FY2026 Plans of Activities

A. Plans of Major Activities

RERF research activities prioritize the evaluation of radiation-related long-term health effects in atomic bomb survivors, and possible transgenerational effects of parental radiation exposure on their children. RERF is grateful for the dedicated support and cooperation of the atomic bomb survivors and their children. Ongoing plans for long-term follow up of epidemiologic studies of atomic bomb survivors and their children to assess risk of cancer and non-cancer disease have been largely covered under research achievements. Here, we provide highlights of new research plans and selected plans of note.

1. Research Projects Examining A-bomb Survivors Health

1.1 Radiation and Cancer

- *Updated Life Span Study (LSS) report on mortality from cancer and non-cancer disease, 1950–2021 (RP 1-75)*: The analysis and publication of LSS Report 15 on mortality among atomic bomb survivors will be one of the highest priority projects over the next several years. Risk analyses will commence after completion of the new J45 organ dose (expected by mid-2026). The anticipated observation period of 1950 to 2021, an 18-year extension of follow-up, will result in more than double the number of deaths among those exposed before age 30 years compared to Report 14, thus providing key information on mortality among those who were young at the time of bombing. The updated analysis will also provide more information on the nature of the dose–response relationship for solid cancers, as well as on emerging mortality risks for non-cancer diseases such as cardiovascular diseases. Following the publication of overall mortality risks, more detailed analyses are planned for major subgroups such as cancer and diseases of the circulatory system.

- *Updated Life Span Study (LSS) report on cancer incidence, 1958-2020 (RPs 1-75, 18-61)*: The new analysis of cancer incidence in atomic bomb survivors, incorporating an additional 11 years of follow-up (through 2020), has been launched with high priority. In recent years, cancer cases have been observed mostly in individuals who were younger than 20 years of age at the time of the bombings. The distribution of observed cancer types differs by calendar time due to factors such as aging of the subjects, changes in risk factors (e.g. viral infections, lifestyle, reproductive factors), and improved diagnostic techniques over the 60-year follow-up period. Modeling for radiation-associated risk estimation will be improved through consideration of these factors, as well as incorporation of revised J45 organ doses, and re-estimated migration rates using contact information for AHS. In addition to an analysis of all solid cancer incidence, more detailed analyses will be conducted and published separately for specific sites of interest.

- *Cancer incidence study series 1958-2009 (RPs 1-75, 18-61)*: A summary of results from the series of site-specific incidence papers for the follow-up period 1958–2009 was completed and published in 2025. A follow-up methodological paper aimed at better understanding the sources of all solid cancer dose–response curvature among males, as well as the heterogeneity of radiation effects across solid cancers, is expected to be completed in 2026. Joint endpoint analyses of site-specific risks according to families of physiologically related cancers (upper gastrointestinal, lower gastrointestinal, hepatobiliary, respiratory, urinary, male reproductive, and female reproductive) have identified several factors that influenced the dose–response curvature for the combined

outcomes, including unaccounted heterogeneity in site-specific baseline rates and models, the form of high-dose adjustment, and the choice of a representative organ dose for superficially located sites. This work has potential implications for how solid cancers may be pooled and analyzed in future research.

- *Completion of site-specific cancer studies with pathological reviews in the LSS cohort*: With changing classification of disease and sub-types over time, very few studies can provide radiation risk estimates applying standardized diagnostic criteria based on pathological review of cases collected over several decades. In 2026, RERF plans to complete and publish analyses of radiation-related risk comparing subgroups of cancers of the breast (1958–2005), uterine corpus (1958–2011), and hematological malignancies (1950–2009). Analyses of soft tissue and bone tumors (1958–2003) and skin cancer (1958–2011) will continue.

- *Pathogenesis of myelodysplastic syndrome (MDS) (RP 1-17)*: A-bomb survivors have a high risk of hematological malignancies, but little is known about the mechanisms of radiation-induced myeloid malignancies. In 2026, we will complete and submit a manuscript on the results of whole exome sequencing (WES) analyses using blood samples before diagnosis of MDS. We will further assess differences in the dynamics of structural variation between low and high dose groups using whole genome sequencing data to better understand the effects of A-bomb radiation.

- *Leukemia among A-bomb survivors (RP-P1-23)*: We will complete and submit a scientific paper regarding the applicability of targeted sequencing in old formalin-fixed paraffin embedded (FFPE) samples. Based on pilot study results, we plan to initiate a related full-scale study "Identification of clinicopathological findings associated with radiation dose in hematological malignancies among atomic bomb survivors."

- *Radiation and Liver Cancer, (RP 9-92)*: The established association between radiation and chronic hepatitis B virus (HBV) infection, together with the known roles of both radiation and HBV in risk of hepatocellular carcinoma imply that HBV is a mediator, but the extent of mediation has not been established. We will complete an analysis of potential mediation and moderation of radiation risk for hepatocellular carcinoma by hepatitis C virus (HCV) infection with concomitant adjustment for possible interaction between HCV and obesity.

- *Hiroshima and Nagasaki tumor/tissue registries (RPs 18-61, 29-60)*: Regular activities in National Cancer Registry and Nagasaki tissue registry continue under contract with each authority. The Dept. of Epidemiology will continue to crosscheck the subjects of RERF major cohorts against newly registered data with approval from each authority.

- *Pathology studies (RPs 5-89, 1-12)*: Efforts to preserve and utilize pathological materials from A-bomb survivors will be continued in collaboration with local hospitals in Hiroshima and Nagasaki. The indexing of FFPE tissue specimens within a new database will continue in collaboration with RERF's Biosample Research Center.

1.2 Radiation and Non-Cancer Effects

- *Updated Adult Health Study (AHS) report on non-cancer disease, 1958-2020 (RP2-75)*: We will conduct the final analysis of associations between the incidence of noncancer diseases and A-bomb radiation dose for all AHS cohort groups except those exposed *in utero* after the revised J45 organ doses become available (expected mid-2026). The

analysis will use updated longitudinal data with 22 years of further follow up and twelve additional disease outcomes compared to the last report (2004). AHS cohort health examinations and collection of clinical/epidemiological data and biosamples will continue.

- *Radiation and Cataracts (RP 5-15)*: Analyses of radiation-related cataract risk in AHS participants using standardized diagnostic criteria were completed and published in 2025. In 2026, we will start analyzing the data of participants exposed *in utero* using the revised J45 organ dose.

- *Radiation and Diseases of the Circulatory System:*
  - *Radiation and Atherosclerosis (RP2-11, RP 1-23-2)*: Radiation effects on measured levels of cytokines were assessed (manuscript submitted in 2025). Further analyses will incorporate cytokines into a Multiple Indicator Multiple Cause (MIMIC) model for analysis of these cytokines as mediators of the effect of radiation on latent atherosclerosis subtypes (expected completion in late 2026). We also expect to begin conceptualizing an analysis of longitudinal measurements of inflammatory markers to study the long-term effects of post-radiation-exposure inflammation on atherosclerosis risk.
  - *Radiation and Stroke incidence (RP 1-21)*: Statistical analysis to determine the association between radiation and incidence of stroke will be completed after the new organ doses become available, and a manuscript will be submitted.
  - *Radiation and Myocardial infarction incidence (RP 1-22)*: An association between exposure to radiation and the incidence of MI from 1958 to 2015 was observed in females, but not in males (submitted for publication in 2025). We will further investigate possible factors underlying the sex difference in the dose–response relationship for MI.
  - *Radiation and Heart disease (RP 2-14):* Analyses of the association between radiation and diastolic dysfunction, heart failure, and valvular heart disease will continue, and a manuscript focusing on diastolic function using conventional echocardiography will be prepared in 2026. Collection of data using speckle-tracking echocardiography is in process.

- *Radiation and Diabetes (RP 1-15)*: We will investigate how radiation exposure affects conditions related to insulin resistance, such as steatotic liver disease.

- *Radiation and Thyroid conditions (RP 4-23)*: A previous AHS study conducted in 2007–2011 reported increased radiation-related risk of thyroid nodules, but not of thyroid dysfunction and autoimmunity. In 2026, following completion of the 3rd examination cycle, we will prepare data for a full-scale analysis on the progression of thyroid nodules (planned for 2027).

- *Radiation and Chronic kidney disease (CKD) (RP-A1-14*): We will complete statistical analysis of the association between radiation and CKD, and prepare a manuscript.

1.3 Underlying Biological Mechanisms of Radiation Health Effects

- *Preparation for AHS Genome Wide Association Study (RP P2-22)*: The analysis of Illumina array data from 12 AHS subjects evaluating call rates and concordance in 10, 20, 30, and 50 year old samples will be completed and submitted for publication in 2026.

Results suggest that reliable genotyping can be achieved using high-density SNP arrays with DNA extracted from stored blood smears following whole genome amplification. This finding creates an opportunity to maximize the sample size for a full-scale GWAS within the AHS.

- *Evaluation of radiation-associated Clonal Hematopoiesis (CH) – Human Studies, (RP 1-23-1)*: This study evaluates the prevalence of CH in approximately 150 AHS participants and characterizes clonal expansion of hematopoietic stem cells (HSCs) in high-dose-exposed individuals through statistical and bioinformatic analyses of whole-exome sequencing (WES), SNP array, and T-cell receptor (TCR) deep-sequencing data. Analyses of radiation effects on CH mutations and T-cell expansion, with regression adjustment for age and sex, are expected to be completed in early 2026.

- *Radiation and Clonal Hematopoiesis (CH) – Animal Studies (RP 1-23-3)*: In 2026, we will:
  - Complete a manuscript on the timing of mutation acquisition and clonal evolution and expansion in mice with radiation-induced CH. The mouse CH study takes a unique approach by integrating clonal phylogenetics with longitudinal trajectories of peripheral blood mutations, enabling time-resolved biodosimetry that may improve our understanding of individual risk trajectories and late health effects in human cohorts, including A-bomb survivor studies.
  - Continue characterizing and longitudinally tracking CH mutants in atherosclerotic LDLR- or APOE-knockout mice following radiation exposure to elucidate the molecular mechanisms underlying inflammatory diseases driven by radiation-associated CH.

- *Preliminary study of chromosome aberration frequency in hematopoietic stem cells (HSCs) following fetal irradiation of mice (RP P4-17)*: To further investigate the mechanisms involved in the process of the disappearance of chromosomal aberrations that occurred in fetal LT-HSCs, we will extend the study and proceed to evaluate the effects of *in utero* radiation exposure through whole genome sequencing (WGS) analysis. The aim is to confirm whether WGS results concerning the effects of *in utero* radiation exposure align with the findings of previous chromosome studies.

- *Preliminary study on possible roles of oxidative stress response in protection against radiation-induced mutagenesis and oncogenesis in mice (RP P3-19)*: A manuscript describing the protective role of NRF2 against radiation-induced somatic mutations in long-term hematopoietic stem cells (LT-HSCs) will be completed and submitted for publication. The analysis of WGS data from LT-HSC-derived clones obtained from WT C57BL/6J mice irradiated at 2 weeks of age (infancy) will be completed to identify somatic mutations, compare them with our published results from mice irradiated at 8 weeks of age (adulthood), and assess differences in mutation frequency and type. We also hope to validate chromosomal aberrations detected in LT-HSC-derived clones to elucidate age-at-exposure effects on radiation-induced somatic mutagenesis.

2. Research Projects on the Health of A-bomb Survivors Children (F_1)

- *Mortality surveillance for In Utero and F1 cohorts (RPs 1-75, 2-61, 4-75):* Mortality follow-up for both cohorts will continue and the data will be completed through 2022. Archiving of early-period materials will continue in collaboration with the Research Resource Center of RERF.

- *F1 Offspring Clinical Study (FOCS), (RP 4-10):* We have completed analyses of potential effects of parental radiation exposure on disease risk in offspring with an illness-death model for any combination of one or more of the primary disease endpoints (hypertension, hyper-LDL cholesterolemia, hyper-triglyceridemia, and diabetes), and with a multistate model for single and multiple disease categories as separate risks. In 2026, we intend to compare the results with a method appropriate for interval-censored data and further investigate self-selection bias.

- *Transgenerational Effects, Trio Genome Study (RP 3-23):* Following formal approval and public announcement of the main project (December 23, 2025), we will proceed with genotyping and analysis of the samples with consent. First, we will identify and confirm de novo mutations (including structural variants) occurring in the children, and determine their parental origins. During FY2026, we expect to complete whole genome sequencing (WGS) on more than half the target samples. We will also continue efforts to obtain informed consent for participation in the Trio Genome Research. Specific procedures for disclosing individual genetic data will be finalized in consultation with domestic and international experts, and patient and public involvement (PPI) initiatives will be continue.

- *Transgenerational Effects, Animal Studies (RP 2-13, RP S3-11)*: A paper describing spontaneous *de novo* structural variants in the mouse germline will be published. We have successfully developed a methodology to capture genomic structural changes at a larger scale than common structural variants, which we plan to confirm using techniques such as ultra-long-read sequencing. Minisatellite region mutations have long been a focus in the field of radiation-induced mutations. If this analysis system can be established successfully, it will enable the study of minisatellite mutations throughout the genome, which we will apply first to mouse models of radiation exposure, and in the future to studies of germline and somatic mutations in A-bomb survivors.

3. Research to Elucidate Individual Doses and Effects from the A-bombs

- *Shielding Survey and Dosimetry (RP 18-59)*: The Department of Statistics will complete work on an updated organ dosimetry system using modern, sophisticated J-45 computational phantoms.

- *Further evaluation of the constant RBE assumption in RERF analysis. Dept. Statistics. PI: Sposto R [RP 18-59]:* Analytic investigation revealed that there can be substantial bias in excess risk estimation if the constant relative biological effectiveness (RBE) of neutron assumed in RERF analyses differs from the true limiting maximum RBE. Most previous analyses aimed at estimating the appropriate RBE from RERF analyses are estimating a quantity that is different from the limiting maximum RBE. Research in the coming year will focus on methods either to unbiasedly estimate the limiting maximum RBE or methods to estimate the neutron / gamma response surface directly with acceptable precision.

- *Dosimetry Error*: Radiation dose estimates are known to contain uncertainty, primarily due to imprecise source information such as individuals' locations at the time of the bombings and the shielding. To address this issue, RERF has been using a method proposed in 1990, originally developed for the DS86 dosimetry system. We plan to update this methodology for use in the next series of LSS analyses.

4. Project to Communicate Research Results and to Collaborate with Other Scientific Organizations

- *Communicating Research Results*: In addition to publication of RERF research in peer-reviewed academic journals, RERF will contribute to high-visibility reports by international dosimetry and radiation risk assessment groups such as the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the International Commission of Radiation Protection (ICRP).

- *Continuing collaboration*: RERF's long-term collaboration with numerous Japanese and international institutions is expected to continue in 2026, including:

  a. Partnerships with the Universities of Hiroshima, Nagasaki, Kurume
  b. Collaboration with the U.S. National Cancer Institute
  c. Collaboration with the University of Washington
  d. Collaboration with Outside Investigators:
     47 Japanese Institutions
     6 North American Institutions
     10 European Institutions
     1 Asian Institution

5. Training programs for domestic and overseas specialists

RERF will hold a training workshop for non-epidemiologist radiation researchers to facilitate their understanding of the basics of epidemiological research and increase their understanding of radiation health risks. In addition, RERF will train staff to work in the fields of radiation protection, radiation emergency medical care, and radiobiological research.

1) RERF plans to accept physicians and researchers from overseas to provide them with training through the MHLW-sponsored FY2026 International Exchange and Research Program.

2) RERF will accept overseas research trainees to support the activities of such organizations like the Hiroshima International Council for Health Care of the Radiation-exposed (HICARE), the Nagasaki Association for Hibakusha's Medical Care (NASHIM), and Nagoya University Graduate School.

3) RERF intends to hold its epidemiological training workshop for radiobiologists in Japan to enhance their understanding of results from epidemiological research on A-bomb survivors.

6. Public Information Programs

These programs aim to communicate the scientific findings obtained from the long-term follow-up on the A-bomb survivors and their children to the study participants (A-bomb survivors and their children) and the general public in an easily understandable manner. By deepening understanding of RERF's research activities and contribution to society, these programs also seek to promote accurate understanding of radiation health effects. In FY2026, RERF will engage in the following activities.

i) PR Activity for RERF Programs

Every year, we accept many visitors from outside organizations and groups and provide them with a summary of the foundation's programs. In FY2026, we will also proactively welcome visitors to deepen their understanding of the foundation's programs and its

societal significance and contributions to expand the scope of those who empathize with the foundation's activities and provide support and cooperation for RERF a continuous basis.

ii) Communication of Research Results

- To enhance the content of the website's portal of the Trio Study Using Genome Analysis initiated last December, we will consider how it will be updated and released in the future.
- We will organize an explanatory meeting on research progress and updates to enhance the study participants' understanding of the foundation's research programs.
- For the media, we will organize study sessions or gatherings to exchange opinions for their accurate understanding of research activities.

iii) Open House

With the Hiroshima Laboratory's relocation, this year's Open House event will be the last to be held at the current facility. The Open House Working Committee and the Public Relations & Publications Office will work together to consider the event's programs and exhibitions. In addition, the issue of holding the event at the new facility after relocation will be considered.

iv) Renewal of Official Website

The objective of renewing the official website is to further strengthen the foundation's information dissemination capabilities, accurately deliver precise and easy-to-understand information to diverse domestic and international target parties, and broadly foster understanding and empathy for the foundation's activities, achievements, and social significance. Concurrently, we seek to deepen trust-based relationships with stakeholders through highly interactive information sharing and promote sustained dialogue with society. In FY2026, we will promptly select a contractor for the website renewal project, and an internal working group will lead the effort to complete the new website.

v) Response to Media Inquiries on Hiroshima Laboratory's Relocation

The Hiroshima Laboratory's relocation scheduled for spring 2027 is attracting significant public attention, and numerous media inquiries are anticipated. We have already received inquiries regarding the transfer of biosamples and will handle such inquiries, including requests for filming existing facilities, carefully to avoid disrupting operations. Regarding Hijiyama Hall, inquiries have come not only from the media but also from those in architecture and the general public. We will explore opportunities for public visits, similar to last year.

vi) Updating Printed Materials

The brief description of RERF, leaflet, and other printed materials will be updated to reflect the Hiroshima Laboratory's relocation. Information on research outcomes and activities will also be updated with the latest content to enhance public understanding of the foundation's role and significance and increase public awareness by communicating information clearly and attractively.

vii) Facility Tours and School Visits

We will continue to present information on its research achievements to date, its contributions to the maintenance of the health and welfare of the A-bomb survivors and

to the enhancement of the health of all humankind, and the significance of its upcoming research by receiving visitors and visiting schools. This will include more than distributing information—we will continue our efforts to ensure the significance of our research is understood by people from all walks of life: A-bomb survivors, their children, researchers, government personnel, peace volunteers, students, members of the communities, overseas visitors, and others.

(Other public relations activities)

- Releasing accessible information about research results through press releases and conferences.
- Regularly tracking coverage in the media and planning the maintenance and enhancement of relationships with the media through close communication.
- Preparing a synopsis for each paper and communicating research results in an accessible manner.
- Actively utilizing our social media accounts, relaunched in FY2025, to enhance the foundation's visibility. This will include disseminating information about our research activities as well as utilizing these channels for releasing recruitment information, etc.
- Responding to everyday inquiries from outside parties in a timely manner as much as possible.
- Creating a digital archive of videos and still images of the historically significant structures of the current Hiroshima Laboratory.

B. Operation and Management of RERF

1. Research Resource Center

In FY2026, the Research Resource Center (RRC) will focus on consolidating and extending the operational framework established in FY2025, with emphasis on practical usability, secure integration, and sustained institutional impact. The Biosample Research Center (BRC) will continue its core mission of high-quality biosample management and stewardship, while supporting expanded linkage of biosample inventory information. The Research Resource Section (RRS) will continue to provide stable technical, computational, and analytical support, ensuring reliable operation of research data environments. The Data Resource Center (DRC) will advance as the central operational component for data integration, access, and visualization. Planned activities for FY2026 include:

- Formalization of the RRC governance framework, clarifying functional relationships among BRC, RRS, DRC, and research support functions.
- Continued build-out of the Data Resource Center (DRC) as the institutional hub for curated research datasets, integrated metadata, and researcher-facing data access.
- Expansion of institution-wide data integration efforts, including linkage of epidemiologic, clinical, biosample, and consent-related data.
- Development and deployment of research dashboards and visualization tools to support study feasibility assessment, cohort characterization, and internal decision-making.

Through these activities, the RRC will transition from initial implementation to an evolving institution-wide research infrastructure supporting modern data-driven research and long-term stewardship of RERF's core scientific assets.

2. Relocation of Hiroshima Laboratory

In FY2026, the steel-framed structure for floors four through ten of the new building will be constructed. Then, plumbing, electrical wiring, and interior finishing work will follow sequentially. Construction of the building, including the exterior, will proceed with a target completion date of January 2027. After the new building is completed and handed over, office and research equipment, as well as other items, will be moved in.

3. Revision of the rules and regulations

RERF revises the current regulations and establishes new regulations based on revisions to laws and regulations and regular reevaluation by the sections in charge. In FY2026, amendments to the RERF Articles of Incorporation and related regulations will be made in accordance with the Hiroshima Laboratory's relocation. Other revisions will also be made as needed to ensure that the foundation's management operations remain appropriate. These amendments and revisions will provide RERF with regulations befitting of a public interest incorporated foundation funded by the U.S. and Japanese government subsidies.