Joy Wilson
04/08/99 09:41 AM

To: Elizabeth White/EH/DOE@EH
cc:
Subject: April Moscow Meeting

FYI

---------- Forwarded by Joy Wilson/EH/DOE on 04/08/99 09:40 AM ----------

Frank Hawkins
04/08/99 09:30 AM

To: akleyev@urcrm.chel.su, romanov@fib1gnc.chel-65.chel.su, rel@envc.chel-65.chel.su, LampittEJ@moscowpoa.us-state.gov, CINDY LERSTEN@NOTES2CC, doemoscow@glas.apc.org, evh@nrc.gov, jol@nrc.gov, john.thomas@dtra.mil, phenry@osophs.dhhs.gov, puskin.jerome@epamail.epa.gov, reeves@nt1.afrri.usuhs.mil, ssy@nrc.gov, walter.schimmerling@hq.nasa.gov, cgj@nrc.gov, rone@epndce.nci.nih.gov, fosterre@acq.osd.mil, LAnspaugh@aol.com, llnlmoscow@glas.apc.org, profhoff@aol.com, sphdah@mail.gwumc.edu, scmiller@hsc.utah.edu, tthomas@usuhsb.usuhs.mil, vysf81a@prodigy.com, ba_napier@pnl.gov, gilberte@epndce.nci.gov, rfilipy@beta.tricity.wsu.edu, edouple@nas.gov, Joseph Weiss/EH/DOE@EH, Barrett Fountos/EH/DOE@EH, Ruth Neta/EH/DOE@EH, Elly Melamed/EH/DOE@EH, Mohandas Bhat/EH/DOE@EH, Frank Hawkins/EH/DOE, Paul Seligman/EH/DOE@EH, David Michaels/EH/DOE@EH, Loretta Young/EH/DOE@EH, Joy Wilson/EH/DOE@EH, Susan Whitmore/EH/DOE@EH, DIANA CLARK@NOTES2CC, BARRY GALE@NOTES2CC, cakessler@aol.com, lofts@nt1.afrri.usuhs.mil, VINCE MCCLELLAND@NOTES2CC, ANN HEINRICH@NOTES2CC, Heather Stockwell/EH/DOE@EH, Barbara Brooks/EH/DOE@EH, Bonnie Richter/EH/DOE@EH, jeh1@nrc.gov, jsamet@phnet.sph.jhu.edu, mgoldman@ucdavis.edu, gh68@columbia.edu, jwp8890@acs.tamu.edu, drush@gis.net, mary_ann_stevenson@dfci.harvard.edu, withers@radonc.ucla.edu, ryanmt@musc.edu, sbelinsk@lrri.org, wlbigbee@pitt.edu, fayed@uic.edu, rguilmet@lrri.org, rkathren@beta.tricity.wsu.edu, jrussell@beta.tricity.wsu.edu, day@ntsrvb.mckee.upmc.edu, fhahn@lrri.org, hg2c@pitt.edu, jamesl@dnfsb.gov, panfilov@ibrae.ac.ru, kisselev@ibrae.ac.ru, bolshov@ibrae.ac.ru, koptelov@ibrae.ac.ru, nagataki@rerf.or.jp, preston@rerf.or.jp, kenneth.chadwick@dg12.cec.be, anna.karaoglou@dg12.cec.be, pha@rah.ks.se, amk.sbi@lrz.uni-muenchen.de, wieser@gsf.de
cc:
Subject: April Moscow Meeting

The Department of Energy has received a letter from Russian Joint Coordinating Committee for Radiation Effects Research (JCCRER) Co-Chair Khetagurov postponing the meetings scheduled for the week of April 26th in Moscow. The Russian letter and an English translation are attached.

Soon, we will share with you the compilation of scientific abstracts that were to be distributed at the meeting. We hope you find this information useful.

I appreciate your flexibility and understanding in this matter. We will keep you informed as we work to find an alternative date and location for the meetings.

Frank Hawkins
Director
Office of International Health Programs
U.S. Department of Energy

S.V. Khetagurov

Vice Minister
Ministry of the Russian Federation for
Civil Defense Affairs, Emergencies and
Elimination of Consequences of
Natural Disasters

To: **Paul J. Seligman** , M.D., M.P.H.

Deputy Assistant Secretary
for Health Studies
Department of Energy
Germantown, MD
20874-1290, USA

Fax: (301) 903-1413

Dear Dr. Seligman,

With my great sorrow I have to inform you that, after discussing the matter with my Russian colleagues from the Joint Coordinating Committee and taking into account the whole plurality of circumstances related to the unsettled issue of JCCRER Agreement extension, I consider it expedient to postpone the Fourth JCC Meeting and the International Scientific Forum dedicated to studies in Southern Urals, both scheduled for the end of April, 1999, to later dates.

I eagerly hope that the position of the Russian side will find your understanding since my suggestion stems, first and foremost, from the feeling of responsibility for the future of the JCCRER Agreement and the desire to keep good relations among all participants in the Agreement, despite today's uncertain situation.

Most sincerely,

Sergei V. Khetagurov

ЗАМЕСТИТЕЛЬ МИНИСТРА

МИНИСТЕРСТВО
РОССИЙСКОЙ ФЕДЕРАЦИИ
ПО ДЕЛАМ ГРАЖДАНСКОЙ ОБОРОНЫ,
ЧРЕЗВЫЧАЙНЫМ СИТУАЦИЯМ
И ЛИКВИДАЦИИ ПОСЛЕДСТВИЙ
СТИХИЙНЫХ БЕДСТВИЙ
(МЧС России)

103012, Москва, Театральный проезд, 3
Тел.: 925-07-50
Телетайп: 114-833 "ОПЕРОН"
Факс: 924-19-46

С.В. Хетагуров

Заместитель Министра
Министерство Российской Федерации
по делам гражданской обороны,
чрезвычайным ситуациям и
ликвидации последствий
стихийных бедствий

_____ № ___

На № _____ от _____

Д-ру Полу Селигману,

Заместителю помощника
Министра энергетики США
по вопросам исследований
в области здравоохранения
Министерство энергетики США
Джермантаун, Мэриленд,
20874-1290, США
Факс: (301) 903-1413

Глубокоуважаемый доктор Селигман,

С сожалением вынужден сообщить Вам, что, принимая во внимание все обстоятельства, связанные с неурегулированностью вопроса о продлении Соглашения по ИРП, и после консультаций со своими коллегами по Объединенному координационному комитету с российской стороны, считаю целесообразным перенос на более поздний срок запланированных на конец апреля 1999 года Четвертого заседания ОКК и Международного научного форума, посвященного исследованиям на Южном Урале.
Надеюсь, что позиция российской стороны найдет у Вас понимание, поскольку это решение продиктовано в первую очередь заботой о будущем Соглашения и стремлением сохранить добрые отношения между всеми его участниками, несмотря на нынешнюю непростую обстановку.

С уважением,

Сергей В. Хетагуров

Development of an Improved Dose Reconstruction System for the General Population Affected by the Operation of the Mayak Production Association (JCCRER Project 1.1)

Principal Investigators:

Marina O. Degteva
Urals Research Center for Radiation Medicine
Medgorodok, Chelyabinsk, 454076 Russia
Telephone: 7-3512-344-351
Facsimile: 7-3512-344-321
Email: marina@urcrm.chel.su

Lynn R. Anspaugh
Radiobiology Division
University of Utah
P.O. Box 171319
Salt Lake City, Utah 84117
Telephone: 801-424-0701
Facsimile: 801-581-7008
Email: lanspaugh@aol.com

Collaborating Scientists:

N.G. Bougrov (URCRM)
D.S. Burmistrov (URCRM)
V.P. Kozheurov (URCRM)
E.I. Tolstykh (URCRM)
M.I. Vorobiova (URCRM)
A.N. Kovtun (Inst.of Marine Transport Hygiene)
A.A. Romanyukha (Inst. of Metal Physics)
B.A. Napier (PNL)

Project Dates: 1995 – 2000

Specific Aims:

This is a comprehensive project to develop improvements in the existing dosimetry system for the members of the Techa River Cohort by providing more in-depth analysis of existing data, further search of existing records, model development and testing, evaluation of uncertainties, and validation studies of results. The specific aim of this project is to enhance reconstruction of external and internal radiation doses for approximately 30,000 individuals in the Techa River Cohort. The purpose of the enhanced dose reconstruction is to support companion epidemiologic studies of radiogenic leukemia and solid cancers (NCI-RERF-URCRM Project and JCCRER Project 1.2). The current database of preliminary individual doses is being expanded and upgraded, and the uncertainty in the doses reconstructed is being evaluated. This project is being conducted in close cooperation with European scientists.

Progress to Date:
Completed work includes development of a source term for releases to the Techa River and a river model that describes radionuclide concentrations in water and sediments (this work has been confirmed by results of JCCRER Project 1.3); upgrading of the unique whole body counter (WBC) that measures ^{90}Sr by counting bremsstrahlung radiation (the physical facilities have been upgraded and new counters and electronics have been ordered); construction of an anthropomorphic phantom containing realistic distribution of ^{90}Sr in bone for recalibration of the WBC; development of a system for the collection of tooth samples for future measurement by electron paramagnetic resonance; and validation of calculated external doses by thermoluminescence measurements of brick samples.

Work is continuing on a broad front of investigations to be concluded in 2000. This includes:

- Accumulation of family histories of lifestyle and source of drinking water (river vs. well);
- Implementation of a mathematical phantom to extend the recalibration of the WBC to additional body sizes;
- Study of the variations in gamma-exposure rate according to distance from river and the effects of location and time spent in streets, gardens, and homes;
- Study of organ-specific doses from external gamma exposure;
- Development of a system to describe accurately the uncertainties (systematic bias and random errors) in all models and measurements and to propagate such uncertainties with proper allowance for correlation structures within the data; and
- Development of the improved Techa River Dosimetry System (TRDS) to provide doses for each member of the cohort and the uncertainty in that dose.

Original Goals that will not be Completed:
One of the original goals that will not be met is the analysis of tooth samples from persons living in the middle Techa region and tooth samples from persons living in non-contaminated areas. These analyses, in combination with the analysis of teeth from persons living in the upper Techa (funded by European sources), were part of an effort to provide validation of calculated doses. This part of the project was terminated by the U.S. Department of Energy. In addition, funding was also withdrawn for further validation studies based on the thermoluminescence measurement of radiation dose in environmental samples.

Recommended Future Directions:
Because of the large number of persons in the TRC, dose calculations currently depend upon group averages for several parameters. It would be desirable to individualize further the doses within the TRDS. For internal dose this could be done by more detailed consideration of individual WBC measurements, autopsy data, and family correlations. For external dose further improvement could be made by detailed consideration of location relative to the Techa River.

The TRDS was designed to consider the doses from the discharges to the Techa River and the lingering effects from the radionuclides absorbed on sediments. There are additional sources of dose to members of the TRC that are potential confounders. These include the East Urals Radioactive Trace (from the 1957 "Kyshtym" explosion), the windblown material from Lake Karachay (when it was dry), and the airborne releases of radioiodine from the Mayak stacks. These sources of additional exposure can be studied and quantified, as was originally proposed.

Stochastic Effects of Environmental Radiation Exposure in Populations Living Near the Mayak Industrial Association (JCCRER Project 1.2b)

Principal Investigators:

Mira Kossenko
Urals Research Center for Radiation Medicine
Medgorodok, Chelyabinsk 454076 Russia
Telephone: 7-3512-344-342
Facsimile: 7-3512-344-321
Email: kossenko@urcrm.chel.su

Daniel A. Hoffman
The George Washington University
School of Public Health and Health Sciences
Ross Hall Deans' Suite
2300 Eye Street, N.W.
Washington, DC 20037
Telephone: 202-994-7770
Facsimile: 202-994-3773
Email: sphdah@mail.gwumc.edu

Terry L. Thomas
Uniformed Services University of the Health Sciences
PMB Room A1039
4301 Jones Bridge Road
Bethesda, Maryland 20814-4799
Telephone: 301-295-3716
Facsimile: 301-295-1854
Email: tthomas@usuhs.mil

Collaborating Scientists:

E.I. Ostroumova (URCRM)
O.V. Vyushkova (URCRM)
L.U. Krestinina (URCRM)
N.V. Gudkova (URCRM)
S.B. Epifanova (URCRM)
E.M. Zhidkova (URCRM)
Donna Cragle (ORISE)

Project Dates: March 1997 – March 2000

Specific Aims:

The overall objective of our long-term epidemiologic project is to assess stochastic (carcinogenic) effects in populations exposed to offsite releases of radioactive materials from the

"Mayak" nuclear facility located in the South Ural Mountains in Russia. Specific study aims for the Techa River cohort are to: (a) evaluate the incidence of cancer among current and former residents of Chelyabinsk Oblast who are in the exposed Techa River Cohort; (b) integrate results from the dose-reconstruction study to estimate doses for risk assessment; and (c) develop a structure for maintaining continued follow-up of the cohort for cancer incidence. Subjects of the present study are those individuals who lived during the period January 1950 through December 1960 in any of the exposed villages along the Techa River in Chelyabinsk Oblast. Krastnoarmeysky, Kunashksky, Argayashsky and Sosnovsky rayons form the 4-rayon "catchment area" in Chelyabinsk Oblast from which death certificates and cancer incidence data have been routinely collected in the past. The registry assembled and maintained by the URCRM for the past 40 years is the basis for identifying study subjects for this project.

The following tasks were proposed for the present funding period: (1) identify subjects who were born before 1949 and were residents of exposed villages in Chelyabinsk Oblast between January 1, 1950 and December 31, 1960; this definition includes both members of the original Techa River cohort which was defined by residence in the exposed villages between 1950 and 1952, as well as late entrants who moved into the exposed villages between 1953 and 1960, bringing the cohort size to approximately 19,000 individuals; (2) update the cancer morbidity registry with information obtained from regional oncology dispensaries from 1991 through 1997; (3) conduct a series of validation procedures to determine completeness and enhance quality of the URCRM cancer morbidity registry (this included the collection of death certificates for the years 1993 and 1994); and (4) conduct analyses of cancer morbidity among the study subcohort.

Progress to Date:
The study cohort was identified and was characterized by demographic features. Death certificates for the time period January 1, 1993 through December 31, 1994 were obtained for the 4-rayon catchment area in Chelyabinsk Oblast, and the mortality registry was updated with information from these certificates. The URCRM cancer morbidity registry was updated with data from 1991 through 1997. Procedures were initiated to verify cancer diagnoses and to assess the completeness of cancer registration.

Recommended Future Directions:
A proposal is being developed to include the rayons comprising Chelyabinsk City in the catchment area in order to obtain vital status and cancer morbidity information on migrants. A plan for data analyses to meet the long range goals is being developed.

Cancer Mortality and External Radiation Exposures Among Mayak Workers; Childhood Mortality and Thyroid Disorders in the Ozyorsk Children Cohort (JCCRER Project 1.2c - NCI funded study)

Principal Investigators:

Nina Koshurnikova
Branch 1 of the Biophysics Institute
Ozersk Rd., 19
Ozersk, 456780 Russia
Telephone: 7-35171-7-66-27
Facsimile: 7-35171-7-25-50
Email: nina@fib.chel-65.chel.su

Dale Preston
Radiation Effects Research Foundation
5-2 Hijiyama Park. Minami-ku
732 Hiroshima
Japan

Collaborating Scientists:

Natalia Shilnikova (FIB-1)
Georgina Mushkacheva (FIB-1)
Kiyohiko Mabuchi (RERF)
Elaine Ron (NCI)
Ethel Gilbert (NCI)

Summary:

The primary aim of this NCI-FIB-1-RERF project is to produce analyses of the cancer mortality risks and external radiation exposure in the Mayak worker cohort. The contract provides support for an assessment of the feasibility of studies of mortality and thyroid disorders in the cohort of children who lived in Ozyorsk for at least one year between 1948 and 1973. The contract also supports, jointly with the Swedish Government, a thyroid screening study focused on current Ozyorsk residents who were born in 1952 and 1953 (the years of highest potential I-131 exposures).

In order to achieve our primary goal the contract provides funds to support and extend mortality follow-up for the Mayak worker cohort, to assess and improve data quality, and to support the expansion of the cohort to include workers from Mayak's auxiliary plants. The original three-year contract was recently (September 1998) extended for additional three years. During the first three years of this contract, follow-up was extended through the end of 1994. As currently defined, the cohort includes 18,830 people. As of the end of 1994, vital status was known for 88% of the cohort (most of the losses to follow-up occurred in the early years of follow-up shortly after workers left Mayak). About 27% of the cohort members had died as of the end of 1994 and cause of death was known for 97% of the deaths.

Analyses of the leukemia and solid cancer risks associated with external exposures for the period through 1994 are currently being carried out. The leukemia analyses confirm earlier reports of a statistically significant dose response and suggest that the excess leukemia risks are most strongly associated with doses received three to five years before death. Analyses of

Retrospective Reconstruction of Radionuclide Contamination of the Techa River Caused by Liquid Waste Discharge from Radiochemical Production at the Mayak Production Association: 1949 – 1956 (JCCRER Project 1.3)

Principal Investigators:

Yuri Mokrov
Yuri Glagolenko
Mayak Production Association
Ozersk, Chelyabinsk Oblast, Russia
Telephone: 7-351-71-21659
Facsimile: 7-351-71-23826

Bruce Napier
Pacific Northwest National Laboratory
P.O. Box 999, MS K3-54
Richland, Washington 99352
Telephone: 509-375-3896
Facsimile: 509-375-2019
Email: bruce.napier@pnl.gov

Collaborating Scientists:

Gennadiy Romanov (MAYAK)

Project Dates: October 1997 – March 1999

Specific Aims:

Project 1.3 was a pilot study designed to strengthen the source term information for the Techa River, supporting JCCRER Project 1.1. The purpose of the feasibility study was to determine if the source term of radioactive materials released to the Techa River from the Mayak facility could be reconstructed from historical environmental measurements.

Progress to Date:

The pilot study investigated the feasibility of reconstructing the releases of a limited number of radionuclides from measurements made at a limited number of downriver locations, using historically measured water flow rates and total-beta radioactivity measurements, and considering the processes of radioactive decay and of sorption/desorption. A simple radionuclide mass balance approach was used, based on a current successful technique for accounting for present-day observed migration of ^{90}Sr. The feasibility study evaluated its applicability to the complete Mayak operating period for radionuclides other than ^{90}Sr. The pilot study indicated that it is possible to determine the historical releases of a wider suite of radionuclides using the historical monitoring data from numerous locations along the river, rather than relying on a more uncertain reconstruction of quantities released at the point of discharge. Radionuclides considered include ^{90}Sr, ^{106}Ru, ^{137}Cs, and ^{144}Ce. Locations included points on the upper, middle, and lower Techa River.

solid cancer risks are complicated by possible associations between internal exposures due to inhalation of 239-Pu aerosols. However, our results suggest that there is an association between external exposure and solid cancer mortality. This association is seen even when analyses are limited to cancers unlikely to be related to internal exposures (i.e. solid cancers at sites other than the lung, liver, or bone). Following a 5 to 10 year latent period, the excess risks do not seem to be related to time since the dose was received. Age and sex patterns in the excess risks are generally similar to those seen for the atomic bomb survivors.
Work on the determination of vital status (and causes of death) at age 15 for all people born between 1934 and 1973 who lived in Ozyorsk for at least one year prior to the age of 15 is continuing in conjunction with efforts to identify thyroid disorders in this cohort (regardless of the age of occurrence). This epidemiologic investigation is being supplemented with a clinical study among current Ozyorsk residents born in 1952 and 1953. Participants are asked to complete a questionnaire and undergo a special thyroid screening examination (involving thyroid palpation, ultrasound, and biochemical blood tests) when they participate in routine annual medical examinations provided by the city of Ozyorsk.

In addition to publication of papers on our current analyses, future plans call for extension of the mortality follow-up through 1997, the expansion of the cohort to include more unexposed and low dose workers, the incorporation of improved dose estimates (from DOE Project 2.4 which is to be terminated in October 2000), and an assessment of the impact of dose errors on risk estimates. Data on the Mayak Children cohort and the thyroid screening study will also be analyzed and reported in the next few years.

Metabolism and Dosimetry of Plutonium Industrial Compounds
(JCCRER Project 2.1)

Principal Investigators:

V.F. Khokhryakov
Branch No. 1 Institute of Biophysics GSC RF
Ozyorsk Road 19
Ozyorsk, Chelyabinsk Region
456780, Russia
Telephone: 7-35171-441-70
Facsimile: 7-35171-441-70
Email: khokh@bib.chel-65.chel.su

R.E. Filipy
United States Transuranium and Uranium Registries
Washington State University, Tri-Cities
2710 University Drive
Richland, Washington 99352
Telephone: 509-372-7316
Facsimile: 509-375-1817
Email: rfilipy@beta.tricity.wsu.edu

Collaborating Scientists:

K.G. Suslova (FIB-1)
V.I. Chernikov (FIB-1
E.E. Aladova (FIB-1)
V.V. Vostrotin (FIB-1)
I.A. Orlova (FIB-1)
J.R. Alldredge (USTUR)
S.E. Glover (USTUR)
R.L. Kathren (USTUR)
D.B. Stuit (USTUR)
Y.C. Ford (USTUR)

Project Dates: April 1, 1997 – September 30, 1999

Specific Aims:

The overall objective of Project 2.1 is to combine data accumulated by both the American and Russian Registries, create a joint database, and perform a mutual analysis of this unique information regarding metabolism and dosimetry of transuranic nuclides, specifically plutonium and americium, in the human body.

A. Comparison of past radioanalytical methods.
B. Establishment of a common database format (complete).
C. Coordination of tissue sampling methods (complete).

To determine the rate of input of radionuclides to the Techa River system, the Techa River was depicted as a series of characteristic sites with controlled hydro-sections. For each site on the river, a system of recurrent (with time) equations was compiled for radioactivity balance accounting for the radioactivity inflow at the inflowing section, activity discharge with water at outflowing section, and the reduction of activity because of radioactive decay. The equations change with time to account for the changing nature of the river regime. Effective (integral for each of the investigated segments of the river) sorption constants which characterize the rate of washing of the radionuclides in the river system components (floodplain soil, bottom sediments) for ^{90}Sr and ^{137}Cs were defined, based on the inventory of the stated radionuclides deposited at each of the studied river sites, and data on water concentration and radioactive removal. All the information on radioactive contamination of the river system components during the period 1949 - 1996 was used. Solution of the series of equations generated provided information on the rate of input of these radionuclides into the upper end of the river.

It was determined that hydrologic and radiation monitoring data kept in "Mayak" PA archives for the period of 1952 – 1998 allow reconstruction of the levels and radionuclide inventory for the Techa River since 1949 (when radioactive waste releases were started).

Average annual concentrations of the main radionuclides were reconstructed for the middle and lower sections of the river (Sr-90, Cs-137, Ru-106, Ce-144). Estimated concentrations of selected radionuclides at various times are presented in the attached tables.

Recommendations:

The pilot project has been completed, and additional funding has not been provided for a full-scale project. However, the following directions are recommended:

- reconstruction of radionuclide inventory of the Techa River contamination in the upper stream of the river (expansion of the spatial area of modelling);
- increased temporal modelling resolution;
- increased spatial modelling resolution of radioactive contamination; and
- assessment of uncertainty in modelling data.

Estimation of the Risk of Stochastic (Cancer) Effects of Occupational Radiation Exposure (JCCRER Project 2.2)

Principal Investigators:

Nina A. Koshurnikova
Branch 1 of the Biophysics Institute
Ozersk Rd., 19
Ozersk, 456780 Russia
Telephone: 7-35171-7-66-27
Facsimile: 7-35171-7-25-50
E-mail: nina@fib.chel-65.chel.su

Ethel S. Gilbert
Radiation Epidemiology Branch
National Cancer Institute
6120 Executive Boulevard
Mailstop 7238
Rockville, Maryland 20852
Telephone: 301-496-6600
Facsimile: 301-402-0207
E-mail: gilberte@epndce.nci.nih.gov

Collaborating Scientists:

M.G. Bolotnikova (FIB-1)
V.V. Kreslov (FIB-1)
P.V. Okatenko (FIB-1)
M.E. Sokolnikov (FIB-1)
N.S. Shilnikova (FIB-1)
L.G. Filippova (FIB-1)
V.F. Khokhryakov (FIB-1)
K.G. Suslova (FIB-1)
S.A. Romanov (FIB-1)
T.I. Kudryavtzeva (FIB-1)
I.A. Orlova (FIB-1)
E.K. Vasilenko (MAYAK)
Elaine Ron (NCI)

Project Dates: April 1, 1997 – March 31, 200[illegible]

Specific Aims:

1. Improvement of the computer database.
2. Update of vital status data.
3. Expansion of the cohort to include additional workers with relatively low occupational doses.
4. Conduct dose-response analyses to evaluate risks of lung, liver and bone cancer resulting from plutonium exposure.
5. Comparison of the results of analyses conducted under this project (2.2) with results from studies in the United States.

Progress to Date:

1. Several logical checks have been performed, and their results summarized in progress reports. Source records for all 18,870 workers were checked, which resulted in some corrections to the database. Documentation that describes the edits that were performed, the specific workers involved, and the changes that were made has been prepared. Occupational histories by time period, plant of employment (reactor, radiochemical and plutonium production) and moves between plants have been computerized for all workers in the registry.
2. The updating of vital status information is being continued in a routine way, and mortality data can now be considered reasonably complete through the end of 1996.
3. The cohort is being expanded to include workers from the mechanical repair and water preparation plants. These workers had lower doses than those employed in the main plants. Dosimetry, employment histories, and vital status data are being obtained for these workers. This effort is expected to add about 1,500 workers from mechanical repair plant and about 1,300 workers from the water preparation plant.
4. A paper on bone tumors in the Mayak cohort is under preparation, and is expected to be completed in the next six-month period. Because plutonium-monitoring data are not yet available for many workers, this paper is primarily descriptive, but includes comparisons by plant, by external dose, and by the estimated plutonium body burden.
5. The paper on bone tumors will include discussion of findings from U.S. worker studies.

Original Goals that will not be Completed:

At this time we anticipate that the tasks listed will be completed. However, because of analyses conducted by others addressing lung cancer risks, we will re-evaluate whether or not additional analyses of this endpoint are needed at this time.

Recommended Future Directions:

Efforts to improve dosimetry, especially estimates of internal dose, are being conducted under Project 2.4. As follow-up of the Mayak cohort is continued, there is a need to re-evaluate risks as more up-to-date mortality data are obtained. Thus, we hope to conduct further analyses of lung, bone, and liver cancer risks based on improved dosimetry and more up-to-date mortality data. In addition, computerized data on detailed occupational histories have been added to the database, and data on workers from the mechanical repair and water treatment plants (with relatively low doses) doses are being obtained. These data need to be evaluated and included in dose-response analyses.

Table 1 – Average annual concentrations of the main radionuclides in Techa River water in the region of Muslyumovo (Brodokalmak) during 1949 – 1965. nCi/l.

Year	^{90}Sr	^{144}Ce	^{106}Ru	^{137}Cs	Short-lived
1949	0	0	0	0	0
1950	14	37	14	6.3	33
1951	81	213	79	33	190
1952	13.7	53.6	19.9	8.0	58
1953	6.52	27.8	10.3	4.2	< 0.5
1954	13.5	14.5	5.4	1.5	0
1955	12.3	7.5	2.8	2.8	0
1956	11.1	3.9	1.44	0.80	0
1957	8.6	2.0	0.75	0.79	0
1958	8.0	1.06	0.39	0.51	0
1959	8.1	0.55	0.20	0.35	0
1960	6.1	0.28	0.104	0.13	0
1961	5.6	0.144	0.053	0.13	0
1962	3.9	0.074	0.028	0.083	0
1963	4.3	0.040	0.015	0.041	0
1964	3.6	0.021	0.0076	0.037	0
1965	1.9	0.014	0.0052	0.016	0

Table 2 – Average annual concentration of main radionuclides in Techa river water in the area of Pershino during 1949 – 1965, nCi/l

Year	^{90}Sr	^{144}Ce	^{106}Ru	^{137}Cs	Short lived
1949	0	0	0	0	0
1950	6.7	11.5	2.6	3.05	29
1951	37	62	14.0	16.3	201
1952	19.4	17.0	3.8	2.7	17
1953	13.5	8.8	2.00	0.94	< 0.1
1954	12.4	4.6	1.00	2.6	0
1955	11.2	2.4	0.52	1.3	0
1956	7.86	1.2	0.27	1.5	0
1957	6.81	0.63	0.14	0.28	0
1958	6.09	0.32	0.07	0.27	0
1959	5.74	0.17	0.04	0.12	0
1960	4.18	0.09	0.02	0.10	0
1961	3.69	0.045	0.01	0.048	0
1962	3.06	0.023	0.005	0.026	0
1963	3.66	0.012	0.003	0.013	0
1964	2.86	0.006	0.001	0.010	0
1965	1.51	0.003	0.001	0.0044	0

fraction in the skeleton than did relatively healthy workers. Also, the fraction of total systemic plutonium excreted per day was significantly greater for workers with liver diseases than for relatively healthy workers (Task H). These observations could have a considerable effect on organ dosimetry in health-impaired workers whose dose assessment was based on urinary excretion rates.

Shielding for an in-vivo counter, formerly in use at the U. S. Rocky Flats Plant, was transported to FIB-1 and installed in a newly constructed building in November 1998. The refurbished detectors, with computer system and software, will be installed and the system will be calibrated and put into operation (Task I) during the next reporting period.

Four publications in the peer-reviewed scientific literature are a direct result of the collaborative research of Project 2.1 and another is in preparation. Two of those publications were Russian-English translations prepared as part of Task J, above. Two other Russian-English translations are in preparation for publication.

Problems:

An interlaboratory comparison of radioanalytical methods by analyses of reference samples prepared by the U. S. National Institute for Standards and Technology (Task A) has been delayed pending FIB-1 authorization from the Russian Government to receive shipment of samples containing transuranic elements.

Recommended Future Directions:

1. Internal dose assessments in former Mayak workers using urinary bioassays, in-vivo counting, and analysis of tissue samples collected at autopsy; tissue samples from those workers will be contributed to the newly established Russian Tissue Repository for molecular epidemiology and other cytogenetic studies.
2. A comparison study of transplacental transfer of plutonium in women who worked at the Mayak production facilities and in women who resided in Ozyorsk.
3. Evaluation of the ability of present ICRP biokinetics models to reliably predict tissue distributions of actinide elements in actual human cases with the combined data of both Registries.
4. Improvement and refinement of combined lung clearance and systemic plutonium biokinetics parameters and models for dose assessment based on urinary and fecal excretion.
5. A study of the influences of modifying factors such as age, smoking, health, and non-uniformity of plutonium lung distribution on lung dose assessment.

D. Modernization of FIB-1 radioanalytical methods.
E. Characterization of workplace aerosols at the Mayak facility (complete).
F. Analysis of relationships between respiratory tract and systemic actinide contents.
G. Analysis of relationships between systemic organ actinide contents.
H. Analysis of relationships between systemic content and urinary excretion of actinides.
I. Calibration of DRMIA in-vivo counters.
J. Translation of Russian documents for publication in English scientific journals.

Progress to Date:
An interlaboratory comparison of radioanalytical methods (Task A) was a first priority task because both Registries had previously collected analytical results from tissues of large numbers of cases and the methods used to obtain those results were quite different. A total of 40 samples were exchanged between laboratories and a comparative analysis of the analytical results from both laboratories indicated no statistically significant differences. It was, therefore, concluded that the data of the two Registries could be included in the joint database, designed with the completion of Task B, above.

The purposes of Tasks C and D, above, was to assure uniformity in the methods of the two Registries for future autopsies and analyses of tissues obtained at those autopsies. The tissue collection protocols of both Registries were very similar; necessitating only minor modifications to ensure compatibility (Task C). As a result of Task D, FIB-1 has significantly modernized its analytical methods for plutonium and americium analysis in biosamples by application of separations resins and reagents currently in use by the USTUR. FIB-1 has acquired a state-of-the-art 16 chamber alpha spectrometry system (EG&G Ortec Octete) to further increase the sensitivity and efficiency of the methods. They have completed the initial background and minimum detectable activity determinations and they are in the process of preparing documentation for certification of their analytical processes in the framework of Russian Federation requirements.

Tasks E, F, G, and H are directly concerned with dosimetry in workers and involve biokinetic modeling for actinide elements. Transportability coefficients (in-vitro solubility) of actinide-containing aerosols (as measured at FIB-1 by the dialysis method) were related to the specific workplaces within Mayak facilities (Task E). The transportability coefficients of inhaled aerosols had a significant effect on the translocation of plutonium from the respiratory tract to the systemic circulation (Task F). Parameters for a simplified lung model, used by FIB-1 and the Mayak Production Association for dose assessment at long times after inhalation of plutonium-containing aerosols, were developed on the basis of joint American and Russian data. This model has separate sets of deposition and transfer parameters for three aerosol transportability groups, allowing work histories of the workers to be considered in the dose assessment process. During the next year, this model will be compared to other biokinetic models such as those proposed by the International Commission for Radiological Protection.

FIB-1 biokinetic models were extended to include the distributions of actinide elements in systemic organs of workers (Task G). It was determined that a relationship existed between the health of individual workers and plutonium distribution in tissues. Workers who suffered from liver diseases generally had a smaller fraction of systemic plutonium in the liver and a larger

Development of an Improved Dosimetry System for the Workers at the Mayak Production Association (JCCRER Project 2.4)

Principal Investigators:

Evgenii Vasilenko
Mayak Production Association
31 Lenin Street
Ozyorsk, 456780 Russia
Telephone: 7-351-7121659
Facsimile: 7-351-7121659
Email: rel@envc.chel-65.chel.su

Valentin Khokhryakov
Branch 1 of the Biophysics Institute
3, Vostochnaya
Ozyorsk, 456780 Russia
Telephone: 7-351-7123826
Facsimile: 7-351-714170
Email: khokh@bib.chel-65.chel.su

Scott C. Miller
University of Utah
Division of Radiobiology
40 N 2030 E Front
Salt Lake City, Utah 84112
Telephone: 801-581-5638
Facsimile: 801-581-7008
Email: scott.miller@hsc.utah.edu

Collaborating Scientists:

Y. Glagolenko (MPA)
E. Drozhko (MPA)
S. Romanov (FIB-1)
K. Suslova (FIB-1)
V. Knyazev (MPA)
Z. Menshikh (FIB-1)
V. Vostrotin (FIB-1)
V. Chernikov (FIB-1)
E. Aladova (FIB-1)
M. Smetanin (MPA)
O. Aleksandrova (MPA)
A. Fevralev (MPA)

The Russian and U.S. scientists are working together on all aspects of this program, but have identified the primary tasks and have assigned leadership roles. These are summarized in the following table:

Tasks	Primary Role	Secondary Role
External dosimetry		
Gamma, beta, neutron doses	Russia	U.S.
Organ dose calculations	U.S.	Russia
Occupations histories	Russia	U.S.
QA/QC	Both	
Internal dosimetry		
Internal model (FIB-1)	Russia	U.S.
New biokinetic model	Both	
Dose uncertainties	U.S.	Russia
Occupational histories	Russia	U.S.
Common identifier	Russia	U.S.
QA/QC	U.S.	Russia

Progress to Date:
The uncorrected internal and external doses have been entered into the databases. QA/QC procedures have been implemented. Worker histories entries in database are about 50% complete. Methods for improved and "corrected" doses are being implemented. Organ dose models for external exposures are also being implemented.

Recommended Future Directions:
Completion of all original tasks. Development of a new biokinetic and dosimetric model for human exposures to plutonium.

D. Slaughter (Univ. of Utah)
M. Krahenbuhl (Univ. of Utah)
J. Wilde (Univ. of Utah)

Project Dates: April 1998 – April 2001

Specific Aims:
The purpose of this project is to create databases which contain verified and updated dosimetry and worker history information for workers at the Mayak Production Association. These data are provided to the epidemiology studies. Project 2.2 (Estimation of the risk of stochastic [cancer] effects of occupational radiation exposure) and Project 2.3 (Deterministic effects of occupational exposure to radiation). Portions of the databases may also be provided to other JCCRER-funded investigators. The database will contain external and internal dose information suitable for these epidemiological studies.

Additional databases used to construct the dosimetry include radiochemical analyses of tissues, bioassay data, air sampling data, whole body counting data, and occupational and worker histories. The entry of the raw data into the database is checked by a quality control (QC) procedure. The procedures, models, methods, and operational uncertainties will be documented and included in the database and technical reports and publications. The cohort of persons to be included in the stochastic epidemiological study (Project 2.2) is expected to include about 19,000 persons currently in the Mayak Worker Registry. The cohort of persons to be included in the deterministic epidemiological study (Project 2.3) is expected to include about 600 persons.

For external dosimetry, workplace gamma, beta and neutron doses are being reconstructed. The models used for this incorporate issues such as known isotopes, composition, shielding, further analysis of film badge sensitivities, and records of direct measurements. Organ doses from external exposures are also being calculated. Methods for calculating uncertainties are being developed. A rigorous quality control procedure (QC) has been implemented.

For internal dosimetry, the organ doses have been calculated using the established FIB-1 biokinetic model. A new biokinetic model is being developed that includes more information of the solubility and biokinetics of the different chemical forms and particulate sizes of Pu that were in the workplace. In addition, updated worker histories will be used to estimate doses to some workers where direct measurements were not made. A rigorous quality control procedure is being implement to ensure that the correct dosimetry data is entering the various databases being used by the epidemiologists.

An Epidemiologic Study of Occupational Chronic Irradiation and Reproductive Health (JCCRER Feasibility Study)

Principal Investigators:

Andre Kurbatov
Senior Scientific Worker
Clinical Department of Biophysics Institute
Ozyorsk Road 19, Ozyorsk
Chelyabinsk Region, Russia 456780
Telephone: 7-351-717-5464
Facsimile: 7-351-717-2550
Email: romanov@fib1gnc.chel-65.chel.ru

Faith G. Davis
Professor and Director
Division of Epidemiology and Biostatistics
School of Public Health, Room 505
University of Illinois at Chicago
2121 West Taylor Street
Chicago, Illinois 60612
Telephone: 312-996-5019
Facsimile: 312-996-0064
Email: fayed@uic.edu

Collaborating Scientists:

Nadezhda Okladnikova (FIB-1)
Irina Vologodskaya (FIB-1)
Laura Schieve (CDC)
John Roeske (Univ. of Chicago)
Bridget McCarthy (Univ. of Illinois)
Arden Handler (Univ. of Illinois)
Loni Castro (Univ. of Illinois)
Dan Hryhorchuk (Univ. of Illinois)

Project Dates: August 1998 – December 1999

Specific Aims:

1. Is there an association between radiation and fertility among females and does this association vary by type, dose, timing and site of radiation exposure?
2. Is there an association between radiation and fertility among males and does this association vary by type, dose, timing and site of radiation exposure?
3. Is there an association between in utero dose and adverse perinatal/child outcomes; specifically low birth weight and preterm delivery?

4. Is there an association between maternal preconceptional dose and adverse perinatal/child outcome; specifically sex-ratio, low birth weight and preterm delivery?
5. Is there an association between paternal preconceptional dose and adverse parent/child outcome; specifically sex-ratio, low birth weight and preterm delivery?

Progress to Date:
Dr. Davis has visited Ozersk and obtained a general overview of the occupational cohort and the scope of the data available. Radiation exposure data are in the form of occupational histories with some estimated doses. For this project exposure estimates will need to be modified to allow for the timing of dose estimates to conception and to estimate selected organ doses to the parents and to the fetus. Coordination with other projects will be important in utilizing microdosimetry and macrodosimetry exposure models. It has been agreed that this project will be restricted to the early cohort of workers (1948-1956) who received the larger radiation exposures. The current family database includes the major reproductive health events proposed, although information on some important confounding factors is lacking. A general description of the database has been developed by the Russian team and shared with U.S. investigators. A more detailed description of each relevant variable is being prepared. One family record with individual data elements has been shared with the U.S. investigators. Summary tables describing proposed exposure groups have been prepared by the Russian investigators and will be discussed in meeting with U.S. collaborators in April. Further assessment of data quality and data collection methods will take place in June. A data access agreement has been worked out by the U.S. and Russian Principal Investigators.

Original Goals that will not be Completed:
Dr. McCarthy had proposed that we look at genetic imprinting of genes involved in fetal growth. To target these efforts we had planned to conduct preliminary analysis which would be utilized to focus the molecular studies. Preliminary analysis was proposed to identify which, if any, of the gender and exposure groups demonstrate a crudely elevated rate of any of the reproductive events. Without the complete data with individual records we are unable to conduct these preliminary analysis and the development of specific genomic imprinting studies will be delayed.

Recommended Future Directions:
1. Extend the organ dose estimations to include individual equivalent doses on the whole body, gonads, uterus, thyroid, breast, liver, bone marrow and fetus.
2. To develop microdosimetry models to describe the distribution of specific energy for gonadal and fetal exposures.
3. To extend our understanding of maternal/fetal plutonium transfer using a human model.
4. Information on the first and second generation families of the workers appears to be available which may enrich the potential for molecular and immunologic studies and allow us to extend the analysis of reproductive events to a second generation.

Improved Dosimetry and Risk Assessment for Plutonium-Induced Lung Disease Using a Microdosimetric Approach (JCCRER Feasibility Study)

Principal Investigators:

Sergey A. Romanov
Branch No. 1 of State Research Center
Biophysics Institute (FIB-1)
Ozyorsk Road 19, Ozyorsk
Chelyabinsk Region, Russia 456780
Telephone: 7-351-717-5464
Facsimile: 7-351-717-2550
Email: romanov@fib1gnc.chel-65.chel.ru

Raymond A. Guilmette
Lovelace Respiratory Research Institute (LRRI)
P.O. Box 5890
Albuquerque, New Mexico 87185
Telephone: 505-845-1096
Facsimile: 505-845-1198
Email: rguilmet@lrri.org

Collaborating Scientists:

Nina A. Koshyrnikova (FIB-1)
Valentina S. Revina (FIB-1)
Klara N. Myksinova (FIB-1)
Kristen J. Nikula (LRRI)
Fletcher F. Hahn (LRRI)

Project Dates: August 15, 1998 – November 14, 1999

Specific Aims:

The risk of developing radiation-induced disease such as lung cancer is currently estimated using models based on epidemiological data from populations exposed either to relatively uniform, low-LET radiation, or from uranium miners exposed to radon and its progeny. It is not clear whether these models published by ICRP and NCRP are the most appropriate for predicting lung cancer risks for inhaled alpha-emitting radionuclides of Pu, Am, U, etc., in which the predominant dosimetric characteristic is nonuniform, chronic irradiation of the parenchymal region of the lung. A better experimental and theoretical basis is needed for relating heterogeneous spatial and temporal radiation dose patterns to the induction of biological lesions, particularly on a microscopic level. Accordingly, scientists at FIB-1 and LRRI are making use of a unique resource at the FIB-1, i.e., a set of about 400 lung specimens fixed in 10% formalin obtained from a population of workers at the Mayak Production Association, many who inhaled significant quantities of Pu and other α-emitting radionuclides during their careers. The principal specific aim of this Phase I study is to determine the feasibility of using the FIB-1

archival lung tissues for measuring the microscopic distribution of Pu by using quantitative autoradiographic techniques. If this prerequisite is satisfactorily demonstrated, then the following specific aims will also be addressed: 1) determine the spatial distribution of Pu in human lung tissue with respect to specific lung structures; 2) determine the heterogeneity of alpha-radiation dose within the lung; and 3) determine the effect of chronic tobacco-smoke exposure on the distribution of local radiation dose.

Progress to Date:

To begin assessment of the usability of the available lung tissue for autoradiography, paraffin-embedded samples of lung tissue from two former Mayak workers having 470 and 4400 Bq Pu lung content at death respectively were transported to LRRI for sectioning and autoradiographic measurement. Concerns had been raised because the lung samples had been fixed and maintained for many years in unbuffered formalin, and the lungs had not been fixed by airway perfusion of fixative under constant pressure. These methods may have resulted in lung sections that would not be adequate for quantitative microscopy. However, the quality of the histological sections was found to be adequate for identifying the various lung structures, and autoradiographic preparations developed at various times ranging from 1 to 45 days showed easily identifiable particles, presumably Pu, as well as a significant number of single α tracks, indicative of soluble forms of Pu. The particles were most often found to be associated with organized lymphoid tissue or in the interstitium associated with respiratory bronchioles or perivascular tissue. The single tracks were associated with alveolar septa, interstitium of bronchioles, perivascular tissue and in the cartilage rings of the bronchi. Having demonstrated the potential usefulness of the lung tissues archived at FIB-1, a second group of fixed lung specimens were obtained from three individuals selected as follows: 1) a cigarette smoker with moderate Pu lung content (430 Bq); 2) a nonsmoker with moderate Pu long content (390 Bq); and 3) a smoker with low Pu lung content (53 Bq). The lung tissue samples from these subjects were obtained using classical stereological sampling techniques at FIB-1, the samples embedded in paraffin and transported to LRRI for autoradiographic measurement. To quantitate the α-activity distribution in the particles observed in the tissue sections, a series of slides are being exposed for times varying from 1 to 60 days. These activity-per-particle distributions will then be compared against similar distributions obtained using monodisperse $^{239}PuO_2$ aerosol particles previously prepared at LRRI. In this way, proper activity-vs.-time calibrations will be maintained throughout the study. To date, a total of about 200 slides per subject have been prepared for autoradiography, and are being developed according to the previously mentioned exposure scheme. Following development, the particle distributions and single-α-track distributions are being enumerated with respect to their locations in the lung, i.e., with respect to the various microscopic lung structures. The volume densities for the various anatomical lung compartments are also being determined using stereological methods. The latter measurements will provide a statistical means for scaling the measured location-specific Pu distributions to the whole lung. It is expected that these analyses will be completed in this Phase I study.

Original Goals that will not be Completed:

Given the quality of the histological materials and the current pace of progress, no impediments to timely completion are anticipated.

Recommended Future Directions:
Assuming satisfactory completion of Phase I, follow-up studies will focus on continuing the microdosimetric analysis on a larger number of subjects. The subjects will be selected to encompass the range of lung burdens available within the FIB-1 study population, will address the potential effects of chronic tobacco smoking on Pu microdistribution, and will correlate the Pu distribution with the distribution of lesions within the lung. Because virtually all subjects died at long times after their major inhalation intakes, kinetic information likely will not become available solely from the human tissue material. As such, the human study will be supplemented with data from microdosimetric measurements done in experimental animals killed at times ranging from a few days to long times after exposure.

Establishment of a Repository Containing Tissues of Organs of Deceased Workers of Mayak Industrial Association Exposed to Actinide Elements
(JCCRER Feasibility Study)

Principal Investigators:

Klara N. Muksinova
Branch No. 1 of State Research Center
Biophysics Institute, FIB-1
19, Ozyorsk Road, Ozyorsk
Chelyabinsk Region, Russia 456780
Telephone: 7-35171-76370, 75464
Facsimile: 7-35171-72550
Email: romanov@fib1gnc.chel-65.chel.su

Ronald L. Kathren
United States Transuranium and Uranium Registries
Washington State University
2710 University Drive
Richland, Washington 99352
Telephone: 509-372-7288
Facsimile: 509-375-1817
Email: rkathren@tricity.wsu.edu

John J. Russell
United States Transuranium and Uranium Registries
Washington State University
2710 University Drive
Richland, Washington 99352
Telephone: 509-372-7315
Facsimile: 509-375-1817
Email: jrussell@tricity.wsu.edu

Collaborating Scientists:

Eugenia N. Kirillova (FIB-1)
Klara G. Suslova (FIB-1)
Sergey A. Romanov (FIB-1)
Valentina S. Revina (FIB-1)
Ronald E. Filipy (USTUR)
Gerald E. Dagle (USTUR)

Project Dates: August 15, 1998 – November 15, 1999

Specific Aims:

1. Establish Russian Human Radiobiology Tissue Repository.
2. Determine equipment and supply requirements for establishment of the repository.
3. Develop protocols of work procedures including how to safely handle preserved materials.
4. Develop inventory of tissue samples fixed in formalin or ethyl alcohol, and the number of paraffin blocks and histological slides.
5. Obtain occupational, radiochemical, dosimetric and medical information on every repository registrant.
6. Establish policies or procedures for the distribution of tissue samples to qualified scientist for study.
7. Establish specific protocols for the collection, packaging, and preservation of human tissues by the repository.
8. Determine and evaluate the most significant impediments to conducting the proposed project and propose strategies to overcome them.

Progress to Date:

1. This U.S.-Russian collaborative research project has helped to establish a Russian Human Radiobiology Tissue Repository (RHRTR) at the First Institute of Biophysics (FIB-1) to systematically collect, preserve, maintain, and make available for scientific study organ and tissue samples from deceased MAYAK facility workers with known occupational radiation exposures.
2. The most urgent supply needs to date have been for formalin, steel shelving, metal casks or containers for tissue storage and a computer with appropriate software to build the tissue repository database. Major pieces of equipment include two freezers capable of maintaining a -70^0 C temperature for long-term storage of tissues for future cytogenetic studies are proposed in Phase II.
3. The NHRTR has extensive experience with handling, collection, packaging, and preservation of human tissues for future use, which is being transferred to the FIB-1. Many of these formal written policies and procedures apply directly to the current operations the FIB-1 tissue repository and will be adopted and or altered as needed (see attachment A).
4. Initial activities accomplished during the first two milestone quarterly report periods, included a comprehensive inventory and characterization of tissue materials from the initial 100 registrants (86 males, 14 females). Formalin-fixed tissue samples of all internal organs including brain were identified and catologed. In addition, there are three or more types of decalcified bone samples fixed in 70% alcohol, paraffin blocks of bone and soft tissue as well as histological slides of soft tissue sections. Samples of primary tumors and/or metastases collected at autopsy.
5. The inventory also includes detailed analysis and documentation of medical records out-patient records, history of diseases, autopsy protocols), information on occupational route of actinide intake, accumulated external γ-exposure doses, Pu body burden and estimated content in the major organs of deposition. The majority of registrants worked at jobs that brought them into direct or indirect contact with plutonium (plutonium manufacturing facility and/or plutonium radiochemical separation plant); the remaining registrants were engaged in maintenance of the first production reactors.
6. As stated above in #3, the current NHRTR policy on acquisition of repository tissues should apply directly to the newly operating FIB-1 repository.

7. See # 3 above.
8. The most significant impediment to the success of this project is expected to be obtaining proper informed consent for the performance of future autopsies because of different Russian cultural, legal and bioethical values.

Original Goals that will not be Completed:

Although we have not actually written and/or altered the existing USTUR policies and procedures that the FIB-1 tissue repository will use, they will be completed very soon. In addition, although it has not been formalized, the faculty members of the USTUR and FIB-1 scientist will form the committee to evaluate the requests from other scientist to obtain tissue samples from the Russian tissue repository.

Future Directions:

1. Extension of the inventory and characterization of RHRTR tissue materials to 500 cases autopsied between 1970-92, including formalin-fixed samples of internal organs, brains, bones as well as paraffin blocks and histology slides.
2. Purchase and install one or more -70^0 C ultracold freezers for storage of newly acquired autopsy tissue materials for pending and future molecular biology and cytogenetic studies.
3. Autoradiographic study of alpha track distribution in normal tissue areas and pathologic lesions in the major organs of plutonium deposition (lung, skeleton) in deceased workers at plutonium manufacturing facility.
4. Completion of computerized database of RHRTR.
5. Prepare and publish a descriptive brochure for the RHRTR.
6. Establish tissue collection, handling and sharing protocols.

Lung Cancer in Workers from the MAYAK Nuclear Enterprise (JCCRER Feasibility Study)

Principal Investigators:

Dr. Steven Belinsky
Lovelace Respiratory Research Institute (LRRI)
P.O. Box 5890
Albuquerque, New Mexico 87185
Telephone: 505-845-1165
Facsimile: 505-845-1198
Email: sbelinsky@LRRI.org

Dr. Vitaliy Telnov
The First Branch of Biophysics Institute (FIB-1)
Ozyorsk St. 19 Ozyorsk
Chelyabinsk Region, 456780
Russia
Email: ond@fib1ko.chel-65.chel.su

Collaborating Scientists:

Dr. Richard Crowell (LRRI)
Dr. Kristen Nikula (LRRI)
Dr. Galina Rysinova (FIB-1)
Dr. Nadezhda Okladnikova (FIB-1)
Dr. Galina Adamova (FIB-1)

Project Dates: August 15, 1998 – November 14, 1999

Specific Aims:

1. Determine the frequency for methylation of the ER and p16 genes in adenocarcinomas from exposed workers and a control population.
2. Determine whether ER and p16 methylation can be used as biomarkers in sputum to identify persons at greatest risk for lung cancer from radiation exposure.
3. Determine whether polymorphisms in DNA repair genes predicts risk for radiation-induced cancer.

Summary:

The molecular mechanisms and gene environment interactions leading to radiogenic lung cancer have not been well characterized. The proposed collaboration between scientists at the Branch 1 Center of Biophysics (FIB-1), Ozyorsk, Russia, and the Lovelace Respiratory Research Institute, Albuquerque, NM, will facilitate a detailed molecular epidemiology study of workers from the MAYAK nuclear enterprise. These workers were gamma irradiated and exposed to airborne ^{239}plutonium. Lung cancers in exposed workers were frequently found in the lower and middle lung lobes and at the periphery, thus reflecting the deposition pattern for inhaled plutonium. Epidemiology studies indicate a significantly higher frequency for adenocarcinoma in workers

than in a control population and a strong correlation between this tumor type and plutonium exposure. Two hypotheses will be evaluated through the proposed studies: (1) radiation exposure targets specific genes for inactivation and these genes can serve as biomarkers for lung cancer risk in population-based studies of exposed workers and (2) inherent deficiency in the repair of DNA double strand or single strand breaks constitute risk factors for lung cancer associated with radiation-induced exposure. These hypotheses will be tested using adenocarcinomas collected retrospectively and through prospective studies of exposed workers and an unexposed population. During Phase I of the proposed studies, scientists from Lovelace are interacting with FIB-1 scientists to exchange ideas, determine sample availability and size of populations for the proposed studies, conduct onsite training, and working with actual tumor specimens to provide preliminary data. The work described in this proposal, if continued in Phase II, will begin to provide fundamental knowledge of the mechanisms leading to radiation-induced lung cancer associated with exposure to airborne plutonium.

Feasibility Assessment of Biodosimetry and Molecular Epidemiology Studies among Mayak PA Workers (JCCRER Feasibility Study)

Principal Investigators

Nadezhda D. Okladnikova, M.D. Ph.D.
Institute of Biophysics, Branch No. 1
Ozyorsk, 456780 Russia
Telephone: 7-35171-6-5487
Facsimile: 7-35171-7-2550
E-mail: ond@fib1ko.chel-65.chel.su

William L. Bigbee, Ph.D.
Department of Environmental and Occupational Health
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, PA 15261
Telephone: (412) 967-6534
Facsimilie: (412) 967-6576
E-mail: wlbigbee+@pitt.edu

Richard D. Day, Ph.D.
Department of Biostatistics
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, PA 15261
Telephone: (412) 624-4077
Facsimilie: (412) 624-9969
E-mail: rdfac@vms.cis.pitt.edu

Collaborating Scientists

Galina G. Rusinova, Ph.D. (FIB-1)
Vitaliy I. Telnov, M.D. (FIB-1)
John D. Boice, Sc.D. (IEI)
H. Gregg Claycamp, Ph.D. (UP)
Susanne M. Gollin, Ph.D. (UP)
Robert E. Ferrell, Ph.D. (UP)
Sofia Shekhter-Levin, M.D., Ph.D. (UP)
Bill Travis, M.D. (AFIP)
Niel Wald, M.D. (UP)

Project Dates: September 1. 1998- November 15. 1999

Phase I (Feasibility) Specific Aims:

1. Establish necessary collaborative relationships with American scientists and institutions.
2. Utilize existing clinical. sociodemographic and epidemiologic information on Mayak PA worker population (Date base of Project 2.3) to ascertain availability of subjects, blood and tissue samples for biodosimetry/biomarker studies.
3. Carry out biodosimetric and molecular epidemiological pilot studies. including: FISH-based cytogenetic analysis of chromosome translocations in peripheral blood lymphocytes; glycophorin A (GPA) locus somatic cell mutation assays in peripheral blood erythrocytes; molecular genetics/DNA sequencing of P53 gene mutations in lung tumor tissues; and DNA microsatellite analysis of germline and somatic genetic effects in workers, spouses and their children.
4. Identify and develop on-site technical resources and capabilities to conduct Phase II study .

Progress to Date:

- An exchange of visits has been carried out between FIB-1 investigators in Ozyorsk and University of Pittsburgh investigators (Ozyorsk. September.1998). The collaborative relationship between Russian and American scientists and institutions was established. work schedule was discussed and the final protocol of studies was signed.
- Subcohort of workers for examination was selected on the basis of registry formed earlier during feasibility study of Project 2.3. According to the final protocol. the first stage of laboratory studies is implemented at FIB-1.
- Informed consent was developed in compliance with all the requirements of Institutional Review Boards of Branch-1 of State Research Center of Public Health Ministry of the Russian Federation and University of Pittsburgh (the USA).
- Joint visit of Dr. Rusinova and Dr. Telnov to University of Pittsburgh took place from January 25 till February 6. 1999. Protocols of joint research were reviewed and tested. During that visit analysis of 5 DNA control assays isolated in FIB-1 was done. The conclusion was drawn regarding the high quality of DNA.
- Invitation of members from 15 families of sampled subcohort was arranged to obtain informed consent for participation in examination. After such consents were signed collecting of blood assay was arranged to isolate DNA.
- 53 samples of DNA (from members of 15 families of selected subcohort) were derived and qualitative and quantitative characteristics of DNA were determined. DNA assays were transferred for long-term storage to DNA bank for their future utilization in joint molecular genetics studies.
- Work pertaining to search for archival chromosome preparations (with storage within a few mouths/years in ordinary conditions) was accomplished for the purpose of estimation of their possible use for retrospective dosimetry by means of FISH-method.

- At present investigations under protocols of obtaining fixed erythrocytes for glucophorin assays and lymphocytes cultivation to derive chromosome preparations are continuing.
- 10 histology preparations were prepared for molecular investigations(gene P- 53).
- Work pertaining to obtaining of informed consent for studies participation is carried on continually among remaining workers residing in the city were selected from the registry study of Project 2.3 feasibility study.
- Ongoing technical discussions are being carried out with regard to the development of these facilities will be developed for the Phase- 2 proposal.

Recommended Future Directions:

It is anticipated that this Phase I (feasibility) project will provide experience and data to facilitate the implementation of a comprehensive study designed to provide biological and molecular data for independently assessing the validity of Mayak PA physical radiation biodosimetry; for determining the quantitative response of these and other biodosimetric and early biological markers to chronic low dose rate radiation exposures, for further elucidating the molecular etiology of radiation-induced carcinogenesis in malignant tissues, and for providing a firmer quantitative and mechanistic basis for epidemiologic estimates of health risks associated with these occupational exposures.