2) children, grandchildren, and younger brothers and sisters who are 22 years old but have not yet arrived at the first March 31 following their 22nd birthday.
(3) children, grandchildren, and younger brothers and sisters who are attending schools accredited under the Education Law, preparatory schools for college entrance or general vocational training schools
(4) parents and grandparents who are 60 years old or over
(5) physically and mentally handicapped persons

Dependents allowance will be paid on a monthly basis at the following rates; ¥16,000 for dependents who come under (1) of the preceding paragraph above, ¥5,500 for each of two dependents who come under (2) to (5) of the preceding paragraph above (¥11,000 for one of the two, if employee has no spouse), and ¥2,000 for each dependent other than above.

When there are among the children who are employee's dependents children who have attained 15 years of age and the first 1st of April after their date of birth has passed, a sum of ¥3,000 will be added for each of those children to the monthly amount of the dependents allowance payable to employee.

Newly hired employees, if they have dependents, and employees to whom either of the three conditions given below pertains must submit promptly a report to that effect, attaching to it documents necessary for ascertaining the conditions.

(1) Acquisition of dependent status
(2) Loss of dependent status
(3) Changes calling for adjustment of the rate of dependents allowance

Dependents allowance will be paid to newly hired employees from the first day of employment if they have dependents. When (1) in the preceding paragraph above has occurred to employees without dependents, the allowance will be paid from the month following the month in which the change occurred (from the month in which the change occurred if it occurred on the first day of the month). When employees eligible for the allowance terminate, payment of the allowance will be discontinued on the date of termination (in case of termination due to death, up to the last day of the month in which death occurred). When the condition in (2) in the preceding paragraph above has occurred to dependents, the allowance will be paid up to the month in which the condition occurred (the month preceding if it occurred on the first day of the month).

When there are changes in the conditions which call for adjustment of the rate of the allowance applied, the rate of the allowance will be adjusted from the first day of the month following the month in which the condition occurred (from the first day of the month in which the condition occurred if it occurred on the first day of the month).

Old

(Dependents Allowance)

Article 22 - Dependents allowance will be paid to employees who have dependents.

2. Dependents eligible for dependents allowance are those who come under the following categories and who have no source of income and are supported primarily by employee. However, those for whom dependents allowance or a corresponding allowance of another business establishment are paid to employee's spouse or siblings and those who are expected to have a regular yearly income of ¥1,300,000 or more will not be eligible as dependents.
   (1) spouse (including common law spouse though not officially registered as married)
   (2) children, grandchildren, and younger brothers and sisters who are 22 years old but have not yet arrived at the first March 31 following their 22nd birthday.
   (3) children, grandchildren, and younger brothers and sisters who are attending schools accredited under the Education Law, preparatory schools for college entrance or general vocational training schools
   (4) parents and grandparents who are 60 years old or over
   (5) physically and mentally handicapped persons
3. Dependents allowance will be paid on a monthly basis at the following rates; ¥16,000 for dependents who come under (1) of the preceding paragraph above, ¥5,500 for each of two dependents who come under (2) to (5) of the preceding paragraph above (¥11,000 for one of the two, if employee has no spouse), and ¥2,000 for each dependent other than above.
4. When there are among the children who are employee's dependents children who have attained 15 years of age and the first 1st of April after their date of birth has passed, a sum of ¥2,500 will be added for each of those children to the monthly amount of the dependents allowance payable to employee.
5. Newly hired employees, if they have dependents, and employees to whom either of the three conditions given below pertains must submit promptly a report to that effect, attaching to it documents necessary for ascertaining the conditions.
   (1) Acquisition of dependent status
   (2) Loss of dependent status
   (3) Changes calling for adjustment of the rate of dependents allowance
6. Dependents allowance will be paid to newly hired employees from the first day of employment if they have dependents. When (1) in the preceding paragraph above has occurred to employees without dependents, the allowance will be paid from the month following the month in which the change occurred (from the month in which the change occurred if it occurred on the first day of the month). When employees eligible for the allowance terminate, payment of the allowance will be discontinued on the date of termination (in case of termination due to death, up to the last day of the month in which death occurred). When the condition in (2) in the preceding paragraph above has occurred to dependents, the allowance will be paid up to the month in which the condition occurred (the month preceding if it occurred on the first day of the month).
7. When there are changes in the conditions which call for adjustment of the rate of the allowance applied, the rate of the allowance will be adjusted from the first day of the month following the month in which the condition occurred (from the first day of the month in which the condition occurred if it occurred on the first day of the month).

New

(Transportation Allowance)

Article 23 - Transportation allowance will be paid on a monthly basis in accord with the following standards:

(1) Definition of commutation
Commutation in these regulations is defined as travel between one's home and the Foundation via a reasonable route and method.

(2) Measuring of distance
Commuting distance will be the distance of the shortest route normally used between home and the Foundation. However, the distance of a roundabout way used by those on night duty to avoid danger may be accepted. The distance between the foot of Hijiyama and the Foundation will be assumed to be two kilometers.

(3) Condition of payment
Transportation allowance will be paid to employees who use public transportation for commuting to work and pay fares and to those who use private vehicles such as bicycles for coming to work, provided that the distance of travel one way is two kilometers or more. Employees who are disabled and have difficulty in walking will qualify for the allowance even if the distance of travel one way is less than two kilometers.

(4) Use of public transportation
Public transportation available for commuting via the most economic and reasonable way in terms of cost, time, distance and the like will be used for the purpose of computing the cost of public transportation.

(5) Rate of transportation allowance

1) Employees who use public transportation
Full cost of transportation (total of cost of commutation passes which are available for one month including corresponding evidences (hereinafter "passes") up to ¥45,000 monthly will be paid. When the monthly cost is more than ¥45,000, one half of the cost exceeding ¥40,000 up to a maximum of ¥5,000 will be paid additionally.

2) Employees who use private vehicles
Payment at the following rates will be made for employees who use private vehicles such as bicycles and where commuting distance one way is

a.	2 kilometers or more but less than 5	¥2,000
b.	5 kilometers or more but less than 10	¥4,100
c.	10 kilometers or more but less than 15	¥6,500
d.	15 kilometers or more but less than 20	¥8,900
e.	20 kilometers or more but less than 20	¥11,300
f.	25 kilometers or more but less than 30	¥13,700
g.	30 kilometers or more but less than 35	¥16,100
h.	35 kilometers of more but less than 40	¥18,500
i.	40 kilometers or more	¥20,900

3) Employees who use public transportation and private vehicles

a. Allowance applicable to travel by private vehicles will be added, if distance of travel by private vehicles one way is two kilometers or more, to cost of public transportation up to a maximum total of ¥50,000 monthly.

b. One-half of the rate of the allowance applicable to cost of public

Old

(Transportation Allowance)

Article 23 - Transportation allowance will be paid on a monthly basis in accord with the following standards:

(1) Definition of commutation
Commutation in these regulations is defined as travel between one's home and the Foundation via a reasonable route and method.

(2) Measuring of distance
Commuting distance will be the distance of the shortest route normally used between home and the Foundation. However, the distance of a roundabout way used by those on night duty to avoid danger may be accepted. The distance between the foot of Hijiyama and the Foundation will be assumed to be two kilometers.

(3) Condition of payment
Transportation allowance will be paid to employees who use public transportation for commuting to work and pay fares and to those who use private vehicles such as bicycles for coming to work, provided that the distance of travel one way is two kilometers or more. Employees who are disabled and have difficulty in walking will qualify for the allowance even if the distance of travel one way is less than two kilometers.

(4) Use of public transportation
Public transportation available for commuting via the most economic and reasonable way in terms of cost, time, distance and the like will be used for the purpose of computing the cost of public transportation.

(5) Rate of transportation allowance

1) Employees who use public transportation
Full cost of transportation (total of cost of commutation passes which are available for one month including corresponding evidences (hereinafter "passes") up to ¥40,000 monthly will be paid. When the monthly cost is more than ¥40,000, one half of the cost exceeding ¥40,000 up to a maximum of ¥5,000 will be paid additionally.

2) Employees who use private vehicles
Payment at the following rates will be made for employees who use private vehicles such as bicycles and where commuting distance one way is

a.	2 kilometers or more but less than 5	¥2,000
b.	5 kilometers or more but less than 10	¥4,100
c.	10 kilometers or more but less than 15	¥6,500
d.	15 kilometers or more but less than 20	¥8,900
e.	20 kilometers or more but less than 20	¥11,300
f.	25 kilometers or more but less than 30	¥13,700
g.	30 kilometers or more but less than 35	¥16,100
h.	35 kilometers of more but less than 40	¥18,500
i.	40 kilometers or more	¥20,900

3) Employees who use public transportation and private vehicles

a. Allowance applicable to travel by private vehicles will be added, if distance of travel by private vehicles one way is two kilometers or more, to cost of public transportation up to a maximum total of ¥45,000 monthly.

b. One-half of the rate of the allowance applicable to cost of public

New

transportation or the full monthly rate applicable to travel by private vehicles, whichever is to the advantage of employees who travel by private vehicles one way and normally use public transportation for the other.

(6) Report
1) When conditions which qualify employees for transportation allowance are satisfied anew, a report to that effect must be made using a separately prescribed form.
2) When there are changes in one's address, travel route, mode of travel or cost of travel or when employees no longer satisfy the conditions which qualify them for transportation allowance, a report to that effect must be made in the same way as in 1) above.

(7) Verification and decision
Upon verification of information reported by employees as provided in the preceding paragraph above by appropriate means such as requesting them to present their passes, the applicable rate of the allowance will be determined or revised.

(8) Commencement and discontinuation of payment
1) Transportation allowance will be paid to newly hired employees from the first day of employment if they are eligible under (3) above or from the first day of the month following the month they become eligible (from the month they become eligible if they become eligible on the first day of the month). When employees eligible for the allowance terminate, it will be paid up to the date of termination (in case of termination due to death, up to the last day of the month in which death occurred). When employees become ineligible under (3) above, it will be paid up to the last day of the month in which the change occurred (of the month preceding if the change occurred on the first day of the month).
2) When there are changes in the conditions which call for adjustment of the rates of the allowance applied, the adjustment will be effected from the month following the month in which the changes occurred (from the month in which the changes occurred if they occurred on the first day of the month).
3) When employees do not report to work from the first day to the last day of a month due to business trip, leave, absence from work or other reasons, the allowance for the month will not be payable.

(9) Investigation
Employees may be required to show their commutation passes or investigations may be conducted from time to time to verify the conditions of commutation reported by employees.

Supplementary Provisions

(Effective Date)
1. These regulations will be promulgated on 27 Descembre 1996 and be effected retroactively to 1 April 1996.
2. Procedures in the Wage Regulations prior to the revision will be applied to employees retiring prior to the date of promulgation of these regulations.

(Partial Payment Salaries)
3. Salaries and allowances paid after 1 April 1996 according to procedures in the Wage Regulations prior to the revision will represent partial payment of the salaries and allowances effective after the revision.

Old

transportation or the full monthly rate applicable to travel by private vehicles, whichever is to the advantage of employees who travel by private vehicles one way and normally use public transportation for the other.

(6) Report
1) When conditions which qualify employees for transportation allowance are satisfied anew, a report to that effect must be made using a separately prescribed form.
2) When there are changes in one's address, travel route, mode of travel or cost of travel or when employees no longer satisfy the conditions which qualify them for transportation allowance, a report to that effect must be made in the same way as in 1) above.

(7) Verification and decision
Upon verification of information reported by employees as provided in the preceding paragraph above by appropriate means such as requesting them to present their passes, the applicable rate of the allowance will be determined or revised.

(8) Commencement and discontinuation of payment
1) Transportation allowance will be paid to newly hired employees from the first day of employment if they are eligible under (3) above or from the first day of the month following the month they become eligible (from the month they become eligible if they become eligible on the first day of the month). When employees eligible for the allowance terminate, it will be paid up to the date of termination (in case of termination due to death, up to the last day of the month in which death occurred). When employees become ineligible under (3) above, it will be paid up to the last day of the month in which the change occurred (of the month preceding if the change occurred on the first day of the month).
2) When there are changes in the conditions which call for adjustment of the rates of the allowance applied, the adjustment will be effected from the month following the month in which the changes occurred (from the month in which the changes occurred if they occurred on the first day of the month).
3) When employees do not report to work from the first day to the last day of a month due to business trip, leave, absence from work or other reasons, the allowance for the month will not be payable.

(9) Investigation
Employees may be required to show their commutation passes or investigations may be conducted from time to time to verify the conditions of commutation reported by employees.

新旧対照表

新

（財）放射線影響研究所

別表一
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

研究員基本給表
REVISED BASE PAY SCALE FOR RESEARCH STAFF

平成8年4月1日
1 April 1996

級 Grade	1級 Grade 1	2級 Grade 2	3級 Grade 3	4級 Grade 4
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1	299,900	316,800	380,300	438,500
2	314,000	333,200	398,100	454,300
3	326,400	349,700	416,000	470,100
4	338,900	366,200	433,900	486,000
5	351,300	383,200	447,600	501,600
6	360,000	400,000	460,800	518,300
7	368,300	416,900	473,500	535,200
8	376,600	429,400	485,800	552,700
9	385,000	440,900	498,000	570,200
10	393,400	451,700	510,200	587,500
11	401,700	461,700	522,000	604,800
12	410,100	470,500	533,600	622,000
13	418,200	478,800	545,300	638,800
14	426,200	486,900	556,900	655,100
15	432,500	494,900	568,200	671,400
16	438,500	502,700	579,300	687,600
17	442,900	510,400	590,200	703,900
18	447,100	517,500	601,100	718,300
19	451,300	523,900	610,600	729,200
20	455,500	529,900	619,900	738,700
21	459,500	535,600	626,900	746,500
22	463,500	541,000	633,000	753,400
23	467,400	546,300	638,100	758,800
24	471,300	550,800	643,200	
25	475,300	555,100		
26	479,200	559,400		
27	483,100	563,700		
28	487,100			
29	491,000			
30	495,000			
31	499,000			

備考： この表は研究員に適用し表別区分は別に定める基準による。

旧

（財）放射線影響研究所

別表一
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

研究員基本給表
REVISED BASE PAY SCALE FOR RESEARCH STAFF

平成7年4月1日
1 April 1995

級 GRADE	1級 GRADE 1	2級 GRADE 2	3級 GRADE 3	4級 GRADE 4
号給 STEP	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON
1	288,600	311,900	374,400	431,900
2	298,900	323,800	387,200	447,600
3	309,100	335,900	400,400	463,200
4	318,700	348,200	413,700	478,800
5	327,900	360,500	427,400	494,500
6	336,900	372,700	441,000	511,400
7	345,600	385,300	454,000	528,400
8	354,200	397,900	466,600	546,200
9	362,500	410,700	479,000	564,100
10	370,700	423,100	491,400	581,800
11	379,100	434,500	503,700	599,400
12	387,600	445,400	515,800	617,100
13	396,100	455,500	527,900	634,500
14	404,400	464,500	539,900	651,300
15	412,800	473,100	551,800	668,000
16	421,200	481,600	563,500	684,800
17	427,800	489,900	575,100	701,600
18	434,200	498,100	586,500	716,000
19	439,000	506,200	597,900	726,900
20	443,500	513,400	607,600	736,400
21	448,100	520,300	617,200	744,300
22	452,500	526,600	624,300	751,200
23	456,800	532,700	630,300	756,600
24	460,800	538,200	635,400	
25	464,800	543,500		
26	468,800	548,000		
27	472,800	552,300		
28	476,800			
29	480,800			
30	484,800			
31	488,800			

備考： この表は研究員に適用し表別区分は別に定める基準による。

新 旧 対 照 表

新

（財）放射線影響研究所

RADIATION EFFECTS RESEARCH FOUNDATION

事務職基本給表

BASE PAY SCALE FOR ADMINISTRATIVE POSITIONS

平成8年4月1日
1 April 1996

2級 Grade 2 月額 Amt/Mon	3級 Grade 3 月額 Amt/Mon	4級 Grade 4 月額 Amt/Mon	5級 Grade 5 月額 Amt/Mon	6級 Grade 6 月額 Amt/Mon	7級 Grade 7 月額 Amt/Mon	8級 Grade 8 月額 Amt/Mon	9級 Grade 9 月額 Amt/Mon	10級 Grade10 月額 Amt/Mon	11級 Grade11 月額 Amt/Mon
	184.800	218.400	237.500	256.500	276.000	297.400	332.500	371.500	420.800
171.000	191.700	226.600	246.100	265.500	285.300	307.400	344.600	384.000	435.500
177.700	198.700	235.000	254.800	274.600	294.900	317.600	356.700	396.600	450.200
184.800	205.700	243.900	263.800	283.700	304.600	328.100	368.600	409.100	465.000
190.600	213.300	252.800	272.800	292.800	314.400	338.600	380.400	421.800	479.800
195.700	221.200	261.400	281.800	302.100	324.300	349.000	392.300	434.200	494.600
200.800	229.000	269.800	290.700	311.500	334.300	359.100	404.200	446.500	509.400
205.900	236.400	278.200	299.600	321.000	344.200	368.900	416.200	458.700	524.500
210.600	242.900	286.400	308.500	330.500	353.900	378.700	428.100	470.700	539.500
215.100	249.300	294.500	317.300	340.000	363.400	388.400	439.600	482.600	554.600
219.500	255.600	302.400	326.000	349.600	372.800	398.100	450.500	493.200	566.500
223.900	261.400	309.900	334.500	359.100	381.900	407.800	461.100	503.000	574.300
228.200	267.000	317.200	342.800	368.400	390.700	417.400	469.800	511.200	581.800
231.600	272.200	324.300	350.900	377.500	398.300	426.600	477.200	518.400	588.000
234.700	277.400	330.700	358.200	385.600	404.900	433.600	484.500	523.000	592.800
237.800	282.100	336.800	364.400	392.000	410.900	440.300	489.600		
240.900	286.300	341.200	369.700	398.200	416.000	444.700	494.200		
243.800	290.000	345.100	373.800	402.400	420.300	449.200	498.500		
245.800	293.400	348.800	377.700	406.500	424.600	453.500			
	296.300	351.900	381.200	410.500	428.700	457.400			
	299.200	355.000	384.800	414.500	432.600	461.200			
	302.100	358.100	388.300	418.400	436.300				
	305.000	361.200	391.700	422.100					
	307.900	364.300	395.000	425.700					
	310.800	367.400	398.400						
	313.700	370.500	401.700						
	316.600	373.600							
	319.500	376.700							
	322.400								
	325.200								
	328.000								
	330.800								

主として事務系業務に従事する職員で別に定める基準により適用する.

旧

（財）放射線影響研究所

別表二①
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

事務職基本給表

BASE PAY SCALE FOR ADMINISTRATIVE POSITIONS

平成7年4月1日
1 April 1995

級 GRADE / 号給 STEP	1級 GRADE 1 月額 AMT/MON	2級 GRADE 2 月額 AMT/MON	3級 GRADE 3 月額 AMT/MON	4級 GRADE 4 月額 AMT/MON	5級 GRADE 5 月額 AMT/MON	6級 GRADE 6 月額 AMT/MON	7級 GRADE 7 月額 AMT/MON	8級 GRADE 8 月額 AMT/MON	9級 GRADE 9 月額 AMT/MON	10級 GRADE10 月額 AMT/MON	11級 GRADE11 月額 AMT/MON
1			182.500	215.200	234.000	252.800	272.000	293.100	327.600	366.400	415.900
2	133.600	169.000	189.300	223.300	242.500	261.700	281.200	302.900	339.600	379.000	430.900
3	137.900	175.600	196.100	231.600	251.100	270.600	290.600	312.900	351.600	391.700	445.900
4	142.400	182.500	202.900	240.300	260.000	279.600	300.100	323.300	363.500	404.300	461.000
5	147.400	188.200	210.200	249.100	268.900	288.600	309.800	333.700	375.400	417.300	476.100
6	153.100	193.200	218.000	257.600	277.700	297.700	319.600	344.000	387.400	430.000	491.300
7	159.000	198.200	225.700	265.900	286.500	307.000	329.500	354.100	399.600	442.500	506.600
8	165.000	203.100	232.900	274.200	295.300	316.400	339.400	364.100	411.800	455.000	522.100
9	169.400	207.700	239.400	282.300	304.100	325.800	349.200	374.100	424.000	467.400	537.500
10	172.900	212.200	245.700	290.200	312.800	335.400	358.900	384.100	435.600	479.800	552.800
11	175.800	216.600	251.900	298.000	321.600	345.200	368.500	394.000	446.800	490.700	564.700
12	178.500	221.000	257.600	305.600	330.300	354.900	377.800	403.900	457.800	500.800	572.600
13	181.200	225.300	263.300	313.100	338.800	364.500	386.800	413.800	467.000	509.300	580.100
14	183.400	228.700	268.700	320.500	347.200	373.800	394.700	423.300	474.600	516.500	586.300
15	185.500	231.800	274.000	327.200	354.700	382.100	401.600	430.700	482.200	521.100	591.100
16	187.100	234.900	278.800	333.500	361.200	388.800	407.800	437.700	487.500		
17		238.000	283.200	338.100	366.700	395.200	413.200	442.300	492.100		
18		240.900	287.000	342.200	370.900	399.600	417.800	446.800	496.400		
19		242.900	290.500	346.200	375.100	403.900	422.300	451.100			
20			293.400	349.300	378.700	408.100	426.400	455.000			
21			296.300	352.400	382.400	412.300	430.300	458.800			
22			299.200	355.500	385.900	416.200	434.000				
23			302.100	358.600	389.300	419.900					
24			305.000	361.700	392.600	423.500					
25			307.900	364.800	396.000						
26			310.800	367.900	399.300						
27			313.700	371.000							
28			316.600	374.100							
29			319.500								
30			322.300								
31			325.100								
32			327.900								

備考： この表は主として事務系業務に従事する職員で別に定める基準により適用する.

新旧対照表

新

（財）放射線影響研究所

別表二②
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

作業・技能職基本給表
BASE PAY SCALE FOR MANUAL & GENERAL TECHNICAL POSITIONS

平成8年4月1日
1 April 1996

級 Grade	1級 Grade 1	2級 Grade 2	3級 Grade 3	4級 Grade 4	5級 Grade 5	6級 Grade 6
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1		164.600	182.900	200.400	226.600	255.000
2	120.900	171.200	188.700	206.400	233.500	262.300
3	124.600	177.000	194.600	212.800	240.400	269.700
4	128.300	182.800	200.400	219.700	247.400	277.700
5	131.800	188.000	206.300	226.500	254.300	285.800
6	135.800	193.100	212.600	233.200	261.100	294.200
7	140.600	198.200	219.200	239.400	267.800	302.700
8	145.300	203.300	225.500	245.300	274.000	311.100
9	151.300	208.600	231.700	251.100	279.900	319.300
10	157.400	213.900	237.500	257.000	285.600	327.200
11	164.400	219.400	243.200	262.400	291.200	335.000
12	171.000	224.500	248.800	267.700	296.800	342.800
13	176.700	229.300	254.100	272.800	302.200	350.400
14	182.100	234.200	259.300	277.900	307.400	357.200
15	186.800	239.000	264.300	282.800	312.600	363.900
16	191.200	243.300	268.900	287.800	317.800	370.500
17	195.700	247.500	273.800	292.200	322.800	376.800
18	199.700	251.400	278.600	296.200	327.400	382.700
19	203.200	254.800	283.100	299.700	331.900	388.100
20	206.300	257.500	287.100	303.000	336.000	392.900
21	209.300	260.200	290.200	306.200	339.800	397.700
22	212.400	262.900	293.100	309.200	343.300	402.000
23	215.300	265.600	296.000	312.200	346.400	405.400
24	218.100	268.300	298.900	315.200	349.500	
25	220.500	271.000	301.800	318.200	352.600	
26	222.800	273.700	304.700	321.200	355.700	
27	225.000	276.400	307.600	324.200	358.800	
28	227.200	279.100	310.500	327.200		
29	229.300	281.800	313.400	330.200		
30	231.300	284.400	316.300	333.200		
31	233.200	287.000	319.200	336.200		
32	235.000	289.600				
33		292.200				

備考： この表は機器の運転操作、施設の保全、その他の業務に従事する職員で別に定める基準により適用する。

旧

（財）放射線影響研究所

別表二②
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

作業・技能職基本給表
BASE PAY SCALE FOR MANUAL & GENERAL TECHNICAL POSITIONS

平成7年4月1日
1 April 1995

級 GRADE	1級 GRADE 1	2級 GRADE 2	3級 GRADE 3	4級 GRADE 4	5級 GRADE 5	6級 GRADE 6
号給 STEP	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON
1		162.900	180.900	197.800	223.300	251.300
2	119.700	169.400	186.500	203.600	230.100	258.500
3	123.400	175.100	192.100	209.900	236.900	265.800
4	127.000	180.800	197.800	216.500	243.800	273.700
5	130.500	185.800	203.500	223.200	250.600	281.600
6	134.500	190.700	209.700	229.800	257.300	289.900
7	139.200	195.700	216.000	235.900	263.900	298.300
8	143.900	200.700	222.200	241.700	270.000	306.900
9	149.800	205.800	228.300	247.500	275.800	315.300
10	155.800	211.000	234.100	253.300	281.400	323.400
11	162.700	216.200	239.700	258.600	287.000	331.400
12	169.200	221.200	245.200	263.800	292.700	339.400
13	174.800	226.000	250.400	268.800	298.300	347.200
14	180.100	230.800	255.500	273.900	303.800	354.200
15	184.600	235.500	260.500	278.900	309.300	361.000
16	188.900	239.800	265.200	284.000	314.700	367.700
17	193.200	243.900	270.200	288.500	319.900	374.200
18	197.100	247.800	275.200	292.800	324.700	380.100
19	200.600	251.400	279.800	296.500	329.300	385.500
20	203.500	254.100	284.000	300.000	333.500	390.500
21	206.500	256.800	287.200	303.400	337.400	395.300
22	209.500	259.500	290.100	306.600	341.000	399.600
23	212.400	262.200	293.000	309.600	344.100	403.000
24	215.200	264.900	295.900	312.600	347.200	
25	217.600	267.600	298.800	315.600	350.300	
26	219.900	270.300	301.700	318.600	353.400	
27	222.100	273.000	304.600	321.600	356.500	
28	224.300	275.700	307.500	324.600		
29	226.400	278.400	310.400	327.600		
30	228.400	281.000	313.300	330.600		
31	230.300	283.600	316.200	333.600		
32	232.100	286.200				
33		288.800				

備考： この表は機器の運転操作、施設の保全、その他の業務に従事する職員で別に定める基準により適用する。

新 旧 対 照 表

新

（財）放射線影響研究所

二③
1条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

医療技術職基本給表（一）
BASE PAY SCALE FOR MEDICAL TECHNICAL POSITIONS (I)

平成8年4月1日
1 April 1996

1 級 Grade 1 月額 Amt/Mon	2 級 Grade 2 月額 Amt/Mon	3 級 Grade 3 月額 Amt/Mon	4 級 Grade 4 月額 Amt/Mon	5 級 Grade 5 月額 Amt/Mon	6 級 Grade 6 月額 Amt/Mon	7 級 Grade 7 月額 Amt/Mon
		205.700	235.600	265.500	307.400	343.200
139.500	176.800	212.600	243.800	275.000	317.600	355.000
145.000	183.300	219.800	252.200	284.500	327.800	366.800
151.700	189.800	227.800	261.000	294.100	337.900	378.600
158.400	196.300	235.900	269.800	303.700	347.900	390.400
165.900	202.700	244.200	278.800	313.400	357.800	402.200
173.400	209.200	252.500	287.900	323.300	367.600	414.400
179.600	215.600	260.800	297.000	333.100	377.400	426.600
185.800	222.400	269.200	306.000	342.800	387.300	438.600
191.000	229.700	277.600	315.000	352.300	397.300	449.900
196.200	236.700	285.900	323.800	361.700	407.200	460.800
201.300	243.400	294.100	332.400	370.600	416.800	469.800
206.300	249.900	302.200	340.900	379.500	426.200	477.200
210.900	256.400	310.100	348.900	387.700	433.400	484.500
215.400	262.200	317.700	356.100	394.500	440.200	491.800
219.800	267.700	325.000	363.000	401.000	444.700	496.300
224.100	272.900	331.800	369.200	406.500	449.200	500.600
228.400	278.100	338.300	375.000	411.700	453.500	
231.900	282.800	343.000	379.500	415.900	457.400	
235.000	287.300	347.600	383.800	420.000	461.200	
238.000	290.600	351.300	387.700	424.100		
240.500	293.500	354.400	391.100	427.800		
242.500	296.400	357.500	394.500	431.400		
	299.300	360.600	397.800			
	302.200	363.700	401.200			
	305.100	366.800	404.500			
	308.000	369.900	407.900			
	310.900	373.000				
		376.100				
		379.200				

：この表は薬剤師、診療放射線技師、臨床検査技師及びこれらに準ずる業務に従事する職員で別に定める基準により適用する。

旧

（財）放射線影響研究所

別表二③
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

医療技術職基本給表（一）
BASE PAY SCALE FOR MEDICAL TECHNICAL POSITIONS (I)

平成7年4月1日
1 April 1995

級 GRADE	1 級 GRADE 1	2 級 GRADE 2	3 級 GRADE 3	4 級 GRADE 4	5 級 GRADE 5	6 級 GRADE 6
号給 STEP	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON
1			202.900	232.300	261.700	302.900
2	138.100	174.500	209.600	240.300	271.000	312.900
3	143.600	180.900	216.600	248.500	280.400	322.900
4	150.200	187.300	224.500	257.200	289.800	332.900
5	156.800	193.600	232.400	265.800	299.200	342.900
6	164.100	199.900	240.600	274.700	308.700	352.800
7	171.400	206.200	248.800	283.600	318.400	362.800
8	177.500	212.400	257.000	292.600	328.100	372.800
9	183.500	219.100	265.300	301.600	337.800	382.900
10	188.600	226.300	273.600	310.600	347.500	393.100
11	193.700	233.200	281.800	319.500	357.100	403.200
12	198.700	239.800	289.800	328.100	366.300	413.200
13	203.500	246.200	297.700	336.500	375.300	422.900
14	208.000	252.600	305.500	344.600	383.700	430.500
15	212.500	258.400	313.300	352.000	390.700	437.600
16	216.900	264.000	320.900	359.200	397.400	442.300
17	221.200	269.400	328.000	365.500	403.000	446.900
18	225.500	274.700	334.700	371.600	408.400	451.100
19	229.000	279.500	339.600	376.200	412.800	455.000
20	232.100	284.100	344.300	380.700	417.000	458.800
21	235.100	287.600	348.200	384.700	421.200	
22	237.600	290.500	351.300	388.100	424.900	
23	239.600	293.400	354.400	391.500	428.500	
24		296.300	357.500	394.800		
25		299.200	360.600	398.200		
26		302.100	363.700	401.500		
27		305.000	366.800	404.900		
28		307.900	369.900			
29			373.000			
30			376.100			

備考：この表は薬剤師、診療放射線技師、臨床検査技師及びこれらに準ずる業務に従事する職員で別に定る　準により適用する。

新旧対照表

新

（財）放射線影響研究所

別表二④
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

医療技術職基本給表（二）
BASE PAY SCALE FOR MEDICAL TECHNICAL POSITIONS （II）

平成8年4月1日
1 April 1996

級 Grade	1 級 Grade 1	2 級 Grade 2	3 級 Grade 3	4 級 Grade 4	5 級 Grade 5
号給 Step	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon	月額 Amt/Mon
1			221.100	243.400	274.700
2	152.600	179.400	227.900	250.800	283.200
3	158.200	187.900	235.700	258.200	291.700
4	164.100	197.000	243.100	265.600	300.200
5	170.200	202.700	250.400	273.100	308.800
6	178.300	208.500	257.800	280.900	317.400
7	186.800	214.400	265.100	288.700	326.000
8	195.300	220.800	272.400	296.600	334.400
9	200.300	227.600	279.800	304.600	342.300
10	205.500	235.000	287.400	312.600	350.100
11	210.600	242.300	295.100	320.500	357.900
12	215.900	249.600	302.800	328.200	365.600
13	221.500	256.900	310.300	335.500	373.400
14	227.100	264.200	317.600	342.700	381.400
15	232.800	271.400	324.800	349.900	389.400
16	238.400	278.600	331.500	356.900	397.300
17	244.100	285.800	338.100	363.900	404.800
18	249.700	293.000	344.600	370.700	411.400
19	255.400	299.900	351.100	377.400	416.600
20	261.000	306.800	357.500	383.400	421.400
21	266.300	313.600	363.900	389.100	426.200
22	271.400	319.900	369.800	394.600	430.300
23	275.700	326.000	375.200	398.900	433.800
24	280.300	332.200	380.500	402.800	437.400
25	284.600	338.100	384.900	406.500	
26	288.700	342.800	388.600	410.100	
27	292.300	346.800	392.100	413.600	
28	295.700	350.600	395.500	417.100	
29	298.500	354.000	398.900		
30	301.000	357.300	402.300		
31	303.400	360.600	405.700		
32	305.600	363.900			
33	307.900	367.200			
34	310.000	370.500			
35	312.100	373.800			
36	314.200	377.100			
37	316.300	380.400			
38	318.500	383.700			
39	320.700				
40	322.900				
41	325.100				

備考： この表は保健婦、看護婦、及び準看護婦で別に定める基準により適用する。

旧

（財）放射線影響研究所

別表二④
（第11条関係）

RADIATION EFFECTS RESEARCH FOUNDATION

医療技術職基本給表（二）
BASE PAY SCALE FOR MEDICAL TECHNICAL POSITIONS （II）

平成7年4月1日
1 April 1995

級 GRADE	1 級 GRADE 1	2 級 GRADE 2	3 級 GRADE 3	4 級 GRADE 4	5 級 GRADE 5
号給 STEP	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON	月額 AMT/MON
1			218.200	239.900	270.700
2	151.100	177.600	224.700	247.100	279.100
3	156.600	185.900	232.300	254.400	287.500
4	162.500	194.700	239.600	261.700	295.900
5	168.500	200.300	246.800	269.100	304.300
6	176.500	205.900	254.000	276.800	312.700
7	184.800	211.700	261.200	284.500	321.100
8	193.000	217.900	268.400	292.300	329.400
9	197.900	224.400	275.700	300.100	337.400
10	202.900	231.600	283.200	308.000	345.300
11	207.900	238.800	290.800	315.700	353.200
12	213.100	246.000	298.300	323.300	361.200
13	218.500	253.200	305.700	330.700	369.200
14	223.800	260.400	313.000	338.100	377.400
15	229.400	267.500	320.300	345.500	385.600
16	234.900	274.600	327.300	352.700	393.800
17	240.500	281.700	334.100	360.000	401.400
18	246.100	288.700	340.900	367.000	408.200
19	251.700	295.400	347.500	374.000	413.500
20	257.200	302.200	354.100	380.200	418.400
21	262.400	309.000	360.700	386.000	423.200
22	267.600	315.400	366.900	391.600	427.300
23	272.100	321.800	372.300	396.000	430.800
24	276.700	328.200	377.600	399.900	434.400
25	281.000	334.400	382.100	403.600	
26	285.200	339.300	385.800	407.200	
27	288.900	343.500	389.400	410.700	
28	292.400	347.600	392.800	414.200	
29	295.200	351.300	396.200		
30	297.900	354.600	399.600		
31	300.500	357.900	403.000		
32	303.000	361.200			
33	305.500	364.500			
34	307.700	367.800			
35	309.900	371.100			
36	312.100	374.400			
37	314.300	377.700			
38	316.500	381.000			
39	318.700				
40	320.900				
41	323.100				

備考： この表は保健婦、看護婦、及び準看護婦で別に定める基準により適用する。

Table of comparison

New

Attachment 3
(re Article 11)

Schedule of Standard Jobs for Pay Scale Grades

1. Professional Base Pay Scale
2. Base Pay Scale for Administrative Positions
3. Base Pay Scale for Manual and General Technical Positions

omission

4. Base Pay Scale for Medical Technical Positions (I)

Grade	Standard Duties
Grade 1	1. Duties of therapeutical radiological technician (includes therapeutical X- ray technician; hereinafter the same) 2. Duties of licensed clinical technician (includes hygiene technician; hereinafter the same) 3. Duties of clinical technician, research technician or autopsy technician (hereinafter, research technician, etc.)
Grade 2	1. Duties of pharmacist 2. Duties of therapeutical radiological technician or licensed clinical technician in charge of difficult work 3. Duties of research technician, etc. in charge of difficult work
Grade 3	1. Duties of pharmacist in charge of difficult pharmaceutical work 2. Duties of senior technician or duties of a comparable level 3. Duties of research technician, etc. in charge of markedly difficult work
Grade 4	1. Duties of chief pharmacist in charge of considerably difficult work 2. Duties of chief of technicians or duties of a Grade 4 comparable level 3. Duties of senior technician in charge of difficult work or duties of a comparable level
Grade 5	Duties of chief of technicians in charge of difficult work or duties of a comparable level
Grade 6	Duties of chief of technicians in charge of markedly difficult work
Grade 7	Duties of chief of technicians for supervising markedly difficult work

5. Base Pay Scale for Medical Technical Positions (II) omission

Old

Attachment 3
(re Article 11)

Schedule of Standard Jobs for Pay Scale Grades

1. Professional Base Pay Scale
2. Base Pay Scale for Administrative Positions
3. Base Pay Scale for Manual and General Technical Positions

omission

4. Base Pay Scale for Medical Technical Positions (I)

Grade	Standard Duties
Grade 1	1. Duties of therapeutical radiological technician (includes therapeutical X- ray technician; hereinafter the same) 2. Duties of licensed clinical technician (includes hygiene technician; hereinafter the same) 3. Duties of clinical technician, research technician or autopsy technician (hereinafter, research technician, etc.)
Grade 2	1. Duties of pharmacist 2. Duties of therapeutical radiological technician or licensed clinical technician in charge of difficult work 3. Duties of research technician, etc. in charge of difficult work
Grade 3	1. Duties of pharmacist in charge of difficult pharmaceutical work 2. Duties of senior technician or duties of a comparable level 3. Duties of research technician, etc. in charge of markedly difficult work
Grade 4	1. Duties of chief pharmacist in charge of considerably difficult work 2. Duties of chief of technicians or duties of a Grade 4 comparable level 3. Duties of senior technician in charge of difficult work or duties of a comparable level
Grade 5	Duties of chief of technicians in charge of difficult work or duties of a comparable level
Grade 6	Duties of chief of technicians in charge of markedly difficult work

5. Base Pay Scale for Medical Technical Positions (II) omission

Table of comparison

New

Attachment 6-2
(re Article 30)

Table of Differential Payment for Seasonal Allowances

Classification	Base Pay Scale for General Employees	Grade
I	Administrative	Grade 11 Grade 10
II	Administrative	Grade 9 Grade 8
	Medical Technical (I)	Grade 7 Grade 6
	Medical Technical (II)	Grade 5 with position allowance class 3 or higher
III	Administrative	Grade 7 Grade 6
	Manual and General Technical	Grade 6
	Medical Technical (I)	Grade 5
	Medical Technical (II)	Grade 5 with position allowance class 4 or lower Grade 4
IV	Administrative	Grade 5 Grade 4
	Manual and General Technical	Grade 5 Grade 4
	Medical Technical (I)	Grade 4 Grade 3 Grade 2
	Medical Technical (II)	Grade 3 Grade 2

Note: 1. I, II, III and IV in the classification column indicate the differential rates of 20%, 15%, 10% and 5%, respectively.
2. Grade 2 employees of Medical Technical Base Pay Scales (I) and (II) require 15 years or more of experience.

Old

Attachment 6-2
(re Article 30)

Table of Differential Payment for Seasonal Allowances

Classification	Base Pay Scale for General Employees	Grade
I	Administrative	Grade 11 Grade 10
II	Administrative	Grade 9 Grade 8
	Medical Technical (I)	Grade 6
	Medical Technical (II)	Grade 5 with position allowance class 3 or higher
III	Administrative	Grade 7 Grade 6
	Manual and General Technical	Grade 6
	Medical Technical (I)	Grade 5
	Medical Technical (II)	Grade 5 with position allowance class 4 or lower Grade 4
IV	Administrative	Grade 5 Grade 4
	Manual and General Technical	Grade 5 Grade 4
	Medical Technical (I)	Grade 4 Grade 3 Grade 2
	Medical Technical (II)	Grade 3 Grade 2

Note: 1. I, II, III and IV in the classification column indicate the differential rates of 20%, 15%, 10% and 5%, respectively.
2. Grade 2 employees of Medical Technical Base Pay Scales (I) and (II) require 15 years or more of experience.

Election／Appointment of directors and others

Election of Officers 役員の選任

Note: Dates in parentheses show time of expiration of term.

注：（ ）内は任期満了の時期

	Present 現 任	New 新 任 Reappointment 再 任
Chairman 理事長	**Dr. Itsuzo Shigematsu** **重松 逸造** (30 / 6 / 97)	**Dr. Shigenobu Nagataki** **長瀧 重信** (30 / 6 / 2001)
Vice Chairman and Chief of Research 副理事長・ 研究担当理事	**Dr. Sheldon Wolff** (30 / 6 / 97)	**Dr. Sheldon Wolff** (30 / 6 / 2001)
Permanent Director 常務理事	**Dr. Shigenobu Nagataki** **長瀧 重信** (30 / 6 / 97)	
Permanent Director 常務理事	**Dr. William J. Schull** (30 / 6 / 97) Retirement on 22 January 1997 1997年1月22日退職	**Dr. William J. Schull** (30 / 6 / 2001) Retirement on 22 January 1997 1997年1月22日退職
Director 理 事	**Dr. Warren K. Sinclair** (30 / 6 / 99)	
Director 理 事	**Dr. Patricia A. Buffler** (30 / 6 / 99)	
Director 理 事	**Dr. Jonathan M. Samet** (30 / 6 / 99)	
Director 理 事	**Dr. Toshiyuki Kumatori** **熊取 敏之** (30 / 6 / 99)	
Director 理 事	**Mr. Kazuaki Arichi** **有地 一昭** (30 / 6 / 99)	
Director 理 事	**Dr. Masumi Oike** **大池 真澄** (30 / 6 / 99)	

Supervisor 監 事	**Mr. David Williams** (30 / 6 / 99)	
Supervisor 監 事	**Dr. Shudo Yamazaki** **山崎 修道** (30 / 6 / 99)	

Election of Scientific Councilors　専門評議員の選任

Note: All the councilors have resigned.　Figures in parentheses show terms of appointment.

注：専門評議員はこのほど全員辞任した。（　）内は任期

Present 現 任	New 新 任 Reappointment 再 任
Dr. Eisei Ishikawa **石川 栄世** Professor Emeritus, Jikei University School of Medicine 東京慈恵会医科大学名誉教授	**Dr. Shinichiro Ushigome** **牛込 新一郎（5 yrs）** Professor, Department of Pathology, Jikei University School of Medicine 東京慈恵会医科大学病理学教授
Dr. Tomio Hirohata **廣畑 富雄** Professor Emeritus, Kyushu University Faculty of Medicine 九州大学医学部名誉教授	**Dr. Tomio Hirohata** **廣畑 富雄（4 yrs）** Professor Emeritus, Kyushu University Faculty of Medicine 九州大学医学部名誉教授
Dr. Hiromichi Matsudaira **松平 寛通** Consultant, Japan Science and Technology Corporation 科学技術振興事業団顧問	**Dr. Hiromichi Matsudaira** **松平 寛通（3 yrs）** Consultant, Japan Science and Technology Corporation 科学技術振興事業団顧問
Dr. Ei Matsunaga **松永 英** Professor Emeritus, National Institute of Genetics 国立遺伝学研究所名誉教授	**Dr. Masao Sasaki** **佐々木 正夫（2 yrs）** Professor, Radiation Biology Center, Kyoto University 京都大学放射線生物研究センター教授
Dr. Shigefumi Okada **岡田 重文** Professor Emeritus, University of Tokyo 東京大学名誉教授	**Dr. Shigefumi Okada** **岡田 重文（1 yr）** Professor Emeritus, University of Tokyo 東京大学名誉教授

Dr. Arno G. Motulsky Professor of Medicine and Genetics, University of Washington School of Medicine 米国ワシントン大学 医学部内科学および遺伝学教授	**Dr.Joe W. Gray（5 yrs）** Professor of Labotatory Medicine, University of California, San Francisco 米国カリフォルニア大学 サンフランシスコ校 実験医学および放射線腫瘍学 教授
Dr. Susan Preston-Martin Professor, Department of Preventive Medicine, University of Southern California Norris Comprehensive Cancer Center 米国南カリフォルニア大学 ノリス総合がんセンター 予防医学教授	**Dr. Susan Preston-Martin（4 yrs）** Professor, Department of Preventive Medicine, University of Southern California Norris Comprehensive Cancer Center 米国南カリフォルニア大学 ノリス総合がんセンター 予防医学教授
Dr. Curtis C. Harris Chief, Laboratory of Human Carcinogenesis,National Cancer Institute 米国がん研究所 人体発癌研究室長	**Dr. Maurice S. Fox（3 yrs）** Lester Wolfe Professor of Molecular Biology, Massachusetts Institute of Technology 米国マサチューセッツ工科大学 Lester Wolfe 分子生物学 教授
Dr. Clark W. Heath, Jr. Vice President for Epidemiology and Statistics, American Cancer Society 米国がん学会疫学 統計学担当副会長	**Dr. Theodore L. Phillips（2 yrs）** Professor and Chairman of Radiation Oncology, University of California, San Francisco 米国カリフォルニア大学 サンフランシスコ校 放射線腫瘍学 教授兼主任教授
Dr. John B. Little Simmons Professor of Radiobiology, Harvard School of Public Health 米国ハーバード大学 公衆衛生学部 Simmons 放射線生物学 教授	**Dr. John B. Little（1 yrs）** Simmons Professor of Radiobiology, Harvard School of Public Health 米国ハーバード大学 公衆衛生学部 Simmons 放射線生物学 教授

Chief of Secretariat　事務局長の指名

Present 現 任	New 新 任 Reappointment 再 任
Mr. Yasukiyo Hirano **平野 康清**	**Mr. Kazumasa Kunitoshi** **国利 一正**

Nomination of Operating Committee　運営委員の指名

Present 現 任	New 新 任 Reappointment 再 任
Dr. Itsuzo Shigematsu **重松 逸造** Chairman　理事長	**Dr. Shigenobu Nagakaki** **長瀬 重信** Permanent Director　常務理事
Dr. Sheldon Wolff Vice Chairman and Chief of Research 副理事長・研究担当理事	**Dr. Sheldon Wolff** Vice Chairman and Chief of Research 副理事長・研究担当理事
Dr. Shigenobu Nagakaki **長瀬 重信** Permanent Director　常務理事	
Dr. William J. Schull Permanent Director　常務理事 Retirement on 22 January 1997 1997年1月22日 退職	
Mr. Yasukiyo Hirano **平野 康清** Chief of Secretariat　事務局長	**Mr. Kazumasa Kunitoshi** **国利 一正** Chief of Secretariat　事務局長
Mr. R. D. Sperry Advisor, Secretariat　事務局参与	**Mr. R. D. Sperry** Advisor, Secretariat　事務局参与
	Mr. Takaaki Hashiguchi **橋口 高明** Assistant Chief of Secretariat 事務局次長

Abridged Curriculum Vitae

Name: Shigenobu Nagataki, M.D.,Ph.D.

Birth date: 18 January 1932

Present position: Permanent Director, Radiation Effects Research Foundation

Educational history:

1961	Graduated from School of Medicine, University of Tokyo, Japan
1965	Graduated from Postdoctoral Course at School of Medicine, University of Tokyo, Japan

Positions:

1961	Research Fellow in Medicine at the Thorndike Memorial Laboratory, Harvard Medical School, Boston, U.S.A.
1963	Assistant in Medicine, Faculty of Medicine, University of Tokyo, Japan.
1980-	Professor of Medicine, Nagasaki University School of Medicine, Nagasaki, Japan.
1994-96	Dean, Nagasaki University School of Medicine, Nagasaki, Japan.
1997	Retired from Professor of Medicine, Nagasaki University School of Medicine, Nagasaki, Japan.

Lecture in the presence of Emperror and Empress:

1995	Patients with radiation-induced disease after the accident of Chernobyl nuclear plant

Prizes:

1991	Sidney H. Ingbar Memorial Lecture (Beth Israel Hospital)
1993	Pitt-Rivers Lecture (The British Endocrine Societies)
1996	Kroc Lecture (Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, U.S.A.)
1996	Samuel Haines Memorial Lecture (Mayo Clinic, U.S.A.)

Honors:

1993	Honorary Member of the Chinese Medical Association (China)
1995	Foreign Member (Academician) of the Academy of Medical Sciences of Ukraine (Ukraine)

WHO:

1994	Director: WHO Collaborating Center for Research on Thyroid Disease
1995	Invited Speaker:Health consequences of the Chernobyl and other

radiological accidents (Geneva, Switzerland)

IAEA:

1996 Invited Speaker:IAEA International Conference: ONE DECADE AFTER CHERNOBYL (Vienna, Austria)

EC:

1996 Invited Speaker:FIRST INTERNATIONAL CONFERENCE: The Radiological Consequences of the Chernobyl Accident (Minsk, Belarus)

Ministry of Foreign Affairs, Japan:

1990- Member: Chernobyl Japan-USSR Specialists Meeting Concerning the Chernobyl Accident

Ministry of Education, Science, Sports and Culture, Japan:

1985 ad-hoc member:Organization of the Science Council (Committee on Scientific Research Grant)

1993 ad-hoc member:Organization of the Science Council (Committee on Scientific Research Grant)

Ministry of Health and Welfare, Japan:

1990 Chairman: Committee of the National Medical Practitioners Examination

1991- Member: Council on Medical Care for the Atomic Bomb Exposed

1994- Chairman: Committee of the Evaluation of the National Medical Practitioners Examination

Nagasaki City:

1996- Chairman, Board of Directors, Nagasaki Foundation for the Promotion of Peace

International Medical Associations (President):

1985- Asia and Oceania Thyroid Association

1991 International Immunology and Diabetes Workshop (Nagasaki, Japan)

1992 International Hashimoto Symposium: 80th Anniversary of Hashimoto Disease (Fukuoka, Japan)

1996 Siebold Memorial International Medical Symposium: 200 years anniversary of Dr. Philipp Franz von Siebold (Nagasaki, Japan)

Permanent Director (Japan)

Abridged Curriculum Vitae

Name: Sheldon Wolff

Birth date: 22 September 1928

Present position: Vice Chairman and Chief of Research, Radiation Effects Research Foundation

Educational history:

1950	B.S. Magna Cum Laude(Biology), Tufts College
1951	M.A.(Biology), Harvard University
1953	Ph. D.(Biology), Harvard University

Occupational history:

1951-52	Teaching Fellow - Harvard University
1952-53	National Science Foundation - Predoctoral Fellow
1953-66	Oak Ridge National Laboratory - Various Positions from Associate Biologist to Member, Senior Research Staff
1962 (Spring)	Visiting Professor of Radiation Biology - University of Tennessee, Zoology Department
1966-94	Professor of Cytogenetics - University of California, San Francisco (UCSF)
1994-present	Professor of Cytogenetics and Radiology Emeritus, UCSF
1983-95	Director, Laboratory of Radiobiology and Environmental Health, UCSF

Honors:

1973	United States Atomic Energy Commission - E.O. Lawrence Memorial Award
1980-81	President, Environmental Mutagen Society
1981	Honorary Vice-President of the third Intentional Conference on Environmental Mutagen
1982	Environmental Mutagen Society Award
1987	Paper selected as a "Citation Classic" by Institute for Scientific Information: Wolff Sheldon,1977, Sister Chromatid Exchange. Annu. Rev. Genet.11:183-201.
1988	Paper selected as a "Citation Classic" by Institute for Scientific Information: Wolff Sheldon and P.Perry 1974, Differential Giemsa Staining of Sister Chromatid Exchanges Without Autoradiography. Chromosoma 48:341-353.
1993	Paper selected as a "Citation Classic" by Institute for Scientific Information: Perry P. and Wolff Sheldon,1974, New Giemsa Method for the Diffcrential Staining of Sister Chromatids. Nature 251:156-158.
1992	Failla Lecturer and gold medal recipient, Radiation Research Society, 1992

Abridged Curriculum Vitae

Name: William Jackson Schull

Birth date: 17 March 1922

Present Position: Director and Ashbel Smith Professor of Academic Medicine, The Human Genetics Center, School of Public Health, The University of Texas Health Science Center, Houston, Texas 77225, U.S.A.

Educational history:

1946 B.S., Marquette University, Milwaukee, Wisconsin, Zoology
1947 M.S., Marquette University, Milwaukee, Wisconsin, Zoology
1949 Ph.D., Ohio State University, Columbus, Ohio, Genetics

Occupational history:

1951-1954 Instructor, Department of Zoology, University of Michigan

1954-1956 Assistant Professor, Department of Zoology, University of Michigan

1957-1962 Associate Professor, Department of Human Genetics, Associate Professor, Department of Zoology, University of Michigan

1962-1972 Professor, Department of Human Genetics and Anthropology, University of Michigan

1963 Visiting Professor, University of Chicago

1969 Visiting Fellow, Australian National University, July-December

1970 Deutsche Forschungsgemeinschaft Gast Professor, University of Heidelberg, January-June

1978-1980 Vice-Chairman and Chief, Department of Epidemiology and Statistics, Radiation Effects Research Foundation, Hiroshima, Japan

1986-1987
1990-1991 Director, Radiation Effects Research Foundation, Hiroshima, Japan

1981-present Director and Ashbel Smith Professor of Academic Medicine, Center for Demographic and Population Genetics, Graduate School of Biomedical Sciences; Professor of Human Genetics, School of Public Health, The University of Texas Health Science Center at Houston, Texas, 1972-1994; Director, Medical Genetics Center, GSBS

Abridged Curriculum Vitae

Name:	Shinichiro Ushigome
Date of Birth:	9 August 1934
Present position:	Professor and Chairman, Department of Pathology(I), Jikei University School of Medicine, Tokyo

Educational history:

Apr. 1953 - Mar. 1956	Tokyo Metropolitan University
Apr. 1956 - Mar. 1960	Jikei University School of Medicine

Occupational history:

Apr. 1960 - Mar. 1961	Internship at the First National Hospital, Tokyo
Jan. 1962 - Jan. 1963	Pathology Resident, United States Air Force Hospital Tachikawa
Jul. 1964 - Jun. 1966	Pathology Resident, Baylor College of Medicine, Houston, Texas (tuteledge by Professsor Harlan J.Spjut, M.D.)
Apr. 1967 - Mar. 1971	Fellow in Pathology, National Cancer Center Hospital, Tokyo
May 1968 - Mar. 1973	Instructor of Pathology, Jikei University School of Medicine, Tokyo
Apr. 1973 - Mar. 1976	Associate Professor of Pathology, St. Marianna University School of Medicine, Kawasaki
Apr. 1976 - Mar. 1987	Professor and Chairman, 2nd Department of Pathology, St. Marianna University School of Medicine, Kawasaki
Mar. 1979	Certified Pathology of Japanese Society of Pathology (Reg. No.19)
Dec. 1986	Certified Cytopathologist of Japanese Society of Clinical Cytology (Reg. No.678)
Apr. 1987 - present	Professor and Chairman, Department of Pathology (I) Jikei University School of Medicine, Tokyo
Apr. 1989 - present	Visiting professor, Kyung-Hee University School of Medicine, Seoul
Apr. 1995 - present	Professor, Jikei University School of Nursing, Tokyo

Rewards:

Apr. 1964	Fulbright Scholarship of United States-Japan Exchange Program

Punishments: No punishment inflicted

Society Membership:

Apr. 1970 -	Japanese Society of Pathology (Councilor)
Apr. 1994 - 1997	Japanese Society of Pathology (a member of the Board of Trustees)
Jan. 1992	Japanese Cancer Association (Councilor)
Jan. 1989 - Dec. 1994	Japanese Division of the International Academy of Pathology (Secretary General)
Jan. 1995-	Japanese Division of the International Academy of Pathology (President-Elect)
1993 -	Japanese Association of Orthopedics (Pathology consultant)
1983 -	International Skeletal Society
	Japanese Society of Clinical Cytology (Councilor, and a member of the Board of the Trustees)
1986 - 1994	Japanese Association of Pathologists (a member of the Board of the Trustees)
	Japanese Society of Reticuloendothelial System (Councilor)
	Japanese Society of Connective Tissue (Councilor)
1966 -	Japanese Medical Association
1995 -	New York Academy of Science
1980 -	Jikei Seiikai Medical Society (Councilor)
1993 -	U.S.-Canadian Academy of Pathology
Dec. 1996 -	International Academy of Pathology (Vice-President for Asia)

Editorial Boards:

1977 - 1987	St. Marianna Medical J
1989 -	Pathology International (Old Name: Acta Pathological Japonica)
1988 - 1992	Surgical Pathology
1993 -	International J Surgical Pathology
1990 -	Pathology and Clinical Medicine (Byori-to-Rinsho)
1993 -	Advances in Anatomic Pathology
1989 -	Jikeikai Medical Journal
1989 - 1995	Editing Consultant, Japanese Journal of Clinical Cytology
1996 -	Pathology Case Reviews

Abridged Curriculum Vitae

Name: Tomio Hirohata

Date of birth: 9 November 1931

Present position: Professor Emeritus, Department of Public Health, School of Medicine, Kyushu University
Professor, Department of Food and Nutrition Sciences, Nakamuta Gakuen University

Educational history:

March 1960	M.D., School of Medicine, Kyushu University, Fukuoka, Japan
1965	Master of Science in Hygiene (in Epidemiology), Harvard School of Public Health, Boston, USA
1968	Doctor of Science in Hygiene (in Epidemiology), Harvard School of Public Health, Boston, USA
1969	Doctor of Medical Science, School of Medicine, Kyushu University, Fukuoka, Japan

Professional Appointment:

1960-1961	Intern, St. Luke's International Hospital, Tokyo
1961-1966	Instructor, Department of Public Health, School of Medicine, Kyushu University, Fukuoka, Japan
1964-1965	Rockfeller Foundation Fellow, Harvard School of Public Health
1967-1970	Assistant Professor, Department of Public Health, School of Medicine, Kyushu University, Fukuoka, Japan
1970-1972	Senior Science Expert, United Nations Scientific Committee on the Effects of Atomic Radiation Primary contributor to the preparation of the U.N. Report of Radiation Carcinogenesis in Man
1970-1971	Visiting Professor of Public Health, School of Public Health, University of Hawaii, Manoa Campus, Oahu, USA
1971-1973	Associate Professor, Department of Public Health, School of Medicine, Kyushu University, Fukuoka, Japan
1973-1976	Head, Demographic Programs, Cancer Center of Hawaii, University of Hawaii, USA
1974-1976	Professor of Public Health, School of Public Health, University of Hawaii, Manoa, Oahu, USA
1976-1984	Professor and Chairman, Department of Public Health, School of Medicine, Kurume University, Kurume, Japan
1976-	Special consultant on occupational medicine for Fukuoka prefecture
1977-1979	Committee member of the International Agency for Research on Cancer

1985-1995	Professor and Chairman, Department of Public Health, School of Medicine, Kyushu University, Fukuoka, Japan
1986-1991	Principal Investigator, Cancer Epidemiology Research Team (Supported by the Ministry of Health and Welfare)
1988	Visiting Professor, School of Public Health, Harvard University, USA
1990-1992	President, Japan Cancer Epidemiology Association
1992-1995	President, Japan Epidemiological Association
1993-	Scientific Councilor, Radiation Effects Research Founfation
1995-	Professor, Nakamura Gakuen University, Fukuoka, Japan

Professional Society Affiliations:

Japan Hygiene Association, Council Member
Japan Cancer Society, Council Member
Editorial Board, Japanese Journal of Clinical Oncology
The Japanese Society of Cancer Epidemiology (Past President)
Editorial Board, Annals of Epidemiology (American College of Epidemiology)
Japan Epidemiological Association (Past President)
Royal Society of Medicine, Fellow, UK
Distinguished Service Awards for Occupational Medicine, Minister of Labor

Publications:

23 books
120 original papers (92 in English)
39 review papers

Abridged Curriculum Vitae

Name: Hiromichi Matsudaira

Date of birth: 19 December 1928

Present position: Adviser to the President, Japan Science & Technology Corporation

Educational history:

March 1948	Graduated from B Science Course, Shizuoka Higher School
March 1952	Graduated from Tokyo University Faculty of Medicine
March 1953	Completed internship at Tokyo University Faculty of Medicine Hospital
April 1953 - December 1954	Department of Biochemistry, Tokyo University Faculty of Medicine(left postgraduate course in midterm)
September 1953	Medical license (registration No. 150011)
January 1960	Doctor of Medical Sciences (Tokyo University)

Occupational history:

January 1955	Assistant, Tokyo University Faculty of Medicine
September 1955 - September 1957	Paris University Faculty of Medicine (fellowship from French Government)
November 1959-1962	Lecturer, Tokyo University Faculty of Medicine
April 1962-1964	Acting Head Radiologist, 3rd Section of Nuclear Medicine, Radiology Division, National Cancer Center Hospital
March 1964-1970	Radiology Division, National Cancer Center Research Institute
April 1970-1988	Chief, Division of Biology, National Institute of Radiological Sciences
1971-1977	Associate Lecturer, Chiba University
May 1988-1993	Director-General, National Institute of Radiological Sciences
December 1993-	Councilor, National Institute of Radiological Sciences
April 1994-1996	President, Research Development Corporation of Japan
October 1996-	Councilor, Japan Science and Technology Corporation

Academic societies:

1965-1996	Councilor, Japanese Cancer Association
1973-1977	President, Japanese Radiation Research Society
1992-1993	Councilor, Japanese Radiological Society
1994-	Councilor, Macromolecule Society
	Japanese Health Physics Society

Japanese Environmental Mutagen Society
Japanese Zoological Society
US Radiation Research Society

Committees:

1971-1987	Member, Radiation Handling Supervisor Examination Committee
December 1975-1993	Expert Member, Nuclear Fusion Board, Atomic Energy Commission
December 1978-1980	Expert Member, Nuclear Reactor Safety Committee, Nuclear Energy Safety Commission
July 1985-1994	Expert Member, Nuclear Energy Safety Commission
February 1986-1988	Expert Member, Japanese Radiation Council
April 1988-	Expert Member, Atomic Energy Safety Association
June 1988-1993	Consultant, Japan Atomic Energy Research Institute
June 1988-1993	Advisory Board Member, Japan Radioisotope Association
June 1988-1993	Member, Management Council, Nuclear Safety and Technology Center
July 1988-1993	Member, Japanese Radiation Council
July 1988-	Consultant, Japan Atomic Industrial Forum
1988-1996	Expert Member, Japanese Science Council
September 1989-	Member, A-bomb Medical Care Council (Ministry of Health and Welfare)
January 1991-1993	Member, Council of Cancer Control Specialists(Ministry of Health and Welfare)
April 1992-1993	Representative Secretary, Chokken-ren(Association of National Laboratories)
July 1993-	Scientific Councilor, Radiation Effects Research Foundation
February 1994-	Board of Director, Environmental Science Institute
April 1994-1996	Councilor, Basic Technology Research Promotion Center
April 1994-1996	Councilor, Institute of Agricultural Machinery (Ministry of Agriculture, Forestry and Fisheries)
April 1994-	Permanent Boars of Director, Japanese Radiation Research Society
April 1994-1996	Councilor, Japan International Scientific and Technology Exchange Center
April 1994-1996	Councilor, Semiconductor Research Promotion Society
April 1994-1996	Councilor, Japanese Patent Information System
April 1994-1996	Board of Director, Tokyo Applied Sciences and Technology Promotion Foundation
April 1994-1996	Board of Director, Mormo Science and Technology Promotion Foundation
April 1994-1996	Board of Director, Kanagawa Academy of Science and Technology
April 1994-1996	Board of Director, New Technology Promotion Watanabe Memorial Society
April 1994	Member, Screening Board for Ichimura Award, New Technology Development Foundation

April 1994-1996	Chairman, Committee for Harushige Inoue Award
1994-1996	Member, Industrial Ownership Screening Board(Patent Office)
1994-	Member, Japanese Radiation Council
1994-	Council, Medicine Side-Effects Aid and Research Promotion Fund
1994-	Vice-Chairman, Board of Director, New Technology Association
June 1996-	Member, Adhoc Commission of Japan Science and Technology Corporation Establishment (Prime Minister)
April 1996-	Member, Committee for Harushige Inoue Award
April 1994-1996	Member, Screening Board for Japanese Industrial Invention Technology Grand Prize, Nikkan Industrial Shimbun Press
July 1994- January 1997	Member, Operating Committee, National Institute of Metal Materials

International activities :

1977-1984, 1989-1992	International Commission of Radiological Protection (Committee 1 Member)
1978-1983	Councilor, International Association of Radiation Research
1988-1993	Japanese Representative, United Nations Scientific Committee on the Effects of Atomic Radiation
1990-	Advisory Editorial Board Member, Advance in Radiation Research (US)
1991-1997	Editorial Board Member, Radioprotection (France)
1992-	Editorial Board Member, Journal of Radiation Hygiene (Russia)
1993-	Main Committee Member, International Commission of Radiological Protection
1994-	Editorial Adviser, Radiation Research (US)
1997-	Editorial Corresponding Member

Abridged Curriculum Vitae

Name:	Masao Sasaki
Date of birth:	28 August 1936
Present position:	Professor, Kyoto University, Radiation Biology Center

Educational history:

March 1959	Graduated from Faculty of Education, Shimane University
March 1961	Master Course, Graduate School, Faculty of Science, Hokkaido University
March 1964	Doctor Course, Graduate School, Faculty of Science, Hokkaido Universit

Occupational history:

April 1964	Research Fellow, Center for the Health Sciences, University of California
October 1966	Associate Professor, Medical Research Institute, Tokyo Medical and Dental University
October 1978 -	Professor, Radiation Biology Center, Kyoto University
April 1979 -	Lecturer, Faculty of Medicine, Kyoto University
	Lecturer, Faculty of Medicine, Osaka University
April 1982 - March 1988	Lecturer, Shiga Medical University
April 1987 - March 1997	Lecturer, Faculty of Medicine, University of Tokyo
September 1993 -	Professor, Nuclear Reactor Research Institute, Kyoto University
April 1993 - March 1997	Director, Radiation Biology Center, Kyoto University
April 1995 -	Lecturer, Faculty of Pharmacology, Nagasaki University
January 1996 -	President, The Japan Radiation Research Society

Abridged Curriculum Vitae

Name: Shigefumi Okada

Date of birth: 13 December 1925

Present position: Professor Emeritus, University of Tokyo

Educational history:

March 1948	B.S. in Chemistry, Department of Chemistry, Faculty of Science, University of Tokyo
June 1956	Ph.D. in Biophysics, Department of Radiation Biology and Biophysics, School of Medicine, University of Rochester

Occupational history:

June 1948	Research Associate, Department of Radiology, Faculty of Medicine, University of Tokyo
September 1956	Post-doctoral Fellow, Department of Chemistry, King's College, University of Durham
June 1958	Post-doctoral Fellow, Department of Radiology, School of Medicine, University of Rochester
June 1959	Instructor, Department of Radiology, School of Medicine, University of Rochester
June 1961	Research Assistant Professor, Department of Radiology, School of Medicine, University of Rochester
August 1964	Research Associate Professor, Department of Radiology, School of Medicine, University of Rochester
July 1965	Associate Professor, Department of Radiation Biology and Biophysics, School of Medicine, University of Rochester
July 1968	Professor, Department of Radiation Biology and Biophysics and Department of Radiology, School of Medicine, University of Rochester
September 1968	Professor, Department of Radiation Biophysics, Faculty of Medicine, University of Tokyo
April 1984	Professor, Radiation Biology Center, Kyoto University
July 1985	Scientific Councillor, Radiation Effects Research Foundation

Scientific memberships:

Radiation Research Society (USA)
Japan Radiation Research Society
Japan Radiological Society
Japan Cancer Association

Current Appointments:

Editor: International Journal of Radiation Biology
International Journal of Radiation Oncology, Biology and Physics
Radiation and Environmental Biophysics
Advances in Radiation Biology

Executive Member, Japan Radiation Research Society

Chairman, Committee on Radiation Research, Science Council of Japan

Abridged Curriculum Vitae

Name: Joe W. Gray

Birth Date: 04/26/46

Present Position: Professor of Laboratory Medicine and Radiation Oncology, University of California, San Francisco

Education:				
	Colorado School of Mines	Professional Engineer	1968	Physics
	Kansas State University	Ph.D.	1972	Physics

Professional Experience:		
	1972-91	Biomedical Scientist, Biomedical Sciences Division, Lawrence Livermore National Lab., University of California, Livermore, CA
	1982-91	Section Leader, Cytophysics Section, Biomedical Sciences Division, Lawrence Livermore National Laboratory, University of California, Livermore, California
	1984-91	Adjunct Professor of Laboratory Medicine, University of California, San Francisco, CA
	1991-1996	Director, Division of Molecular Cytometry, University of California, San Francisco, CA
	1990-present	Member, NIH Human Genome Advisory Council
	1991-present	Professor of Laboratory Medicine and Radiation Oncology, University of California, San Francisco
	1992-present	Senior Scientist (faculty), Biophysicist, Lawrence Berkeley Laboratory
	1992-present	Director, Resource for Molecular Cytogenetics, Lawrence Berkeley Laboratory
	1995-present	Interim Director, UCSF Cancer Center, University of California, San Francisco
	1996-present	Program Director, Cancer Genetics Program, UCSF Cancer Center, University of California, San Francisco

Honors: Research Award, Radiation Research Society, 1985
E.O. Lawrence Award, Department of Energy, 1987
Fellow, American Association for the Advancement of Science, 1996

Current Research Interests: Molecular cytogenics, analytical cytology, genetic disease diagnosis, tumor cytogenetics, and biological dosimetry.

Abridged Curriculum Vitae

Name: Susan Preston-Martin

Birth Date: 1942

Present Position: Professor of Preventive Medicine

Education:	Swarthmore College, PA	B.A. 1963	Experimental Psychology
	Univ. of California, Los Angeles	M.P.H. 1972	Health Services/ Epidemiology
	Univ. of California, Los Angeles	Ph.D. 1978	Epidemiology

Professional Experience:	1972-77	Head of Field Operations, Los Angeles Cancer Surveillance Program
	1978-1983	Assistant Professor of Preventive Medicine, University of Southern California (USC)
	1984-1989	Associate Professor of Preventive Medicine, USC
	1990-	Professor of Preventive Medicine, USC

Honors:

Swarthmore College: full scholarship; Mortar Board Honor Society; Honors Program; 1959-1963

UCLA: Delta Omega; Medical Center Award; Outstanding Graduate Scholar; 1972-1978

International Agency for Research on Cancer, Visiting Scientist Award, 1984-1985

Fogarty Senior International Fellowship, 1991-1992

Committees:

NIH Cancer Research Manpower Review Committee, 1985-1989

NIH Reviewer's Reserve, (ad hoc reviewer), 1989-1993

Editorial Board, Cancer Causes and Control, 1994-1997

Scientific Advisory Board, Electric Power Research Institute, 1995-1999

Board of Directors, Central Brain Tumor Registry of the United States, 1995-

Scientific Councilor, Radiation Effects Research Foundation, 1996-

Research Interests: Cancer epidemiology and biostatistics.

Abridged Curriculum Vitae

Name: Maurice S. Fox

Birth Date: 10/11/24

Present Position: Lester Wolfe Professor of Molecular Biology, Massachusetts Institute of Technology

Education:	University of Chicago	B.S.	1944	Meteorology
	University of Chicago	M.S.	1951	
	University of Chicago	Ph.D.	1953	Chemistry

Professional Experience:	1951-53	Instructor, University of Chicago
	1953-62	Assistant, Assistant Professor, Associate Professor, The Rockefeller Institute
	1962-66	Associate Professor, Massachusetts Institute of Technology
	1966-present	Professor, Massachusetts Institute of Technology Lester Wolfe Professor of Molecular Biology
	1979-present	Massachusetts Institute of Technology
	1985-1989	Head, Department of Biology, MIT

Honors:
Fellow, United States Public Health Service, 1952-1953
Nuffield Research Fellow, 1957
Lalor Award, 1959
Fellow, American Association for the Advancement of Science, 1963
Member, Institute of Medicine, 1980
Member, National Academy of Sciences, 1988

Committees: Board on Radiation Effects Research, National Research Council, 1996-1999

Current Research Interests: The molecular mechanisms of genetic recombination; cancer diagnosis, treatment, and natural history.

Abridged Curriculum Vitae

Name: Theodore L. Phillips

Birth Date: 06/04/33

Present Position: Professor of Radiology
Chair, Division of Radiation Oncology
Research Physician, Donner Laboratory and
Lawrence Berkeley Laboratory
University of California, School of Medicine, San Francisco

Education:			
	Dickinson College	B.S.	1955
	Univ. of Pennsylvania	M.D.	1959

Professional Experience:		
	1959-60	Intern, University Hospital, Cleveland, OH
	1960-63	Resident Therapeutic Radiologist
	1965-68	Assistant Professor of Radiology
	1968-70	Associate Professor of Radiology
	1970-present	Professor of Radiology, University of California, San Francisco, CA
	1973-present	Chairman, Division of Radiation Oncology

Honors: Janeway Medal and Lecture, American Radium Society, 1993
C. Chester Stick Award, Memorial Sloan Kettering Cancer Center, 1993
Gold Medal of the American Society for Therapeutic Radiology and Oncology, 1993

Committees: Past-president of the American Society for Therapeutic Radiology and Oncology, the Radiation Research Society, and the North American Hyperthermia Society.

Current Research Interests: Normal tissue effects, neutron radiobiology, and the study of fractionation and pharmacological effects on tissue injury and recovery.

Abridged Curriculum Vitae

Name: John B. Little

Birth Date: 10/05/29

Present Position: Simmons Professor of Radiobiology
Department of Cancer Biology
Harvard School of Public Health

Education:

Harvard University	A.B.	1951	Physics
Boston University	M.D	1955	
Harvard School of Public Health	Fellow	1963	Physiology & Radiobiology

Professional Experience:

1955-56	Intern (Medicine) Johns Hopkins Hospital, Baltimore, MD
1958-61	Resident in Radiology, Massachusetts General Hospital, Boston, MA
1963-65	Instructor in Physiology (Radiobiology) Harvard School of Public Health
1965-	Consultant in Radiology, Massachusetts General Hospital, Boston, MA
1965-69	Assistant Professor of Radiobiology, Harvard School of Public Health
1969-	Lecturer on Radiology, Harvard Medical School
1969–1975	Associate Professor of Radiobiology, Harvard School of Public Health
1975-	Professor of Radiobiology, Harvard School of Public Health
1980-83	Chairman, Dept. of Physiology, Harvard School of Public Health
1982-	Director, Kresge Center for Environmental Health, Harvard University
1987-	James Stevens Simmons Professor of Radiobiology

Committees: Chairman, Board on Radiation Effects Research, National Research Council, 1996

Current Research Interests: Molecular and genetic mechanisms of mutagenesis and transformation.

(Candidate for Chief of Secretariat, Radiation Effects Research Foundation)

KAZUMASA KUNITOSHI

Date of birth:	26 January 1943 (54 years old)
Place of birth:	Hiroshima prefecture
Education:	Graduated from Chuo University (Department of Law) in March 1965.
Qualification:	Passed national public service examination for middle class position in February 1965.
Grade/step:	Administrative position (-), Grade 10, Step 15 (next salary increase due on 1 April 1997).

Occupational history:

April 1965	Employed by Chugoku Regional Finance Bureau.
July 1975	Chief, Financing Unit, Economic Section, Yamuguchi Finance Department, Chugoku Regional Finance Bureau.
July 1978	Chief, Credit Management Unit, Collection Department, Yamaguchi Custodial Department, Chugoku Regional Finance Bureau.
July 1980	2 Chief, Medium- & Small- Financing Unit, Financing Section, Yamaguchi Economic Department, Chugoku Regional Finance Bureau.
July 1983	Senior Investigator, Economic Investigation Section, Yamaguchi Economic Department, Chugoku Regional Finance Bureau.
July 1984	Chief, Economic Section, Tottori Finance Department, Chugoku Regional Finance Bureau.
July 1986	Senior National Property Official, Guidance Section, Tottori Property Custodial Department, Chugoku Regional Finance Bureau.
July 1988	Chief, Finance Inspection Section, Tottori Economic Department, Chugoku Regional Finance Bureau.
July 1990	Chief, Housing Section, Tottori Property Custodial Department, Chugoku Regional Finance Bureau.
July 1991	Chief, Personnel Section, Tottori General Affairs Department, Chugoku Regional Finance Bureau.
January 1993	Manager, Okayama Finance Office, Chugoku Regional Finance Bureau.
July 1995	Assistant Chief, Economic Department, Kyushu Regional Finance Bureau.
July 1996	Chief, Property Custodial Department, Chugoku Regional Finance Bureau.
July 1997	Resignation due.

Schedule of next board meeting

PLACES AND DATES OF RERF BOARD MEETINGS

1st Board Meeting:	Hiroshima:	14 April 1975
2nd Board Meeting:	Hiroshima:	24 - 25 September 1975
3rd Board Meeting:	Hiroshima:	8 - 10 June 1976
4th Board Meeting:	Hiroshima:	31 January - 2 February 1977
5th Board Meeting:	Hiroshima:	22 - 23 June 1977
6th Board Meeting:	Nagasaki:	24 - 25 January 1978
7th Board Meeting:	Hiroshima:	27 - 28 June 1978
8th Board Meeting:	Hiroshima:	23 - 24 January 1979
9th Board Meeting:	Hiroshima:	23 - 24 May 1979
10th Board Meeting:	Nagasaki:	22 - 23 January 1980
11th Board Meeting:	Hiroshima:	10 - 11 June 1980
12th Board Meeting:	Hiroshima:	27 - 28 January 1981
13th Board Meeting:	Hiroshima:	9 - 10 June 1981
14th Board Meeting:	Hiroshima:	26 - 27 January 1982
15th Board Meeting:	Washington, DC:	16 - 18 June 1982
16th Board Meeting:	Nagasaki:	17 - 18 February 1983
17th Board Meeting:	Hiroshima:	8 - 9 June 1983
18th Board Meeting:	Hiroshima:	13 - 15 June 1984
19th Board Meeting:	Washington, DC:	17 - 19 June 1985
20th Board Meeting:	Nagasaki:	10 - 12 June 1986
21st Board Meeting:	Hiroshima:	9 - 11 June 1987
22nd Board Meeting:	Washington, DC:	22 - 24 June 1988
23rd Board Meeting:	Nagasaki:	21 - 23 June 1989
24th Board Meeting:	Hiroshima:	6 - 8 June 1990
25th Board Meeting:	California, Irvine	19 - 21 June 1991
26th Board Meeting:	Nagasaki:	24 - 26 June 1992
27th Board Meeting:	Hiroshima:	10 - 12 June 1993
28th Board Meeting:	Hiroshima:	22 - 24 June 1994
29th Board Meeting:	Hiroshima	26 - 28 June 1995
30th Board Meeting:	Hiroshima	5 - 7 June 1996
31st Board Meeting:	Washington, DC:	11-12 June 1997

Any other business