

APPROVED

at IRB meeting of SEP 29 1988

University of California



Lawrence Livermore National Laboratory

Meeting of Institutional Review Board

718030

June 2, 1988

Trailer 3675, Room 106, 9:00 a.m.

Attendees:

Committee Members:

John Beatty
Max Biggs
Alan Brautigam
Max Creamer
Bart Gledhill

Jim Johnson
Brian Mayall
Kathleen Noonan
Jack Shearer
Vivian Shepherd
Gerry Wyman

Principal Investigators:

B. Brandriff
Deborah Kruchten, Larry Anderson
Rich Langlois for R. Jensen
Paul Meyer
Andy Wyrobek

Administrative Matters

1. Minutes of the Board meeting of 3/14/88 were approved with no additions or corrections.
2. Two new Board members were introduced. Brian Mayall has been appointed to replace R. Lowry Dobson, and Kathleen Noonan has been appointed to replace George Lawton. Both Lawton and Dobson recently retired from LLNL.
3. Bart discussed human subjects issues during his recent visit to DOE/HQ. Regardless of funding institution, DOE-HQ (OHER) wants a complete packet from the Institutional Review Board for each proposal involving human subjects to include: (1) informed consent forms; (2) experimental subjects bill of rights; (3) minutes of meetings; (4) approval letter from IRB to PI; (5) complete research protocols (grant applications)--even though they already get this through the Work For Others process; (6) signed copies of HHS-596 (NIH form). Bart will contact Susan Rose to discuss this process. Bart will write a memo to all PIs detailing items required for DOE-HQ.
4. Copies of a revised IRB membership list were distributed.
5. Copies of the latest draft P.I. Handbook were distributed for review. Please give comments to Gerry Wyman by June 10. Brian Mayall has a copy of the UCSF Committee on Human Research Guidelines that he will give to Bart to review.
6. The next IRB meeting will be held on Tuesday, July 18 at 1:30 p.m. in Building 361, Room 1155. A written confirmation of this date will be sent to Committee members. Bart Gledhill will not be available, and asked Max Biggs to chair the meeting. A notice of the next meeting will be sent to P.I.'s who have active projects with renewals expiring in June-August 1988.

REPOSITORY LLNL B361 Rm 940A

COLLECTION Institutional Review Board

BOX No. IRB Minutes

FOLDER June 2, 1988 Institutional Review Board Mtg

1122501

Protocol Reviews:

1. *Effects of PCE on Male Reproduction* (renewal), P.I. Andy Wyrobek (deferred from 3/14/88 meeting)
IRB No. 87-107 - last approval 3/17/87

This project involves analyzing sperm count and morphology as part of a UC Berkeley School of Public Health study of the effects of PCE on human semen.

Andy receives coded semen samples from a collaborating physician and returns data in coded form. This is the second year continuation for this project. Sample collection is finished. Only data analysis will be done. Samples are encoded. Data collection phase should be completed by the end of June. He is into the final phase of project. This project is in collaboration with UC Berkeley. Copies of the current UC Berkeley Human Subjects Committee approval document and an informed consent form have been submitted for IRB records. Approval is requested to do data analyses and a few more sample analyses if needed. Funding is still active. No changes in protocol from last approval.

Action: One-year renewal of approval of this project was voted unanimously.

2. *Specific Locus Mutations in Human Sperm* (renewal), P.I. Andy Wyrobek (deferred from 3/14/88 meeting)
IRB No. 86P-106 - last approval 3/17/87

This project, started in 1978, involves collecting sperm from local donors and preparation of sperm nuclei for analyses by dual beam flow cytometry and other methods. This project will develop a new assay for measuring gene mutations directly in sperm by using antibodies that detect sperm with mutated proteins. Source of sperm samples is ongoing LLNL donor program. Approximately 15 samples per month are collected. Same donors have participated over several years. Some of the samples are also used in Brandriff's project (to be reviewed later in this meeting). Andy is only one who knows donor identities. There are no changes in this protocol since the last IRB review.

Action: One-year renewal of approval of this project was voted unanimously.

3. *Human Studies of Somatic Germinal and Heritable Genetic Damage* (renewal), P.I. Andy Wyrobek (deferred from 3/14/88 meeting)
IRB No. 84P-102 - last approval 3/17/87 (Expedited Review 9/18/87)

This project is to study the effects of chemotherapy on sperm using image analyses equipment. This project was funded at NIEHS until March 1988; EPA picked up part of the funding in October 1987 due to a job change by Andy's collaborator, R. Everson. Funding will continue. The work to be done is slightly different from last year. The EPA project has three components: (1) perform cytogenetic analyses of stable aberrations on glass slides; preps made earlier under the NIEHS study; (2) perform sperm morphology and morphometry of slides and smears obtained earlier--also study sperm of local donors; and (3) perform glycophorin analyses using frozen bloods from NIEHS study or blood from local donors. Components 1 and 3 are not new; component 2 was not part of NIEHS study in the past.

Sources of samples: (1) LLNL local donor group (slides collected over past 10 years)
(2) M.D. Anderson Hospital, collaborating since 1978. Collaboration and procedure have been approved by the M.D. Anderson IRB.

Action: One-year renewal of approval of this project was voted unanimously with minor changes to consent form and protocol form.

4. *Chromosomal analysis of human sperm chromosomes visualized in hamster eggs* (renewal), P.I. Brigitte Brandriff
IRB No. 84P-101 - last approval 6/30/87

This project will characterize numerical and structural aberrations in human sperm chromosomes, and investigate mechanisms leading to some of these aberrations. This project will use some semen samples from LLNL local donors (see #2 above). Brigitte is only collecting semen at this point but may collect blood samples in the future. Collaborations with M.D. Anderson and Vanderbilt University; they do blood analysis, we do sperm analysis.

Action: One-year renewal of approval of this project was voted unanimously with minor changes to LLNL consent form for local donors and protocol form. Also, P.I. is to provide the IRB with a copy of Brandriff letter to Vanderbilt University requesting that they list LLNL/Brandriff as collaborator on their consent form.

5. *Biological Dosimeter Using a New Cyto-Immunological Method: Glycophorin-Based Flow Cytometric Analysis of Human Red Blood Cells* (new project--expedited review on 5/20/88), P.I. Ron Jensen
IRB No. 88-105 - Expedited Review by B. L. Gledhill on 5/19/88

This project is to perform assays for somatic mutations in red blood cells. Samples from individuals with a wide range of radiation exposures will be provided from survivors and workers at Chernobyl, U.S.S.R, through the International Atomic Energy Agency, interagency technical contract #4990/RBTC.

The IRB was advised that B.L. Gledhill gave this project expedited review and approval on May 19, 1988, under category 4 of CFR criteria for expedited review.

Action: One-year renewal of approval of this project was voted unanimously.

6. *Estimating adipose tissue in the chest wall using ultrasonic and alternate biometric measurements* (renewal), P.I. Deborah Kruchten
IRB No. 87-111 - last approval 6/30/87

The percentage of adipose tissue in the chest-wall must be known to accurately measure plutonium in the human lung. Methods using simple biometric measurement techniques may be possible to obtain reasonably accurate estimates of adipose tissue content of the chest wall. Personnel from the Whole Body Counter made circumference measurements in attempt to correlate these measurements with those derived by weighing under water for a representative portion of the LLNL population. A follow-up of these employees will be performed at a later date using an ultrasonic examination of specific body sites, such as the chest-wall to further correlate fat content obtained from the circumference data to that obtained by direct ultrasonic measurement.

There are no changes to the protocol or consent form from last year. Some of the ultrasound measurements still need to be done because of earlier equipment problems. The ultrasonic levels are at diagnostic levels. No studies are known that show harmful effects of using ultrasound at diagnostic levels.

Action: One-year renewal of approval of this project was voted unanimously with minor change to protocol form.

7. *Protocol to Measure Chromosomal Aberration Frequencies in Patients Undergoing Radiation Therapy with X-rays or Fast Neutrons* (approval of new collaboration), P.I. Tore Straume
IRB No. 80G-102 - last approval 3/14/88

This protocol is submitted to request approval for a new collaboration. Project was deferred to next meeting as P.I. was unavailable to come before the IRB.

8. *Pulmonary gas rates in man* (renewal - deferred from last several meetings),
P.I. Paul Meyer
IRB No. 80P-109 - last approval 11/25/86

This project is designed to obtain quantitative measures of nitrogen and argon gas exchange rates using radioactive tracers. Data will be used to evaluate physiological models of gas exchange and provide a data base for decompression calculations necessary for safer decompression procedures of deep sea divers.

Paul Meyer gave a brief summary of the project purposes for the benefit of the two new IRB members. IRB members participated in a lengthy discussion of various aspects of this project, including institutional documentation, necessity of radiation exposure to humans, available literature to support continuation of this project, and efforts to minimize total radiation exposure to humans. Over the past several months, Paul Meyer has provided correspondence and literature to the IRB. An LLNL operational safety procedure will be prepared documenting aspects of this procedure. The risk to humans exposed to radiation in this project of developing cancer is 2×10^{-4} . A copy of the last approved consent form was handed out. This work will be done at ambient pressure, which is significant relative to decompression. Paul has no means of doing the experiment at high pressure. The IRB understands that there are no current smokers in the group of Navy divers who will participate in this experiment. Actual doses need to be recorded and tracked by the P.I.

Action: One-year renewal of approval of this project was voted as follows:

Beatty: approve	Johnson: approve
Biggs: approve	Mayall: approve
Brautigam: approve	Noonan: abstain (new member, lacking background info)
Creamer: approve	*Shearer: disapprove
Gledhill: approve	Shepherd: approve

The following are conditions of approval:

1. Actual doses need to be recorded and tracked by the P.I.
2. Add to protocol:
 - a. Total number of individuals who will participate in this project.
 - b. State specific date that human subjects will be at LLNL.
 - c. Reference applicable OSP.
3. Add to consent form the fact that each individual is a non-smoker.

*Note: The IRB requested that Paul Meyer give a bibliography to Jack Shearer of animal experiments related to studies of decompression sickness. Jack Shearer will communicate to the IRB within a maximum of four weeks. Based on the adequacy and timeliness of the bibliography, the IRB requests that Shearer provide either a written minority opinion, or documentation of a change of his vote. This document will become a part of these minutes.

9. *Total encapsulating suit leakage rate* (renewal)
P.I. Jim Johnson
IRB No. 82P-101 - last approval 6/30/87

At the request of the P.I., review of this protocol was deferred to the next meeting.

10. *Urine bioassay for heavy metals as an early indicator of occupational exposure* (renewal),
P.I. Kathleen Noonan
IRB No. 87-105 - last approval 6/30/87

This procedure will determine normal background levels of selected metals in the urine of an occupationally unexposed healthy group of LLNL employees, and determine if a group of LLNL employees, potentially occupationally exposed to select metals, have urinary levels of metals differing from the occupationally unexposed healthy group. There are two parts to this protocol: (1) workplace monitoring ; and (2) collecting data, databases, and studies of effects of rare metals. Interpretation of CFR is that the protocol for review and approval by the IRB will only apply to the volunteer group (controls). Analyses of worker data is considered to be workplace monitoring and not subject to the purview of the IRB.

Action: One-year renewal of approval of this project with minor changes to the consent form was voted as follows:

Beatty: abstain (project participant)
Biggs: approve
Brautigam: approve
Creamer: approve
Gledhill: approve

Johnson: approve
Mayall: approve
Noonan: abstain (project P.I.)
Shearer: approve
Shepherd: approve

Meeting adjourned at 12:35 p.m.

Respectfully submitted:


Geraldine F. Wyman, Secretary

DRAFT

University of California



Lawrence Livermore National Laboratory

Meeting of Institutional Review Board

June 2, 1988

Trailer 3675, Room 106, 9:00 a.m.

Attendees:

Committee Members:

John Beatty
Max Biggs
Alan Brautigam
Max Creamer
Bart Gledhill

Jim Johnson
Brian Mayall
Kathleen Noonan
Jack Shearer
Vivian Shepherd
Gerry Wyman

Principal Investigators:

B. Brandriff
Deborah Kruchten, Larry Anderson
Rich Langlois for R. Jensen
Paul Meyer
Andy Wyrobek

Administrative Matters

1. Minutes of the Board meeting of 3/14/88 were approved with no additions or corrections.
2. Two new Board members were introduced. Brian Mayall has been appointed to replace R. Lowry Dobson, and Kathleen Noonan has been appointed to replace George Lawton. Both Lawton and Dobson recently retired from LLNL.
3. Bart discussed human subjects issues during his recent visit to DOE/HQ. Regardless of funding institution, DOE-HQ (OHER) wants a complete packet from the Institutional Review Board for each proposal involving human subjects to include: (1) informed consent forms; (2) experimental subjects bill of rights; (3) minutes of meetings; (4) approval letter from IRB to PI; (5) complete research protocols (grant applications)--even though they already get this through the Work For Others process; (6) signed copies of HHS-596 (NIH form). Bart will contact Susan Rose to discuss this process. Bart will write a memo to all PIs detailing items required for DOE-HQ.
4. Copies of a revised IRB membership list were distributed.
5. Copies of the latest draft P.I. Handbook were distributed for review. Please give comments to Gerry Wyman by June 10. Brian Mayall has a copy of the UCSF Committee on Human Research Guidelines that he will give to Bart to review.
6. The next IRB meeting will be held on Tuesday, July 18 at 1:30 p.m. in Building 361, Room 1155. A written confirmation of this date will be sent to Committee members. Bart Gledhill will not be available, and asked Max Biggs to chair the meeting. A notice of the next meeting will be sent to P.I.'s who have active projects with renewals expiring in June-August 1988.

1122506

DRAFT

Protocol Reviews:

1. *Effects of PCE on Male Reproduction* (renewal), P.I. Andy Wyrobek (deferred from 3/14/88 meeting)
IRB No. 87-107 - last approval 3/17/87

This project involves analyzing sperm count and morphology as part of a UC Berkeley School of Public Health study of the effects of PCE on human semen.

Andy receives coded semen samples from a collaborating physician and returns data in coded form. This is the second year continuation for this project. Sample collection is finished. Only data analysis will be done. Samples are encoded. Data collection phase should be completed by the end of June. He is into the final phase of project. This project is in collaboration with UC Berkeley. Copies of the current UC Berkeley Human Subjects Committee approval document and an informed consent form have been submitted for IRB records. Approval is requested to do data analyses and a few more sample analyses if needed. Funding is still active. No changes in protocol from last approval.

Action: One-year renewal of approval of this project was voted unanimously.

2. *Specific Locus Mutations in Human Sperm* (renewal), P.I. Andy Wyrobek (deferred from 3/14/88 meeting)
IRB No. 86P-106 - last approval 3/17/87

This project, started in 1978, involves collecting sperm from local donors and preparation of sperm nuclei for analyses by dual beam flow cytometry and other methods. This project will develop a new assay for measuring gene mutations directly in sperm by using antibodies that detect sperm with mutated proteins. Source of sperm samples is ongoing LLNL donor program. Approximately 15 samples per month are collected. Same donors have participated over several years. Some of the samples are also used in Brandriff's project (to be reviewed later in this meeting). Andy is only one who knows donor identities. There are no changes in this protocol since the last IRB review.

Action: One-year renewal of approval of this project was voted unanimously.

3. *Human Studies of Somatic Germinal and Heritable Genetic Damage* (renewal), P.I. Andy Wyrobek (deferred from 3/14/88 meeting)
IRB No. 84P-102 - last approval 3/17/87 (Expedited Review 9/18/87)

This project is to study the effects of chemotherapy on sperm using image analyses equipment. This project was funded at NIEHS until March 1988; EPA picked up part of the funding in October 1987 due to a job change by Andy's collaborator, R. Everson. Funding will continue. The work to be done is slightly different from last year. The EPA project has three components: (1) perform cytogenetic analyses of stable aberrations on glass slides; preps made earlier under the NIEHS study; (2) perform sperm morphology and morphometry of slides and smears obtained earlier--also study sperm of local donors; and (3) perform glycophorin analyses using frozen bloods from NIEHS study or blood from local donors. Components 1 and 3 are not new; component 2 was not part of NIEHS study in the past.

Sources of samples: (1) LLNL local donor group (slides collected over past 10 years)
(2) M.D. Anderson Hospital, collaborating since 1978. Collaboration and procedure have been approved by the M.D. Anderson IRB.

Action: One-year renewal of approval of this project was voted unanimously with minor changes to consent form and protocol form.

4. *Chromosomal analysis of human sperm chromosomes visualized in hamster eggs* (renewal), P.I. Brigitte Brandriff
IRB No. 84P-101 - last approval 6/30/87

This project will characterize numerical and structural aberrations in human sperm chromosomes, and investigate mechanisms leading to some of these aberrations. This project will use some semen samples from LLNL local donors (see #2 above). Brigitte is only collecting semen at this point but may collect blood samples in the future Collaborations with M.D. Anderson and Vanderbilt University; they do blood analysis, we do sperm analysis.

Action: One-year renewal of approval of this project was voted unanimously with minor changes to LLNL consent form for local donors and protocol form. Also, P.I. is to provide the IRB with a copy of Brandriff letter to Vanderbilt University requesting that they list LLNL/Brandriff as collaborator on their consent form.

5. *Biological Dosimeter Using a New Cyto-Immunological Method: Glycophorin-Based Flow Cytometric Analysis of Human Red Blood Cells* (new project--expedited review on 5/20/88), P.I. Ron Jensen
IRB No. 88-105 - Expedited Review by B. L. Gledhill on 5/19/88

This project is to perform assays for somatic mutations in red blood cells. Samples from individuals with a wide range of radiation exposures will be provided from survivors and workers at Chernobyl, U.S.S.R, through the International Atomic Energy Agency, interagency technical contract #4990/RBTC.

The IRB was advised that B.L. Gledhill gave this project expedited review and approval on May 19, 1988, under category 4 of CFR criteria for expedited review.

Action: One-year renewal of approval of this project was voted unanimously.

6. *Estimating adipose tissue in the chest wall using ultrasonic and alternate biometric measurements* (renewal), P.I. Deborah Kruchten
IRB No. 87-111 - last approval 6/30/87

The percentage of adipose tissue in the chest-wall must be known to accurately measure plutonium in the human lung. Methods using simple biometric measurement techniques may be possible to obtain reasonably accurate estimates of adipose tissue content of the chest wall. Personnel from the Whole Body Counter made circumference measurements in attempt to correlate these measurements with those derived by weighing under water for a representative portion of the LLNL population. A follow-up of these employees will be performed at a later date using an ultrasonic examination of specific body sites, such as the chest-wall to further correlate fat content obtained from the circumference data to that obtained by direct ultrasonic measurement.

There are no changes to the protocol or consent form from last year. Some of the ultrasound measurements still need to be done because of earlier equipment problems. The ultrasonic levels are at diagnostic levels. No studies are known that show harmful effects of using ultrasound at diagnostic levels.

Action: One-year renewal of approval of this project was voted unanimously with minor change to protocol form.

7. *Protocol to Measure Chromosomal Aberration Frequencies in Patients Undergoing Radiation Therapy with X-rays or Fast Neutrons* (approval of new collaboration), P.I. Tore Straume
IRB No. 80G-102 - last approval 3/14/88

This protocol is submitted to request approval for a new collaboration. Project was deferred to next meeting as P.I. was unavailable to come before the IRB.

8. *Pulmonary gas rates in man* (renewal - deferred from last several meetings),
P.I. Paul Meyer
IRB No. 80P-109 - last approval 11/25/86

This project is designed to obtain quantitative measures of nitrogen and argon gas exchange rates using radioactive tracers. Data will be used to evaluate physiological models of gas exchange and provide a data base for decompression calculations necessary for safer decompression procedures of deep sea divers.

Paul Meyer gave a brief summary of the project purposes for the benefit of the two new IRB members. IRB members participated in a lengthy discussion of various aspects of this project, including institutional documentation, necessity of radiation exposure to humans, available literature to support continuation of this project, and efforts to minimize total radiation exposure to humans. Over the past several months, Paul Meyer has provided correspondence and literature to the IRB. An LLNL operational safety procedure will be prepared documenting aspects of this procedure. The risk to humans exposed to radiation in this project of developing cancer is 2×10^{-4} . A copy of the last approved consent form was handed out. This work will be done at ambient pressure, which is significant relative to decompression. Paul has no means of doing the experiment at high pressure. The IRB understands that there are no current smokers in the group of Navy divers who will participate in this experiment. Actual doses need to be recorded and tracked by the P.I.

Action: One-year renewal of approval of this project was voted as follows:

Beatty: approve	Johnson: approve
Biggs: approve	Mayall: approve
Brautigam: approve	Noonan: abstain (new member, lacking background info)
Creamer: approve	*Shearer: disapprove
Gledhill: approve	Shepherd: approve

The following are conditions of approval:

1. Actual doses need to be recorded and tracked by the P.I.
2. Add to protocol:
 - a. Total number of individuals who will participate in this project.
 - b. State specific date that human subjects will be at LLNL.
 - c. Reference applicable OSP.
3. Add to consent form the fact that each individual is a non-smoker.

*Note: The IRB requested that Paul Meyer give a bibliography to Jack Shearer of animal experiments related to studies of decompression sickness. Jack Shearer will communicate to the IRB within a maximum of four weeks. Based on the adequacy and timeliness of the bibliography, the IRB requests that Shearer provide either a written minority opinion, or documentation of a change of his vote. This document will become a part of these minutes.

9. *Total encapsulating suit leakage rate* (renewal)
P.I. Jim Johnson
IRB No. 82P-101 - last approval 6/30/87

At the request of the P.I., review of this protocol was deferred to the next meeting.

10. *Urine bioassay for heavy metals as an early indicator of occupational exposure* (renewal),
P.I. Kathleen Noonan
IRB No. 87-105 - last approval 6/30/87

This procedure will determine normal background levels of selected metals in the urine of an occupationally unexposed healthy group of LLNL employees, and determine if a group of LLNL employees, potentially occupationally exposed to select metals, have urinary levels of metals differing from the occupationally unexposed healthy group. There are two parts to this protocol: (1) workplace monitoring ; and (2) collecting data, databases, and studies of effects of rare metals. Interpretation of CFR is that the protocol for review and approval by the IRB will only apply to the volunteer group (controls). Analyses of worker data is considered to be workplace monitoring and not subject to the purview of the IRB.

Action: One-year renewal of approval of this project with minor changes to the consent form was voted as follows:

Beatty: abstain (project participant)
Biggs: approve
Brautigam: approve
Creamer: approve
Gledhill: approve

Johnson: approve
Mayall: approve
Noonan: abstain (project P.I.)
Shearer: approve
Shepherd: approve

Meeting adjourned at 12:35 p.m.

Respectfully submitted:

Geraldine F. Wyman, Secretary