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Revision C

JSC Committee for the Protection of Human Subjects

Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations

Space and Life Sciences Directorate

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http://stic.jsc.nasa.gov/dbase/iso9000/master/master.cgi)

February 2004

National Aeronautics
and Space Administration

Lyndon B. Johnson Space Center
Houston, TX

Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS)

Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations

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Handbook Revision Process

This Handbook has been reviewed by each major organizational element involved (denoted by Handbook signature page). Requests for changes shall be submitted in writing to the Director for Space and Life Sciences. The quality record for this review and update process will be the current document with the appropriate updated revision number and date, signed by the Director, Space and Life Sciences. The Director, Space and Life Sciences, can update the document within any fiscal year as required, and will provide notification that a new version is available. This Handbook shall remain in effect until the Director, Space and Life Sciences, cancels it through such notification. Once a change, revision, or cancellation of this document has been approved, the appropriate information will be provided to the Master List Custodian for placing the change on the Space and Life Sciences Master List.

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Acronyms and Abbreviations

f	frequency
μA	microampere
a.c.	alternating current
AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care
AAMI	Association for the Advancement of Medical Instrumentation
ACES	Advanced Crew Escape Suit
ACHRE	Advisory Committee for Human Research Experiments
ACLS	Advanced Cardiac Life Support
ALARA	as low as reasonably achievable
AMB	Aerospace Medical Board
AMERD	Astronaut Medical Evaluation Requirements Document
ANSI	American National Standards Institute
AO	Announcement of Opportunity
ASDMB	Aerospace Support and Dive Medicine Board
BCD	Bioastronautics Control Board
BDC	baseline data collection
BLS	basic life support
cc	cubic centimeter (same as ml)
CDR	commander (of Space Shuttle or ISS Increment)
Center	Lyndon B. Johnson Space Center
CFR	Code of Federal Regulations
Co-I	co-investigator
CPHS	Committee for the Protection of Human Subjects
CSA	Canadian Space Agency
CSE	Clinical Status Evaluation
d.c.	direct current
DCB	Directorate Control Board
DHEW	Department of Health, Education, and Welfare (now the Department of Health and Human Services (DHHS)
DHHS	Department of Health and Human Services
DMO	Designated Medical Officer
DSO	Detailed Supplementary Objective
DTO	Detailed Test Objective
DTP	Detailed Test Procedure
ECG	electrocardiogram, electrocardiography
EMG	electromyogram, electromyography
EMU	External Maneuvering Unit
EOG	electro-oculogram
ESA	European Space Agency
EVA	extravehicular activity
FDA	Food and Drug Administration
FRR	Flight Readiness Review

GOJ	Government of Japan
HEPA	high-efficiency particulate air
HERD	Human Experimental and Research Data Records
HIMS	Health Information Management System
HRMRB	Human Research Multilateral Review Board
HSEC	Health, Safety, and Environmental Compliance Officer
HTSF	Human Test Subject Facility
ICU	intensive care unit
IDE	investigational device exemption
IEC	International Electrotechnical Commission
IND	investigational new drug
IRB	Institutional Review Board
ISS	International Space Station
JAXA	Japan Aerospace Exploration Agency
JHB	Johnson Space Center Handbook
JPD	Johnson Space Center Policy Directive
JPG	Johnson Space Center Procedures and Guidelines
JSC	Lyndon B. Johnson Space Center
KC-135	NASA microgravity aircraft (parabolic flight)
kg	kilogram
kHz	kilohertz
LBNP	lower body negative pressure
LD50	lethal dose-50
mA	milliampere
MER	Medical Evaluation Requirement
MO	medical officer
MOU	memorandum of understanding
ml	milliliter (same as cc)
MOCR	Mission Operations Control Room
MPA	Multiple Project Assurance
MS	mission specialist (of Space Shuttle)
MSD	Medical Sciences Division
NASA	National Aeronautics and Space Administration
NASDA	National Space Development Agency of Japan
NFPA	National Fire Protection Association
NFQ	NASA Flight Quality
NIH	National Institutes of Health
NMI	NASA Management Instruction
NPD	NASA Policy Directive
NPG	NASA Procedures and Guidelines
NRA	NASA Research Announcement
NRC	Nuclear Regulatory Commission
NSTS	National Space Transportation System (no longer used)

OBPR	Office of Biological and Physical Research
OHRP	Office of Human Research Protections
ORR	operational readiness review
OSTP	Office of Science and Technology Policy
PCN	page change notice
PCO	Protocol Compliance Officer
PHS	Public Health Service
PI	principal investigator
PLT	pilot (of Space Shuttle)
PPO	Policy and Procedure Order
PS	payload specialist (of Space Shuttle)
PSRP	Payload Safety Review Panel
QR	quality record
RAHF	Research Animal Holding Facility
RCP	Radiation Constraints Panel
RDRC	Radioactive Drug Research Committee
RME	Risk Mitigation Evaluation
RPWG	Radioactive Payloads Working Group
RSA	Russian Space Agency
RSC	Radiation Safety Committee
S&LSD	Space and Life Sciences Directorate
SMART	Safety and Mission Assurance Review Team
SMO	Supplemental Medical Objective
SMP	Space Medicine Program
SPA	Single Project Assurance
SR&QA	Safety, Reliability, and Quality Assurance
SR&T	Scientific Research and Technology
STS	Space Transportation System
TC	test conductor
TD	test director
TEDP	Test Equipment Data Package
TRR	Test Readiness Review
TRRB	Test Readiness Review Board
UL	Underwriters Laboratories, Inc.

Glossary

Co-Investigator — a scientist who works closely with the principal investigator on flight experiments that have been selected for a specific mission or on ground-based studies that support flight experiments.

Crew Surgeon — a flight surgeon assigned to a particular mission. The crew surgeon is responsible for maintaining the overall health of the astronauts assigned to a given mission.

Human Test Subject Facility Recruiter — the individual responsible for locating suitable test subjects for JSC CPHS-approved ground-based experiments.

Medical Monitor — a physician appointed by the JSC CPHS to monitor experiments to ensure compliance with CPHS requirements. The qualifications and certifications required of the medical monitor(s) are determined by the JSC CPHS.

Mission Scientist — the NASA science supervisor responsible for the overall scientific conduct of a mission.

Mission Manager — the NASA manager responsible for allocating and negotiating mission resources, designing and developing mission-unique integration hardware, developing and operating mission training facilities, and ensuring payload element safety compliance and integration of payload elements in the orbiter.

Principal Investigator — a scientist whose proposed flight experiment has been selected for a specific mission or ground-based study.

Project Scientist — the NASA field center scientist/manager responsible for the detailed development and integration of flight experiments, for representing the interests of selected investigators, and for interfacing their experiments with the various mission organizations.

Protocol Compliance Officer — a medical monitor whose primary function is to verify that all experiments are conducted in accordance with JSC CPHS requirements and ethical principles. The PCO is a representative of the JSC CPHS and a voting member of the JSC CPHS.

Secretary/Recorder — the individual who provides clerical support to the JSC CPHS by ensuring the collection of accurate records and the publication of JSC CPHS activities, including agendas, proceedings, and action items. The Secretary/Recorder supports the JSC CPHS and serves as a point of contact for investigators submitting protocols to the JSC CPHS for review, and for annual renewal of protocol approval.

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Intra- and Internet Access

JSC forms may be accessed electronically from the JSC Internal Home Page: http://www4.jsc.nasa.gov. Under General Information, go to JSC Forms.

Investigators may access Johnson Procedures and Guidelines (JPG) 1700.1H, Safety and Total Health Handbook at http:www4.jsc.nasa.gov/safety/Handbook.

NASA JSC (center-wide) management directives, policies, and procedures may be accessed through the JSC Internal Home Page Intranet address http://www4.jsc.nasa.gov. Under General Information, go to Management Directives.

Investigators may access their digitized images from KC-135 flights via a password-protected system at http://zerog.jsc.nasa.gov.

Investigators may obtain general information about the KC-135 Reduced Gravity Program and Aircraft Operations at http://jsc-aircraft-ops.jsc.nasa.gov.

Research use of drugs for indications not in the package insert is subject to Food & Drug Administration (FDA) restrictions. FDA forms (Appendix M) are also available online and may be accessed at http://www.fda.gov/opacom/morechoices/fdaforms/fdaforms.html.

The Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) internet address is http://ohrp.osophs.dhhs.gov.

Information associated with the Code of Federal Regulations may be accessed through the following internet address: http://www.access.gpo.gov/nara/cfr/index.html.

INTRODUCTION

This document is intended to provide investigators with a thorough understanding of the role of the Lyndon B. Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS). In addition, the process of submitting a research protocol for consideration and the methods of monitoring the research protocol for safety and compliance are defined in Appendix G. The authority and scope of the JSC CPHS derive from JPG 1107.1A (Appendix C), NASA Policy Directive (NPD) 7100.8D, and NASA Procedures and Guidelines (NPG) 7100.1 (Appendix D). The JSC CPHS charter, some definitions, and the ethical principles that guide the Committee are described below.

1.0 OVERVIEW OF THE JSC CPHS

The JSC CPHS is the oversight organization charged with assuring the health, safety, and well-being of human research subjects in any JSC investigation or NASA-sponsored space flight investigation.

1.1 Guiding Principles of the CPHS

A. Human research must always be based on fundamental ethical principles. These principles include the following:

- Participation of a human test subject must be entirely voluntary, without coercion in any form
- A subject may withdraw from an experiment at any time, for any reason, without penalty.

The Federal policy for the protection of human research subjects, referred to as the "Common Rule" (45 CFR Part 46, Subpart A), establishes the ethical framework for all federally funded human research. A brief overview of the policy is given in Appendix A. Additional guidelines describing basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects may be found in Appendix B.

B. Coercion to participate in research can take many forms and must be diligently avoided. No agreements can be made that imply consent before a subject is informed, in detail, of the risks of the experiment. The principal investigator (PI) has the primary responsibility for the safe and ethical conduct of human experiments. In addition, PIs shall be required to disclose any and all potential conflicts of financial interest that they have or that are imputed to them in connection with their proposals or research, as set forth in section 1.6C of Appendix G.

1.2 Charter of the JSC CPHS

A. Research protocols using human test subjects must be approved by the JSC CPHS when research is funded or sponsored by NASA JSC or conducted in spacecraft, at NASA JSC facilities, on NASA JSC aircraft, or at other centers or institutions when JSC civil service or contractor personnel are directly involved in the research activities. All research involving space-flight crews must be approved by the JSC CPHS. All institutions proposing human research shall give written institutional assurance as described in 14 CFR 1230.103 and 45 CFR 46.103. In lieu of requiring submission of an assurance, the JSC CPHS may accept the existence of a current assurance, appropriate for the research in question, on file with the Office for Human Research Protections (OHRP) of the Department of Health and Human Services (DHHS), and approved for Federal Government-wide use by that office. This requirement is in addition to, and not in lieu of, JSC CPHS approval of a research protocol.

Procedures normally followed in foreign countries to protect human subjects may differ from those set forth in this policy. When research covered by this policy takes place in a foreign country, if NASA determines that the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in this policy, the JSC CPHS may approve the substitution of the foreign procedures in lieu of the procedures required in this policy, in accordance with 14 CFR. 1230.101 and 45 CFR 46.101.

B. Most institutions will require that their own Institutional Review Board (IRB) review protocols for research involving human test subjects at their institutions. Such a review does not obviate the review by the JSC CPHS. This duplication of effort is unavoidable because two different sets of requirements must be met.

C. With respect to proposals for research to be done on the International Space Station (ISS), each NASA ISS partner will initially conduct its own review of its individual experiments through appropriate national IRBs or equivalents. Protocols that have been approved by the appropriate national IRBs or equivalents will be submitted to the Human Research Multilateral Review Board (HRMRB). The HRMRB was established in accordance with Article 11.5 of the Memorandum of Understanding (MOU) (Appendix Y).

1.3 Composition of the JSC CPHS

A. The JSC CPHS consists (at a minimum) of these members:

- The Chairperson
- An alternate Chairperson
- A life scientist
- A flight surgeon
- A representative from the Legal Office
- A representative from the Safety, Reliability, and Quality Assurance (SR&QA) Office, Safety & Test Operations Division
- An astronaut
- A non-life-sciences employee
- A non-NASA, full-time Federal employee

B. Members of the Committee are appointed by the Center Director. CPHS members are expected to attend regularly. At least one third of the members are physicians. Up to three *ad hoc* members in specialized disciplines may be added to the JSC CPHS on a temporary, non-voting basis as deemed appropriate by the Chairperson (Appendices C and D). The member position filled by a non-life-sciences employee may be rotated among the Center directorates and offices.

C. The permanent Chairperson will periodically designate a Committee member as acting Chairperson to give others experience in conducting the meetings, while the permanent Chairperson retains overall control of the standing Committee.

D. All members of the JSC CPHS are voting members. The Chairperson will vote only in the event of a tie. A majority of the JSC CPHS members present is required to review and approve a protocol. This majority must include the Chairperson (or alternate Chairperson) and representatives of the Astronaut Office (presence of Astronaut Office representation is mandatory for evaluation of flight studies), SR&QA Office, and Medical Operations. Every member is required to vote on each issue except when a member would have a conflict of interest, or when a member's lack of technical familiarity with aspects of a protocol would render that vote inappropriate.

1.4 Working Principles of the JSC CPHS

A. The JSC CPHS meets regularly and uses only written documents for the evaluation of research protocols. Verbal assurances or explanations are not acceptable, although PIs or their representatives may be invited to explain parts of a protocol and answer questions as necessary to clarify the written research protocol.

B. The JSC CPHS does not duplicate the efforts of the Payload Safety Review Panel (PSRP) in its review of equipment for payload experiments (Appendix E), or the efforts of SR&QA Office personnel in their review of equipment for ground-based experiments. Detailed Supplementary Objectives (DSOs), Supplemental Medical Objectives (SMOs), and Detailed Test Objectives (DTOs) relating to life sciences or involving equipment that requires human interaction are reviewed by the JSC CPHS, even if they are also reviewed by the PSRP and/or the SR&QA Office. The Committee requires documented evidence of appropriate safety reviews. The particulars of each study will dictate which group reviews the research hardware.

C. No JSC CPHS member may participate in the review of any research protocol in which that member has a conflicting interest, except to provide information requested by the Committee. Any JSC CPHS member who is a PI, co-investigator (Co-I), immediate supervisor, or relative of the investigator(s) of a research protocol before the Committee, or has any known or perceived conflict of interest, may not participate in the discussion of, or vote on, that protocol. Members may also abstain from voting if they are not technically familiar with aspects of a protocol. A simple majority vote of those present is required for approval (See section 1.3 D for additional specifications of members who must approve). Absent a consensus of the Committee, each individual's vote will be recorded. JSC CPHS decisions are documented in writing. The minutes will reflect the rationale for abstentions.

D. The Chairperson, or one or more experienced reviewers designated by the Chairperson from among the members of the JSC CPHS, may approve human research protocols by the expedited review procedure, using the same criteria for approval as are used for non-expedited review but without the necessity for consideration by the entire JSC CPHS (Appendices C and D). Only research protocol changes involving "minimal risk" or minor changes in "reasonable risk" protocols may be so approved. Approvals will be reported to the full JSC CPHS at its next meeting in accordance with the current NPD and NPG.

E. The JSC CPHS is autonomous and impartial. Committee members may not be added or deleted to alter Committee membership for the purpose of influencing a decision. Individual members must feel free to express opinions and concerns without fear of career repercussions.

F. The Secretary/Recorder and the Protocol Compliance Officer (PCO) supports the Committee. The Secretary/Recorder will ensure the collection of accurate records and the publication of JSC CPHS activities, including agendas, proceedings, and action items. Minutes and action requirements shall be published and distributed to NASA Headquarters, and to appropriate JSC Directors, JSC CPHS members, meeting attendees, and action assignees. The PCO, as medical monitor for the Committee, must ensure that all experiments are conducted in accordance with JSC CPHS requirements. The PCO will routinely participate in tests as a monitor and representative of the JSC CPHS. As such, the PCO is fully authorized to halt any research or test activity that is judged to be in violation of JSC CPHS recommendations, accepted medical practice, or accepted safety guidelines.

1.5 Purpose of JSC CPHS Review

The fundamental responsibility of the JSC CPHS is to ensure the health, safety, and well-being of human research subjects while ensuring the ethical conduct of experiment operations. All PIs bear responsibility for implementation of the JSC CPHS guidelines. The Committee approves only those investigations involving "minimal" or "reasonable" risk to the human subject. Animal research is of interest to the JSC CPHS particularly in the context of human health and safety.

1.5.1 Definitions of Risk Levels

Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research protocol are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams or tests. Examples of "Minimal Risk" activities are found in Appendix F.

Reasonable Risk: The probability and magnitude of harm or discomfort anticipated in the research protocol are greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological exams or tests, but these risks are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

1.6 Authority and Responsibility of the JSC CPHS

1.6.1 Actions

The JSC CPHS can approve, disapprove, or require changes in any research protocol submitted for review. The JSC CPHS has the authority to terminate approval of research activity that is not conducted in accordance with the approved research protocol or generates unexpected harm or excessive discomfort to a subject. In the event that approval is terminated, the JSC CPHS will promptly communicate its rationale to the PI, who may appeal the decision by meeting with the JSC CPHS or by writing to the Chairperson. Experiment operations will be suspended until the matter is resolved.

1.6.2 Sanctions for Violations

A. Any research protocol may be immediately suspended because of non-compliance with JSC CPHS recommendations in accordance with the "Common Rule" (Appendix A), or for scientific misconduct or unethical practice by an investigator. A review panel may be convened to investigate the circumstances surrounding these events.

B. A protocol may be suspended when a research subject suffers an adverse event. In this case, the JSC CPHS will vote on whether to recommend initiating a formal investigation.

C. NASA may invoke disciplinary action against investigators whose conduct has not been in accordance with JSC CPHS standards. Sanctions for non-compliance by researchers include loss of investigator privileges and funding. Sanctions may also include reprimands, and suspension or termination of employment (Appendix D).

2.0 APPLICATION: SUBMISSION OF A RESEARCH PROTOCOL[1]

2.1 Types of Research Protocols Reviewed by the JSC CPHS

Research protocols reviewed by the JSC CPHS are of three types:

- Ground-based Research Protocol: Protocol for research to investigate and measure parameters associated with life science goals and objectives. Investigators must submit their protocol to the JSC CPHS for review. The format for this type of protocol is given in Appendix G. Approval of a ground-based research protocol is valid for only 12 months.

- KC-135 Research Protocol: Research protocol to investigate, test, or evaluate procedures associated with the altered gravitational environment of NASA's KC-135 aircraft. Investigators must submit their protocol to the JSC CPHS for review according to the guidelines in Appendix G. Additionally, a Test Equipment Data Package (TEDP) must be included as an attachment to the protocol. This documentation must include the test plan, engineering drawings and schematics, structural analysis, electrical load analysis, and an analysis of any identifiable hazards. Detailed information outlining the test plan is given in Appendix G. Additional information about testing aboard the KC-135 aircraft is in the JSC Reduced Gravity Program User's Guide (JSC-22803). Upon approval of the research protocol by the JSC CPHS, a copy of the research protocol should be forwarded to the JSC Reduced Gravity Office for processing. Approval of KC-135 research protocols is valid for only 12 months.

- Space Flight Research Protocol: A life science research protocol associated with a space-flight mission(s). Investigators must submit their protocol to the JSC CPHS for review. The format for this protocol is given in Appendix G. Additionally, the Training/Baseline Data Collection Protocol must be reviewed by the JSC CPHS. The format for this protocol is given in Appendix H. A detailed description of procedures for each training session must be submitted by investigators for all in-flight experiments. Protocols for training and baseline data collection sessions must include objectives of the session as well as a daily schedule of the training procedures and equipment to be used. Experience gained from training sessions and baseline data collections may result in protocol modifications. The JSC CPHS therefore requires that the exact protocol for each training or baseline data collection session be reviewed and approved. Training/baseline data collection protocols need to be submitted to the JSC CPHS 6 weeks before crew training begins. Approvals for space flight research and training/baseline data collection protocols are valid for only 12 months.

2.2 Submission Process for JSC CPHS Approval

A. In some cases, additional approval may be required by one or more of the following review committees or JSC elements before a protocol is submitted to the CPHS:

- JSC Radiation Safety Committee

- Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee

[1] For the purpose of this handbook, the term "research protocol" denotes a more specific procedural document than that conveyed by the phrase "research proposal."

For the above two committees, use the forms and information provided in Appendix I as appropriate.

- Payload Safety Review Panel (for in-flight experiment equipment)
- Safety, Reliability, and Quality Assurance Office (for ground-based experiments)

B. Once approved by the required board(s), research protocols (for space flight, KC-135, or ground-based research) must be submitted to the JSC CPHS per the Life Sciences Research Protocol format (Appendix G). Investigators must provide the Secretary/Recorder with 20 copies. When applicable, include pre-, in-, and postflight activities. Applicable flight studies should be routed through the designated mission/increment scientist or equivalent before JSC CPHS review. Research protocols for flight investigations should be submitted for initial approval no later than 12 months before the mission. All research protocols submitted to the Committee must be signed and dated by the PI.

C. For space-flight studies, at least 6 weeks before a training session, the investigator shall provide the JSC CPHS with 20 copies of the Training/Baseline Data Collection Protocol to be used (Appendix H). If applicable, the training/baseline data collection protocol will be routed first through the mission/increment scientist or equivalent, then to the JSC CPHS. All training/baseline data collection protocols submitted to the Committee must be signed and dated by the PI.

D. If the research protocol changes, the PI must provide, in writing, details of the Page Change Notice (PCN) to the JSC CPHS for review. The format for this notice is given in Appendix V. The PCN replacement pages must be dated and identified, with the appropriate changed sections indicated by bars in the margins. The PCN replacement pages must be submitted to the Secretary/Recorder of the JSC CPHS as soon as feasible. The mission/increment scientist or equivalent must receive similar PCN replacement pages.

E. When the Secretary/Recorder has received a satisfactory and complete research protocol, the PI is informed officially, in writing, of the date of the meeting at which the protocol will be reviewed. The Secretary/Recorder ascertains that all required components of the protocol have been submitted. Non-compliant or incomplete research protocols are returned to the PI with the discrepancies noted. Research protocols and agendas are distributed to Committee members at least 2 weeks before the scheduled meeting. The Committee considers only written documents for evaluation of protocols. It may be desirable to have a representative familiar with the study available to answer detailed questions or to note action items from the JSC CPHS.

F. No crew training or ground-based investigation will start unless its master research protocol has received CPHS approval. All additional research protocols must be approved before any baseline data collection (BDC), training session, or KC-135 flight starts. Informed consent statements must be filed with the Secretary/Recorder of the JSC CPHS and the mission/increment scientist or equivalent, when appropriate. Responsibility for meeting these requirements lies entirely with the PI.

2.3 Renewal of a Training/Baseline Data Collection Protocol

The PI must submit renewal material (Appendix J) to the JSC CPHS 30 days before the 12-month approval period for a training/baseline data collection protocol expires. The PI must include appropriate consent statement(s) (Appendix K). If substantive changes have been made to the training/baseline data collection protocol, these revisions must be submitted for review by the JSC CPHS before the next training session starts.

3.0 BOARD DECISION AND NOTIFICATION

3.1 Disposition of a Research Protocol

Any of four dispositions is possible for a research protocol. A simple majority vote of the members present is required for approval. The PI will be notified in writing; a sample letter is shown in Appendix L.

A. Approval

The research protocol is acceptable as written. Any subsequent deviations or changes must be submitted to the JSC CPHS. The PI is informed of such approval in writing (Appendix L).

B. Approval with Recommendations (Mandatory Action Items)

In some cases where minor deficiencies are found, the proposal may be "approved with recommendations." In these cases, responses to the JSC CPHS action items must be formally closed in a written document addressed to the Committee Chair. The JSC CPHS Protocol Action Item Response (Appendix W) must be submitted to and reviewed by the JSC CPHS. When all recommendations have been reviewed and approved, a JSC CPHS letter of notification (Appendix L) is sent to the PI.

C. Tabled

This disposition indicates that the JSC CPHS did not have enough information to make a decision, or major changes are required to make the research protocol acceptable. The PI is informed of the JSC CPHS decision in writing (Appendix L). New information should be submitted at least 2 weeks before the next scheduled CPHS meeting. For Training/Baseline Data Collection Protocols, it is imperative that the approval process be initiated at least 6 weeks before the planned training session.

D. Disapproval

The research protocol is not acceptable. The PI is notified of the JSC CPHS decision in writing (Appendix L). A decision of disapproval cannot be overturned without substantial modifications to the risk-benefit aspect of the protocol. The revised protocol must be resubmitted for all required approvals.

4.0 CONDUCT OF THE RESEARCH PROTOCOL

4.1 Normal Process

A. All activities conducted at JSC, whether by JSC employees or visiting PI teams, shall comply with JPG 1700.1H, Safety and Total Health Handbook Policy, Requirements, Instructions and Guidelines (Appendix Q), which provides requirements for test activities.

B. Safe and ethical conduct of all research, in conformance with JSC CPHS-approved research protocols, is the primary responsibility of the PI and his or her management. All research protocols must contain a section with a detailed medical monitoring plan. The plan should include provisions to pre-screen subjects, when possible, for hypersensitivity to any administered substances before the experiment starts. The JSC CPHS considers the adequacy of the plan. If a study requires the intravenous administration of any substance,

at least one Co-I and a licensed physician must be present. Research use of Food and Drug Administration (FDA)-approved drugs for indications not in the package insert, as well as investigational new drugs (INDs), are subject to FDA restrictions. FDA forms (Appendix M) are also available online and may be accessed at http://www.fda.gov. These forms are to be submitted as attachments as part of the Life Sciences Research Protocol format. The JSC CPHS reviews all protocols for compliance with FDA requirements.

C. Members of the JSC CPHS and the PCO will occasionally participate in formal, announced visits to the various facilities in which JSC CPHS-approved investigations are conducted. In addition, members of the Committee and the PCO may observe tests in progress on an irregular, unannounced basis to ensure that JSC CPHS recommendations are being followed. These individuals are responsible to the Chairperson of the JSC CPHS and must have no relationship to the research or to the researchers (that is, no conflict of interest).

D. A medical monitor attends ground-based investigations and training sessions as deemed necessary by the JSC CPHS. Qualifications and certifications required of the medical monitor shall be determined by the JSC CPHS.

E. Minor equipment and procedural changes may be approved by the medical monitor during the session. Any changes that the monitor does not approve are deferred to the full JSC CPHS, and the part of the training that may be changed will be delayed until the JSC CPHS has ruled on the changes.

F. For space-flight studies, to ensure that having a subject perform protocols for two or more juxtaposed experiments does not increase risk, an integrated plan for pre-, in-, and postflight experiment operations must be presented to the JSC CPHS for approval. This plan must include proposed experiment activities, medical operations requirements (such as sampling of blood and other body fluids), and crew scheduling requirements for all phases of the mission.

G. The results of ground-based (bed rest, KC-135) preliminary research, if such has been required, are reviewed before any research is approved for space flight. This must be done to ensure feasibility of the protocol, as well as an adequate risk/benefit ratio assessment of the research.

H. Subject Qualifications

- Ground-based, KC-135: No subject who has had an allergic diathesis (predisposition) or a reaction to a medication or diagnositc agent, particularly an anaphylactoid or frank anaphylactic reaction, up to the time the experiment is performed will be selected for research involving provocative procedures, or intravenous/intramuscular administration of any drug. Using the results of the physical exam and a review of the medical history, the examining physician certifies that all subjects meet the medical standards for participation and are at no additional risk.

- Space flight: Space flight personnel with history of any above reactions will not be selected for research involving provocative procedures or intravenous/intramuscular administration of any drug. If at any time crew surgeon believes, on the basis of his/her specific knowledge of the crew member's medical history, a crew member's participation presents an unacceptable risk, the crew surgeon can prohibit the crew member from participation in a study. The crew member can obtain a waiver for participation from the Aerospace Medical Board (AMB).

I. No human research flight protocol will be manifested until and unless it is approved by the Bioastronautics Control Board (BCB).

J. Responsibilities

- PIs and monitoring physician(s) have the responsibility to discuss frequently, with crew members and other subjects, all risks associated with provocative procedures or intravenous/intramuscular drug administration. These risks should be reiterated both verbally and in writing (layman's terms as appropriate) in the informed consent statement (Appendix G, Section 14.0). The principals must also ensure that appropriate experiment-specific and general support medications are available for any mishap that might occur.

- During presentation at the Flight Readiness Review (FRR) for space-flight studies, the crew surgeon focuses on the risks associated with provocative procedures or intravenous/intramuscular administration of drugs.

- The mission scientist (and/or project scientist) and crew surgeon for each flight evaluate the potential for interactive risks to astronaut test subjects that result from participating in multiple experiments on the same flight. Their evaluation includes examining the sequence of experiments for each participant. Potential hazards that must be excluded or minimized include but are not limited to drug interactions and the impact of experimental medical hardware on crew performance or emergency egress. Attention should be directed toward the combined physiological and psychological impact of all procedures on the subject. The mission scientist and the crew surgeon present the profile of interactions for consideration by the JSC CPHS (Appendix G, Section 10.0). This plan must be approved by the JSC CPHS before training or baseline data collection starts. For life science intensive flights and ISS missions, this approval must occur by L–6 months; for all other missions, by L–4 months.

4.2 Informed Consent

A. Before any medical study starts, the PI obtains signed informed consent forms [NASA/JSC Human Research Informed Consent, JSC Form 1416; Multinational Space Station Human Research Informed Consent, JSC Form 1418; or NASA/JSC Human Research Informed Consent for Grants/Other Agreements Where Research Is Conducted at Locations Other than JSC, JSC Form 1419 (Appendix K)] from all subjects. If non-astronaut test subjects are required, the PI submits a request for human subjects (Appendix N) to the Human Test Subject Facility (HTSF) Recruiter.

B. A complete description (in layman's terms) (Appendix G, Section 14.0) of the experiment, including all procedures involving subjects, must be included in a research protocol. A detailed description of any medical risks involved (such as exposure to ionizing radiation, use of medications, and reactions to these medications) must also be included. Experiment-specific prohibitions related to subjects' exercise, diet, medications, weight control, etc. must also be included as an attachment.

4.3 Privacy of Biomedical Research Data

A. Each investigator must submit details of a data-sharing plan (Appendix G), and a plan to protect privacy of medical data that includes safeguards for electronically stored data. No data attributable to an individual will be publicly released without written permission of the

subject. This concept encompasses non-disclosure of an individual's name, and also requires sufficient pooling of data to preclude determining an individual's identity by combining or cross-referencing data (for example, height, weight, sex, and flight number may identify a specific individual).

B. The JSC CPHS requires investigators to comply with JPD 1382.5B "Maintaining the Privacy of Biomedical Research Data" (Appendix P).

4.4 Government Access to and Use of Human Research Data

All research data collected under NASA contracts and grants is to be delivered to NASA as summarized in Appendix Z, "Policy Regarding Human Research Data."

4.5 Test Readiness Review

A. A test readiness review (TRR) is conducted before each "reasonable risk" test or series of tests. Documents must be provided for review at least 5 days before the TRR. The review outlines the test plan, determines the readiness of the facility and test equipment, and verifies the qualification and certification of the test team. All test team personnel receive a briefing detailing possible adverse reactions to the protocol, and review emergency procedures. Appendix Q provides additional detail concerning TRR requirements.

The PI will ensure that all questions are properly raised and answered. A medical monitor will attend the TRR and be informed of all procedures, reasonable risks, and known hazards. The TRR should include all key members of the test team, including those persons who will have hands-on responsibility for test operations and data collection and analysis. A TRR must be completed, and all assigned actions must be closed, before any manned evaluation of equipment or test setup is conducted.

B. The Test Readiness Review Board (TRRB) signs a readiness statement to indicate approval for the test to proceed. As required, the TRRB may include representatives from the SR&QA Office, and medical monitoring and laboratory support personnel.

C. A post-test debriefing is held with all significant test team members to discuss the test results and any test or facility anomalies. The SR&QA Office must be notified of the post-test debriefing if safety issues or significant anomalies arose during the test activities.

4.6 Appropriate Medical Monitoring

The PI proposes the level of medical monitoring for all "reasonable risk" protocols. The JSC CPHS evaluates the medical monitoring plan for each portion of the protocol. The JSC CPHS typically categorizes medical monitoring into four levels. Quarterly emergency drills must be conducted as part of training for investigator teams whose protocols require Level 1 or 2 monitoring. The PI or Co-I must be physically present during performance of all protocols that require Level 1 monitoring, unless the CPHS has approved an alternate to the PI or Co-I for this purpose. The PI, Co-I, or designee must also supply the PCO with an up-to-date testing schedule. Responsibility for maintaining JSC crash carts and training all ancillary medical personnel in the use of equipment lies with the Occupational Medicine and Test Support Group. Experiments conducted during flight typically will not have equivalent monitoring because of programmatic constraints. Certain flight protocols will have ground-based real-time monitoring requirements to compensate. These are the medical monitoring levels for ground-based studies:

Level 1: The Advanced Cardiac Life Support (ACLS)-certified physician must be physically present in the room at the time of the test (active monitoring). An up-to-date "crash cart" is located in the immediate vicinity of the test. Two basic life support (BLS)-certified test operators also are present during testing.
Level 2 : An up-to-date crash cart is immediately available in the building where the test is being conducted and an ACLS-certified physician is able to reach the testing area within 2 minutes. Two BLS-certified operators are present at all times.

Level 3: The ACLS-certified physician is available within 15 minutes of notification.

Level 4: The ACLS-certified physician is aware of the specific testing and available for consultation.

4.7 Corrective Action

The purpose of this section is to help investigators become aware of the basic concepts of corrective action at JSC. Investigators must be aware of how to participate in the corrective action process. Investigators must report instances of medical problems resulting from a subject's participation in experiment activities to the JSC CPHS Chair and the JSC Safety Office. The following five-step Corrective Action Plan must be submitted by investigators for JSC CPHS review.

4.7.1 Corrective Action Plan

Immediate Action: Describe the immediate action that will be taken on the spot to deal with the observed problem.

Interim Action: Describe the temporary action that will be taken to alleviate the problem until the permanent corrective action is implemented.

Remedial Action: Describe the remedial action taken to treat any reactions or discomfort produced by a subject's participation in experiment activities, and to ensure that similar problems are unlikely to result from related activities.

Root Cause: Describe the underlying reason for, or cause of, the observed problem that, when corrected, will eliminate or minimize the recurrence of the problem.

Permanent Action: Describe the permanent action taken to eliminate the root cause of the observed problem.

4.8 Reporting of Adverse Events and Anomalous Data

A. The activity will be immediately suspended if injury, unexpected illness, or significant anomalous data occurs, unless such suspension would endanger the subject. Procedures to follow if such an event occurs are shown as a flow chart in Appendix BB (starting with Serious Adverse Events* near bottom of page, just to right of center). Immediate notification of the crew surgeon (when applicable), medical monitor, Chairman CPHS, and Safety Office is required for injury, illness, or anomalous data involving test subjects. The crew surgeon, medical monitor, or designated medical officer will exercise clinical judgment in determining the significance of anomalous data. Within 24 hours of such an event, the PI or Co-I must also notify the Chairperson (or Alternate Chairperson) of the JSC CPHS, and submit to the Chairperson of the CPHS a detailed written report within 48 hours.

Within 24 hours of such an event, the PI or Co-I must also notify the Director of the SR&QA Office and submit a NASA Mishap Report (Appendix R). Reporting of these anomalous incidents applies to training sessions as well as to research and test activities. Adverse reactions that occur during flight or in ground-based facilities will be reported to the medical monitor. In addition, such reactions or anomalies will be reviewed during medical postflight or post-test debriefings. Any such discussion shall be regarded as privileged information and shall be protected in accordance with the provisions of the Privacy Act.

Such incidents will include (but not be limited to) the following:

- Adverse reactions to drugs, trauma, eye irritations, equipment failure (anomalous operation), animal bites or scratches, thrombophlebitis, burns, etc.
- Any illness or injury of a subject that may be related to the experiment.
- Any change in the environment, or in a subject's response, that could lead to some medical disturbance.
- Any substantive change from the approved research protocol.
- Any subject complaint related to or occurring after the protocol activity if there is reason to believe the complaint is related to the protocol activity.

B. Any one of the following individuals has the authority to terminate the test and initiate a review of the circumstances by the JSC CPHS before test activities are allowed to resume:

- Principal investigator
- Medical monitor, PCO, or crew surgeon
- Test subject
- NASA test director (if applicable)
- Mission manager or equivalent
- JSC CPHS Chairperson

If any one of the people listed above decides to terminate the test, the others must abide by the decision. When a protocol is suspended because an adverse event occurred, the JSC CPHS reviews the occurrence and may recommend a formal investigation if appropriate.

C. A database of adverse events is maintained by the PCO and communicated to the JSC CPHS, appropriate future investigators, medical personnel, and subsequent subjects for similar tests. This information is protected as private medical data (Appendix P).

D. For non-astronaut test subjects, the medical aspects of an adverse event or mishap are recorded in detail by the medical officer in the test subject's medical record maintained in the Human Test Subject Facility.

E. Some of the data collected from astronauts may lie outside the expected norms for the given experiment conditions of the research protocol. Information of this category must be reported to the CPHS.

4.9 Withdrawal of Flight Crew Subjects from Human Research

A. When astronauts spend a protracted period in training to be subjects and/or operators for a number of experiments (as for a dedicated life sciences Spacelab mission), the withdrawal of a crew member from participation in one or more experiments is a serious step that may

have a cascading effect on other experiments and on the success of the mission. Specific instances exist in which subjects cannot or may not withdraw from participation in human research without prejudice or penalty. These contingencies are detailed in NPD 7100.8D and NPG 7100.1 (Appendix D).

B. The Space and Life Sciences Directorate and the Astronaut Office will determine by formal agreement which experiments on a mission will be treated as core experiments; withdrawal from those may lead to replacement of a crew member on the mission. Core experiments will be indicated in the briefing before crew assignment is made.

4.10 Studies Involving Animals

A. Studies involving animals must adhere to the guidelines that are outlined in Appendices G, S, and T. Appendix G describes precautions to be taken to maintain NASA Flight Quality (NFQ) status and tests used to ascertain NFQ status before training or flight begins. Appendix S describes animal care procedures to be used during preflight crew training activities. Appendix T describes animal care procedures to be used during flight simulations and space flight.

B. Potential biohazards from all animals to be used in an experiment must also be assessed.

5.0 MISCELLANEOUS GUIDELINES AND STANDARDS

All approved flight protocols must be implemented in accordance with NASA regulations, including crew scheduling constraints.[2]

5.1 Recommended JSC CPHS Electrical Standards for In-flight Instrumentation

Because of the risk from electrical hazards, the JSC CPHS has set limits for leakage currents from surface electrodes of biomedical instruments, as well as for currents from invasive instruments powered by voltage sources or power amplifiers with frequencies in the range from direct current to 1 kHz. Electrical stimuli applied to research subjects will be evaluated for electrical safety on a case-by-case basis. Instrumentation of subjects with multiple bioelectric systems will be assessed in the context of possible system interactions (normal or failure modes) to ensure that the electrical standards are not exceeded by any interactions. Details of these electrical standards are given in Appendix U.

5.2 Crew Venipuncture and Blood Volume Constraints

The following guidelines have been established to help investigators, management personnel, and the JSC CPHS evaluate venipuncture and blood volume requests for a given space-flight mission or ground-based study. The intent is to establish blood volume collection and venipuncture schedules that are acceptable to Medical Operations and to crew member or test subjects, while maintaining the integrity of the investigation or mission. Investigations or missions that deviate from these guidelines will identify the specific deviation and provide appropriate supporting rationale in the required research protocol documents.

The allowable experiment blood volume may be reduced if, in the judgment of the crew surgeon, the subject has a medical condition that warrants this. Crew members weighing less than 110 pounds are eligible for blood draws, but the CPHS, in consultation with the medical monitor or crew surgeon, will approve on a case-by-case basis.

[2] JSC 22359, "Crew Scheduling Constraints. Appendix K of the Space Shuttle Crew Procedures Management Plan, Revision B, January 1992."

Medical Operations currently requires blood analyses as part of the standard health care for crew members. With crewmember consent, data from Medical Operations analyses can be made available to investigators. Procedures for sharing information should be outlined in a data-sharing plan. For a complete list of the tests that are run, see the "Astronaut Medical Evaluation Requirements Document" (AMERD), JSC 24834.

5.2.1 Specific Guidelines

A. Blood sample collection should minimize the number of needle sticks and catheter insertions, grouping data collections as much as possible for all studies. The number of proposed sticks (venipunctures and finger sticks) must be part of the CPHS review package for the individual proposal as well as for the final plan in which all the studies for a mission or ground-based study are combined. The CPHS has the right to reduce the number of sticks.

B. The CPHS has established different standards for the total amount of blood (including the blood volumes required for medical care) that may be drawn under 3 types of conditions: 1) a space flight shorter than 30 days, 2) a space flight longer than 30 days, and 3) a study (ground-based) not involving space flight. All volumes listed are per crew member.

1) Space Flights Shorter than 30 Days

   The total volume of pre-, in- and postflight blood draws will not exceed 450 ml per mission. The preflight phase begins 6 weeks before launch, and the postflight phase ends 6 weeks after landing. In-flight blood draws cannot exceed 50 ml per week. The volume of blood drawn outside this timeline may not exceed 450 ml per 56 days (Appendix X, "21 CFR Part 640: Additional Standards for Human Blood and Blood Products."

2) Space Flight Longer than 30 Days

   - Up to 6 months before launch (L–6 months): blood volumes must meet Federal guidelines (maximum of 450 ml per 56 days).
   - L–6 months to L–20 days: 250 ml per month, not to exceed a maximum volume of 500 ml.
   - L–20 days to launch: maximum of 100 ml during those 20 days.
   - During space flight: 100 ml per 30 days, not to exceed a maximum total in-flight volume of 300 ml.
   - No blood may be drawn within 24 hours of the planned first opportunity for descent.
   - Landing day: maximum of 120 ml.
   - Postflight phase, day after landing (R+1) to R+45: maximum is 300 ml.
   - After R+45 days: must meet Federal guidelines (maximum of 450 ml per 56 days) beginning on day R+46.

3) Ground-based Studies

   These include closed-chamber and bed-rest studies as well as any other studies that require blood. Blood volume must meet the Federal guidelines of no more than 450 ml per 56 days.

Note: The rationale for the above guidelines is derived from the general recommendations for blood donations. Donations are allowed only from individuals who

weigh more than 110 pounds (50 kg) and who have a hematocrit greater than 35%. Every 8 weeks, a donation center can accept one (1) unit (400-450 ml) from a given person. This schedule assumes a blood replacement rate of 10 ml per day. Autologous blood donors may give up to 2 units per week for 2 to 3 weeks before elective surgery. This is based on a more realistic blood replacement rate of 50 to 200 ml per day, assuming adequate iron stores.

5.2.2 Responsibilities

A. The final schedule approved by the JSC CPHS will be strictly followed. The mission manager (or equivalent) or project scientist must report any significant discrepancy in blood draw amounts to the crew surgeon and the JSC CPHS.

B. Non-astronaut studies: Total blood sample volumes are recorded in a data base in the Human Test Subject Facility to ensure that participants in multiple studies do not exceed JSC CPHS recommendations for total volume of blood drawn.

5.3 Practice Guidelines for Anesthetic Procedures Immediately After Landing

Purpose: This section outlines briefly the anesthetic concerns unique to procedures performed within three (3) days of recovery (landing). It is formatted for rapid transmission to and review by anesthesia personnel who are suddenly confronted with a patient newly returned from space. It is not intended as a "cookbook" for such procedures, nor is it meant to pre-empt the clinical judgment of the attending anesthesiologist. The reader is cautioned that, although these guidelines represent the best expert opinion currently available, the strength of evidence behind many of the recommendations is weak.

5.3.1 Anesthetic Concerns Unique to Post-flight Patients

A. Gastrointestinal dysfunction: Nearly all crew members have some degree of motion sickness after landing. Gastric motility is known to decline very early in the course of motion sickness, even before any symptoms develop. Therefore, all crew members are at risk for gastric stasis. Furthermore, because no restrictions are placed on fluid and solid intake during recovery, and, indeed, fluid intake is usually encouraged before de-orbit operations, most crew members will be in violation of usual "nil per os" guidelines. Consequently, it seems reasonable to assume that the patient has a "full stomach."

B. Neurovestibular dysfunction: After space flight, profound neurovestibular dysfunction is common, producing disturbances of station and gait as well as bouts of intense neurosensory illusions such as vection and vertigo. These phenomena can be triggered and exacerbated by passive movements, so that some patients have intense symptoms after even minor postural repositioning. This neurovestibular dysfunction may contribute to other physiologic dysfunction, such as gastric stasis and cardiovascular instability. Highly symptomatic patients must be transported with the gentleness appropriate for a victim of deep hypothermia.

C. Cardiovascular dysfunction: Orthostatic instability is very common after space flight. The cause seems to be multi-factorial and includes intravascular hypovolemia, poor baroreceptor and/or sympathetic responsiveness to orthostatic stimuli, and cardiovascular deconditioning. The maximum heart rate produced by orthostatic stress is reduced. Consequently, a post-flight surgical patient may have less cardiovascular reserve than one might assume for an individual from a relatively young, fit population. Unusual autonomic phenomena may occur, and intravascular hypovolemia may be poorly tolerated.

The responsiveness of the systemic vasculature to direct-acting sympathomimetic drugs seems largely intact, so these agents are preferable to indirect-acting drugs. Ventricular and supraventricular dysrhythmias may be more common after landing. Unrecognized, pre-existing coronary artery disease has been discovered in the past after landing and, no doubt, will be encountered in the future.

D. Neuromuscular junction dysfunction: Prolonged space flight seems to carry a small but credible risk of producing changes in the neuromuscular junction similar to those from extended bedrest (such as the "ICU syndrome") and resulting from disuse. Consequently, succinylcholine, a depolarizing blocker, is not the neuromuscular blocker of first choice immediately after space flight.

E. Altered pharmacokinetics/pharmacodynamics: Experience to date with both humans and non-human primates suggests that the clinical effects of many drugs are altered after landing. In particular, unexpectedly profound and prolonged depression of consciousness may be produced by agents that inhibit the central nervous system. Such agents should be used with caution, preferably through careful titration of short-acting drugs.

5.3.2 Conduct of Anesthesia

A. The decision to proceed: If possible, surgery should be delayed for 3 days after space flight. The decision to proceed without delay should be entertained only in the face of disease or injury that threatens prolonged or permanent disability or organ dysfunction, or death.

B. Choice of anesthetic technique: If possible, local or regional blockade with minimal or no sedation should be used. However, because complications may ensue from these blocks or a switch to a general anesthetic may be necessary, the fact that a wholly elective surgical procedure might be able to be completed with a regional block does not justify performing such procedures immediately after landing (see "The decision to proceed" above). Very little evidence currently exists to compel a choice between neuraxial blockade (such as spinal and epidural anesthetics) and general anesthesia. General endotracheal anesthesia, using carefully titrated, short-acting agents and close hemodynamic monitoring, may offer the best opportunity to detect and correct unexpected physiologic dysfunction. The rest of this discussion primarily concerns this approach.

C. Pre-induction: Administration of a fluid bolus (such as 2 liters of a crystalloid solution) should be considered. Aspiration prophylaxis, including a non-particulate antacid (such as Bicitra), metoclopramide, and an H_2 antagonist (such as ranitidine), should be administered unless contraindicated. An arterial line should be placed in a peripheral artery under local anesthesia. Central venous access should be considered, particularly if cannulation of peripheral veins is difficult. Monitors should be used that, at a minimum, meet the Standards for Basic Anesthetic Monitoring of the American Society of Anesthesiologists. Specifically, the following should be monitored: arterial oxygen saturation, inspired oxygen concentration, intra-arterial blood pressure, expired carbon dioxide content, body temperature, electrocardiogram, and neuromuscular function (via a nerve stimulator capable of delivering "train-of-four" and sustained tetanus stimuli). If possible, an automated record-keeping system should be used to conserve the very valuable data that will be generated by this procedure. The collaboration of a second anesthesiologist may be very helpful. A transcutaneous pacer should be immediately available.

D. Induction: If difficulty (such as cervical or facial trauma) with direct laryngoscopy is expected and the patient is somewhat cooperative, then an awake fiberoptic endotracheal

intubation should be considered. Otherwise, a rapid sequence induction with cricoid pressure is indicated. Etomidate and rocuronium are preferred induction drugs.

E. Intra-operative period: The urinary bladder should be catheterized, and urine output should be quantified. Abnormalities of blood pressure should be treated with short-acting, direct agents (after exclusion of more immediate problems, such as hypoemia, hypercapnia, pain, hypovolemia, etc.) as follows: hypotension with phenylephrine; hypertension with sodium nitroprusside. Recognize that a moderate tachycardia (such as 130 beats per minute) may represent the cardiovascular system's maximal response after space flight. Conversely, a heart rate of less than 70 is abnormal after flight—such a heart rate may not alone mandate treatment, but an explanation should be sought. If narcotics are used intra-operatively, small doses of short-acting agents are preferred. Prophylaxis against deep venous thrombosis should be implemented.

F. Emergence: Neuromuscular blockade should be reversed with conventional agents (such as neostigmine and glycopyrolate). Extubation should be considered only on the basis of objective criteria. The decision to extubate should be made by the attending anesthesiologist. Full reversal of neuromuscular blockage should be established on the basis of full "train-of-four," sustained tetanus, sustained head lift, and tongue protrusion. Intact pulmonary function should be established on the basis of measured tidal volume, respiratory rate, end-tidal or arterial carbon dioxide, and maximum inspiratory force. The patient should be fully awake and following commands.

G. Transport to a recovery area: Supplemental oxygen should be delivered. If the patient is still intubated, use of a transport ventilator is preferable to "hand-bagging." A transport monitor that includes electrocardiogram, invasive or non-invasive blood pressure monitor, and oxygen saturation should be used. The patient should be accompanied by the attending anesthesiologist. All postural changes, transitions between beds, and gurney movements should be accomplished slowly.

H. Post-anesthetic care: Post-operative nausea and vomiting may result from conventional causes (such as narcotics and other drugs) as well as post-flight motion sickness. The importance of this distinction lies in the fact that newer anti-emetics, such as the 5-HT_3 antagonists, are not effective against the latter. Therefore, one should not rely solely on these drugs to treat nausea and vomiting in this setting. Pain should be treated with conventional agents but with incremental, small doses. Discharge should be based on an objective scoring system such as the Aldrete score. The patient should spend at least three (3) hours in post-anesthetic care under the direct supervision of an anesthesiologist.

I. Subsequent care: The patient should spend at least 24 hours in the functional equivalent of an intensive care unit (ICU). Transport during this period by vehicles equipped and staffed to provide ICU-level care is not contraindicated.

5.4 Safety Reporting Requirements for Investigations Performed at Off-site Locations

For human research investigations not conducted at JSC but involving JSC personnel as investigators or subjects, the following elements shall be included in the appropriate research protocol:

- A detailed system description documenting all of the systems and hardware of the research and/or training, and their functions and relationship to the research.

- Facility information identifying all of the requirements and services that must be met or provided by the facility.

- A hazard analysis, with particular emphasis on stored energy, procedures, and interfaces between the test subject and hardware, and the means by which the hazards are eliminated or controlled. The level of effort of the hazard analysis will be consistent with the hazard potential to the test subject.

- Existing flight hazard analyses may be used for ground-based investigations, provided that no differences exist between flight and ground hardware with regard to function, use, or hazards associated with the hardware.

- A letter of "safety certification" from the resident safety office or the JSC CPHS stating that all hardware items have been reviewed and, in the opinion of the off-site safety organization, are considered safe for their intended use.

Appendix A

Current Ethics Policies and Research Oversight Practices for Federally Sponsored Research[3]

Introduction

In 1991, sixteen federal departments adopted a single, general set of regulatory provisions governing human subjects protections. This common federal policy, known as the "Common Rule", 45 CFR Part 46, Subpart A, specifies how research that involves human subjects is to be reviewed, the protections that such research must afford human subjects in order to be approved for funding by each signatory federal agency, and what must be included in the process of obtaining subjects' informed consent.

The Federal Policy for Human Subjects Protection (Common Rule)

The basic organizational structure for ensuring that the rights and well-being of human subjects are protected are institutional review boards (IRBs), panels often composed of physicians, scientists, administrators, and community representatives, usually at the local research institution, that review and approve any research proposal before it is submitted to a federal agency for funding. The Common Rule requires that research institutions, as a condition for receiving federal research support, form IRBs and delegate to them the authority to review, stipulate changes in, approve or disapprove, and oversee human subjects protections for all research conducted at the institution. The IRB has the authority to suspend the conduct of any research found to entail unexpected or undue risk to subjects, or that is not in conformity with the Common Rule or the Institution's additional protections.

A prominent feature of the Common Rule is the requirement for the informed consent of the subject. The informed consent of a competent subject, is a cornerstone of modern research ethics. Ideally, informed consent should be viewed as an ongoing process of communication between researcher and the subjects of their research. The required elements of informed consent as enumerated in the Common Rule are summarized as follows:

- a statement that the study involves research, an explanation of the purposes of the research, and a description of the procedures to be followed;
- a description of any reasonably foreseeable risks or discomforts to the subject;
- a description of any benefits to the subjects or to others that might reasonably be expected;
- a disclosure of alternative procedures or courses of treatment;
- a statement describing the extent to which confidentiality of records identifying the subject will be maintained;

[3] Excerpts taken from: Final Report - Advisory Committee on Human Radiation Experiments, October 1995, Chapter 14, Part III, pp.675-693 (Pittsburgh: US Government Printing Office).

- for research involving more than minimal risk, an explanation of the availability and nature of any compensation or medical treatment if injury occurs;

- identification of whom to contact for further information about the research and about subjects' rights, and whom to contact in the event of a research-related injury;

- a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time.

Research Involving Ionizing Radiation

Beyond the strictures of the Common Rule, research involving either external radiation or radioactive drugs usually undergoes additional review for safety and risk (including a review of radiation dose) prior to IRB review at the local research institution. Most medical institutions have a radiation safety committee (RSC) responsible for evaluating the risks of medical activities, whether for diagnostic, treatment, or research purposes, and limiting the exposure of both employees and subjects to radiation. In addition, research and medical institutions that perform basic research involving human subjects and radioactive drugs must have such studies reviewed and approved by a radioactive drug research committee (RDRC) -- a local institutional committee approved by the Food and Drug Administration (FDA) to ensure that safeguards, including limitations on radiation dose, in the use of such drugs are met. Notwithstanding the prior review and approval of either or both of these radiation committees, the IRB must also assess the risks and potential benefits of the proposed research before approving it.

Administrative Structures and Procedures for Research Oversight

Some (federal) departments audit or review IRB performance routinely while others conduct investigations only when problems emerge. The method, intensity and frequency of research oversight and inspection activities are a direct function of the level of staffing and budgetary resources.

The IRB is an administrative unit that must itself comply with certain requirements of the Common Rule in terms of its composition, review procedures, and substantive review criteria; it must also direct researchers to comply with other requirements of the rule, such as adequate informed consent and fair subject selection procedures.

Effectiveness of IRBs

The success or failure of the federal regulations governing human subjects research depends on the effectiveness of IRBs in carrying out their responsibilities: assessing research proposals prior to their funding, stipulating any changes in the research protocol or informed consent procedure that strengthen the protections afforded the subjects, disapproving inadequate or excessively risky research proposals, reviewing ongoing research at least every twelve months to ascertain that the research poses no undue risks to subjects, and taking action quickly to correct any failing in safeguarding subjects' rights and welfare.

Federal agencies overseeing human subjects research conducted in-house or supported extramurally establish a structure whereby research proposals involving human subjects are peer reviewed for scientific merit as well as for IRB approval and the adequacy of subject protections, negotiate assurances with research institutions that ensure that adequate protections will be in place for research subjects, verify that institutions, their IRBs, and researchers is complying with the federal human subjects regulations, and investigate complaints of noncompliance and adverse outcome for subjects of research.

Principal investigators are required to report any adverse outcomes to the IRB and the IRB must have procedures to ensure that the appropriate institutional officials and the funding agency are informed as well. The method, intensity and frequency of research oversight and inspection activities are a direct function of the level of an agency's staffing and budgetary resources.

Sanctions for Violation of Human Subjects Protections

Withdrawal of assurance and, with that action, of research funding; suspension or termination of IRB approval of research; and disciplinary action against agency employees engaged in human subjects research are the sanctions available under the Common Rule. The Common Rule authorizes IRBs to suspend or terminate their approval or research that is not conducted according to the IRBs requirements or when a research subject suffers an adverse event in the course of participation that requires investigation.

Federal agencies may also take disciplinary action against employees involved in human subjects research for failure to follow human subjects protection rules. Sanctions for noncompliance by intramural researchers include loss of investigator privileges. Sanctions may also include reprimands, suspension, or termination of employment.

THE NUREMBERG CODE

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personalduty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods, or means of study, and not random and unnecessary in nature.

3. The experiment should be designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the to an end if the physical or mental state where continuation of the experiment seems to be impossible has been reached.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if there is probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

1947	The Nuremberg Code
1953	NIH Clinical Center Policy *In addition to a statement of principles similar to the Nuremberg Code, this policy required prior review of research involving healthy volunteers and patients that would be exposed to hazardous research procedures by an independent, local group of researchers*
1962	Kefauver-Harris amendments to the Food, Drug and Cosmetic Act *Required the informed consent of subjects participating in drug research*
1964	Declaration of Helsinki
1965	National Advisory Health Council resolution requires prior review and protection for informed consent
1966	PHS-wide policy for the protection of human subjects in extramural clinical research, Policy and Procedure Order No. 129 (PPO #129) *Required that an awardee institution, through a committee of institutional associates, review proposed research in terms of protections afforded the rights and welfare of subject, informed consent, and its risks and potential medical benefits*
1967	PPO#129 expanded to include intramural research and Contracts
1971	PHS policy extended to all human subjects research conducted or supported by HEW, published as the "Institutional Guide to DHEW Policy on Protection of Human Subjects" *Required documentation of the informed consent process and the signature of the research subject or the subject's representative*
1974	Title II of the National Research Act (P.L. 93-348) *Required codification of DHEW policy in regulation, imposed a moratorium on federally funded fetal research, and established requirements for IRB review of all human subjects research at any institution receiving DHEW funding* DHEW regulations for the protection of human research subject. 45 C.F.R. 46 *Established IRB review procedures in accordance with Title II. Later in the same year DHEW published regulations providing additional protection for pregnant women and fetuses*
1974-1978	National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research *Issued reports and recommendations on fetal research; on research involving prisoners, psychosurgery, children, and the mentally infirm; on IRBs and informed consent; and, in The Belmont Report, discussed criteria for distinguishing research form the practice of medicine and ethical principles underlying the protection of subjects*
1978	Revised DHEW regulations governing protections for pregnant women, fetuses, and in vitro fertilization (subpart B of 45 C.F.R. 46), and prisoners (subpart C) published
1980-1983	President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research *Charged with, among responsibilities, reviewing federal policies governing human subjects research and determining how well those policies were being carried out. Recommended that all federal agencies adopt the DHHS regulations for the protection of human subjects (1981)*

1981	DHHS published a revision of 45 C.F.R. 46, responding to recommendations of the National Commission *The revision set out in greater specificity IRB responsibilities and the procedures IRBs were to follow* FDA regulations at 21 C.F.R. 50, governing informed consent procedures, and at 21 C.F.R. 56, governing IRBs, revised to correspond to DHHS regulations to the extent allowed by FDA's statute
1982	President's Science Advisor, Office of Science and Technology Policy (OSTP), appointed an interagency committee to develop a common federal policy for the protection of human research subjects
1983	DHHS regulation governing protections afforded children in research (subpart D of 45 C.F.R. 46) published
1986	Proposed common federal policy for the protection of human research subjects published
1991	Final common federal policy published on June 18, codified in the regulations of fifteen federal agencies and adopted by the CIA under executive order *This common policy, known as "the Common Rule", is identical to the basic DHHS policy for the protection of research subjects, 45 C.F.R. 46, subpart A. Other sections of the DHHS regulation provide additional protections for pregnant women, fetuses, in vitro fertilization (subpart B), prisoners (subpart C), and children (subpart D). Several agencies have adopted these additional provisions as administrative guidelines. The FDA made conforming changes in its informed consent and IRB regulations*

APPENDIX B

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Office of the Secretary
Protection of Human Subjects

Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Commission for the Protection of Human Subjects Biomedical and Behavioral Research, April 18, 1979[4]

AGENCY: Department of Health, Education, and Welfare.

ACTION: Notice of Report for Public Comment.

SUMMARY:

On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, there-by creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk/benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402. Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

[4] Reprinted from U.S. Government Printing Office: 1988-201-778/80319; GPO 887-809

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

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Belmont Report

Ethical Principles and Guidelines for Research Involving Human Subjects

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the Nuremberg code was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on
concentration camp prisoners. This code became the prototype of many later codes[5] intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, which guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called “experimental” when the terms “experimental” and “research” are not carefully defined.

For the most part, the term “practice” refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable

[5] Since 1945, various codes for the proper and responsible conduct of human experimentation in medical research have been adopted by different organizations. The best known of these codes are the Nuremberg Code of 1947, the Helsinki Declaration of 1964 (revised in 1975), and the 1971 Guidelines (codified into Federal Regulations in 1974) issued by the U.S. Department of Health, Education, and Welfare Codes for the conduct of social and behavioral research have also been adopted, the best known being that of the American Psychological Association, published in 1973.

expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment, or therapy to particular individuals.[6] By contrast, the term "research" designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental," in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.[7]

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence, and justice.

1. *Respect for Persons.* - Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

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[6] Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; it is practice and need not be reviewed as research.

[7] Because the problem related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities that may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences. The
extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

2. *Beneficence*. - Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these

imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research-involving children - even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not so unambiguous. A difficult ethical problem remains, for example, about research that
presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

3. *Justice*. - Who ought to receive the benefits of research and bear its burden? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell largely upon poor ward patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged,

rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to consideration of the following requirements: informed consent, risk/benefit assessment, and the selection of subjects of research.

1. *Informed Consent*. - Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.

While the importance of informed consent is unquestioned, controversy prevails over the nature and possibility of an informed consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative procedures (where therapy is involved), and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of “the reasonable volunteer” should be proposed; the extent and nature of information

should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy or invalidate the research from cases in which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice.

Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension.

Special provision may need to be made when comprehension is severely limited for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm. Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm.

The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of informed consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable.

Unjustifiable pressures usually occur when persons in positions of authority or commanding influence - especially where possible sanctions are involved - urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. *Assessment of Risks and Benefits*. - The assessment of risks and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to the subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that informed consent be obtained is derived primarily from the principle of respect for persons.

The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted to probability of benefits, and benefits are properly contrasted with harms rather than risks of harm. Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harms and anticipated benefits. Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.

Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and Federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to

society in the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research.

The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.

Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject - or, in some rare cases, to the manifest voluntariness of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgements, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the informed consent process.

3. *Selection of Subjects.* - Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects.

Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought,

and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. Thus injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects.

Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments. When research is proposed that involves risks and does not include a therapeutic component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits.

One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition. [FR Doc. 79-12065 Filed 4-17-79; 8:45 am]

APPENDIX C

Excerpted from the JPG 1107.1A, The JSC Organization, Section 4, Committee, Boards, and Panels, Part 4.8, JSC Committee for Protection of Human Subjects (CPHS)

JPG 1107.1A

4.8 JSC Committee for the Protection of Human Subjects

4.8.1 Purpose

To establish the JSC Committee for the Protection of Human Subjects (CPHS) and to delegate authority to approve the conduct of human research and recommend expedited review(s) of human research protocols to the Director, Space and Life Sciences.

4.8.2 Applicability

4.8.2.a. JSC: The policy set forth applies to JSC and will be followed by all members of investigative teams in all research experiments involving human test subjects which are funded or sponsored by JSC; conducted in spacecraft, JSC facilities or aircraft; or which involve JSC to any degree.

4.8.2.b. Cooperative Arrangement or Agreement: All human research conducted under a cooperative or reimbursable arrangement or agreement entered into by JSC and another Government agency, private entity, non-Federal public entity, or foreign entity must also comply with the terms and conditions of this document and NASA Policy Directive (NPD) 7100.8D and NASA Procedures and Guidelines (NPG) 7100.1.

4.8.3 Establishment The JSC CPHS is established by the Center Director in accordance with NPD 7100.8D and NPG 7100.1 "Protection of Human Research Subjects." The JSC CPHS will review all ground-based and aeronautical flight research involving human subjects that is conducted at JSC, or extramural research in which JSC personnel and/or facilities are involved. Additionally, all research involving human subjects, including flight crews, performed in NASA spacecraft will be reviewed by the JSC CPHS.

4.8.4 Membership

4.8.4.a. The minimum membership of the JSC CPHS is:

Chairperson	Chief Scientist for Bioastronautics
Member	Alternate Chairperson (Executive Secretary)
Member	A life scientist appointed by the Chairperson
Member	A flight surgeon
Member	A representative from the Legal Office
Member	A representative from the Safety, Reliability, and Quality Assurance Office
Member	An astronaut
Member	A non-life-sciences employee
Member	A non-NASA, full-time Federal employee

4.8.4.b. Members of the JSC CPHS are appointed by the Center Director. Members are expected to attend regularly and actively participate in all discussions. Approximately one third of the membership will be physicians. Up to three ad hoc members in specialized disciplines may be added to the JSC CPHS on a temporary, non-voting basis as deemed appropriate by the Chairperson. The member position filled by a non-life-sciences employee will be rotated among the Center directorates and offices.

4.8.4.c. The permanent Chairperson will periodically designate an alternate Chairperson to afford experience in conducting the meetings while the former will retain overall control of the standing JSC CPHS.

4.8.4.d. All members of the JSC CPHS are voting members. The Chairperson will vote only in the event of a tie. A majority of the JSC CPHS members present is required to evaluate and approve a protocol and must include the Chairperson (or alternate Chairperson) and representatives of the Astronaut Office (a representative from the Astronaut Office is required for evaluation of flight studies), SR&QA Office, and Medical Operations. Every member is required to vote on each issue except in conflict-of-interest cases or when lack of technical familiarity with aspects of a protocol would impede the decision process. If there is no consensus of the Board, the vote of each member will be recorded and the reason for a negative vote or abstention will be stated.

4.8.5 Authority

4.8.5.a. The JSC CPHS has the authority to approve, disapprove, or require changes in the proposed human research protocols and procedures covered by NPD 7100.8D and NPG 7100.1.

4.8.5.b. The JSC CPHS may conditionally approve a protocol or recommend changes to disapproved protocols that may result in their approval. The JSC CPHS has the authority to suspend or terminate its approval of research activities that are not being conducted in accordance with approved protocol or the policies set forth in NPD 7100.8D and NPG 7100.1 or that have been associated with unexpected serious harm to subjects.

4.8.6 Responsibility The fundamental responsibility of the JSC CPHS is to assure the health, safety and well-being of human research subjects while ensuring ethical conduct of experimental operations.

4.8.7 Functions

4.8.7.a. The JSC CPHS will provide advice and counsel to the authorized JSC official on matters within the scope of this document and as required by referenced management instructions, including, but not limited to:

- Review of all NASA ground-based or aeronautical flight and all space-flight proposed human research protocols submitted to the authorized JSC official prior to funding, approval, or execution;

- Review of all flight payloads experiments or procedures involving humans as test subjects, ensuring that protocols and safety procedures conform to NASA policy;

- Issue guidelines to be followed in the conduct of all human research measurements and experimental procedures, flight and ground-based;

- Maintain documentation of JSC CPHS activities as prescribed in NPD 7100.8D and NPG 7100.1.

4.8.8 Reporting The Chairperson and members of the JSC CPHS report to the Center Director for all matters involving the Board.

4.8.9 Meetings Meetings will be convened by the Chairperson of the JSC CPHS on a monthly basis or more frequently when a request is made by the authorized JSC official, program director, JSC's Center Director, or a test subject to evaluate a human research experiment which may affect the health or well-being of any human subject.

4.8.10 Records and Staff Supporting Services

4.8.10.a. A secretary-recorder will ensure accurate recording and publication of JSC CPHS activities, including agendas, proceedings, and action items. Minutes and actions shall be published and distributed to JSC CPHS members, meeting attendees, and action assignees.

4.8.10.b. The Chairperson will appoint a Protocol Compliance Officer (PCO) to verify that all experiments are conducted in accordance with JSC CPHS requirements. The PCO will report any protocol violation immediately to the Chairperson.

4.8.10.c. All JSC human research protocols must have passed scientific merit peer review, prior to submission to the JSC CPHS. All protocols will have been submitted to and approved by one or more of the following review committees or JSC elements as appropriate:

- JSC Radiation Safety Committee
- Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee
- Payload Safety Review Panel (reviews equipment for in-flight experiments)
- Safety, Reliability, and Quality Assurance (reviews equipment for ground-based experiments)

4.8.10.d. The Legal Office representative to the CPHS will provide assistance with the Informed Consent Statements.

4.8.11 Subcommittees The Chairperson, or one or more experienced reviewers designated by the Chairperson from among the members of the JSC CPHS , may approve human research protocols by the expedited review procedure, using the same criteria for approval as is used for non-expedited review but without the necessity for consideration by the entire JSC CPHS . Only low hazard or "minimal risk" protocols or previously approved protocols with minor changes are eligible for expedited review. Such reviews shall be communicated to the JSC CPHS by the Chairperson at the next meeting of the full JSC CPHS.

4.8.12 Conflict of Interest No JSC CPHS member may participate in the review of any research protocol in which that member has a conflicting interest, except to provide information requested by the Board. Any JSC CPHS member who is a Principal Investigator, Co-Investigator, immediate supervisor or relative of the investigator(s) of a research protocol before the Board, or has any known or perceived conflict of interest, may not participate in the discussion or vote on that protocol.

4.8.13 Duration The JSC CPHS will remain in effect until dissolved by the Center Director.

4.8.14 References

- NPD 7100.8D, “Protection of Human Research Subjects.”
- NPG 7100.1, “Protection of Human Research Subjects.”
- NMI 8900.1, “Medical Operations Responsibilities for Manned Space Flight Programs.”
- JSC-20483C, “JSC Institutional Review Board - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations.”

APPENDIX D

NASA	Directive: NPD 7100.8D
POLICY	Effective Date: May 31, 2002
DIRECTIVE	Expiration Date: May 31, 2007

Responsible Office: AM/Chief Health and Medical Officer

Subject: PROTECTION OF HUMAN RESEARCH SUBJECTS

1. POLICY

a. This NPD sets forth NASA's policies for the protection of human research subjects, which is of primary importance in the conduct of any human research. All human research conducted, or supported by NASA, whether on the ground, in aircraft, or in space, will follow the provisions of NASA regulations contained in 14 CFR Part 1230 and Department of Health and Human Services (HHS) regulations contained in 45 CFR Part 46.

b. The authorized NASA official for the protection of human subjects is the Chief Health and Medical Officer (CHMO), NASA Headquarters. All human research, funded, sponsored, conducted, or supported by NASA, will be reviewed by an Institutional Review Board (IRB), approved by NASA or the Office of Human Research Protection (OHRP) at HHS. IRB's will be established at NASA Centers to review all ground-based and aeronautical flight research, involving human subjects, that is conducted at the Centers or which utilizes NASA Centers, equipment, or personnel. All research performed on NASA spacecraft, involving crewmembers, will be reviewed by the IRB at the Johnson Space Center (JSC)

c. The IRB has authority to approve, disapprove, or require changes in the proposed human research protocols and procedures and to suspend or terminate its approval of research activities that are not conducted in accordance with the approved protocol or that have been associated with serious harm to subjects.

d. No Principal Investigator (PI) may involve a human being as a subject in research covered by this policy, unless the written informed consent of the subject or the subject's legally authorized representative has been obtained. Such consent shall be sought only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights or which releases or appears to release the PI, the sponsor, the institution, or its agents from liability for negligence.

The conditions under which an IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent or under which an IRB may waive the requirements to obtain informed consent, must include all of the following elements, which must be documented by the IRB:

(1) The research involves no more than minimal risk;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration;

(4) Whenever appropriate, the subjects shall be provided with additional pertinent information after participation; and

(5) Astronaut and other human experimental data derived from, or associated with such approved research, must be non-attributable to any individual.

e. All classified human research must have informed consent of the subjects.

f. All institutions proposing human research, funded by NASA, shall be required to give written assurance, as provided in 14 CFR 1230.103, to the authorized NASA official. A Multiple Project Assurance (MPA) on file with the HRP will satisfy this requirement. Assurances from institutions for projects utilizing NASA facilities, equipment, or personnel will not be accepted, NASA IRB review and approval shall be obtained. NASA Centers conducting human research or studies shall file MPA's with the authorized NASA official every 5 years and submit an annual report on the research and IRB activities. NASA Centers not conducting human research or studies will file a letter with supporting documentation certifying this fact to the authorized NASA official every year.

g. When research covered by this policy takes place in foreign institutions, procedures normally followed in the foreign countries to protect human subjects may differ from those set forth in this policy. Studies funded or sponsored by NASA must follow this NPD. In these circumstances, if NASA determines that the procedures prescribed by the foreign institution afford protections that are greater than those provided in this policy, the Agency may approve the use of the foreign procedures in addition to the procedural requirements provided in this policy, in accordance with 14 CFR Part 1230.101 (h) and 45 CFR 46.101 (h).

h. PI's are required to familiarize themselves with Agency and Center policies and procedures for the conduct of human research. Any NASA PI or a PI supported by NASA involved in human research, who does not comply with the policies and procedures of this NPD or with the protocol as approved, may have his or her research immediately suspended or terminated when such noncompliance becomes known to the appropriate IRB, NASA Center Director, Associate Administrator of the Office of Biological and Physical Research, or the CHMO. Evidence of noncompliance may be cause for the application of sanctions.

2. APPLICABILITY

a. This NPD applies to NASA Headquarters and all NASA Centers, including Component Facilities, and will be followed by all members of the research teams in all research experiments involving human subjects that are funded or sponsored by NASA or conducted in NASA facilities, aircraft, or spacecraft.

b. All human research conducted under a cooperative or reimbursable arrangement or agreement entered into by NASA and another Government agency, private entity, non-Federal public entity, or foreign entity must also comply with the terms and conditions of this NPD.

c. Research activities, involving the collection or study of existing data, documents, records, pathological or diagnostic specimens, are exempted from this NPD, if these sources are publicly available, or if its information is recorded in such a manner that subjects cannot be identified directly or through identifier links to the subjects.

3. AUTHORITY

a. 42 U.S.C. 2473 (c)(1), Section 203 (c)(1), The National Aeronautics and Space Act of 1958, as amended.

b. 14 CFR Part 1230 and 45 CFR Part 46, Protection of Human Subjects.

4. REFERENCE

World Medical Association Declaration of Helsinki adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and amended by the 29th World Assembly, Tokyo, Japan, October 1975; 35th World Medical Assembly, Venice, Italy, October 1983; and the 41st World Medical Assembly, Hong Kong, China, September 1989.

5. RESPONSIBILITY

a. The authorized NASA official for the protection of human subjects is the CHMO, NASA Headquarters.

b. The authorized NASA official is responsible for ensuring that the written institutional assurances related to NASA-supported human research, NASA Center MPA's and any NASA Center letters certifying that human research or studies are not being conducted at the Center, are filed in a timely manner with NASA Headquarters. All or part of the authority may be re-delegated, without power of further re-delegation, to a senior NASA Headquarters employee, usually the Deputy CHMO, who reports to the authorized NASA official.

c. The authorized NASA official is responsible for ensuring that the Administrator, the appropriate Enterprise Associate Administrator, the Office of Safety and Mission Assurance, the NASA General Counsel, and the NASA Inspector General (when appropriate) are kept fully and currently informed, through official channels, of significant actions, problems, or other matters of substance related to the exercise of this authority.

D. The NASA Center Directors are responsible for implementing this NPD within their assigned areas of responsibility. The Center Directors are responsible for ensuring that the written institutional assurances related to Center-supported human research, Center MPA's, and any NASA Center letters certifying that human research or studies are not being conducted at the Center, are filed in a timely manner with the authorized NASA official. In addition, the Center Directors are responsible for establishing an IRB at their respective

Centers to review all ground-based, aeronautical, and aerospace flight research, involving human subjects, that is conducted at their Center.

e. All research involving human subjects, including flight crews, which is performed in NASA spacecraft will be reviewed by the IRB at the JSC. In addition, flight surgeons are responsible for monitoring the health of the crew during the conduct of research protocols and assessing the crewmembers' continued suitability as a subject.

f. The primary responsibility of the IRB is to protect the rights of and ensure the safety of every person who is a subject of any research in NASA facilities, including NASA aircraft or spacecraft, or is a subject of NASA-funded or NASA sponsored research. Specifically, the IRB's are responsible for the following:

(1) Approving, disapproving, or requiring changes in the proposed human research protocols and procedures;

(2) Ensuring that the human subjects have given informed consent and reviewing such informed consent, or documenting the reasons and safeguards in all cases where the informed consent procedure, or any element of such procedure, has been altered or waived; and;

(3) Suspending or terminating approval of research activities that are not being conducted in accordance with the approved protocol or that have been associated with serious harm to subjects.

g. All PI's are responsible for complying with Agency and Center policies and procedures for the conduct of human research.

6. DELEGATION OF AUTHORITY

None.

7. MEASUREMENTS

Measurements of Agency compliance with this policy for the protection of human subjects in NASA research are contained in the attachment.

8. CANCELLATION

NPD 7100.8C, Protection of Human Research Subjects, dated February 1, 1999.

Sean O'Keefe
Administrator

ATTACHMENT A: (TEXT)

Metrics or measurements of Agency compliance with this policy for the protection of human subjects in NASA research are the following:

(1) Percentage of NASA Centers with active MPA and certifying letters on file with the authorized NASA official;

(2) Percentage of NASA Centers filing timely MPA's or certifying letters;

(3) Number of research proposals reviewed by IRB's;

(4) Number of research proposals approved by IRB's;

(5) Number of complaints to IRB's;

(6) Timeliness of response to complaints, including Headquarters notifications;

(7) Number and type of sanctions imposed; and

(8) Number of audits conducted and corrective measures adopted.

Appendix: Astronaut Health Care and Biomedical Research

Supplemental Guidance to NPD 8900.3E and NPD 7100.8(D)

PURPOSE:

This Appendix sets forth guidelines for bridging the policies on NPD 8900.3E, Astronaut Medical and Dental Observation, Study and Care Program, and NPD 7100.8D, Protection of Human Research Subjects, when both apply simultaneously during the performance of an astronauts' duties.

These guidelines address the multiplicity of issues surrounding the medical support of astronauts and of the NASA-supported space crews as well as their participation in biomedical research as research subjects. They provide guidance and direction in the ethical practice of medical care and conduct of human research in support of space missions.

POLICY:

a. Medical support of astronauts and of the NASA-supported space crews prior to space flight, while in space, and after space flight is guided by practices established or approved countermeasures. Medical management is the responsibility of the attending flight surgeon. Basic medical monitoring, countermeasures, and clinical treatment protocols, and their frequency will be independently evaluated periodically by an expert team reporting to the Medical Policy Board and CHMO. This evaluation will assess the actual risk, benefit, and value of treatments.

This medical support plan and requirements should be based on--

(i) evidence-based knowledge of physiological responses to space-flight;

(ii) knowledge of the specific mission scenario and crewmember's activities timeline;

(iii) knowledge of the specific, all-inclusive research protocol in which the crewmember participates as a research subject and the research protocol timelines;

(iv) monitoring of select environmental parameters and their changes, for possible interactions with the research protocols, countermeasures or medical monitoring or treatment.

Flight surgeons are responsible for--

(i) monitoring the health of the crew during the conduct of research protocols and assessing the crewmember's continued suitability as a subject;

(ii) remaining cognizant of the particular experimental research outcomes when they are reported, after the flight is completed;

(iii) developing and continuously updating requirements for operational clinical research.

b. Biomedical Research:

Biomedical Research is designed to--

(i) develop the understanding of the mechanisms underlying the changes during and after space-flight;

(ii) design, evaluate, and validate appropriate countermeasures and rehabilitation procedures based on the knowledge from (i);

(iii) provide the pathophysiological evidence required for safe and effective medical care in space and after flight.

All monitoring or testing other than that essential to medical care and health maintenance of astronauts and the NASA-supported space crews should be considered biomedical research in that it is presumed that a hypothesis has been formulated, that similar procedures or data are required from more than one subject, and the proposal was designed in a scientifically valid manner.

All research will be independently peer reviewed. All flight experimental research conducted concurrently on the same crewmember will be integrated into a single protocol and will be reviewed by the IRB at the JSC for risk, taking into account interactions with mission activities, environmental data, and medical care activities.

c. Coordination of Medical Care and Biomedical Research:

This Appendix is designed to ensure full integration of methods to foster a commitment among the astronaut corps, the NASA-supported space crews, the flight surgeons, and the research community to define and optimize biomedical operational and research objectives for each flight mission or Space Station operation. The Space and Life Sciences Directorate at JSC will be responsible for ensuring this integration.

(i) Research protocols and health care monitoring requirements will be coordinated, when possible, into a single activity and timeline to avoid duplication and unnecessary interference with the crewmember.

(ii) Mission timelines and research protocols will be planned in coordination with the medical operational activities to minimize impact on health and safety of crewmembers and ensure integrity of research data.

(iii) Research data obtained from astronauts is not to be used for medial or flight certification purposes. It may be available as background information to be used when required for medical care or for medical emergency purposes during and after flight.

(iv) The following guidance applies:

Before a researcher has access to medical data, a crewmember's informed consent and an assurance of confidentiality will be required to be on file in order to preclude the inappropriate release or use of any medical data.

Investigators should identify in their proposals and revise as necessary, prior to the mission, applicable health, environmental, or mission activities data that might impact the research protocol(s). Applicable deviations in the mission profiles and appropriate data will be reported to the PI in a timely fashion to ensure research integrity.

Research data will not be presented or published in any way that allows identification of the participating crewmember or other subjects without their explicit written consent(s).

d. Bioethics of crewmembers volunteering as research subjects.

(i) Prior to selection as astronauts, applicants should be provided with information to ensure that they understand that they will be asked to volunteer to participate as research subjects during the course of their employment with NASA. Additionally, they should be informed that, as research subjects, they have certain rights, including the right to refuse to participate and the right to withdraw from participation. This information should be presented fairly and objectively to avoid real or perceived coercion.

(ii) Informed consent and consent forms should be comprehensive and in simple, layman's language and should also address the purpose of the research and the disposition of the data. Research subjects can withdraw consent at any time, including after the commencement of the research.

(iii) Potential crew members expected to volunteer as human subjects will receive an in-depth briefing of all biomedical experiments, including attendant risks and integrated risks, to obtain informed consent for participation prior to assignment as a crewmember to that flight.

(iv) Data and results from the research and their significance should be appropriately briefed to the participating crewmembers before publication in the open literature.

(v) Periodic informational and educational briefings on major biomedical findings and their implications from space missions will be provided by the PI or life sciences research personnel to the astronaut corps.

e. Effective date: This guidance is effective with the date of issuance and the signature of the Chief Health and Medical Officer, NASA.

Richard S. Williams, M.D., FACS, Date 4/16/2002

APPENDIX D

NASA Procedures and Guidelines

NPG 7100.1

Effective Date: March 28, 2003
Expiration Date: March 28, 2008

PROTECTION OF HUMAN RESEARCH SUBJECTS

Responsible Office: AM/Office of the Chief Health and Medical Officer

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Preface

P.1 PURPOSE

P.1.1 This NASA Procedures and Guidelines (NPG) outlines the implementing procedures and guidelines for the Agency to conduct or support research involving human subjects. These guidelines follow the provisions of "Federal Policy for the Protection of Human Subjects" as codified for NASA in Title 14 CFR Part 1230, and for the U. S. Department of Health and Human Services (DHHS) in Title 45 CFR Part 46. These regulations are implemented by the DHHS, Office for Human Research Protections (OHRP).

P.1.2 The primary intent of these guidelines is to provide instructions on setting up oversight protection for the rights, medical safety, and well-being of human subjects involved in research. This shall cover all volunteers who participate in any research utilizing NASA facilities, including NASA aircraft and spacecraft, directed by NASA personnel or onsite contractors, and in any NASA-conducted or supported research.

P.2 APPLICABILITY

P.2.1 These guidelines apply to NASA Headquarters (HQ), and all NASA Centers and component facilities engaged in experiments involving human subjects conducted or supported by NASA, conducted in NASA facilities, aircraft and spacecraft, or which involve NASA to any degree. The terms and conditions of this NPG, as applicable, are required to be incorporated in any contract, cooperative agreement, grant, or reimbursable arrangement, which involves human subject research entered into by NASA and another Government agency, private entity, non-Federal public entity, or foreign entity.

P.2.2 Research activities are exempted from this NPG if their involvement of human subjects is limited solely to the use of surveys or interviews unless (1) the information obtained is recorded in such a manner that human subjects are identified directly or can be identified indirectly through designators or through identifiers linked to the subjects, and (2) disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk for criminal or civil liability or could damage their financial standing, employability, or reputation. Also exempt is research involving the collection or study of existing data, documents, records, and pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded by the Principal Investigator (PI) in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects. Research activities using identifiable specimens archived after space flight are not exempt from the guidelines of this NPG.

P.3 AUTHORITY

a. 42 U.S.C. 2473(c)(1), Section 203(c)(1) of the National Aeronautics and Space Act of 1958, as amended.
b. 14 CFR Part 1230, Protection of Human Subjects.
c. 45 CFR Part 46, Protection of Human Subjects.

P.4 REFERENCES

a. 5 U.S.C. 552, The Freedom of Information Act (FOIA), as amended.
b. 5 U.S.C. 552a, The Privacy Act of 1974, as amended.
c. NPD 8621.1H, NASA Mishap and Close-Call Reporting, Investigating, and Recordkeeping Policy.
d. NPG 1441.1D, NASA Records Retention Schedules.
e. NPD 8900.1F, Medical Operations Responsibilities in Support of Human Space Flight Programs.
f. NPD 8900.3F, Astronaut Medical and Dental Observation Study and Care Program.
g. NPD 7100.8D, Protection of Human Research Subjects.
h. NPG 8621.1, NASA Procedures and Guidelines for Mishap Reporting, Investigating, and Recordkeeping.

P.5 CANCELLATION

None.

/s/ Richard Williams, M.D.
Chief Health and Medical Officer

CHAPTER 1. Responsibilities

The purposes of this NPG is to comply with the following:

1.1 Authorized NASA Official (ANO): The ANO shall be responsible for the protection of human subjects and is empowered, subject to conditions and limitations imposed by immediate superiors, to authorize research involving human subjects. All or part of the authority may be redelegated, without power of further redelegation, to (a) a senior NASA HQ employee who reports to the ANO, or (b) the NASA Center Director(s).

1.2 Inform the Administrator: The ANO shall ensure that the Administrator, the appropriate Associate Administrators (AA) sponsoring research involving humans, the AA for Office of Safety and Mission Assurance (OSMA), and NASA Chief Scientist, are kept fully and currently informed, through official channels, of significant actions, problems, or other matters of substance related to the exercise of this authority.

1.3 Approval of Multiple Project Assurances (MPA): The ANO is responsible for approving all NASA Center MPA's or Single Project Assurances (SPA), indicating that NASA-conducted or -sponsored research complies with NASA policy and the body of existing law pertaining to research involving human subjects. The ANO is responsible for approving each NASA Center's annual summary of the research and Institutional Review Board (IRB) activities for the preceding year including review of compliance activities, membership, initial and continuing education, and an updated IRB membership list.

1.4 NASA Center Directors: Shall be responsible for ensuring that their MPA is filed with the ANO. For NASA Center Directors not filing an MPA or SPA, the Center Director must certify to the ANO that research involving human subjects will not be conducted or sponsored by that Center during the following calendar year.

1.5 Establish IRB: The NASA Center Directors may establish a Center IRB to review all ground-based, aerospace, and aeronautical flight research that their respective Centers conduct or that utilize NASA facilities, equipment, or personnel (NASA-conducted or -sponsored research). If this is not done, then another NASA IRB, by prior arrangement, shall review the research proposals using human subjects.

1.6 Protection of Rights: The NASA Contracting Officers (NCO) shall ensure that all research proposals involving human subjects (including grants, contracts, cooperative agreements, memoranda of understanding, or other similar legal arrangements) are reviewed by an approved IRB prior to funding. The NCO shall maintain a record of all such IRB approvals.

1.7 Other Institutions Responsibilities: Academic institutions, nonprofit institutions, or business enterprises performing NASA-funded research involving human subjects at non-NASA facilities, and not involving NASA permission to use Government equipment are responsible for obtaining approval for their proposed research from an approved IRB, which will generally be the IRB at the institution performing the research. NASA reserves the right to have all such research reviewed by a NASA IRB prior to funding or implementation of this research involving human subjects.

CHAPTER 2. NASA Institutional Review Boards (IRB)

2.1 IRB Authority

2.1.1 The IRB has authority to approve, disapprove, or require changes in the proposed research protocols and procedures involving human subjects covered by this NPG. Another authority cannot overturn a decision of disapproval; however, a decision of ANO, Center Director, or their designee may change a decision of approval to disapproval.

The IRB may conditionally approve a protocol or recommend changes to disapproved protocols that could result in protocol approval. Any changes must be approved by the IRB prior to initiation or continuation of the protocol. The IRB has the authority to suspend or terminate its approval of research activities that are not being conducted in accordance with the approved protocol, or the policies set forth in this NPG, or that have been associated with serious harm to human subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be promptly reported to the PI, the NASA Center Director, and the ANO. If an IRB disapproves, suspends, terminates, or conditionally approves a research activity, the PI shall be given the opportunity to respond to the decision by either meeting with the IRB or through written correspondence with the Chairperson of the IRB.

2.1.2 When a NASA Center funds research involving human subjects not involving NASA facilities, personnel or equipment, the Center IRB may evaluate such proposals prior to their funding, or the NASA IRB may accept IRB certification for the research proposal from a DHHS OHRP approved non-NASA IRB.

2.2 IRB Responsibility

The primary responsibility of the IRB is to protect the rights and ensure the safety of every person who is a research subject in any NASA facility, including NASA aircraft or spacecraft. This applies to subjects involved in any research conducted or supported by NASA.

2.3 IRB Functions

2.3.1 The IRB reviews all proposals for NASA-conducted or -sponsored, ground-based, aeronautical, and space flight research, that apply to human subjects (the latter applies to the NASA Flight IRB (NFI) only chapter 6), prior to funding, approval, or execution of research. Except when an expedited review procedure is used, this review of proposed research shall be held only at convened meetings at which a majority of the members of the IRB are present including at least one member whose primary concerns are in a nonscientific area. For the research to be approved by the IRB, it must receive the approval of a majority of those members present at the meeting. If human subjects are to participate in multiple research protocols at the same time, the IRB shall review all the research proposals as an integrated protocol to assess the risks and benefits to the research subject.

2.3.2 The IRB conducts a continuing review of research involving humans at intervals appropriate to the degree of risk, but not less than once per year. This continuing review shall include the informed consent particulars, the adequacy of safety precautions taken to date, and a determination as to whether or not proper and comprehensive information was

given to the subject during the process. The IRB shall review all adverse events (whether expected or not), which occur during the conduct of research. In all cases in which there has been an adverse incident reported to the IRB, the IRB must notify the appropriate NASA safety and legal representatives, the ANO, and if appropriate other AA's.

2.3.3 The IRB defines for each approved experiment the extent to which the actual consent process and/or the conduct of the research shall be monitored. If monitoring is deemed necessary, this may be accomplished by appointment of a monitor with specified responsibilities or direct monitoring by selected members of the IRB.

2.3.4 The IRB maintains documentation of IRB activities as prescribed in chapter 6 of this NPG.

2.3.5 The appropriate NASA IRB must review and monitor non-NASA research using NASA facilities, equipment, or personnel involving human subjects.

2.3.6 The appropriate NASA IRB shall review human-used, ground-based simulators. The IRB shall determine the potential risks of the simulator operations to the research subjects. The IRB may then determine that all or some of the operations in the simulator may be IRB exempt, requires expedited review or requires full IRB review.
2.3.7 The ANO or designee will be responsible for developing and administering a NASA Human Protection Training program that is congruent with requirements for Federal funding by DHHS. This or similar training will be mandatory for all NASA IRB members and investigators using human subjects receiving NASA funds or involved in NASA-sponsored research.

2.3.8 The NASA Center IRB overseeing any human subject research for units responsible to that Center shall be responsible for appropriate oversight.

CHAPTER 3. Center IRB Membership

3.1 Membership Requirements

Each IRB shall have at least five members. The IRB shall consist of persons of varying backgrounds knowledgeable of the experimental environment and conditions to provide a complete and adequate review of research activities conducted by the institution or investigator. The IRB members shall be experienced, possess adequate expertise, and sufficient familiarity to exercise due diligence and consideration in the sensitive matters of race, gender, ethnic, and cultural backgrounds, and prevalent community attitudes toward human experimentation, to promote respect for IRB advice and counsel in safeguarding the rights and welfare of human research subjects. The cognizant NASA Center Director shall appoint the members of the IRB and select a full-time, senior-level NASA employee as the Chairperson. The members must have the competence required to review the research activities involving human subjects covered by this NPG and to determine the acceptability of the proposed research relative to applicable laws, safety regulations, health standards, and ethical codes. The Chairperson shall designate one of the members as his or her alternate.

3.2 Cultural Diversity

The IRB shall include culturally diverse members not entirely of one gender or race and shall include (1) a member of the Center's Safety and Mission Assurance Office; (2) at least one member whose expertise is in a nonscientific area such as medical ethics; (3) at least one
member cognizant of the operational aspects of the aerospace or aeronautic environment if appropriate; (4) at least one member who is not otherwise affiliated with NASA who is not a part of the immediate family of a person affiliated with NASA; and (5) a subject representative. In the case of Johnson Space Center (JSC) IRB, an astronaut usually serves in this function. The JSC IRB shall also include a NASA-employed physician. The Center Office of Chief Counsel shall provide legal advice to the IRB.

3.3 IRB Conflict of Interest

No IRB member may participate in the review of any proposal in which that member has a conflicting interest, except to provide information requested by the Board.

3.4 Nonvoting Expert Consultation

The IRB may invite nonvoting experts to help review and resolve special or difficult issues which require competence beyond or supplementing that available on the Board.

3.5 Recording Secretary

The recording secretary shall be appointed by the Chairperson of the IRB for recordkeeping and for general administrative Board functions.

3.6 Term of Appointment

IRB members shall be appointed for a 3-year term and can be reappointed at the end of their term. The Center Director cannot remove IRB members from their positions before the end of their terms except in cases of misconduct.

CHAPTER 4. NASA IRB Convening Authority

Meetings shall be convened by the Chairperson of the IRB on a regular basis or when a request is made by the Director of Bioastronautics Research Division (DBRB), Office of Biological and Physical Research (OBPR); the Chief Health and Medical Officer (CHMO), NASA HQ; the Mission Manager; a NASA Center Director; or a test subject to evaluate a research protocol which may affect the health or well-being of participating human subject(s).

CHAPTER 5. NASA IRB Records

5.1 Preparation and Maintenance of Records

The IRB shall prepare and maintain documentation of its activities including the following:

5.1.1 Copies of all research proposals reviewed; scientific evaluations, if any, that accompany the proposals approved; final consent documents; progress reports submitted by PI's; and reports of illness or injuries to subjects.

5.1.2 Minutes of IRB meetings shall include members, alternates, and visitors in attendance at the meetings; actions taken by the IRB; the vote on these actions, including the number voting for, against, and abstaining; the basis for requiring changes in or disapproving research; a written summary of the discussion of controversial issues and resolutions of same; and a statement for each approved proposal that the proposal is approved and all IRB
concerns have been addressed. Minority reports shall be filed in all cases in which there is no consensus.

5.1.3 Records of continuing review and monitoring activities.

5.1.4 Copies of all correspondence between the IRB, the investigators, and between other NASA Centers, including NASA HQ.

5.1.5 A list of IRB members identified by name, earned degrees, representative capacity, areas of proficiency such as board certification and licenses, and any current or previous employment or other relationship between each member and NASA or NASA contractors. A copy of this list and changes including IRB members' continuing education thereto shall be forwarded to the ANO yearly or as updated.

5.1.6 Written procedures for the operation of the IRB.

5.1.7 Statements of significant new findings provided to subjects, as required below by section 7.5.5 of this NPG.

5.1.8 Written procedures for assuring prompt reporting to the IRB and the ANO of any problems, whether anticipated or not, involving risks to subjects or to others; serious noncompliance or continuing noncompliance with NASA research policy, with the PI's protocol, or with the requirements of the IRB; or suspension or termination of IRB approval.

5.1.9 An annual report of IRB activities based on the minutes.

5.2 Record-Retention Requirement

IRB records relating to research conducted by an investigator shall be retained for at least 3 years beyond the last action of the IRB on that protocol or specific issue. The IRB shall retain records that shall then be dispositioned in accordance with NPG 1441.1, NASA Records Retention Schedules. All records shall be entered into a secure database, under the management of the Recording Secretary of the IRB, and accessible for inspection and copying by authorized representatives of NASA at reasonable times and in a reasonable manner. The information contained in the records and the database shall be maintained in conformity with prescribed NASA policies, guidelines, and procedures.

CHAPTER 6. NASA Flight IRB (NFI)

6.1 Establishment of NASA Flight IRB

The ANO shall establish a NASA Flight IRB whose function is to review all research proposals that (1) propose the use of crewmembers as research subjects and/or research technicians; (2) all space flight or aircraft research proposals that use noncrew human

research subjects; (3) all aircraft research proposals that use noncrew as research technicians if it is deemed that their participation could effect their health or safety; and (4) all space flight or aircraft research proposals that use animals, biological, or toxic materials that could be expected to interact with the humans onboard the space or aircraft. The NFI may also evaluate other proposals at the discretion of the ANO.

6.2 NFI at Johnson Space Center (JSC)

The NFI shall be located at JSC; however, meetings of the NFI may be at any appropriate location.

6.3 Membership

In consultation with the JSC Center Director, the ANO shall appoint the membership of the NFI which shall include (1) the Chairperson; (2) a NASA safety representative; (3) an active NASA Astronaut; (4) a NASA flight surgeon (5) a non-NASA employee from the bioethics or health profession communities; and (6) other members as required to have sufficient expertise and diversity to adequately evaluate research proposals. The Center Office of Chief Counsel or the Headquarters Office of General Counsel (OGC), as appropriate, shall provide legal advice to the NFI.

6.4 Conflict of Interest

No NFI member may participate in the review of any proposal in which that member has a conflicting interest, except to provide information requested by the Board.

6.5 Ad hoc Members

The NFI may invite nonvoting experts to help review and resolve special or difficult issues, which require competence beyond or supplementing that available on the Board.

6.6 Recording Secretary

The recording secretary shall be appointed by the Chairperson of the NFI for recordkeeping and for general administrative Board functions.

6.7 Term of Membership

NFI members shall be appointed for a 3-year term and can be reappointed at the end of their term. NFI members may not be removed from their positions before the end of their terms except in cases of misconduct.

6.8 Research Monitor

The NFI may require that a NASA safety and health monitor (may be the crew surgeon) must be available to observe all research studies involving NASA crewmembers.

6.9 PI Certification of Safety and Health Risks

If human subjects are to participate in multiple flight research protocols at the same time, the NFI shall review all the research proposals as an integrated protocol to assess the risks to the research subject.

6.10 Integrative Proposal Review

All research proposals that are required for review by the NFI shall be approved by the NFI prior to the initiation of crew or subject briefing.

6.11 IRB Approval Prior to Beginning of Training

The NFI will review only those proposals that have undergone successful scientific peer review, are funded for definition and/or feasibility studies, and are proposed as part of a flight payload complement.

6.12 No Waiver or Reciprocity With Any Other IRB

No waiver or reciprocity with any other IRB shall be accepted for any research proposal falling under chapter 6.

6.13 NFI Conform With NPG

The NFI shall conform to all appropriate parts of this NPG.

CHAPTER 7. Informed Consent

7.1 Required Informed Consent

Except as provided in section 7.6 below, no PI may involve a human subject in research covered by this NPG unless the PI has obtained the informed consent of the subject or the subject's legally authorized representative. Such consent shall be sought only under circumstances that provide the prospective subject, or the subject's representative, with sufficient latitude and opportunity to decide whether or not to participate, while minimizing the possibility of coercion or undue influence. All information that is provided shall be in language understandable to the subject or the representative. No informed consent may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or which releases, or appears to release the PI, the sponsor, the institution, or its agents from liability for negligence.

7.2 Elements of Informed Consent

The following basic elements of informed consent information shall be provided to each subject in nontechnical, easily understood language:

7.2.1 A statement that explains that the study involves research. An <u>explanation</u> of the purposes of the research and the expected duration of the subject's participation, a <u>description</u> of the procedures to be followed, and <u>identification</u> of any procedures which are experimental.

7.2.2 A description of foreseeable risks or discomforts to the subject.

7.2.3 A description of any benefits to the subject, or to others which may reasonably be expected from the research, or a statement that the research is of no benefit to the subject.

7.2.4 A disclosure of appropriate alternative procedures or courses of action or treatment that could be advantageous to the subject.

7.2.5 A statement describing the extent to which confidentiality of records identifying the subjects shall be maintained. (Special attention should be given to explaining the problem of maintaining confidentiality with electronically stored databases.)

7.2.6 For research involving more than minimal risk, an explanation as to whether any compensation and medical assistance are available if injury or illness occurs and, if so, of the specifics relating thereto and any other relevant information.

7.2.7 Identification of contacts for answers to pertinent questions concerning specifics of the research and the research subject's rights. The contact in the event of a research-related injury or illness to the subject should also be identified.

7.2.8 Except as provided in sections 7.4.2 and 7.4.4 below, a statement that participation is voluntary, and that subjects have the right to refuse to participate and to discontinue participation in the research at any time and that they may do so without penalty or loss of benefits to which they would be otherwise entitled. If the subject, in fact, cannot withdraw at any given time (because it would be unwise, dangerous, or impossible), the circumstances must be explained to the subject in writing as part of the informed consent document.

7.2.9 Subjects concerned about protocol violations may request a meeting with the relevant IRB.

7.3.1 Subject Withdrawal From Nonspace-Based Research

7.3.1 Consideration for withdrawal from nonspace-based research is predicated upon the following:

7.3.2 Research subjects may withdraw from participation at any time without penalty or loss of benefits to which they are otherwise entitled.

7.3.3 In the event that a subject withdraws from nonspace flight research involving human subjects, NASA reserves the right to replace that individual with another test subject.

7.4 Subject Withdrawal From Space-Based Research

Consideration for withdrawal from space-based research includes the following:

7.4.1 Research subjects may withdraw from participation at any time without penalty or loss of benefits to which they are otherwise entitled.

7.4.2 In the event that the research subject is a crewmember,

7.4.2.1 The IRB-approved life science experiment is part of the central or core function of the mission,

7.4.2.2 The crewmember was clearly and completely informed of the experiment prior to assignment to the mission,

7.4.2.3 The crewmember formally consented to participate in the experiment,

7.4.2.4 No substantial change has occurred in the protocol since the crewmember's consent; and

7.4.2.5 No new interim scientific information has surfaced indicating that the initial protocol presents a more than minimal increase in health or medical safety risk and no new, safer techniques have become available; then
7.4.2.6 Withdrawal from research may result in removal of that individual from that mission. This action shall be based on the determination that it is in the best interest of the Government and to ensure mission success.

7.4.3 The determination of whether all conditions in section 7.4.2 have been met shall rest with the IRB that approved the initial protocol. In the case of NASA or international astronauts, or payload specialists, a review shall be conducted by the ANO to validate the findings of the IRB under section 7.4.2 and formulate a recommendation. Approval of the recommendation and final disposition shall rest with the AA for OSF in consultation with the mission-sponsoring organization.

7.4.4 When a crewmember has withdrawn and all conditions in section 7.4.2 have been met, such withdrawal shall not influence career opportunities; however, it could be used in the decision process regarding assignments to a future mission in which similar life science experiments are central or core to the mission.

7.5 Supplementary Elements of Informed Consent

Additional elements of informed consent may include, when appropriate, one or more of the following elements of information:

7.5.1 A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant), which are currently unforeseeable.

7.5.2 Anticipated circumstances under which the subject's participation may be terminated by the PI without regard to the subject's consent.

7.5.3 Any additional monetary costs to the subject that may result from participation in the research.

7.5.4 The consequences of a subject's decision to withdraw from the research and prescribed procedures for an orderly termination of participation by the subject.

7.5.5 A statement that the subject shall be informed of significant new findings developed during the course of the research, including adverse reactions of other subjects participating in this research, which may affect the subject's willingness to continue participation.

7.5.6 The approximate number of subjects in the study.

7.5.7 Any collective impact of multiple protocols, if applicable.

7.5.8 PI disclosure of financial interest in the research study, to include benefits the PI will derive from the study, or drugs or devices being developed through the study.

7.6 Waiver of Consent Elements

An IRB may approve a consent procedure that either does not include or otherwise alters some or all of the elements of informed consent set forth in this NPG; or the IRB may waive the requirements to obtain informed consent, provided that the IRB finds and documents each of the following:

7.6.1 The research involves no more than minimal risk to the subjects.

7.6.2 The waiver or alteration shall not adversely affect the rights and welfare of the subjects.

7.6.3 The research could not practically be carried out without waiver or alteration.

7.6.4 Whenever appropriate, the subjects shall be provided with additional pertinent information after participation.

7.6.5 Published or released astronaut data and other human experimental data derived from or associated with approved research shall not be attributable to any individual.

7.7 NPG Shall Not Preempt Current Laws

The informed consent requirements in this NPG shall not preempt any applicable Federal, State, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

7.8 Physician Right to Practice Emergency Medicine

Nothing in this NPG is intended to limit the authority of a physician to provide emergency medical care to the extent that the physician is permitted to do so under applicable Federal, State, or local law.

CHAPTER 8. Documentation of Informed Consent

8.1 Written Consent Required

Informed consent shall be documented by the use of a written consent form approved by the IRB, and signed and dated by the subject or the subject's legally authorized representative. The PI shall keep the original signed consent for at least 3 years after the

completion or termination of the research protocol; and a copy shall be given to the person signing the form. The PI must make the signed consent form available to the IRB for inspection and copying.

8.2 The Consent Form May Be Either of the Following

8.2.1 A written consent document containing the elements of informed consent required in chapter 7 of this NPG. This form may be read to the subject or the subject's legally authorized representative, but in all instances, the PI shall give either the subject or the representative adequate opportunity to read, understand, ask questions, and consult with additional experts if so desired before it is signed.

8.2.2 A "short form" written consent document stating that elements of informed consent required in chapter 7 has been presented orally to the subject, or subject's legally authorized representative. When this method is used, there shall be an independent witness to the oral presentation. Also, the IRB shall approve written summary of that which is to be said to subject or representative. Only the "short form" itself is to be signed by subject or representative. However, the witness shall sign both the "short form" and a copy of the summary. The person actually obtaining the consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the "short form."

CHAPTER 9. Criteria for IRB Approval of Research Involving Human Subjects

9.1 The following requirements must be satisfied for the IRB to approve the research involving human subjects covered by this NPG:

9.1.1 The PI shall always protect the safety and minimize health risk to subjects: (1) by selecting methodologies and procedures which are consistent with sound research design and conduct and which do not unnecessarily expose subjects to undue risk; and (2) whenever possible, by using procedures already being performed on the subjects for other experiments, so as to minimize the collective impact of multiple protocols on the subject.

9.1.2 In evaluating safety risks and benefits, the IRB shall ensure that risk to subjects be reasonable in relation to anticipated benefits, if any, and the importance of the new knowledge that may reasonably be expected to result. The IRB should consider only those risks and benefits, taking into account the collective impact of multiple protocols that may result from the research. The IRB should not consider possible long-range effects of new knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks or benefits that are its responsibility.

9.1.3 The PI shall obtain and document voluntary informed consent of each prospective subject or the subject's legally authorized representative. The human research consent form shall contain at least all elements listed in section 7.2 (section 7.5, if appropriate). The PI shall inform the subject not all risks are readily identifiable.

9.1.4 The PI may ensure that the subject or the subject's beneficiaries receive compensation by means of insurance, worker's compensation, or the like in the event that the subject suffers illness, disease, injury, loss, or death as a direct result of the research. The lack of this provision <u>may</u> serve as a basis for disapproval of the research. Such provisions for compensation shall be required for all studies performed at a NASA Center.

9.1.5 Where applicable, the research proposal shall contain provisions for monitoring the data collected to ensure the safety of the subjects. Other informational items that should be included in a human research proposal are listed in Appendix A.

9.1.6 The PI shall provide safeguards to protect the privacy of subjects and the confidentiality of data, especially electronically stored data. Biomedical data, if held by NASA and if retrievable by personal identifier, are subject to the Privacy Act of 1974, as amended, 5 U.S.C. 552a, and are maintained under the NASA System of Records, Human Experimental and Research Data (HERD) Records. Such data held by other institutions must have similar safeguards. The PI shall maintain the records relating to the conducted research and shall retain these records for at least 3 years after completion of the research.

9.1.7 No human subject shall participate in any portion of the research until the protocol is approved by the IRB.

9.1.8 The PI shall ensure that selection of subjects is equitable and representative of population that its biomedical research intends to represent. The IRB should assess purposes and setting of the research. In the case of space flight, considerations should be given to habitability conditions and level of medical care available in event of illness or injury.

CHAPTER 10. Expedited Review

10.1 Minimal Risk

In the case of research involving minimal risk to human subjects (Appendix B), the IRB may conduct an expedited review. This shall consist of a review by the Chairperson or one or more experienced reviewers designated by the Chair from among the members of the IRB. It shall be based on the same criteria as a nonexpedited review but shall not require consideration by the entire IRB. The IRB may also use the expedited procedure to review minor changes in previously approved research during the period for which approval is authorized.

10.2 Authority of Expedited Reviewer

In conducting an expedited review, the reviewer(s) exercises all the authority of the IRB, except that the reviewer(s) may not disapprove the research. A research activity may be disapproved only through the nonexpedited procedure described in this NPG. A reviewer must recommend that the proposal be reviewed by the full IRB if the research involves more than minimal risk.

10.3 Report to the IRB for Expedited Review

The reviewer(s) who approves research proposals using the expedited review procedure shall either directly or through the Chairperson report to the Board on such approvals at the next meeting of the IRB. The minutes of the IRB shall reflect the expedited approval with the concurrence of the full IRB.

CHAPTER 11. Reports on Injuries, Illness, or Disease and Medical Care

11.1 PI Responsibility for Reporting

The PI shall immediately inform the IRB Chairperson and initiate appropriate investigations in the event of the following:

11.1.1 Any injury, illness, disease, or death, whether expected or not, incurred by the subject as a possible result of a research protocol.

11.1.2 Any change in the experimental environment or in the subject that could forecast medical problems.

11.2 PI Responsibility for Recordkeeping

The occurrence of any instance requiring medical attention. The PI shall note any such occurrences in the subject's research records and make them available to the subject's physician.

11.3 Determination of Suspension of Research

The IRB Chairperson or designate shall determine whether the research should be immediately suspended with subsequent IRB concurrence.

11.4 Reporting to NASA Headquarters

The PI shall report all such events immediately to the IRB. If appropriate, the PI shall report all such events additionally to NASA. A non-NASA PI shall notify all institutional IRB's that approved his or her proposal. It shall be the responsibility of said IRB's holding approved MPA's from other Federal agencies to communicate such incidents to that Agency directly.

11.4.1 When the injury results in a loss of life, a permanent disability, or when a person requires hospitalization, and/or a person requires extensive first aid or lost workday(s), the mishap must be reported to NASA HQ immediately (within 1 hour) in accordance with NPD 8621.1, NASA Mishap and Close-Call Reporting, Investigating, and Recordkeeping Policy, and NPG 8621.1, NASA Procedures and Guidelines for Mishap Reporting, Investigating, and Recordkeeping.

11.4.2 The IRB Chairperson shall notify the NASA Center Safety Officer; the ANO; and the Crew Medical Officer especially in the case of crew involvement in the event of a reportable incident. The IRB Chair shall initiate an investigation as soon as possible per NPG 8621.1, NASA Procedures and Guidelines for Mishap Reporting, Investigating, and Recordkeeping.

11.4.3 When NASA conducts a mishap investigation to investigate an injury or illness resulting from the research, all researchers shall cooperate with the NASA mishap investigators, grant interviews, and provide data as requested.

11.5 Review by IRB Required to Resume Research

Once a research protocol involving human subjects is suspended, IRB review and approval are required before the experiment can resume.

11.6 Health Care Provisions for Research Subjects

11.6.1 The NASA IRB shall review the health care provisions provided to the research subject, and/or available for possible injury or illness that could occur during the research.

11.6.2 The provisions for access to medical care shall be included in the consent form as appropriate.

11.6.3 The medical care for astronaut research subjects shall include the assigned NASA flight surgeon. The flight surgeon shall have access to all research data that pertains to the health of the astronaut research subject. The flight surgeon may use this data for the ongoing health monitoring of the astronaut.

CHAPTER 12. Protocol Modifications

12.1 IRB Review of Protocol Modifications

The protocol shall not be modified unless the IRB or the reviewer (in the case of an originally expedited review) approves a formal request with appropriate justification. If the IRB determines that the modification increases the risk(s) to the subject, a revised informed consent shall be required.

12.2 Peer Review Suggested Modifications

Space flight experiment research protocols may require modification during flight, as procedures are refined to comply with operational constraints. Substantive human research protocol changes during flight require the majority approval of a quorum of the IRB. The Chairperson or designee shall expeditiously seek this approval in a meeting or by teleconferencing, if appropriate, with members of the IRB. The Mission Operations Control Room Surgeon must be immediately informed of this requested substantive change and has the authority to temporarily suspend the experiment until the IRB can review the request. All such approved changes to the research protocol shall also be approved by the crewmember volunteering for the research prior to the initiation of the research protocol changes.

CHAPTER 13. Assurances from Participating Instructions

13.1 MPA on File

All NASA Centers or other institutions proposing research involving human subjects supported by NASA shall give written institutional assurance, provided in 14 CFR 1230.103, to the ANO. MPA on file with the DHHS OHRP shall satisfy this requirement. Assurances from international institutions must follow U.S. ethical and legal standards.

13.2 NASA IRB Approvals and Non-NASA Research

NASA IRB review and approval shall be required for protocols by a non-NASA investigation, which utilizes NASA facilities, equipment, or personnel in addition to IRB of the extramural participants. Therefore, in this instance, other institutional assurances certified by DHHS OHRP or international oversight bodies for extramural projects shall not suffice.

13.3 Format for MPA

Institutions submitting MPA's and SPA's to NASA should use the sample documents from the DHHS OHRP deleting DHHS, or OHRP and substituting NASA.

13.4 Term of MPA

The term of an MPA shall not exceed 5 years.

CHAPTER 14. The Approval of Assurances

14.1 Approval by Authorized Official

The ANO with the concurrence of the OGC shall evaluate the MPA's from NASA Centers and shall certify such MPA's that are deemed appropriate for the protection of human subjects if the submissions are satisfactory and meet the requirements in NPD 7100.8, Protection of Human Research Subjects, and this NPG (NASA Centers not conducting or supporting human research shall file an annual notice with the ANO).

14.2 Non-NASA Institutions

Other interested institutions, including public, private, and international institutions may submit an application for a NASA-approved MPA. The ANO with the concurrence of the OGC may evaluate these MPA's and may certify such MPA's that are deemed appropriate for the protection of human subjects if the submissions are satisfactory, meet the requirements in NPD 7100.8, and this NPG, and are in NASA's best interests.

14.3 Site Review

A site visit may be required for evaluation of either a new or renewal MPA to assess the adequacy of the NASA Center or other institution's procedures for protecting human research subjects. The site visit for a new approval shall evaluate the facilities to determine (1) the institution's ability to safely perform research involving human subjects, (2) the expertise of the officials who shall oversee the assurances, (3) the facilities for maintaining adequate records, and (4) the institutional commitment for adequately funding the oversight efforts. Compliance may be audited at a site visit for renewal or at other times. Training of IRB and staff members shall also be monitored.

14.4 Evaluation of Requirements for MPA Approval

Approval of an MPA shall be based on the evaluation of the following factors: (1) administration including jurisdiction of the IRB, establishment and membership of the IRB, recordkeeping, institutional responsibilities, the assurance itself, staff, space, and supplies, communication, institutional procedures and guidelines, identification of the

authorized NASA Center or other institutional official, training of IRB and staff members, and process for internal audits; (2) regulations and policies regarding Federal laws and the common rule and their use by the IRB;(3) description of the way the IRB interacts with other interested oversight bodies, e.g. safety, legal, (4) basic IRB review policies including risk or benefit analysis, requirement for the disclosure of risks and benefits in the consent form, continuing review and monitoring of data, requirements and documentation for the informed consent; (5) policies for monitoring and observation of research activities; and (6) appropriate guidelines for the use of special classes of subjects.

CHAPTER 15. Assurance Compliance Oversight Procedures

15.1 Allegations on Noncompliance

The ANO shall investigate any allegation or indication of noncompliance with NPD 7100.8, or with this NPG, which comes to his or her attention with regard to NASA-conducted or supported research. The ANO may at any time modify an MPA to require interim corrective actions to remedy such noncompliance. The ANO may also suspend an MPA during an investigation if it is necessary to protect human research subjects.

15.2 Center Responsibility

The ANO may request the NASA Center or other institution to either acknowledge the institution's report of noncompliance or notify the NASA Center or institution's Assurance Signatory Official (ASO) of the possible noncompliance and, as necessary, request that the institution investigate the matter and report back. The ANO may communicate directly with other affected institutional officials or personnel or, if the noncompliance involves a specific research investigator, may notify that investigator directly.

15.3 Onsite Evaluation

The ANO may initiate an onsite evaluation of protections under an MPA even in the absence of specific allegations or indications of noncompliance. The ANO may convene a NASA HQ review panel to investigate the circumstances surrounding any cases of noncompliance. A designated senior NASA HQ official who has no apparent or real conflict of interest shall chair the review panel. The membership shall consist of five members, as a minimum, with participation from the OGC and the OSMA. After review of the circumstances, the ANO in consultation with the OGC may prescribe and publicize sanctions, as appropriate.

15.4 Reporting Requirements

If the Authorizing Official determines that a formal report of findings is warranted, he or she shall notify the NASA Center or other institution's ASO that a formal report is required. The report may include (1) an invitation to the Signatory Official for institutional identification of errors of fact, and/or (2) the complainant(s), as appropriate, with an invitation for individual identification of errors of fact.

15.4.1 The Authorizing Official will establish a Data Safety Monitoring Board (DSMB) to review clinical studies as appropriate.

15.4.2 The DSMB membership will be multidisciplinary in nature and, as a minimum, will include experts in biostatistics, experimental design, and bioethics. The DSMB will be established for particularly high-risk research, or research where the blinded nature of data might put subjects at risk in ways that are not immediately apparent to blinded researchers.

15.4.3 The relevant IRB's, in consultation with the Office of CHMO, will determine which protocols warrant the establishment of particular levels of DSMB oversight.

15.4.4 All investigators who work with human subjects must be trained in basic principles of human subjects protection. Minimum training should include the history and basic principles of human subject research protections, risk or benefit assessment and informed consent procedures, and institutional responsibilities. Research investigators must demonstrate that they have completed such training to be eligible to submit research proposals to a NASA IRB.

CHAPTER 16. Sanctions and Potential Disciplinary Action

16.1 PI Research Suspended

Any NASA PI participating in research involving human subjects, who does not comply with this NPG or with the IRB-approved protocol, may have his or her research immediately suspended or terminated by the appropriate IRB, NASA Center Director, OBPR Director of Bioastronautics Research, or the ANO. Such noncompliance may be cause for revocation of funding. It may also be the cause for other appropriate remedies including disciplinary action against the PI, i.e. sanctions addressed in this section do not exclude possible personnel actions.

16.2 Non-NASA PI

PI's not employed by NASA, who are responsible for research involving human subjects sponsored by NASA or performed in NASA facilities, aircraft, or spacecraft and who do not comply with this NPG or do not comply with the NASA IRB approved protocol, may have their research immediately suspended or terminated and shall also be subject to appropriate sanctions. NASA shall suspend or terminate funding approval if the investigator's research is suspended or terminated by the originating institution for any reason. NASA may immediately suspend or terminate grant approval for research involving human subjects from non-NASA institutions funded by NASA if that institution's MPA is suspended or terminated.

16.3 Funding of Suspended Research

16.3.1 If an MPA for a NASA Center or any institution is suspended or terminated for cause, the ANO with the concurrence of the OGC and the Office of Procurement may recommend to the NASA Administrator that all NASA funding for human research to that institution be suspended or terminated.

16.3.2 Any evidence of alleged criminal wrongdoing at any level related to information obtained from IRB activities and oversight by the Office of the CHMO shall be forwarded to the NASA Office of the Inspector General.

CHAPTER 17. Measurements

17.1 The following metrics are required:

17.1.1 Number of research proposals reviewed by the IRB and tracking of timely responses to the Board's recommendations (action items) by the PI's.

17.1.2 Number of research proposals reviewed by the IRB and tracking of timely PI responses to the Board's recommendations (action items) and the number of proposals approved and disapproved by the IRB.

17.1.3 Number of research proposal renewals.

17.1.4 Number of adverse reactions, equipment failures or modifications reported to the IRB by the PI, the IRB Compliance Officer (if mandated), crew surgeon, or other responsible monitors or officials.

17.1.5 Tracking of action item responses from PI's.

17.1.6 Number of IRB letters of reprimand or more serious sanctions imposed.

17.1.7 Number of audits and followup corrective actions adopted as a result of complaints to the IRB.

17.1.8 Number of official mishap investigations instituted or completed and corrective action taken to avoid repetitions.

17.1.9 Number of cases of research misconduct occurring in IRB-approved protocols.

17.1.10 Number of investigators taking the NASA Bioethics training. Number of first-time training certifications versus number of recertifications.

17.1.11 Number of DSMB reviews, corrective actions, and lessons learned.

APPENDIX A: DEFINITIONS

1. Assurances are either a Single Project Assurance (SPA) or Multiple Project Assurance (MPA) which is a formal, written statement in which an institution promises to comply with applicable rules governing research with human subjects. An SPA or MPA must be provided by the IRB prior and accepted by the appropriate Federal agency prior to commencing of any NASA research involving human subjects. An SPA or MPA must cover all research conducted, supported, or otherwise subject to regulation by the Federal Government outside the United States.

2. Authorized NASA Official (ANO) is the official designated by the NASA Administrator who is empowered, subject to conditions and limitations imposed by an immediate supervisor, to authorize research involving human subjects. This has been designated in NPD 7100.8D as the Chief Health and Medical Officer (CHMO).

3. Conducted Research is research involving a PI or subordinate researcher who is a NASA employee.

4. Crewmember is an astronaut, payload specialist, or aviation personnel assigned to a spacecraft or an aircraft mission who may volunteer as a research subject and/or participate as a research technician for a research experiment as part of their employment.

5. Funded Research is research that is partially or completely underwritten by NASA through a contract, cooperative agreement, grant, or other funding mechanism, and which does not also involve permission by NASA to utilize NASA, U.S. Government, or foreign agency facilities, equipment, or personnel, including space and aircraft vehicles.

6. Human Subject is a living person who is an integral part of a test, or other substantive evaluative procedure and about whom the PI (whether professional or student) obtains (1) research data through intervention or interaction; or (2) identifiable private information.

7. Informed Consent consists of oral or written acknowledgement by a research subject that he/she understands the nature of the research to be performed and his/her obligations in participating in the research, the potential risks to health and well-being by participating as a research subject, and other tests or therapies available if the subject is a medical patient seeking health care; that he/she has been allowed to ask questions relating to the research to be performed; and is allowed to quit the research activity at any time (except if it would cause greater harm to the subject). The elements of informed consent are full disclosure, adequate comprehension, and voluntary choice to and for the research subject.

8. An Institutional Review Board (IRB) is a committee approved by NASA and established in accordance with this NPG or approved by the DHHS under a current Multiple Project Assurance (MPA) to review research involving human subjects and their activities for the adequacy of procedures that protect human subjects in research.

9. Interaction includes communication or interpersonal contact between the investigator and the subject.

10. Intervention includes both physical testing procedures by which data are collected (for example, equipment used on a person) and manipulation of the subject or the subject's environment for research purposes.

11. Life Sciences Research includes biomedical, biological, human factors, psychological, environmental health, and life-support experimentation.

12. Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. Persons employed in hazardous occupations are not expected to submit to greater risks than persons employed in non-hazardous occupations. Examples of minimal risk activities are presented in Appendix B.

13. Principal Investigator is the researcher who has overall responsibility for all aspects of the funded and/or sponsored research project.

14. Private information includes information provided for specific purposes about a subject's medical, physiological, or behavioral status or history about which the individual can reasonably expect that no observation or recording is taking place and which the individual can reasonably expect shall not be made public.

15. Research is a systematic investigation, including development, testing, and evaluation, which may be designed to test a hypothesis, enable conclusions to be drawn and, thereby, develop or contribute to knowledge in general. The research is described in a formal protocol that sets forth an objective and a set of procedures designed to reach the stated objective.

16. Risk the probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk."

17. Serious Harm is a temporary or permanent illness, injury, disability, or death.

18. Sponsored Research is investigative and commercial experimental work approved by NASA to permit the utilization of NASA, U.S. Government, or foreign agency facilities, equipment, or personnel, including space and aircraft vehicles, whether or not NASA funds are used to support the research.

19. Supported Research is NASA-funded or -sponsored research.

APPENDIX B: MANDATORY PORTION OF A NASA HUMAN SUBJECT RESEARCH PROPOSAL

The following information shall be included with the proposal submitted for IRB review:

1. Name of the organization conducting the research or for which the research is being conducted.

2. Name and qualifications of persons who shall conduct the research involving human subjects.

3. The reasons for the use of human subjects and a plan to ensure equitable selection of research subjects with reference to race and gender.

4. Possible inconveniences, discomforts, illnesses, diseases, injuries, pain, and risks to the subject.

5. A description of the hazard controls and safety precautions to be applied.

6. Expected duration of the study, including approximate beginning and ending dates.

7. The extent of any physical examinations to be given by medical personnel:

   a. Initially, to ascertain the subject's health status and to certify that the subject is capable of undertaking the proposed research,

   b. During the course of the research, and

   c. At the completion of the research.

8. Wage, salary, or other payment, if any, to be paid to the subject for participating in the research.

9. Source (Federal or State compensation acts and insurance) and general description of compensation, if any, to be received by a subject or the subject's legally authorized representative in the event of injury or death. Assistance in the preparation of this information may be obtained from the appropriate NASA Center OGC or, if the subject is or shall be a Government employee, from the NASA Center Personnel Office.

10. Availability of medical personnel, if applicable, and an adequate medical facility within a reasonable distance of the location where research is performed. Indicate whether a physician shall be present at all times or on call; if on call, the physician's location during the research.

11. Information about the research involving human subjects that shall be given to the subject while obtaining the subject's informed consent.

12. The research involving human subjects consent form, including the provision that subjects concerned about protocol violations may request a meeting with the relevant IRB.

13. Evidence of review and approval by the sponsoring organization's IRB.

14. A plan for ensuring privacy and protecting the confidentiality of data with particular attention to data contained in an electronic database.

15. Data Safety Monitoring plan, where applicable.

APPENDIX C: TYPES OF RESEARCH ACTIVITIES THAT MAY BE REVIEWED THROUGH EXPEDITED REVIEW PROCEDURES

Research activities involving no more than minimal risk and in the involvement of human subjects shall be in one or more of the following categories (carried out through standard methods), may be reviewed by IRB through expedited review procedure authorized in Federal Policy Regulations cited 45 CFR 46.110 and 14 CFR 1230.110.

1. Collection of hair and nail clippings, in a nondisfiguring manner, deciduous teeth, and permanent teeth if normal preventive patient care indicates a need for extraction.

2. Collection of excreta and external secretions, including sweat, noncannulated saliva, and placentas removed at delivery, and amniotic fluid at the time of membrane rupture prior to or during labor.

3. Recording of data from subjects 18 years of age or older, using noninvasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body, or at a distance, and do not involve input of matter or significant amounts of energy into the subject or an invasion of privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, and detection of naturally occurring radioactivity, diagnostic sonography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (e.g., X-rays, microwaves, ultraviolet light, and infrared lights).

4. Collection of both supra and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

5. Voice recordings made for research purposes such as investigations of speech defects or stress.

6. Moderate exercise performed by healthy subjects.

7. The study of existing data, documents, records, pathological specimens, or diagnostic specimens. In the latter two instances, a new informed consent statement must be obtained.

8. Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, in which the PI does not manipulate the subject's behavior and the research does not involve stress to the subjects.

APPENDIX E

Memorandum of Understanding
JSC Committee for the Protection of Human Subjects (CPHS) and JSC Payload Safety Review Panel (PSRP)

Purpose

To define and clarify the joint responsibilities of JSC Committee for the Protection of Human Subjects (CPHS) and JSC Payload Safety Review Panel (PSRP) in reviewing NASA-sponsored experiments involving human research subjects. The CPHS shall combine their biomedical expertise with the technical expertise and engineering capability of the PSRP in an effort to ensure that NASA-sponsored experiments involving human research subjects (i.e., human physiology experiments) are safe.

Roles and Responsibilities

1. The role of the physicians, human physiologists, and other professional support personnel of the CPHS in ensuring the safety of human test subjects for in-flight and NASA-sponsored ground-based experiments is as follows:

a. The CPHS shall review, from a biomedical perspective, all human research protocols for potential hazards and hazard controls with respect to all in-flight and NASA-sponsored ground-based experiments. The CPHS will ensure that all credible hazards are identified and are adequately controlled. Potential hazards and their controls to be addressed by the CPHS include excessive electrical shock, ultrasound, personal fatigue, adverse effects of drugs or injectable solutions, excessive collection of blood, or other single or combined physiological stress factors.

b. The CPHS or their appointed representative shall establish safe physiological limits for intentionally applied electrical, ultrasound, laser, and other types of electromagnetic impulses to the various parts of the body, as required for a given experiment system.

c. The CPHS shall be responsible for ensuring the safety of all equipment used in human in-flight research. In this context, the CPHS shall rely on the PSRP to review the design and operation of <u>all</u> custom-made equipment and modifications of off-the-shelf devices that could be hazardous to the in-flight test subjects or nearby participants in an experiment.

d. The CPHS shall be responsible for ensuring that a planned sequence of human experiments does not create excessive risk or other adverse effects for the test subjects.

e. The CPHS through the Safety and Test Operations Division (NS) shall verify that all ground-based human research (experiment) hardware is safe for use in human surroundings in accordance with JPG 1700.1 (JSC Safety and Health Handbook).

2. The role of the engineers and other support persons on the PSRP in this joint responsibility to ensure crew safety is as follows:

a. The PSRP shall review the design and operation of payload experiment hardware for compliance with the safety requirements in NSTS 1700.7B, "Safety Policy and Requirements for Payloads Using the Space Transportation System," or in the NSTS 1700.7B, ISS Addendum, "Safety Policy and Requirements for Payloads Using the International Space Station." The PSRP will ensure that all identified hazards are adequately controlled, and that these controls have been adequately verified.

b. The PSRP shall forward to the CPHS for their resolution any potential hazard identified at a payload safety review that requires the biomedical expertise of the CPHS to determine its risk potential. This will help the PSRP confirm that controls for this hazard are adequate.

c. The PSRP shall send to the CPHS requests for the establishment of physiological limits for ultrasound, electrical shock, and other physiological stresses that could result from either planned use or a malfunction during use of the equipment. These physiological limits will be used by the PSRP in determining whether the design and controls on the equipment items under review are adequate.

To facilitate the flow of information between the CPHS and the PSRP, a representative of the Space and Life Sciences Directorate will be a member of both groups. This individual shall attend all safety reviews of flight experiments involving human test subjects. This person will also keep each group informed of the deliberations and actions of the other group regarding human research experiments of common interest to both groups.

Original signed by:

_____

Axel M. Larsen/MA2 Date
Chairman,
Shuttle/ISS Payload
Safety Review Panel (PSRP)

Original signed by:

_____

Charles F. Sawin, Ph.D./SA Date
Chairman,
JSC Committee for the Protection
of Human Subjects (CPHS)

INFORMATIONAL NOTE:
The name of the JSC Institutional Review Board (IRB) was changed to the JSC Committee for the Protection of Human Subjects (CPHS). The name change was announced at the July 13, 2001 board meeting and recorded in the minutes. (See exert below.)

JSC-IRB Name Change to JSC Committee for the Protection of Human Subjects (JSC-CPHS)

Dr. Sawin informed the Board that the name of the JSC-IRB is now changed to JSC Committee for the Protection of Human Subjects (JSC CPHS). He explained that this title was becoming more commonly used in the academic environment and would better represent the function of the Board.

APPENDIX F

Examples of Research Activities for "Minimal Risk" Protocols or Previously Approved "Reasonable Risk" Protocols With Minor Changes

(1) Collection of hair and nail clippings, in a non-disfiguring manner; deciduous teeth, and permanent teeth if patient care indicates a need for extraction.

(2) Collection of excreta and external secretions including sweat, uncannulated saliva, placenta removed at delivery, and amniotic fluid at the time of rupture of the membrane prior to or during labor.

(3) Recording of data from subjects 18 years of age or older using noninvasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject, or an invasion of the subject's privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, diagnostic echosonography, and electroretinography. It does not include exposure to electromagnetic radiation outside the visible range (for example, x-rays, microwaves).

(4) Collection of blood samples by venipuncture, in amounts not exceeding 450 millliters in an 8-week period and no more than two venipunctures per week, from subjects 18 years of age or older and who are in good health and not pregnant.

(5) Collection of both supra-and subgingival dental plaque and calculus, provided the procedure is not more invasive than routine prophylactic scaling of the teeth, and the process is accomplished in accordance with accepted prophylactic techniques.

(6) Voice recordings made for research purposes such as investigations of speech defects.

(7) The study of existing data, documents, records, pathological specimens, or diagnostic specimens.

(8) Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate subjects' behavior and the research will not involve stress to subjects.

APPENDIX G

Lyndon B. Johnson Space Center
Committee for the Protection of Human Subjects

LIFE SCIENCES RESEARCH PROTOCOL FORMAT

The Lyndon B. Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS) reviews both ground-based and space flight related human research protocols. Life sciences protocols using human test subjects must be approved by the JSC CPHS when research is conducted in spacecraft, JSC facilities, JSC aircraft, or at other centers or institutions when JSC civil service or contractor personnel are directly involved in the research activities. In addition, all research protocols involving space flight crews must be approved by the JSC CPHS. Only complete protocols will be reviewed by the JSC CPHS. Verbal agreements are not satisfactory and all protocols must be presented to the JSC CPHS in writing. Refer to JSC 20483C, "JSC Committee for the Protection of Human Subjects - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations" for additional information.

GENERAL INFORMATION

- The format described here is to be used by investigators preparing the documentation required by the JSC CPHS for protocol review. It is important to be thorough and detailed. Do not eliminate anything. Prepare the package in the order presented below. Incomplete protocols WILL be returned.

- A completed, signed PROTOCOL COMPLETION CHECKLIST (Appendix G, Section 17.0) must be submitted with the protocol.

- The Principal Investigator must forward 20 copies of the signed LIFE SCIENCES RESEARCH PROTOCOL to the secretary/recorder of the JSC CPHS if the protocol requires full JSC CPHS review. Forward 3 copies of the signed Life Science Research Protocol if the protocol will be reviewed by the expedited review process.

SPACEFLIGHT STUDIES

Full Committee Review: 1 year prior to mission.

Expedited Review (minimal risk protocols and previously approved reasonable risk protocols with only minor changes): These protocols may be submitted at any time. If you have questions whether a protocol qualifies for expedited review or not, please contact Dr. Charles F. Sawin, JSC CPHS Chairperson, (281) 483-7202.

GROUND-BASED STUDIES AND KC-135 STUDIES

Full Committee Review: 6 months prior to intended start date.

As a matter of general practice, all JSC human research protocols must show evidence of favorable scientific peer review prior to submission to the JSC CPHS. However, proposals in response to NASA Research Announcement (NRA), Announcement of Opportunity (AO), etc. must follow the schedule imposed by Headquarters and the announced JSC CPHS review schedule.

Expedited Review ("minimal" risk protocols and previously approved "reasonable" risk protocols with minor changes) (Appendix F) may be submitted any time. If you have questions whether a protocol qualifies for expedited review or not, please contact Dr. Charles F. Sawin, JSC CPHS Chairperson, (281) 483-7202 .

- If you require assistance with the completion of the protocol, or have questions regarding the process, please contact Ms. Mary Flores, the JSC CPHS secretary/recorder, at (281) 244-6491. The JSC CPHS Chairperson and the Alternate Chairperson are also available to assist you.

- "NASA/JSC Human Research Informed Consent", JSC Form 1416, the Multinational Space Station Human Research Informed Consent", JSC Form 1418, and "NASA/JSC Human Research Informed Consent for Grants/Other Agreements Where Research is Conducted at Locations Other than JSC" JSC Form 1419 are available on the JSC Internal Home Page "http:www4.jsc.nasa.gov" (without the quotes).

- Investigators may access their digitized images from KC-135 flights via a password-protected system at "http://zerog.jsc.nasa.gov/" (without the quotes).

- Investigators may obtain general information about the KC-135 Reduced Gravity Program and Aircraft Operations at "http://jsc-aircraft-ops.jsc.nasa.gov/" (without the quotes).

- Investigators may access full text of JPG 1700.1H, Safety and Total Health Handbook Policy, Requirements, Instructions and Guidelines at "http:www4.jsc.nasa.gov/safety/Handbook" (without the quotes).

- Research use of drugs for indications not in the package insert is subject to Food & Drug Administration (FDA) restrictions. FDA forms (Appendix M) are also available online and may be accessed at http://www.fda.gov (without the quotes).

- NASA (center-wide) Management Directives, policies and procedures may be accessed through the JSC Internal Home Page Intranet address "http://www4.jsc.nasa.gov (without the quotes) under General Information, go to Management Directives.

- Information associated with the Code of Federal Regulations may be accessed through the following Internet address "http://access.gpo.gov/nara/cfr/index.html" (without the quotes).

LIFE SCIENCES RESEARCH PROTOCOL FORMAT

The format below is to be used during the preparation of the protocol. Deviation from this format will result in the protocol being returned to the Principal Investigator. Number each section as shown.

1.0 COVER PAGE

Each protocol is to have a cover page that contains the following information:

1.1 Spacelab or Shuttle Flight Designation (if applicable)

1.2 Experiment Designation

1.3 Functional Objective Designation(s) (if applicable)

1.4 Title of Project

1.5 Organization Conducting the Research

A. Name the organization conducting the research or for which the research is being conducted. Normally it is the institution with which the Principal Investigator (PI) is affiliated.

B. Research protocols submitted by JSC civil service investigators must include the signature of the authorizing NASA official (Branch or Division Chief).

1.6 Investigators

A. List all investigators starting with the PI. Include each individual's position and affiliation, mailing address, telephone and fax numbers, and e-mail address if available. Attach a curriculum vitae for each investigator as an appendix at the end of the protocol. *The PI must sign the cover page*.

B. List technical personnel who will aid in and/or conduct the research. Attach qualifications as an appendix at the end of the protocol. The JSC CPHS is interested in the qualifications of the technical staff that will be interacting with the test subjects, because they will be operating equipment or performing procedures on them.

C. List any financial interests <u>in companies or entities involving your proposal</u> <u>or research</u> that <u>any of the following</u> have: (1) yourself; (2) your spouse; (3) your minor (under 18 years of age) or dependent children; (4) your general (vice limited) partner; (5) an organization in which you serve as an officer, director, employee, trustee or general partner; or (6) a person or organization with whom/which you are seeking, negotiating, or have an arrangement concerning prospective employment.

Financial interests may include, <u>but are not limited to</u>, the following: (a) stock or stock options; (b) salary or other compensation; (c) employment welfare or benefit plans (e.g., pension, 401 K, retirement, profit sharing, stock bonus, and annuity plans); (d) ownership, partnership, lease, or other property interests; (e) patents, royalties, licenses, or similar interests; (f) bonds; (g) mutual funds; (h) trusts; or (i) liens, loans or indebtedness.

2.0 TABLE OF CONTENTS

All protocols must include a Table of Contents that divides the protocol into major sections identical with those presented in this guideline. Appendices should be numbered or lettered sequentially.

3.0 ABSTRACT

Briefly describe the purpose, general implementation plan, and expected results. This description of the overall project should be a stand-alone summary and should not be more than half a page (500 words).

4.0 HYPOTHESIS(ES)

The hypothesis(es) should be clearly and succinctly stated. The JSC CPHS must consider scientific merit as a factor in weighing risk vs. benefits. This summary should abstract the details to be included in the Section 5.0 below.

5.0 PURPOSE OF RESEARCH

This section may be handled by attachment (as an appendix) of information submitted in the original proposal. However, the investigator should ensure that the following information is included:

Background and Significance - Discuss briefly the development of key factors or principles that lead to the formulation of hypothesis. Reference to pertinent scientific literature is essential. Provide an account of the preliminary studies by the principal investigator or other associated personnel that are pertinent to the proposed study. References and titles of appropriate related publications should be included; reprints (no more than five) may be attached to the protocol.

New Information Expected - Explain the results that may be expected and their relevance to the aforementioned overall goals of the project.

6.0 STATISTICAL ANALYSIS

Describe how the data will be analyzed. Indicate the statistical methods to be used, power of the statistical method, number of subjects required, etc.

7.0 RATIONALE FOR USE OF HUMAN SUBJECTS

Explain why humans are a necessary part of the study. Include a plan for ensuring equitable selection of research subjects with particular reference to race and gender.

8.0 RESEARCH PLAN AND SCHEDULE (FOR ALL STUDIES)

Management Plan - Clearly identify the roles of each of the investigators in reference to the conduct of the study. Include any laboratory or medical support staff required and their responsibilities.

Consultants & Collaborators - Succinctly describe the expertise of consultants and/or collaborators and their responsibilities in the study. Attach a letter of confirmation from each member stating their consent to participate in the project, and in the specified capacity or role.

Data Privacy/Confidentiality - Briefly describe the procedures which you will employ to maintain confidentiality of subject identity and results. Include a plan for ensuring the privacy and protecting the confidentiality of data as required by JMI 1382.5A, with particular attention to electronic databases. Indicate where the information is to be stored, the type of format to be used to store the information, and most importantly, who will have access to the information and under what circumstances. The investigator should also develop a plan for the ultimate long-term archiving at JSC of both raw and reduced data.

Data Sharing - Data and/or specimens may be shared among investigators as specified in each investigator's initial protocol. Identify other investigators with whom you wish to share data/samples. If appropriate, a table summarizing venipuncture and blood volume limits for the investigation should be provided. Values should be consistent with the guidelines in the JSC CPHS Handbook, JSC 20483.

Anomalous Data/Adverse Reactions Reporting – Instructions relating to this topic can be found on page 13, Section 4.8 "Reporting of Adverse Events and Anomalous Data".

Injury/Illness Reporting Plan - Include a plan for reporting any illness or injury of a subject possibly related to the experiment.

SPACEFLIGHT STUDIES

Give an overview of what will be accomplished during preflight training/baseline data collections sessions, in-flight experimentation, and postflight data acquisitions. For example, familiarization with the concepts of the experiment, procedures to be learned, equipment to be used, data collection, etc.

Dates/Duration - Give the expected duration of the study, which will include approximate beginning and ending dates. Provide as close an approximation as possible. Detailed schedules for Spacelab investigations should be included in the Training Protocol.

Place(s) of Training/Test/Baseline Data Collection - List the location(s) where data collection will be performed.

Subjects - Provide flight personnel designation, e.g., Mission Specialist (MS) MS1, MS2, MS3, Payload Specialist (PS) PS1, PS2, PS Backup, Commander (CDR), and Pilot (PLT).

GROUND-BASED STUDIES AND KC-135 STUDIES

State the overall general goals of the project; list specific and realistic objectives the proposed research is intended to accomplish. The relevance of the objectives to the overall goal must be clearly stated.

Study Schedule - Provide an estimate of the study duration, and a tentative start date. Present a timetable that reflects the progression of the study phases described above,

including the dates of the testing. List all of the important milestones for the conduct of the study.

Facilities and Performance Site - Describe all the facilities in which the study will be conducted including any training facilities that will be used.

9.0 EXPERIMENTAL PROTOCOLS AND EQUIPMENT

This section contains some of the most important information used by the JSC CPHS . It is from this section that the JSC CPHS may identify potential problems that might be overlooked by the investigators. Experience has shown that incompleteness of this section is one of the major reasons for JSC CPHS non-approval.

SPACEFLIGHT STUDIES

Preflight Training and Baseline Data Collection - Describe preflight training and baseline data collection in terms of step-by-step procedures and equipment used. All equipment must be identified. In those instances where any hardware is used for training or ground-based testing, the PI is responsible for providing detailed descriptions and hazard analyses as an attachment to the protocol. The PI is also responsible for maintaining configuration control of the hardware to prevent any modifications that would compromise the hazard analyses. Inspection records must be provided to assure the hardware configuration and to assure adherence to test requirements and procedures. Functional test and checkout of equipment utilizing non-flight crew personnel is required. All equipment, whether commercial, modified commercial, or custom designed, used for fit and functional testing, must be inspected by the Safety, Reliability, and Quality Assurance (SR&QA) Office. These results, together with equipment safety certification, must be submitted by the PI to the JSC CPHS prior to flight crew usage.

In-Flight Activities - List step-by step procedures and equipment used, approximate duration of the testing, how many crew subjects are necessary, and how many times the experiment will be performed.

Postflight Activities - If postflight testing of flight personnel is necessary, note how many times the test will be done, when, where, and what procedures and equipment will be used.

Samples - For all activities describe the methods for collection, processing, and disposal of biological samples with particular attention to the handling of radioactive and other hazardous materials.

GROUND-BASED STUDIES AND KC-135 STUDIES

Outline all the details of the experiment design and procedures to be used to accomplish the specific aims of the project. If the study involves more than one phase, or multiple protocols, summarize the interrelation of these component parts here. The description of the design and methods should include the following:

Protocol Design - Describe details of all the methods, materials, and procedures to be employed in the study and their sequencing and frequency. If new methodologies are

proposed, clearly describe them and justify their need by discussing their advantages over currently approved/accepted ones.

Samples - Describe the methods for collection, processing, and disposal of biological samples with particular attention to the handling of radioactive and other hazardous materials.

Equipment - List all the required hardware for conducting the experiment and processing the samples. Include separate lists of ground-based equipment and flight hardware.

10.0 HAZARD ANALYSES AND SAFETY PRECAUTIONS (FOR ALL STUDIES)

Medical Safety Risks and Hazards

- Detail the conceivable hazards that might be encountered during the study and the precautions that will be taken to avoid them. Describe all anticipated hazards from the procedures (especially biological sample collections, new diagnostic procedures and treatments), materials (radioactive substances, etc.), or any other experiment-related conditions, including immediate, delayed, or long-term effects. Include assessment of degree of risk (minimum, reasonable, or high) and proposed acceptable risk-benefit ratio. Make sure to include assessment of residual risk. The sample analysis form (Attachment 1) may be used if desired.

- Describe details of medical intervention procedures in the event of an adverse reaction. Include information on the availability of a physician and medical facilities during and after the study, and post-experiment medical check up requirements, and precautionary measures to avoid any complications (immediate and delayed) that are experiment related.

- If *animals* are used in an experiment, the protocol MUST include:

    - Precautions to be used to maintain the NASA Flight Quality (NFQ) status and tests used to ascertain NFQ status prior to training or flight (if applicable).

    - An assessment of potential biohazards from all experimental animals.

    - A list of precautions employed for minimizing zoonoses for research involving animal handling.

- If *radioactive* materials are administered to subjects in the study, provide evidence of approval by the JSC Radiation Safety Committee. While the same protocol can be undergoing simultaneous review by both committees, final approval from the JSC CPHS will be withheld until evidence of approval by the JSC Radiation Safety Committee has been received.

- For spaceflight studies, include a statement in the protocol such as: "All experiments are to be tested if possible on non-flight-crew personnel prior to each mission."

- For KC-135 studies see instructions for preparation of the required Test Equipment Data Package (Appendix G, section 16.0)

HAZARD ANALYSIS FORMAT

Below is the specific format to be used when preparing hazard analyses and safety plans for any study. This is the same format shown in Attachment 1. For spaceflight and KC-135 studies, preflight, inflight, and postflight hazard analyses should be individually documented according to this same format:

a. POTENTIAL HAZARD CAUSE
b. EFFECTS OF THE HAZARD
c. ASSESSMENT: SEVERITY & PROBABILITY
   Severity categories: Reasonable/Minimal
   Probability categories: High/Medium/Low/Extremely Low
d. PROTECTION TO MINIMIZE RISKS
   Include level of medical coverage required during experimental activities

11.0 POSSIBLE INCONVENIENCES OR DISCOMFORTS TO SUBJECTS

List additional factors that do not fall into the category of hazards, but that should be considered.

12.0 EXTENT OF PHYSICAL EXAMINATIONS

SPACEFLIGHT STUDIES

In many cases, reliance on the annual physical examination for flight personnel is all that need be stated. Include a statement that subjects are flight personnel and their annual physical will be relied upon. If a special physical examination or special test is required, describe it and state why it is needed.

GROUND-BASED STUDIES AND KC-135 STUDIES

- In addition to listing qualifying and disqualifying medical conditions for test subjects, indicate the extent of any physical examinations to be given by medical personnel as follows:

  a. Initially, to ascertain that the subject's health status has been adequately established to certify that the subject is capable of undertaking the research;
  b. During the course of the research (if applicable); and
  c. At the completion of the research (if applicable).

- For KC-135 studies also indicate how requirements for physiological training will be met.

13.0 AVAILABILITY OF A PHYSICIAN AND MEDICAL FACILITIES

SPACEFLIGHT STUDIES

State if a flight surgeon and/or medical facilities will be required preflight, in-flight, or postflight.

GROUND-BASED STUDIES AND KC-135 STUDIES

Indicate the anticipated level of medical monitoring that will be required and the qualifications/certifications required of the physician/medical monitor (section 4.5 of Introduction and Appendix R).

ALL STUDIES

This section should include provisions to pre-screen subjects when possible for hypersensitivity to any administered substances prior to experimentation.

14.0 INFORMED CONSENT

The Principal Investigator has the difficult task of explaining the proposed activity to potential subjects in enough detail and in appropriate language so as to assure that the potential subjects fully understand what they are consenting to and that the consent is based on complete knowledge of the nature and risk of the procedure.

The JSC Committee for the Protection of Human Subjects has the equally difficult task of determining whether or not the consent procedure proposed by the Principal Investigator adequately assures legally informed consent by the subject. The Principal Investigator should consider the following when preparing subject consent:

- Include information concerning human research to be communicated to the subjects in the course of obtaining their informed consent. Along with a signed *NASA/JSC Human Research Informed Consent Multinational Human Research Informed Consent, and/or NASA/JSC Human Research Informed Consent for Grants/Other Agreements Where Research is Conducted at Locations Other than JSC statement,* attach a summary, signed by the subject, describing in layman's terms the procedures the subject will undergo. The detailed layman's summary of the research procedures must specifically list the risks associated with the procedures to be employed, the possible adverse reactions of all medications to be administered, and the risk/hazards resulting from exposure to ionizing radiation. Further, the investigator must clearly specify all forms of subject behavior interdicted by the research protocol (exercise, diet, medications, etc.).

- The subject will be free to withdraw from the research at any time. (Describe any circumstances under which it would be hazardous or unwise to do so).

- The identity of human subjects will not be released to the general public without his or her consent unless specifically required by law.

- There will be no additional wage, salary, or other remuneration of any form paid, given, or in any manner delivered to the test subjects of this investigation where the subjects are National Aeronautics and Space Administration (NASA) employees.

- The human research subjects are NASA employees, NASA contractor employees or independent contractors, and the training/testing is part of their employment or contractual circumstances. Therefore, NASA is responsible for compensation for injury, death, or property damage to the extent required by the Federal Employees Compensation Act or the Federal Tort Claims Act.

- If applicable, include the following statement in the consent, "Since the KC-135 is considered to be a public aircraft within the meaning of the Federal Aviation Act of 1958, as amended, and as such does not hold a current airworthiness certificate issued by the Federal Aviation Administration, any individual manifested to board the KC-135 should determine before boarding whether their personal life or accident insurance provides coverage under such conditions."

- A statement is required if the study involves the use of a drug or device that is still under an investigational new drug (IND) number or investigational device exemption (IDE) number and the records may therefore require inspection by the Food and Drug Administration.

"I have a right to privacy, and all information that is obtained in connection with this study and that can be identified with me will remain confidential as far as possible within state and federal law. Information gained from this study that can identify me will be released to no one other than the investigators, my physician, (insert name of pharmaceutical or medical device company) and the United States Food and Drug Administration, which, through its regulatory powers, may inspect records involving research participants. The results of this study may be published in scientific journals without identifying me by name."

- Include the provision that subjects concerned about protocol violations may request a meeting with the relevant CPHS .

- The subject consent form must identify the activity to be conducted, name(s) and the phone number of the individual(s) who are to conduct the activity and state the purpose of the activity. It must describe any procedures that are deemed to be experimental in nature and indicate the risks attendant thereto. It must also refer to any prior experience gained in human use or state that no prior human use has occurred and indicate the experience gained in human use or state that no prior human use has occurred and indicate the experience which has been acquired in animal studies.

- A statement should be made about expected or potential reactions resulting from all procedures to be performed that are not deemed to be experimental. The benefits, if any, that could accrue from the activity should be described and a statement made as to whether the benefit would accrue to the individual subject or to society in general. Alternative procedures that could be used in lieu of the experimental procedures must be described. An offer to answer any inquires concerning the procedure should be made in writing. Subjects should also be informed in writing that they may discontinue participation in the activity at any time without prejudice.

- If personal data are to be acquired from surveys, questionnaires, or medical records it is necessary to inform the subject of the criteria used by which he or she was selected to be a subject. Describe the purpose for which the data are being collected, indicate any benefits to be gained by the subject's participation in the activity, and state what risks (physical, psychological, or social) or possible detrimental effects that may accrue to the subject.

- When the activity proposes to use healthy subjects, they should be informed that no benefit would be derived from their participation. The inducements offered to a healthy subject should be consistent with the degree of remuneration and shall not unduly influence the subject to participate in the activity.

- If randomization (by chance) is used to select a subject population, subjects must be so informed. If a placebo (inactive agent) is involved, subjects must also be informed that they may receive the experimental modality or a placebo (inactive agent). The consequences of placebo therapy must be explained.

- The investigator should incorporate into the subject consent the length of time required for participation in the activity (whether this is continuous or intermittent), any requirement for follow-up examinations or studies, and whether or not there will be limitations or constraints on the physical activities of the subject after the activity is completed.

- If monitoring procedures are required during the activity, the type, number and frequency of such procedures should be explained and the risks of discomforts of each should be described. If the performance of such procedures will incur additional expenses incurred by participation in the research protocol, this must be explained in the consent form.

REGARDLESS OF THE TYPE OF STUDY, THE INFORMED CONSENT PROCESS SHOULD INCLUDE THE FOLLOWING:

Subject Briefing - Describe all the necessary information concerning the study that will be explained to the subjects at the briefing session. Include a list of personnel that will attend the briefing and the procedures that will be explained or demonstrated at the briefing.

Subject Information Handout - Attach a handout to the consent form that clearly states in simple language all the procedures employed in the study, hazards and risks involved, safety precautions during and after the study, benefits and coverage, subjects' rights and remuneration, and any post-experiment instructions.

Consent Forms - Include the appropriate JSC Form 1416, , 1418, or 1419 required by the JSC Committee for the Protection of Human Subjects that is duly filled with information regarding the study and the investigator. The Subject Information Handout must be attached to the consent form.

Each subject must be given a copy of the consent statement that they have signed as well as any attachments thereto.

15.0 OTHER FUNDING SOURCES

Include a statement regarding any funding source (other than NASA) supporting this research, e.g., NIH, or NSF. Attach a copy of the Single Project Assurance or Multiple Project Assurance, as appropriate. The Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP) maintains information relating to human and animal grant research through the following Internet address "http//ohrp.osophs.dhhs.gov" (without the quotes).

16.0 ADDITIONAL ATTACHMENTS TO LIFE SCIENCES RESEARCH PROTOCOL

ALL STUDIES

- Curriculum vitae (all Investigators)
  Qualifications for Technical Personnel

- Approval letter from the PI's Institutional Review Board (Human Research or Ethics Committee)

- Evidence of favorable scientific peer review (i.e., Approval letter)

- A copy of the Institutional Safety Authority's most recent certification of all related equipment

- Research use of drugs for indications not in the package insert is subject to Food & Drug Administration (FDA)-approved drugs for indications not in the package insert, as well as investigational new drugs (INDs), are subject to FDA restrictions. FDA forms are available online and may be accessed at http://www.fda.gov" (without the quotes) and are to be submitted as attachments to the Life Sciences Research Protocol (Appendix G).

- If applicable, approval from one of more of the following committees:

  - JSC Radiation Safety Committee
  - Medical Isotopes Operations Subcommittee of the JSC Radiation Safety Committee
  - Payload Safety Review Panel
  - Safety, Reliability, & Quality Assurance

- If external radiation sources or radionuclides are employed at JSC, their use must have the approval of the JSC Radiation Safety Committee. Attach a copy of JSC Form 1942 or JSC Form 1944 (Appendix I). In addition, the following forms must be completed as appropriate: JSC Forms 44, 44a, 44b, 44c, 44d, 44e, 44f, and 44g (Appendix I).

KC-135 STUDIES

General information about the KC-135 Reduced Gravity Program and Aircraft Operations may be obtained by internet access "http://jsc-aircraft-ops.nasa.gov/" (without the quotes) or by contacting the JSC Reduced Gravity Office at 281-244-9809. Investigators wishing to conduct life science related experiments or hardware evaluations on the KC-135 should contact Mr. Noel Skinner at 281-244-5163. Digitized images from the KC-135 flights may be accessed via a password-protected system at "http://zerog.jsc.nasa.gov/" (without the quotes).

A Test Equipment Data Package (TEDP) must be submitted to the JSC Reduced Gravity Office at least 6-weeks prior to KC-135 flights. This package must include the test plan, engineering drawings and schematics, structural analysis, electrical load analysis, and hazard analysis (Appendix G, section 10.0). The test plan should contain the following:

a. Synopsis
b. Test objectives
c. Test description
d. Equipment description (narrative, drawing, schematics, photographs, block diagrams, etc.)
e. Structural load analysis
f. Electrical load analysis (if applicable)
g. Pressure vessel certification (if applicable)
h. In-flight test procedures (checklist type is required)
i. Parabola requirements, number, and sequencing
j. Test support requirements; ground and flight
k. Data acquisition system
l. Test operating limits or restrictions
m. Proposed manifest for each flight
n. Photographic requirements
o. Hazard analysis (Appendix G, section 10.0)
p. Safety certification (if applicable)

17.0 PROTOCOL COMPLETION CHECKLIST

It is the responsibility of the PI to verify that all required information has been included in the protocol. A checklist has been developed to help eliminate possible confusion regarding the content of a protocol (Appendix G, Attachment 2). Protocols will not be accepted by the JSC CPHS without a completed, signed checklist.

ANALYSIS OF POTENTIAL HAZARDS

TITLE: _____ PAGE_____OF _____
RESPONSIBLE PERSON(S) _____DATE _____

NO.	POTENTAL HAZARD	CAUSE	EFFECT	ASSESSMENT SEV: REAS/MIN PRB: H/M/L/EL	PROTECTION TO MINIMIZE RISKS

PROTOCOL COMPLETION CHECKLIST

1.0	COVER PAGE (signed by PI)	_____
2.0	TABLE OF CONTENTS	_____
3.0	ABSTRACT	_____
4.0	HYPOTHESIS(ES)	_____
5.0	PURPOSE OF RESEARCH	_____
	Copies of Reprints/Supporting Information	_____
6.0	STATISTICAL ANALYSIS	_____
7.0	RATIONALE FOR USE OF HUMAN SUBJECTS	_____
8.0	RESEARCH PLAN AND SCHEDULE	_____
	Expected Study Duration & Location	_____
	Confirmation Letter(s) from Consultants/Collaborators	_____
	Protection Plan for Personnel and Medical Data	_____
	Data Sharing Plan	_____
	Venipuncture Plan (pre, in-, and post)	_____
	Anomalous Data/Adverse Reaction Reporting Plan	_____
	Injury/Illness Reporting Procedures	_____
9.0	EXPERIMENTAL PROTOCOLS AND EQUIPMENT	_____
	Hardware Description/Hazard Analysis	_____
	Protocols and procedures	_____
	Flight Training Protocols	_____
	Flight Crew Procedures	_____
10.0	HAZARD ANALYSIS/SAFETY PRECAUTIONS	_____
	Description of all Medical Risks	_____
11.0	INCONVENIENCES OR DISCOMFORTS TO SUBJECTS	_____
12.0	EXTENT OF PHYSICAL EXAMINATIONS	_____
13.0	AVAILABLITY OF PHYSICIAN AND MEDICAL FACILITIES	_____
14.0	INFORMED CONSENT	_____
	Human Research Informed Consent	_____
	Summary of Risk In Layman's Terms	_____
	Statement of Insurance for Subjects	_____
	Subject withdrawal policy	_____
	Subject payment and source of funds	_____
15.0	OTHER FUNDING SOURCES	_____
	Copy of SPA or MPA sent to NIH (if required)	_____
16.0	ATTACHMENTS TO LIFE SCIENCES PROTOCOL	_____
	Curriculum vitae (all Investigators)	_____
	Qualifications for Technical Personnel	_____
	IRB Approval from PI's Institution	_____
	Human Subject Training Certification	_____
	Other JSC Committee Reviews and Approvals	_____
	FDA Forms	_____
	KC-135 Test Equipment Data Package (if applicable)	_____

APPENDIX H

Training/Baseline Data Collection Protocol

Spaceflight Designation: _____
Training Session #: _____
Location of Training: _____
Dates of Training: _____
Subjects: _____

1. Title

2. Organization Conducting the Research

3. Investigator and Technical Personnel

List the name of the Principal Investigator and technical personnel. Information such as addresses, and telephone numbers must be included. Changes in investigator and/or personnel status must be indicated.

4. Objectives of the Tour

State the objectives of the session. Include background history as well as any information relevant to the activity.

5. Training Activity Schedule

Include step-by-step procedures. Changes must be identified with the appropriate changed sections indicated by bars in the margins.

6. Hazard and Safety Analyses

Include the hazard and safety analyses for the equipment to be used.

7. Consent Form and Layman's Summary

Include the consent form as well as the layman's summary of the experiment.

8. Additional Attachments

- Safety certificates (e.g., inspection and certification of ground-based equipment).
- Equipment calibration record.
- Institutional Review Board approval letters from host institutions.
- CVs of technical support personnel.

APPENDIX I

Guidelines for Radionuclide Use in Space Flight Payloads

The large number of permutations of radionuclide type, amount, chemical and physical form, and degree of containment requires that each experiment involving radionuclides be evaluated on its own merit. Nonetheless, some general guidelines can be set forth. These guidelines are not hard and fast and may be waived if other safety features or procedures are deemed adequate.

1. No payload containing radioactive material or other sources of ionizing radiation shall create a situation whereby:

a. Radiation levels which, if an individual were continuously present in the area, could result in the individual's receiving a dose in excess of 2 millirems in any 1 hour, or

b. Radiation levels which, if an individual were continuously present in the area, could result in the individual's receiving a dose in excess of 50 millirems in a 365-day period.

2. No payload or experiment, by design, shall cause quantities of radioactive material to be released into an occupied space which could result in uniform air concentrations in excess of the values as specified as part of the Nuclear Regulatory Rules and Regulations 10 CFR Part 20 Subpart B. For calculation purposes, the volume of the crew compartment is 65 m^3 and that of the Spacelab is 77 m^3.

   The maximum permissible dose and the maximum permissible concentrations of radionuclides as recommended are primarily for the purpose of keeping the average dose to the individual members of the public as low as reasonably achievable (ALARA) and not because of the likelihood of specific injury to an individual.

   The annual occupational dose limit for radiation workers are: 5 rems for the total effective dose equivalent; 50 rems for the sum of the deep-dose equivalent to any individual organ or tissue other than the lens of the eye; 15 rems to the lens of the eye; and 50 rems to the skin or any extremity as shallow-dose equivalent. The ALARA principle should be applied to all experimental design.

   In no case should the accumulated occupational dose from radioactive material and external radiations to any crewmember exceed the monthly, annual, or career dose limits accepted by NASA.

3. General rules for safe use of radioactive materials shall be followed:

   - Wear disposable gloves and a surgical-type mask at all times while handling radioactive liquids or powders. The gloves should prevent contamination of the hands and a mask should reduce chances of inhalation and/or ingestion.

   - Do not eat or drink in any area where radioactive material is being used.

   - Wipe all work surfaces after use of radioactive materials.

- Practice good personal hygiene habits by always thoroughly cleaning hands after handling radioactive sources.

- Never mouth-pipette liquids containing radioactive materials. To the maximum extent possible minimize handling and transfers of radioactive materials in flight.

- Dispose of radioactive waste only in specifically designated receptacles that are properly shielded and labeled.

- Confine radioactive solutions, specimens, powders, and waste in double containment, plainly identified and labeled. Containment must be leakproof and puncture resistant. (Hood, glove box, or vented workbench could be considered one of the containers, but not stowage bins.)

- All transfers of radioactive liquids should be accomplished by the "buddy system." The individual performing the transfer will be assisted by an assistant to catch or trap droplets, aerosols, etc., with absorbent material to ensure that no trap droplets or aerosols are released in the occupied areas.

4. Contingency plans for all conceivable off-nominal situations shall be developed and tested.

5. Individuals trained in Health Physics shall be involved with the stowage, the post-mission handling of payloads utilizing radioactive materials capable of producing radioactive contamination, and post-mission survey for contamination of the spacecraft.

Adherence to the guidelines is important for radiological protection of the operator and other crewmembers in the Spacelab or crew compartment. Moreover, such adherence is important in minimizing contamination buildup in the spacecraft which can interfere with other investigators' experiments.

Table 1. Magnitude of Radioactive Releases

EVENT (NUMBER)	LOCATION	YEAR (S)	CURIES RELEASED (TOTAL)	ISOTOPES	RISK (FATAL CANCERS)
Chernobyl	Ukraine, Soviet Union	1986	950,000 1,900,000 17,000,000	Cs-234; Cs-137; I-131	17,400 expected/ 2.9 billion exposed
Household radon	United States	Lifetime	N/A	Ra-222	14,000 per year expected/240 million
Atomic weapons testing (atmospheric)	Worldwide	1945-1980	~26 million (Cs-137); ~18 million (Sr-90); ~19 billion (I-131); ~6.5 billion (H-3); ~6 million (C-14)	Cs-137; Sr-90; I-131; H-3; C-14	12,000 expected/ 5 billion
First A-bombs	Hiroshima & Nagasaki,	1945	~250,000,000	short-lived fission	300 estimated/ 76,000 tracked

	Japan			products	
Early Hanford operations	Hanford, Washington	1945-1947	700,000	I-131	~1.6 cases of thyroid cancer expected/ 3,200
Three Mile Island	Harrisburg, Pennsylvania	1979	15 10,000,000	I-131; noble gases	0.7/2 million exposed
RaLa tests (254)	Los Alamos, New Mexico	1944-1962	250,000	La-140	0.4 cases/ 10,000 exposed
Green Run	Hanford, Washington	1949	8,000 20,000	1-131; Xe-133	0.04 expected/ 30,000 exposed
RW field tests (65)	Dugway, Utah	1949-1952	13,000	Ta-182	Unknown

Table 1, minus all footnotes, was reprinted from: Final Report – Advisory Committee on Human Radiation Experiments, October 1995, Chapter 11, Part II, p.534 (Pittsburgh: US Government Printing Office).

Table 2. Examples of Common Radiation Exposures

Radiation Exposure Source	Approximate Dose (rem)
Transcontinental Round Trip, Jet (New York – London; 37,000 ft)	0.004
Chest X-ray (Lung Dose)	0.010
Living One Year in Houston	0.100
Living One Year in Denver	0.200
Xeromammography (Breast Dose)	0.100
Barium Enema (Intestinal Dose)	0.875
Living One Year in Kerala India	1.300
Maximum Allowable in One Year to an Earth-based Radiation Worker	5
Maximum Allowable in One Year to a Space-based Radiation Worker	50

Table 3. Chest X-ray Standards

(Aviator Standards)

AGENCY	FREQUENCY OF CXR EXAM
NASA (Class I, II, III)	Every 5 years
Navy (Service Grade 1)	Age 21, 24, 27, 30, 36, 39, and annually at 40 and older
Air Force (Class I, II, III, ACC)	Only when clinically indicated
Army FAA (Class 1, II, III)	Only when clinically indicated
Russian Military	Every year (ref: Oleg Ryumin, MD)
Russian Cosmonauts	Every year (ref: Oleg Ryumin, MD)
US Previous Service Task Force	Not recommended as screening method for asymptomatic patient
American Cancer Society	Not recommended as screening method for asymptomatic patient

Table 4. Chest X-ray Doses at JSC Clinic

TYPE	DOSE	WHOLE BODY DOSE EQUIVALENT
PA; 90-100 kVp	4-8 mrem	Male: 1.64 mrem Female: 1.08 mrem
Lateral; 120-125 kVp	13-30 mrem	Male: 5.77 mrem Female: 3.61 mrem
Average dose	17 mrem	

IV. TEST DATA	
DATA SOURCE LEAK TESTED	RESULTS (MICROCURIE)
THERMO-VACUUM QUALIFIED TO: _____ MM Hg _____ DEGREE C.	DATE

V. PRE-FLIGHT TRANSFERS		
LOCATIONS WHERE SOURCE IS TO BE USED OR STORED AND APPROXIMATE DATES		
LOCATIONS	DATED FROM:	TO:
SOURCE CUSTODIAN/RADIATION SAFETY OFFICER	TELEPHONE	

VI. POST-FLIGHT DISPOSITION
OUTLINE REQUIREMENTS

PART B. IONIZING RADIATION PRODUCING EQUIPMENT

I. EQUIPMENT CHARACTERISTICS		
TYPE OF RADIATION PRODUCED		
MAXIMUM ENERGY LEVEL	OPERATING ENERGY LEVEL	
DURATION OF OPERATION _____ HOURS TOTAL, ALL UNITS	NO. OF UNITS	PULSED UNIT DUTY CYCLE

II. RADIATION CHARACTERISTICS		
RADIATION INTENSITY OF FLIGHT CONFIGURED UNIT	SECONDARY RADIATIONS PRODUCED	
	ENERGY LEVEL	TYPE
_____ RAD/HR @ _____ METERS	_____ KeV	

III. EQUIPMENT USE DATA	
CREW INVOLVEMENT/PROCEDURES	
RADIATION PRODUCTION WARNING SYSTEM ☐ YES *(Describe)* ☐ NO	SAFETY INTERLOCK SYSTEM ☐ YES *(Describe)* ☐ NO

RADIO FREQUENCY/MICROWAVE HAZARD EVALUATION DATA

(PLEASE TYPE OR PRINT LEGIBLY)

NAME	ORGANIZATION/MAIL CODE	DATE	REFERENCE NO.

I. SYSTEM DESCRIPTION

A. SYSTEM DESIGNATION	B. TYPE OF SYSTEM	C. LOCATION OF USE	QUANTITY

D. SYSTEM CHARACTERISTICS/CAPABILITIES

1. Fixed, mobile or temporary system: _____
2. Size, type, and quantity of antennas: _____
3. Height above occupied areas: _____
4. Azimuth capability: _____
5. Elevation capability: _____
6. Azimuth stops: _____
7. Elevation stops: _____
8. Type transmission lines: _____
9. Qty. and type power tubes: _____
10. Peak voltage to tubes: _____
11. Interlocked doors to H.V. Cab: _____
12. Frequency capability: _____

E. OPERATING PARAMETERS (Indicate parameters used for normal operations)

1. Continuous or pulsed emission: _____
2. Pulse width(s): _____
3. Pulse repetition frequency: _____
4. Pulse code: _____
5. Maximum rated duty cycle: _____
6. Normal operating frequency: _____
7. Peak power to transmitter: _____
8. Insertion loss (transmitter to antenna): _____
9. Antenna gain: _____
10. Type of illumination: _____
11. Beam width/skew: _____
12. Polarization of transmitted wave: _____
13. Scan rate (RPM): _____
14. Estimated hazard distance (meters): _____

II. AREA DESCRIPTION

A. Bldg. no: _____ Room no.: _____

B. Site plans: _____

C. System drawings: _____

D. Adjacent areas/facilities: _____

(Submit copies as attachments)

III. PROCEDURES

A. Operating procedures: _____

B. Accident/emergency proc.: _____

C. Maintenance procedure: _____

D. Brief description of project: _____

(Submit copies as attachments)

IV. SYSTEM USERS

A. User org.: _____ B. Maint. org.: _____

C. Area radiation officer: _____

V. PERIOD OF USE

From: _____ To: _____

VI. RADIATION PROTECTION REQUIREMENTS

- ☐ Accountability
- ☐ Compliance with ACGIH TLV's
- ☐ Compliance with JPD 1860.4
- ☐ Other

VII. REVIEW

(Radiation Safety Use)

Additional Information Required: Yes _____ No _____ Date Received: _____

Disposition: _____

JSC Radiation Safety Officer Signature	Recommend ☐ Approval ☐ Disapproval	Date:
JSC Radiation Safety Committee Chairperson Signature	☐ Approved ☐ Disapproved	Date:

JSC Form 44A (Rev May 96) (MS Word May 96)

LASER/OPTICAL DEVICE HAZARD EVALUATION DATA

(Please type/print legibly)

Name	Mail Code	Date	Reference No.

I. LASER DESCRIPTION

A. Type of Laser Media	B. Manufacturer	C. Model No. and Year	D. Serial No.	E. ANSI Class

F. Emission Characteristics *(Use supplemental sheets as needed)*

Mode of Operation	Peak Power	Pulse Width Sec.	PRF	Wavelength(s)*	Max. Exposure Time	Beam Dia. @ i/e (cm)	Beam Div. @ i/e (rad)

*For multiple wavelength lasers, specify power levels of individuals wavelength

II. OPTICAL DEVICE DESCRIPTION

A. Type Device	B. Manufacturer	C. Model No. and Year	D. Serial No.

E. Operating characteristics (including power output, wavelength(s), dimensions associated with optics where applicable, etc.)

III. AREA DESCRIPTION

A. Location: _____

B. Site Plans: _____

C. System Drawings: _____

D. Adjacent Areas/Facilities: _____

(Submit copies as attachments)

IV. PROCEDURES

A. Operating Procedures: _____

B. Accident/Emergency Proc.: _____

C. Maintenance Procedure: _____

D. Brief Description of Project: _____

(Submit copies as attachments)

V. HAZARD ANALYSIS

A. ANSI MPE: _____ B. Eyewear O.D. Required: _____

C. @ Wavelength: _____

D. Estimated Hazard Zones: Direct Beam: _____ m Lens: _____ m

Diffuse: _____ m Other: _____ m

VI. SYSTEM USERS

A. User Org.: _____

B. Maint. Org.: _____

_____

VII. RADIATION PROTECTION REQUIREMENTS

- ☐ Accountability
- ☐ Compliance with Am. Nat'l. Standards Institute (ANSI)
- ☐ Safety Levels
- ☐ Compliance with JPD 1860.4

VIII. REVIEW

Additional Information Required: ☐ YES ☐ NO Date Received: _____

Disposition: _____

JSC Radiation Safety Officer	Recommend ☐ Approval ☐ Disapproval	Date:
	☐ Approved ☐ Disapprove	Date:

JSC Form 44B (Rev May 96) (MS Word May 96)

WORKSHEET FOR TISSUE DOSES FROM RADIOPHARMACEUTICALS

This form is to be used for each radionuclide and individual receiving radiopharmaceuticals. For reference information see Report 53 of the International Commission on Radiological Protection, *Radiation Dose to Patients from Radiopharmaceuticals*. Annals of the ICRP, Vol 18(1-4), 1987.

Principal Investigator and Address	Radiopharmaceutical

Brief Title of Study

Tissue	Absorbed dose per unit activity (mrad/microcurie) or (mGy/MBq)	Total radioactivity administered (microcurie) or (MBq)	Tissue absorbed dose (mrad) or (mGy)
Adrenals			
Bladder			
Bone			
Breast			
Stomach			
Small intestine			
Upper large intestine			
Lower large intestine			
Kidneys			
Liver			
Lungs			
Ovaries			
Pancreas			
Red marrow			
Spleen			
Testes			
Thyroid			
Uterus			
Skin			
Eyes			
Effective dose equivalent			

JSC Form 44C (Rev May 96) (MS Word May 96)

WORKSHEET FOR TISSUE DOSES FROM DIAGNOSTIC X-RAY EXAMINATIONS

This form is to be used for each projection and view to be performed on each individual. For reference information see HHS Publication (FDA) 89-8031, *Handbook of Selected Tissue Doses for Projections Common in Diagnostic Radiology*, Center for Devices and Radiological Health, Rockville, Maryland 20857.

Principal Investigator and Address	Projection and View

Brief Title of Study

Tissue	Skin entrance exposure (R)	Tissue dose (mrad) or (mGy)
Adrenals		
Bladder		
Bone		
Breast		
Stomach		
Small intestine		
Upper large intestine		
Lower large intestine		
Kidneys		
Liver		
Lungs		
Ovaries		
Pancreas		
Red marrow		
Spleen		
Testes		
Thyroid		
Uterus		
Skin		
Eyes		
Effective dose equivalent		

JSC Form 44D (Rev May 96) (MS Word May 96)

RADIOPHARMACEUTICAL HUMAN USE INFORMATION FORM

Organization	☐ New Request ☐ Modification	Date prepared
Title or brief description of project		
Name and address of principal investigator	U.S. N.R.C. and/or state license no.	☐ Yes ☐ No Authorized to use proposed nuclides with given license?
Name and license of attending physician	License expiration date	☐ Yes ☐ No Has the use of non-radioactive materials been investigated?

Pre-flight Usage

Radionuclide	Compound	Activity (microcurie) per injection/dose	Number of administrations per subject	Total dose per astronaut/ test subject (microcurie)	Location (NASA Center, bldg. no., room) and frequency or flight-days of usage (ex: L-90)

In-flight Usage

Radionuclide	Compound	Activity (microcurie) per injection/dose	Number of administrations per subject	Total dose per astronaut/ test subject (microcurie)	Flight days, mission elapsed time (MET) and usage location on orbiter

Post-flight Usage

Radionuclide	Compound	Activity (microcurie) per injection/dose	Number of administrations per subject	Total dose per astronaut/ test subject (microcurie)	Location (NASA Center, bldg. no., room) and frequency or flight-days of usage (ex: R+2)

JSC Form 44E (May 96) (MS Word May 96)

RADIOPHARMACEUTICAL UNIT DOSAGE RECEIPT AND USE LOG

Authorized User: _____

Study: _____ Radiopharmaceutical: _____

Date Received	Supplier	Lot No.	Dosage (microcurie)	Label Time	Date Dispensed	Time Dispensed	Measured (microcurie)	Subject	Init.

JSC Form 44F (May 96) (MS Word May 96)

RADIOPHARMACEUTICAL MULTIDOSE VIAL PREPARATION AND USE LOG

Authorized User: _____

Study: _____ Radiopharmaceutical: _____

Date Prepared	Time	Date Generator Received	Kit Manufacturer	Kit Lot No.	microcurie/cc	cc	Measured (microcurie)	Subject	Init.

JSC Form 44G (May 96) (MS Word May 96)

RADIOACTIVE MATERIAL USE AUTHORIZATION			REF. NO.
Request Originator *(Please Type)*	Organization	☐ New Request ☐ Modification	Date

1. Description of Proposed Use *(Additional information may be attached.)*

2. Written Procedures and Safety Precautions *(Submit as an attachment.)*	3. Completion Date

4. Location of Use

a. Site ☐ JSC ☐ WSTF ☐ Other	b. Building	Room

If other, submit data for the site location, written authorization, and a copy of its license, if available.

c. Laboratory

d. Will radioactive waste be generated? (If yes, attach the WASTE PROFILE)	☐ Yes	☐ No
e. Will this proposed use generate airborne radioactive material?	☐ Yes	☐ No
f. Is radiation monitoring equipment accessible to the users?	☐ Yes	☐ No

5. Radioactive Material Requirements

a. Element and Isotope	b. Millicurie Activity per Experiment	c. Physical Form			d. Leak test required?		e. Maximum Amount at one time. Millicurie(s)
		solid	liquid	gas	Yes	No	

6. Submit a JSC 1944, Radiation User Approval form for each proposed user.

7. Area Responsible User	a. Area Responsible User Signature	b. Telephone No.	c. Mail Code

8. NASA Technical Manager or NASA Supervisor Signature	a. Title or Position	b. Telephone No.

9. JSC Radiation Safety Committee Action	Date

☐ Approved ☐ Approved, Subject to Conditions Noted in Item 10 ☐ Disapproved

JSC Radiation Safety Committee Chairperson Signature	Radioactive Material Use Authorization Expiration Date

10. This Use Authorization shall be subject to all applicable rules, regulations, and orders of the JSC Radiation Safety Committee now or hereafter in effect along with the specified below:

a) Standard Conditions
(1) The responsible authorized user shall insure compliance with JPD 1860.2, Radiological Health Manual, and with the statements and procedures contained within this request.
(2) Additionally, the responsible authorized user shall provide for the security and control of the radioactive material and for training of radiological health and safety precepts to each individual using such radioactive material

b) Special Conditions (Required by the Radiation Safety Committee): _____

INSTRUCTIONS FOR JSC FORM 1942

Reference Number: Leave blank. To be filled in by Radiation Safety Office.

Request Originator and Organization: Self-explanatory.

New Request: Initial submittal or major rewrite.

Modification: For renewal or minor changes in users, location, etc.

1. Title and objective of project.

2. Include special techniques, safety precautions, labeling and safe practice statements along with the inhouse training and posting information to be made available to area employees conducting this task. The following should be considered:

Are general procedures written and posted?
Are emergency procedures written and posted?
What are the methods of containment (hoods, spill trays, absorbents, work surfaces, floors, etc.)?
What is estimated waste activity/gram of media? How is the waste to be handled and documented?
Is there controlled access to use area?
What are the proposed training and requirements for assistants and peripheral personnel?
What considerations are given to women of child-bearing age and pregnant women?

3. Enter date if one-time only. For a continuous operation, enter the day's date plus one year.

4a. *Other* refers to temporary job site. Does not include buildings leased or located outside JSC or White Sands location fences. The use of temporary job sites requires advanced written approval from that location's management. If the job site has a state or federal license for radioactive material, so note.

4b. If multiple locations, list all.

4c. Required only if the proposed use is for radioisotopes in liquid form. Consult with the Radiation Safety staff to determine the proper classification for the laboratory or use location.

4d. If yes, attach a waste profile identifying any EPA-classified hazardous waste, and a summation of total activity with a separate breakdown of microcuries/grams of material.

5a. List all isotopes needed.

5b. How much activity will be utilized per each one-time use?

5c. If different for each isotope, identify each form as gas, liquid, sealed, plated, powder, solid.

5e. What is the maximum activity the area will contain at any one time, for each isotope? This total should include stock solutions in the area.

6. Attach a Radiation User Approval form (JSC Form 1944) for each person who will use or handle the radioactive material. The JSC Radiation Safety Committee will review each application to determine if the requester qualifies as an "authorized user". Each "authorized user" must have a minimum of a B.S. degree and 40 hours of radiation safety training, or equivalent job-related experience and training. Training must include the use of radiation detection instrumentation, and the biological hazards of exposure to radiation appropriate to the types and forms of radioactive materials requested. Additional requirements are identified in the Code of Federal Regulations 10 CFR Part 35.910, when radiopharmaceuticals are to be administered to human subjects.

7. Area Responsible User - refers to the individual that will be responsible for overall compliance with the requirements set forth by the JSC Radiation Safety Committee's approval of this Radioactive Material Use Authorization request.

a. Area Responsible User signature
b. Telephone number of the Area Responsible User
c. Mail Code of the Area Responsible User

9-10. Leave blank.

All questions should be directed to SD23/Radiation Safety Office, Building 229, Extension 37082.

RADIATION USER APPROVAL

Please Type

Name _____ Telephone Number _____

Employer _____ Mail Code _____

Proposed Radiation Use _____

List Isotopes _____ Total Activity (millicuries) _____

RADIATION TRAINING

	FORMAL	INFORMAL	NO. OF HOURS	LOCATION
1. Principles and practices of radiation protection.	☐ Yes ☐ No	☐ Yes ☐ No	_____	_____
2. Radioactivity measurements standardization and monitoring techniques and instruments.	☐ Yes ☐ No	☐ Yes ☐ No	_____	_____
3. Biological effects of radiation.	☐ Yes ☐ No	☐ Yes ☐ No	_____	_____

Have you had forty hours of radiation training? ☐ Yes ☐ No Are you an M.D.? ☐ Yes ☐ No

EXPERIENCE

(Check applicable area(s))

An "authorized user" on license no. _____ ☐ NRC ☐ State ☐ Certified in medical X-ray

☐ Administered isotopes to humans ☐ Used radiation monitoring equipment

☐ X-ray machine(s) ☐ Radioactive material ☐ College lab isotopes ☐ Multi-Curie sources

☐ Certified in radiography ☐ Radiation exposure limits ☐ Gas chromatography source(s)

☐ Other Explain _____

Nuclide(s) _____ Amount Curie(s) _____ X-ray Equipment Output kvp _____

Purpose _____

Location(s) _____

Duration _____

I certify that I have read the following:

1. NRC Regulations, Parts 19 and 20, and OSHA 1910.96
2. Radiological Health Manual. (JPG 1860.2)
3. Local Procedures and Methods of Control.

Date _____

Signature _____
(Requester)

JSC Radiation Safety Committee Action:

Approved ☐ Yes ☐ No

Date _____

Signature _____
Chairperson, JSC Radiation Safety Committee

Special Conditions _____

Attach additional information if necessary

JSC Form 1944 (May 96) (MS Word May 96)

APPENDIX J

National Aeronautics and
Space Administration
Lyndon B. Johnson Space Center
2101 NASA Road 1
Houston, Texas 77058-3696

JSC COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS (CPHS) PRINCIPAL INVESTIGATOR REQUEST TO RENEW APPROVAL OF HUMAN RESEARCH PROTOCOL

Use this form only to request annual renewal of an existing protocol. All information must be typed.

RESEARCH PROGRAM: _____

PREVIOUS JSC-CPHS APPROVAL PERIOD FROM: _____TO _____

TITLE OF RESEARCH PROTOCOL: _____

JSC-CPHS CONTACT: Ms. Mary Flores E-MAIL: Mary.p.flores1@.jsc.nasa.gov
TELEPHONE: (281) 244-6491 FAX: (281) 212-1210
MAIL CODE: WYLE/SA ADDRESS: Wyle Laboratories
1290 Hercules, Suite 120
Houston, TX 77058

_____

INVESTIGATOR(S): _____ E-MAIL: _____
TELEPHONE: _____ FAX: _____
MAIL CODE: _____ ADDRESS: _____
DIVISION: _____ _____

JSC COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS (CPHS)
PRINCIPAL INVESTIGATOR REQUEST TO RENEW APPROVAL OF HUMAN RESEARCH PROTOCOL

_____

SPONSOR: (funding source): _____

What is the total number of test subjects needed to complete the entire study _____

Is this research project still enrolling subjects: ( ) YES ( ) NO
If no, when did enrollment end? _____

Total number subjects enrolled in study to date: Male ____ Female ____
Total number subjects who have completed the study to date: Male ____ Female ____

How many subjects did you enroll during the last review period? Male _____ Female ____

Number of withdrawals to date: _____

General reason(s) for withdrawals to date: _____

Number of adverse events to date:_____

Summary of all adverse events:_____

_____

_____

Preliminary results of study: _____

_____

_____

_____

JSC COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS (CPHS)
PRINCIPAL INVESTIGATOR REQUEST TO RENEW APPROVAL OF HUMAN RESEARCH PROTOCOL

Since the last approval, have there been additions or deletions of co-investigators that have not already been communicated to the Board? ( ) YES ( ) NO
If yes, list:

REQUIRED ATTACHMENTS

Consent Form(s)
- Consent Form from Principal Investigator's Home Institution
- NASA/JSC Human Research Informed Consent Form (Form 1416) – (To be Used for Shuttle Flight and Ground-based Studies)
- Multinational Space Station Human Research Informed Consent (Form 1418) – (To be Used for International Space Station Flight Studies)
- NASA/JSC Human Research Informed Consent for Grants/Other Agreements Where Research is Conducted at Locations Other than JSC (Form 1419) – (To be Used for NASA Grant Studies)

Layman's Summary/Subject Information Handout
- A detailed description of the investigation to be written in layman's terms that the subject understands of the procedures required of their participation and the risks associated therewith

Progress Report
- A report that provides the status/progress of the research project

Budget
- A copy of the remaining budget for the project

Conflict of Interest
- Principal Investigators must provide a signed conflict of interest statement that discloses any potential conflicts of financial interest that they have or that are imputed to them in connection with their proposal or research. This statement must be written on letterhead from the Principal Investigator's host institution

_____ _____
Signature of Principal Investigator Date

_____ _____
Office Chief Date

APPENDIX K

NASA/JSC HUMAN RESEARCH INFORMED CONSENT

1. I, the undersigned, do voluntarily give my informed consent for my participation as a test subject in the following research study, test, investigation, or other evaluation procedure:

NAME OF INVESTIGATION _____

_____

FLIGHT TO WHICH ASSIGNED _____

PRINCIPAL INVESTIGATOR _____

RESPONSIBLE NASA PROJECT SCIENTIST_____

I understand or acknowledge that:

(a) This procedure is part of an investigation approved by NASA.

(b) I am performing these duties as part of my employment with _____.

(c) This research study has been reviewed and approved by the JSC Committee for the Protection of Human Subjects (CPHS) which have also determined that the investigation involves_____ risk to the subject.
(minimal or reasonable)

(d) Definitions:

"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

“Reasonable risk” means that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but that the risks of harm or discomfort are considered to be acceptable when weighted against the anticipated benefits and the importance of the knowledge to be gained from the research.

“Protected Research Data” means that the individually identifiable research data maintained or shared will be protected.

(e) The research procedures were explained to me prior to the execution of this form. I was afforded an opportunity to ask questions, and all questions asked were answered to my satisfaction. A layman's description was provided to me. **

(f) I am medically qualified to participate in the investigation.

(g) I know that I can refuse to participate in the tests at any stage of their performance, and my refusal will be honored, except in those cases when, in the opinion of the responsible physician, termination of the tests could have detrimental consequences for my health and/or the health of the other subjects. I further understand that my withdrawal or refusal to participate in this investigation will not result in any penalty or loss of benefits to which I am otherwise entitled.

(h) In the event of physical injury resulting from this study and calling for immediate action or attention, NASA will provide or cause to be provided, the necessary treatment. I also understand that NASA will pay for any claims of injury, loss of life or property damage to the extent required by the Federal Employees Compensation Act or the Federal Tort Claims Act. My agreement to participate shall not be construed as a release of NASA or any third party from any future liability, which may arise from, or in connection with, the above procedures.

(i) Except as provided for by Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of my participation as a research subject in this study shall be maintained so that no data may be linked with me as an individual. I understand, however, that if a "life-threatening" abnormality is detected, the investigator will notify the JSC Flight Medicine Clinic and me. Such information may be used to determine the need for care or medical follow-up, which, in certain circumstances, could affect my professional (flight) status.

Signature:		Signature:	
_____		_____	
Test Subject	Date	Witness	Date

2. I, the test subject, do further understand that the responsible Principal Investigator for the research investigation for which I am participating, must meet the following elements as a condition for valid authorization for disclosure of my protected research data:

(a) Provide specific and meaningful description of the types of information to be used or disclosed.

(b) Identify the person(s) or class of persons who will be allowed the use of my protected research data.

(c) Identify the person(s) or class of persons to whom the research institution may release my protected research data.

(d) A description of the purpose of the requested use or disclosure of my protected research data.

(e) Provide an explanation indicating that the use or disclosure of my protected research data will be used till the end of the research study.

Signature		Signature	
_____		_____	
Test Subject	Date	Principal Investigator	Date

3. I, the Principal Investigator of the investigation, certify that:

(a) I have thoroughly and accurately described the research investigation and procedures to the test subject and have provided him/her with a layman's description of the same.

(b) The test setup involves _____risk to the test subject
(minimal or reasonable)
All equipment to be used has been inspected and certified for safe and proper operation.

(c) The test subject is medically qualified to participate.

(d) Except as provided for by Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of the test subject's participation in this study shall be maintained so that no data may be linked to him/her as an individual

(e) The test protocol has not been changed from that originally approved by the JSC CPHS.

Signature:		Signature:	
_____		_____	
Principal Investigator	Date	NASA Project Scientist	Date

Notes:

* This form is valid for the period including preflight, in-flight and postflight data collection sessions for the mission. Before the first baseline data collection, the Principal Investigator will repeat the briefing concerning risks involved in the investigation. A signed, dated copy of this form with attachments must be forwarded to Chairperson, Johnson Space Center Committee for the Protection of Human Subjects, Mail Code SA, Lyndon B. Johnson Space Center, Houston, Texas 77058.

** A detailed description of the investigation will be attached to this consent form. The Principal Investigator is responsible for formulating this document, which should be in layman's terms such that the subject clearly understands what procedures will be required of him/her and the risks associated therewith.

The detailed description of the research must, at a minimum, include the following:

(1) An explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject, including, but not limited to, possible adverse reactions of all medications to be administered and any risks/hazards resulting from exposure to ionizing radiation;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternate procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) Clarification of all forms of behavior, if any, interdicted by the research protocol (e.g., exercise, diet, medications, etc.);

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

When appropriate, the following information shall also be provided in the detailed description:

(8) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforseeable;

(9) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(10) Any additional costs to the subject that may result from participation in the research;

(11) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(12) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;

(13) The approximate number of subjects involved in the study.

APPENDIX K

MULTINATIONAL SPACE STATION HUMAN RESEARCH INFORMED CONSENT

1. I, _____the undersigned, do voluntarily give my informed consent for my participation as a test subject in the following research study, test, or investigation:

NAME OF INVESTIGATION _____

_____

MISSION TO WHICH ASSIGNED_____

PRINCIPAL INVESTIGATOR_____

RESPONSIBLE PROJECT SCIENTIST _____

I understand or acknowledge that:

(a) This procedure is part of an investigation approved by participating agencies.

(b) I am performing these duties as part of my employment with or assignment to this particular mission and the _____ agency.

(c) This research study has been reviewed and approved by the Human Research Multilateral Review Board (HRMRB) which has also determined that the investigation involves _____ risk to the subject.
(minimal or reasonable)

(d) Definitions:

"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

"Reasonable risk" means that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but that the risks of harm or discomfort are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

(e) The research procedures were explained to me prior to the execution of this form. I was afforded an opportunity to ask questions, and all questions asked were answered to my satisfaction. A layman's description was provided to me.**

(f) I consider myself physically and mentally qualified to participate in the investigation.

(g) I know that I can refuse to participate in the tests at any stage of their performance, and my refusal will be honored, except in those cases when, in the opinion of the responsible physician, termination of the tests could have detrimental consequences for my health and/or the health of the other subjects. However, understanding the significance of the investigations (tests), I will give every effort to perform the full scope of the program.

(h) In the event of injury resulting from this study, I understand that I will receive medical attention and available treatment. I also understand that I will be compensated for any injuries to the extent permitted under current_____ laws
agency
and regulations and the provisions of the contract between me and _____. My
agency

agreement to participate shall not be construed as a release of _____ or any
(agency)
third party liability which may arise from, or in connection with, the above procedures.

(i) Consistent with statutory and Agency-approved routine uses under _____

(agency)
regulations, the confidentiality of any data obtained as a result of my participation as a research subject in this study shall be maintained, so that no data may be linked with me as an individual without my written permission. However, if a "life-threatening" abnormality is detected, the investigator will notify me and the _____. Such information may be used to determine the need for care or
(agency)
medical follow-up, which, in certain circumstances, could affect my professional (flight) status.

_____
Test Subject Date

2. I, the undersigned, the Principal Investigator of the investigation designated above, certify that:

(a) I have accurately described the procedure and related risk(s) to the test subject.

(b) The test setup involves _____ risk to the test subject as
(minimal/reasonable)
determined by the HRMRB.

(c) All equipment to be used has been inspected and certified for safe and proper operation.

(d) The test subject is qualified to participate in my experiment protocol.

(e) The test protocol has concurrence of the HRMRB.

_____
Principal Investigator Date

Notes:

* This form is valid for the period including preflight, in-flight, and postflight data collection sessions for the mission. Before the first baseline data collection, the Principal Investigator will repeat the briefing concerning risks involved in the investigation. A signed,

dated copy of this form with attachments must be forwarded to Chair, Human Research Multilateral Review Board.

** A detailed description of the investigation will be attached to this consent form. The Principal Investigator is responsible for formulating this document, which should be in layman's terms such that the subject clearly understands what procedures will be required and the risks associated therewith. The detailed description of the research procedures must specifically list the risks associated with the procedures to be employed, the possible adverse reactions of all medications to be administered, and the risks/hazards resulting from exposure to ionizing radiation. Further, the investigator must clearly specify all forms of subject behavior interdicted by the research protocol (exercise, diet, medications, etc.)

APPENDIX K

NASA/JSC HUMAN RESEARCH INFORMED CONSENT FOR GRANTS/OTHER AGREEMENTS WHERE RESEARCH IS CONDUCTED AT LOCATIONS OTHER THAN JSC

1. I, the undersigned, do voluntarily give my informed consent for my participation as a test subject in the following research study, test, investigation, or other evaluation procedure:

NAME OF GRANT/OTHER AGREEMENT _____

_____

PRINCIPAL INVESTIGATOR _____

RESPONSIBLE NASA GRANT/TECHNICAL OFFICER _____

I understand or acknowledge that:

(a) This procedure is part of an investigation approved by NASA.

(b) I am performing these duties as part of my employment with _____.

(c) This research study has been reviewed and approved by the JSC Committee for the Protection of Human Subjects (CPHS) which have also determined that the investigation involves _____ risk to the subject.
(minimal or reasonable)

(d) Definitions:

“Minimal risk” means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or test.

"Reasonable risk" means that the probability and magnitude of harm or discomfort anticipated in the research are greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests, but that the risks of harm or discomfort are considered to be acceptable when weighed against the anticipated benefits and the importance of the knowledge to be gained from the research.

“Protected Research Data” means that the individually identifiable research data maintained or shared will be protected.

(e) The research procedures were explained to me prior to the execution of this form. I was afforded an opportunity to ask questions, and all questions asked were answered to my satisfaction. A layman's description was provided to me. **

(f) I am medically qualified to participate in the investigation.

(g) I know that I can refuse to participate in the tests at any stage of their performance, and my refusal will be honored, except in those cases when, in the opinion of the responsible physician, termination of the tests could have detrimental consequences for my health and/or the health of the other subjects. I further understand that my withdrawal or refusal to participate in this investigation will not result in any penalty or loss of benefits to which I am otherwise entitled.

(h) In the event of physical injury resulting from this study and calling for immediate action or attention, the necessary treatment will be provided (or be caused to be provided) by _____.
(Name of Grantee or Organization)

I also understand that NASA will pay for any claims of injury, loss of life or property damage to the extent required by the Federal Employees Compensation Act or the Federal Tort Claims Act. My agreement to participate shall not be construed as a release of NASA or any third party from any future liability, which may arise from, or in connection with, the above procedures.

(i) Except as provided for by Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of my participation as a research subject in this study shall be maintained so that no data may be linked with me as an individual. I understand, however, that if a “life-threatening” abnormality is detected, the investigator will notify me. Such information may be used to determine the need for care or medical follow-up.

Signature: Signature:

_____ _____

Test Subject Date Witness Date

2. I, the test subject, do further understand that the responsible Principal Investigator for the research investigation for which I am participating, must meet the following elements as a condition for valid authorizaton for disclosure of my protected research data:

(a) Provide specific and meaningful description of the types of information to be used or disclosed.

(b) Identify the person(s) or class of persons who will be allowed the use of my protected research data.

(c) Identify the person(s) or class of persons to whom the research institution may release my protected research data.

(d) A description of the purpose of the requested use or disclosure of my protected research data.

(e) Provide an explanation indicating that the use or disclosure of my protected research data will be used till the end of the research study.

Signature Signature

_____ _____

Test Subject Date Principal Investigator Date

3. I, the Principal Investigator of the investigation certify that:

(a) I have thoroughly and accurately described the research investigation and procedures to the test subject and have provided him/her with a layman's description of the same.

(b) The test setup involves _____risk to the test subject.
(minimal or reasonable)

All equipment to be used has been inspected and certified for safe and proper operation.

(c) The test subject is medically qualified to participate.

(d) Except as provided for by Agency-approved routine uses under the Privacy Act, the confidentiality of any data obtained as a result of the test subject's participation in this study be maintained so that no data may be linked ot him/her as an individual.

(e) The test protocol has not been changed from that originally approved by the JSC CPHS.

Signature: Signature:

_____ _____

Principal Investigator Date NASA Grant/Technical Officer Date

* A signed, dated copy of this form with attachments must be forwarded to the Chairperson, Johnson Space Center Committee for the Protection of Human Subjects, Mail Code SA, Lyndon B. Johnson Space Center, Houston, Texas 77058

** A detailed description of the investigation will be attached to this consent form. The Principal Investigator is responsible for formulating this document, which should be in layman's terms such that the subject clearly understands what procedures will be required and the risks associated therewith.

The detailed descriptions of the research must, at a minimum, include the following:

(1) An explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject, including, but not limited to, possible adverse reactions of all medications to be administered and any risks/hazards resulting from exposure to ionizing radiation;

(3) A description of any benefits to the subject or to others which may reasonably be expected from the research;

(4) A disclosure of appropriate alternate procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) Clarification of all forms of behavior, if any, interdicted by the research protocol (e.g., exercise, diet, medications, etc.);

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

When appropriate, the following information shall also be provided in the detailed description:

(8) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforseeable;

(9) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(10) Any additional costs to the subject that may result from participation in the research;

(11) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(12) A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject;

(13) The approximate number of subjects involved in the study.

APPENDIX L

National Aeronautics and
Space Administration
Lyndon B. Johnson Space Center
2101 NASA Road 1
Houston, Texas 77058-3696

Date

Principal Investigator/Mail Code
Address
City, Zip Code

RE: [Submission Identifer]

[Title of JSC-CPHS Research Submission]

Approval valid from [Date] to [Date]

Dear [Principal Investigator]:

1. The Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS) has taken the following action with respect to the above named proposal:

( ) Accept the governance of the local Institutional Review Board (IRB).
( ) Proposal is approved for 1-year.
( ) Proposal is approved with minor Board recommendations (See CPHS minutes).
( ) Proposal is tabled with Board recommended actions (See CPHS minutes).
( ) Proposal is rejected (See CPHS minutes).
( ) Medical Monitoring designation; ( ) Not Required; ( ) Level I; ( ) Level II; ( ) Level III; ( ) Level IV

2. Additional review of this proposal will be required:

(X) Annually.
(X) If there is any substantive change in protocol.
(X) Should unexpected problems or unusual complications develop.

3. Method of review utilized:

( ) JSC CPHS Screening Process (NASA Funded Grants)
( ) JSC CPHS Full Board Review
( ) JSC CPHS Expedited Review.

_____ _____

Charles F. Sawin, Ph.D. Date
Chair, JSC Committee for the Protection of Human Subjects

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

INVESTIGATIONAL NEW DRUG APPLICATION (IND)

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

Form Approved: OMB No. 0910-0014.
Expiration Date: September 30, 2002.
See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR	2. DATE OF SUBMISSION
3. ADDRESS (Number, Street, City, State and Zip Code)	4. TELEPHONE NUMBER *(Include Area Code)*
5. NAME(S) OF DRUG (Include all available names: Trade, Generic, Chemical, Code)	6. IND NUMBER *(If previously assigned)*

7. INDICATION(S) (Covered by this submission)

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED:
☐ PHASE 1 ☐ PHASE 2 ☐ PHASE 3 ☐ OTHER _____ *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES (21 CFR Part 314.420), AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER ___ ___ ___

11. THIS SUBMISSION CONTAINS THE FOLLOWING: (Check all that apply)

☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND) ☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):	INFORMATION AMENDMENT(S):	IND SAFETY REPORT(S):
☐ NEW PROTOCOL	☐ CHEMISTRY/MICROBIOLOGY	☐ INITIAL WRITTEN REPORT
☐ CHANGE IN PROTOCOL	☐ PHARMACOLOGY/TOXICOLOGY	☐ FOLLOW-UP TO A WRITTEN REPORT
☐ NEW INVESTIGATOR	☐ CLINICAL	

☐ RESPONSE TO FDA REQUEST FOR INFORMATION ☐ ANNUAL REPORT ☐ GENERAL CORRESPONDENCE

☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED ☐ OTHER _____ *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION FOR FURTHER INFORMATION.

☐ **TREATMENT IND 21 CFR 312.35(b)** ☐ **TREATMENT PROTOCOL 21 CFR 312.35(a)** ☐ **CHARGE REQUEST/NOTIFICATION 21 CFR 312.7(d)**

FOR FDA USE ONLY

CDR/DBIND/DGD RECEIPT STAMP	DDR RECEIPT STAMP	DIVISION ASSIGNMENT:
		IND NUMBER ASSIGNED:

12. **CONTENTS OF APPLICATION**

This application contains the following items: *(Check all that apply)*

- ☐ 1. Form FDA 1571 *[21 CFR 312.23(a)(1)]*
- ☐ 2. Table of Contents *[21 CFR 312.23(a)(2)]*
- ☐ 3. Introductory statement *[21 CFR 312.23(a)(3)]*
- ☐ 4. General Investigational plan *[21 CFR 312.23(a)(3)]*
- ☐ 5. Investigator's brochure *[21 CFR 312.23(a)(5)]*
- ☐ 6. Protocol(s) *[21 CFR 312.23(a)(6)]*
  - ☐ a. Study protocol(s) *[21 CFR 312.23(a)(6)]*
  - ☐ b. Investigator data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - ☐ c. Facilities data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
  - ☐ d. Institutional Review Board data *[21 CFR 312.23(a)(6)(iii)(b)]* or completed Form(s) FDA 1572
- ☐ 7. Chemistry, manufacturing, and control data *[21 CFR 312.23(a)(7)]*
  - ☐ Environment assessment or claim for exclusion *[21 CFR 312.23(a)(7)(iv)(e)]*
- ☐ 8. Pharmacology and toxicology data *[21 CFR 312.23(a)(8)]*
- ☐ 9. Previous human experience *[21 CFR 312.23(a)(9)]*
- ☐ 10. Additional information *[21 CFR 312.23(a)(10)]*

13. IS ANY PART OF THE CLINICAL STUDY TO BE CONDUCTED BY A CONTRACT RESEARCH ORGANIZATION? ☐ YES ☐ NO

IF YES, WILL ANY SPONSOR OBLIGATIONS BE TRANSFERRED TO THE CONTRACT RESEARCH ORGANIZATION? ☐ YES ☐ NO

IF YES, ATTACH A STATEMENT CONTAINING THE NAME AND ADDRESS OF THE CONTRACT RESEARCH ORGANIZATION, IDENTIFICATION OF THE CLINICAL STUDY, AND A LISTING OF THE OBLIGATIONS TRANSFERRED.

14. NAME AND TITLE OF THE PERSON RESPONSIBLE FOR MONITORING THE CONDUCT AND PROGRESS OF THE CLINICAL INVESTIGATIONS

15. NAME(S) AND TITLE(S) OF THE PERSON(S) RESPONSIBLE FOR REVIEW AND EVALUATION OF INFORMATION RELEVANT TO THE SAFETY OF THE DRUG

I agree not to begin clinical investigations until 30 days after FDA's receipt of the IND unless I receive earlier notification by FDA that the studies may begin. I also agree not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. I agree that an Institutional Review Board (IRB) that complies with the requirements set fourth in 21 CFR Part 56 will be responsible for initial and continuing review and approval of each of the studies in the proposed clinical investigation. I agree to conduct the investigation in accordance with all other applicable regulatory requirements.

16. NAME OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	17. SIGNATURE OF SPONSOR OR SPONSOR'S AUTHORIZED REPRESENTATIVE	
18. ADDRESS (Number, Street, City, State and Zip Code)	19. TELEPHONE NUMBER *(Include Area Code)*	20. DATE

(**WARNING:** A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CBER (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
5516 Nicholson Lane
Kensington, MD 20859

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

STATEMENT OF INVESTIGATOR

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)
(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014.
Expiration Date: September 30, 2002.
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFIES THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS ATTACHED.

☐ CURRICULUM VITAE ☐ OTHER STATEMENT OF QUALIFICATIONS

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED.

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY.

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES).

6. NAMES OF THE SUBINVESTIGATORS *(e.g., research fellows, residents, associates)* WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION(S).

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR.

8. ATTACH THE FOLLOWING CLINICAL PROTOCOL INFORMATION:

☐ FOR PHASE 1 INVESTIGATIONS, A GENERAL OUTLINE OF THE PLANNED INVESTIGATION INCLUDING THE ESTIMATED DURATION OF THE STUDY AND THE MAXIMUM NUMBER OF SUBJECTS THAT WILL BE INVOLVED.

☐ FOR PHASE 2 OR 3 INVESTIGATIONS, AN OUTLINE OF THE STUDY PROTOCOL INCLUDING AN APPROXIMATION OF THE NUMBER OF SUBJECTS TO BE TREATED WITH THE DRUG AND THE NUMBER TO BE EMPLOYED AS CONTROLS, IF ANY; THE CLINICAL USES TO BE INVESTIGATED; CHARACTERISTICS OF SUBJECTS BY AGE, SEX, AND CONDITION; THE KIND OF CLINICAL OBSERVATIONS AND LABORATORY TESTS TO BE CONDUCTED; THE ESTIMATED DURATION OF THE STUDY; AND COPIES OR A DESCRIPTION OF CASE REPORT FORMS TO BE USED.

9. COMMITMENTS:

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64.

I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR:

1. Complete all sections. Attach a separate page if additional space is needed.
2. Attach curriculum vitae or other statement of qualifications as described in Section 2.
3. Attach protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND ATTACHMENTS TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND).

10. SIGNATURE OF INVESTIGATOR	11. DATE

(**WARNING:** A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CBER (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

Food and Drug Administration
CDER (HFD-94)
5516 Nicholson Lane
Kensington, MD 20895

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Please **DO NOT RETURN** this application to this address.

APPENDIX N

Date Submitted _____

Request for Human Test Subject Recruiting

This form should be completed, approved by the appropriate Laboratory Supervisor and Principal Investigator, and submitted with the CPHS Approval Letter and Test Subject Information Handout packet, prior to the start of subject recruitment for a study. . Please allow sufficient time (typically six weeks) for the initial phase of recruiting before the projected start date of the study. If newspaper advertising will be necessary, more time will be needed. If a second group of test subjects is needed after the first group completes the study, an additional request for test subjects must be submitted in sufficient time for new recruitment.

Submit this form, the CPHS Approval Letter, and the Test Subject Information Handout to the Human Test Subject Facility (HTSF) B. 37, Rm 1068 (Telephone 3-7284 or 3-7240).

Principal Investigator:_____ Ph. No: _____ Mail Code: _____

Requester: _____ Ph. No: _____ Mail Code: _____

Study Name:_____

Short Version of Study Name:_____

Job Order No. test subject pay will be charged to:_____

Projected Study Schedule: From:_____ To: _____

The Purpose of this study is: _____

_____

Study Description: (Briefly describe study in layman's terms, i.e., testing procedures, any hospital admission, length of stay, any invasive procedures, special diet, etc.)

_____

_____

Subject Qualifications: (Age, weight, height, sex, etc.)_____

_____

Page 2 (Subject Recruiting)

Specific Subject Information Requirements: (Pre-test requirements, i.e., Bruce TMET, Physiological Training Class, medications not permitted, fitness level, restrictions on exercise, etc.)

_____

_____

Drug Study Description: (Include information test subjects should know about the medication)

_____

_____

Drug Screens Needed: (Illicit drug screening is routinely done on all Test Subjects prior to study. List any additional screens needed (i.e., prescription drugs, nicotine, alcohol, caffeine, etc.)

_____

_____

Payment of Test Subjects: (Total study pay, daily pay, etc.) _____

Approximate radiation exposure during the study: _____ (mrem)

Amount of blood to be drawn during the study: _____(ml)

Number of Subjects: Male _____ Female _____

Sessions per Subject: _____ Hours per session: _____

Laboratory Supervisor:

Signature: _____ Date _____

Principal Investigator:

Signature: _____ Date _____

APPENDIX O

JSC Policy Directive

JPD 7170.2B

EFFECTIVE DATE: September 17, 2003

EXPIRATION DATE: September 17, 2008

This Directive is uncontrolled when printed.

RESPONSIBLE OFFICE: SA/Space and Life Sciences

SUBJECT: Scientific Misconduct With Regard to Human Research

1. PURPOSE. To define the policy with regard to scientific misconduct as it applies to human research.

2. REFERENCES.

2.a. NASA Policy Directive (NPD)) 7100.8D, "Protection of Human Research Subjects"

2.b. NASA Procedures and Guidelines (NPG) 7100.1, "Protection of Human Research Subjects"

2.c. JSC Procedures and Guidelines (JPG) 1107.1, "The JSC Organization"

2.d. JSC Policy Directive (JPD) 1382.5, "Maintaining the Privacy of Biomedical Research Data"

2.e. JPD 7170.3, "Disposition and Reporting of Anomalous Human Research Data"

2.f. JSC-20483, "JSC Committee for the Protection of Human Subjects - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigation"

3. APPLICABILITY.

3.a. JSC. Applies to all members of investigative teams, including research subjects, in all research and experiments involving human subjects that are funded or sponsored by JSC; conducted in JSC facilities, aircraft, or NASA spacecraft; or which involve JSC to any degree.

3.b. Contracts and Agreements. All human research conducted under contracts, grants, cooperative agreements, and Space Act agreements entered into by JSC and another Government agency, private entity, non-Federal public entity, or foreign entity must comply with this Management Instruction and NPD 7100.8D and NPG 7100.1.

4. DEFINITIONS. There are at least two definitions of scientific misconduct. One definition concerns scientific investigators who may be guilty of willful fabrication, falsification of data or records, plagiarism, or some other serious deviation from accepted practice in proposing, implementing, or reporting research. A complementary definition concerns research subjects who willfully and knowingly engage in one or more forms of behavior specifically prohibited in the relevant research proposal or protocol.

5. POLICY.

5.a. Scientific Investigators. No scientific investigator funded by a NASA grant or contract shall at any time be permitted to engage in scientific misconduct as defined in Paragraph 4. Allegations of such behavior will be considered serious. Procedures for disposing of such allegations are outlined in Paragraph 6a.

5.b. Research Subjects. No subject will willfully, knowingly, and purposefully engage in any form of behavior specifically interdicted by the investigator in his/her experimental protocol or requirements that would thwart the objectives of the research or result in spurious and/or uninterpretable data.

(1) The interdicted behavior on the part of the subject must be done willfully and knowingly and not be a simple unintentional omission or commission due to forgetfulness or misinterpretation of requirements. In this context, it will be the responsibility of the investigator and/or the Project and Mission Scientists to remind the subjects of permitted and proscribed behavior at repeated intervals, namely, at appropriate times prior to each session of baseline data collection, training exercises, KC-135 flights, etc.

(2) The proscribed types of behavior must be clearly detailed by the Principal Investigator in the document attached to the NASA Informed Consent Statement or form. This description of the experiment must be in non-technical terms such that a person without a scientific background could clearly understand what will be done to the subject. The document should also clearly indicate what behavior is or is not permitted. Thus, time and types of exercise, hours of sleep, dietary limits, interdicted foods, over-the-counter or prescription medications, and a detailed description of the known medications to be administered to the subject must be provided to include their principal pharmacological actions, undesirable side-effects, idiosyncratic reactions, and any other pertinent information that may be of importance. The risks associated with certain pharmaceuticals (including radionuclides) must be stated insofar as these are known. The importance of this

document cannot be overstressed, since it may serve as a basis for crew selection and will serve as the source document in determining whether allegations of subject scientific misconduct may have occurred.

6. PROCEDURES.

6.a. Scientific Investigators. Allegations of investigator scientific misconduct shall be treated with the utmost sensitivity and shall be brought to the attention of the Chairperson, *JSC Committee for the Protection of Human Subjects (CPHS). Depending upon the gravity of the allegations, the CPHS may elect to remand the matter to the Office of the Inspector General for substantiation of the allegations, since the CPHS has limited investigative authority. If such allegations are verified, appropriate higher NASA management shall be apprised of the facts of the matter and may wish to consider what sanctions may be warranted. At this point, NASA may elect to report the matter to appropriate administrative personnel of the investigator's parent organization. The possible penalties for investigator misconduct are given in Paragraph 7a.

6.b. Research Subjects. Should scientific misconduct on the part of any subject be suspected or alleged, the problem should be resolved utilizing the initial part of the procedure prescribed for in JMI 7170.3

7. PENALTIES FOR SCIENTIFIC MISCONDUCT. Penalties for Scientific Investigators: Sanctions or penalties for scientific investigators guilty of scientific misconduct shall be assessed on a case-by-case basis by the appropriate level of NASA management. In the case of JSC employees, they may be subject to appropriate disciplinary actions up to and including dismissal. Non-JSC investigators and contractor employees may be subject to similar sanctions as deemed appropriate by their respective employer. In addition, NASA may take additional actions severing all relationships with the individual and/or employer, including termination of grants, cooperative agreements, contracts, or Space Act agreements.

8. DISPOSITION. Ultimate disposition will be on a case-by-case basis with management decision based on an evaluation of the inputs from as many of the elements listed in Paragraph 6 as may be required. Penalties and/or sanctions, if appropriate, will be prescribed or recommended by Center management.

9. RESCISSION: JMI 7071.2A, dated January 31, 1996.
* Denotes Change

Original signed by:

Jefferson D. Howell, Jr.
Director

APPENDIX P

JSC Policy Directive

JPD 1382.5B

EFFECTIVE DATE: January 27, 2004

EXPIRATION DATE: January 27, 2009

This Directive is uncontrolled when printed

RESPONSIBLE OFFICE: SA/Space and Life Sciences Directorate

SUBJECT: Maintaining the Privacy of Biomedical Research Data

1. **PURPOSE.** This Policy Directive establishes a policy for protecting the privacy of data collected during voluntary medical research involving active, inactive, or retired space flight crew members and for ground-based and in-flight data collection. This addresses the protection of the privacy of the crew members's data, as well as the protection of NASA's interests for safety of flight by allowing the collection of data necessary for the development of countermeasures to the adverse effects of space flight on human physiology.

2. **SCOPE.** This Policy Directive applies to medical payload experiments as well as Detailed Supplementary Objectives and includes preflight, in-flight, and post-flight data.

3. **AUTHORITY.**

3.a. NASA Policy Directive (NPD) 7100.8D, "Protection of Human Research Subjects."

3.b. NASA Procedural Requirements (NPR) 7100.1, "Protection of Human Research Subjects."

4. **REFERENCES.**

4.a. NASA 10HERD, "Human Experimental and Research Data Records," Privacy Act of 1974, Systems of Records.

4.b. NASA 10HIMS, "Health Information Management," Privacy Act of 1974, Systems of Records.

4.c. JPG 1107.1, "The JSC Organization."

4.d. JSC-20483, Revision C , "JSC Committee for the Protection of Human Subjects - Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

5. **POLICY**. Medical research data shall be handled in accordance with the references in Paragraph 4 and with the additional specific provisions set forth below:

5.a. Each investigator must submit with the research proposal a plan for maintaining the privacy of the data collected. For currently approved investigations, the investigator must submit an updated plan for maintaining the privacy of the data collected to the JSC Committee for the Protection of Human Subjects (CPHS) for approval prior to the next flight on which the investigation is manifested.

5.b. Data may be shared among investigators as specified in each investigator's initial proposal. These plans for data sharing must be approved by the CPHS prior to implementation.

5.c. Data collected during medical research protocols will not be used to determine the aero-medical certification of crew members. Data that indicate a life-threatening condition may, however, require additional medical evaluation necessary for appropriate medical follow-up for the individual and aero-medical certification.

5.d. Should an abnormality be detected that is life-threatening, the investigator shall provide and/or obtain medical care for the crew member. The Flight Medicine Clinic shall be notified to provide this care.

5.e. Preflight, in-flight, and postflight medical research tests will be monitored by the investigator and by a medical monitor as required by the IRB. In-flight data collection will also be monitored by the flight surgeons in the Mission Control Center when the CPHS determines that the investigation represents a potential hazard to the crew's health during space flight.

6. **BACKGROUND**. Data collected during medical research can potentially affect crew member's careers should an abnormality be detected. Confidentiality of data collected, data will be managed to references in Paragraph 4 by all data collection personnel and investigators of each proposal. General group results may be released, but individual crew member will not be identified except noted in Paragraph 5d.

7. **RESCISSION**. JMI 1382.5A, dated December 27, 1995.

Original signed by:

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Jefferson D. Howell, Jr.
Director

APPENDIX Q

Guidelines for Test Readiness Review

Excerpted from JPG 1700.1H Safety and Total Health Handbook Policy, Requirements, Instructions and Guidelines

1. This appendix covers the basic safety requirements and references for all tests, including medical research testing / baseline data collection (hereafter know as test), conducted at that involve JSC personnel JSC and for tests conducted at other locations or property or that are sponsored by JSC. This appendix also applies to equipment being tested, test personnel, test facility interfaces with test equipment and personnel, test conduct, and test documents. Test hardware and operations must also comply with the requirements of other chapters in this handbook. The term "testing," as used in this appendix, includes hazardous activities designed to accomplish training, demonstrations of test hardware or procedures, medical research, data acquisition, and hardware evaluation, qualification, or acceptance.

2. This appendix does not cover testing of institutional systems and equipment, diagnostic medical tests, or medical treatment procedures.

3. The Safety, Reliability and Quality Assurance Branch (SR&QA) must be informed of upcoming test activities by test request, schedule, or by other means. The following requirements must be followed:

   a. For non-hazardous test, follow Paragraphs 4, 8, 9, and 10 (operating procedures, test systems, and test team members) of this appendix and any other requirements from this appendix that you or SRQA decide to include. Test documentation should be made available to SR&QA on request.

   b. For hazardous tests, follow all the requirements in this appendix that apply to your tests. You or the SR&QA Branch may also decide to follow more stringent requirements.

4. The following personnel must be present during each test as required below or in other sections of this appendix. These personnel may not be required to be present throughout the entire test. The testing organization's research protocol, operating procedures or detailed test procedures (DTPs) must specify when each member is to be present.

If you are the . . .	*Your duties are . . .*	*Your certification requirements are .*

Test Director / Principal Investigator (TD / PI)	To be the central authority and have overall responsibility for all aspects of the test.	The responsibility of the testing organization
Test Conductor (TC) (Optional)	Described in the testing organization's operating procedures or DTPs.	The responsibility of the testing organization
Test Safety Officer (TSO)	To monitor all phases of test activities for certain human or especially hazardous tests, and to advise the TD of any activities deemed to be hazardous to JSC personnel or property. To advise SR&QA of any safety concerns that surface during the test	The responsibility of the SR&QA Branch
Medical Officer or Medical Representative (MO or MR)	To monitor (as required) the test activities, provide medical assistance or opinions when necessary, and advise the TD any time the health of anyone involved in the test is being compromised.	Defined by the Medical Operations Branch & JSC 20483
Facility or Test Support Personnel Facility or test support personnel include all other personnel necessary to support a test such as console operators, divers, test article support personnel, audiovisual personnel, or pressure suit engineers	Listed in the testing organization's operating procedures, test plan, or DTPs.	Specified in the testing organization's operating procedures, test plan, or DTPs.
Test Subject (the human subjected to the test or research environment)	To inform the TD if you feel that you maybe in danger and desire to stop the test.	Specified in the operating procedures, test plan, or DTPs.

5. Medical Officer (MO) or Medical Representative (MR):

   a. The MO must certify the fitness of test team personnel to perform hazardous operations and of test subjects to participate before any hazardous testing begins.

   b. An MR must monitor the medical conduct of tests under the following conditions unless excluded by, and as deemed necessary by, the Medical Operations Branch.

      - Personnel in hypobaric, hyperbaric, and oxygen-enriched environments

- Suited underwater neutral buoyancy operations
- Ambient pressure suit operations using other than ambient air or where the suit pressure is greater than 8.8 psid
- Level 1 and Level 2 “Reasonable Risk” Protocols as defined in JSC 20483

6. All test team members or support persons, you must be trained for your job as described in the operating procedures. Certification is also required under JMI 5330.5 "JSC Personnel Training and Certification Requirements."

7. The testing organization must follow JPG 1700.1H, Part 10, "Safety and Health Requirements for Test, Vacuum, and Oxygen-enriched Facilities". The operating procedures may contain more stringent requirements than those of this handbook if you and SR&QA believe they are required.

8. The following requirements apply to all hazardous and non-hazardous test systems.

   a. Test systems must be designed and constructed so that a single-point failure, loss of utilities, fluctuation of utilities, or software command can’t cause injury or property damage. Follow fault tolerance requirements in Paragraph 109 of NHB 1700.1 (V1-B), "NASA Safety Policy and Requirements Document."

   b. Test systems used in oxygen-enriched, high-vacuum, or enclosed environments must undergo materials scrutiny as defined by the testing organization’s material control process. If the facility does not have a material control process, the test system’s materials must follow the material control requirements of Part 10 of 1700.1H.

   c. Safety instrumentation must be calibrated and certified before the test and as required by the test documentation or the testing organization’s operating procedures.

   d. Test systems are approved for testing after the Test Readiness Review Board (TRRB) has signed the TRRB approval sheet.

   e. Software that controls test systems must meet NASA-STD-8719.13, "NASA Software Safety Standard."

   f. Make sure that no test team member can be exposed to hazardous materials used in the system.

9. In addition to the requirements above, human test systems must meet the following requirements:

   a. Have a means of immediately detecting an incipient fire or other hazardous condition in each occupied compartment of any test area. Automatic

detection must be provided for critical areas not suitable for visual monitoring.

b. Be designed for rescue of an incapacitated test subject.

c. Be designed for safe test termination and removal of test subjects if a power failure, fire, or other emergency occurs.

d. Have software controlling test systems analyzed to make sure no command can cause death or injury to test subjects.

e. Provide manual overrides for software commands to ensure the safety of test subjects. The commands must support safe test termination and egress of the test subject.

10. The following documentation must be completed as part of the test process. Everything but the test report and the mishap report must be completed before the test:

a. The ***test plan* / research protocol** is a top-level summary of the study. A test plan must be written for each new study and must include the following as a minimum:

- Test objectives
- Safety and medical planning provisions and known medical issues
- Test requirements
- Special safety considerations for test
- Other items, if required by the testing organization. Test plans containing final DTPs (as described below) must be approved in the same manner as a DTP document.

b. The ***DTP*** describes the steps that will be used to run the test. Test procedures should be made available for critical review at least 1 to 5 days before the TRR. DTPs must include the following as a minimum:

- Operating procedures to accomplish the test
- Measures to prevent mishaps
- Emergency procedures to be taken in the event of systems failure or malfunction such as fire, smoke, power outages, and system failure
- Test rules which define equipment and instrument limits, operating limits, off-nominal conditions, and operational situations which would require abort, hold, or proceed decisions for each test or checkout operation
- The safety requirements, individual tasks, and personnel involved in hazardous operations
- Special considerations and procedural steps that address specific hazards identified during the hazard analysis process; these and steps containing

actions critical to the protection of life or property must be flagged as safety critical steps for easy identification by test team personnel

c. A ***safety assessment*** that identifies the hazards associated with the test, the hazard controls, and verifications. The operating procedures must outline the safety assessment process and identify specific assessment subjects. The process should begin in the early phases of test planning and operations and should involve SR&QA at every step. All hazards should be eliminated, controlled/closed or the risk accepted before testing begins.

- Operating procedures will state how you document the results of safety assessment. You must update your safety assessments for changes to the hardware or operations.
- "Hazard and job safety analysis," of 1700.1H describes system safety requirements and concepts. You may use JSC 17773, "Instructions for the Preparation of Hazard Analysis for JSC Ground Operations," as a guideline for format or thought processes for conducting safety assessments. Other information sources on safety assessments include MIL-STD-882, "System Safety Program Requirements," and NHB 1700.1(V3), "System Safety."

d. If you prepare a ***test report***, you should include any anomalies, safety implications, and safety lessons learned. Send a copy of the report to SR&QA. You may send lessons learned by means other than the report.

e. You must submit a ***mishap report*** for any incident causing damage or injury or for any incident that could cause damage or injury (close call).

11. Principal Investigators (PIs) should give the reviewers 3 - 5 days to carefully review the test documentation before the TRR. The more complex the test, the more time you should give them. You should also follow these rules:

a. Each DTP containing safety-critical steps must state that on its cover.

b. Emergency procedures must be immediately available to personnel at their duty stations unless it isn't practical (such as divers).

c. You must have SR&QA concurrence on DTPs.

12. Test Readiness Reviews (TRRs)

a. A TRR should be held for each test involving human subjects, other hazardous tests, or a series of tests. A TRR determines:

- The readiness of the test facility and the test protocol.
- The adequate completion of the safety assessments.
- The status and closure of key issues.
- The test's constraints.
- The open items.

- The qualification or certification of the test team.

b. A management official or designee from the testing organization who is not personally involved with the test will chair the TRR Board. The board's membership will include representatives from:
   - The SR&QA Test Safety Officer
   - The SR&QA Quality Assurance Group (for tests supported by the Quality Assurance Group)
   - The Medical Operations Branch or CPHS Compliance Officer

The board chairman or the testing organization might add other members who are selected for their special knowledge. The TRRB members will sign a TRRB summary sheet to indicate their approval to proceed with the test.

b. A TRRB summary sheet generally will include:
   - The test's objective.
   - A statement covering test article's readiness.
   - The test's schedule.
   - Approval of the staffing, operation, procedures, and safety assessments.

13. Tests utilizing previously approved configurations and procedures may be repeated with out another TRR within a 12 month period, as long as the test complies with the constraints of the original and the documentation has not changed. Modified procedures and safety analysis shall be approved in accordance with the testing organization's operating procedures.
14. Real Time and Quick-Turnaround Testing refers to testing that is required real time to support a mission or permission testing required to support a space mission. This is defined as testing that is essential for timely start or safe continuation of the mission. For this type of testing, the test procedures shall be prepared and approved and a TRR held. SR&QA shall be notified of such tests as soon as possible. An SR&QA representative shall be present for any procedure reviews, the TRR and the test is required by paragraph 21.7.1c(3) of this document.

15. Other requirements for tests involving human subjects

    a. Keep in voice and visual contact with test subjects. Provide backup voice communications if feasible. Deliberate loss of voice or visual (but not both simultaneously) communications as part of a test is allowed if you document it in the approved test procedures.
    b. Appropriate emergency medical equipment should be made available as deemed necessary by the Medical Officer

c. Keep a hyperbaric treatment chamber on standby during the following test operations with human subjects:
   - Pressure-suited operations in a vacuum or underwater environment
   - Ambient pressure suit operations where the suit pressure is greater than 8.8 psi above ambient
   - Pre-breathe studies, vacuum chamber runs or other studies utilizing a hypobaric environment
d. Have an MO certify the fitness of each test team member to test subjects doing hazardous operations before a test.
e. Stop the test when a test subject requests that the test be discontinued.
f. Use instruments on test subjects to monitor critical physical parameters the MO requires.
g. Make sure appropriate emergency medical treatment is available.

16. Perform hazard analyses to make sure your job or system is as safe as possible. These analyses use systematic methods to:

    a. Find the hazards in your job or system.
    b. Remove those hazards if possible or take steps to control them in a timely, cost effective manner and reduce the risk to an acceptable level.

17. A hazard analysis is an organized method for identifying hazards and hazard controls in a system at any point in its life cycle. JSC 17773, "Instructions for Preparation of Hazard Analysis for JSC Ground Operations," gives you more details on how to recognize hazards and do a hazard analysis.

18. A system safety program may be simple or complex, depending on the project. As part of your system safety program, you should:

    a. Start with a preliminary hazard analysis on each proposed concept.
    b. Use the preliminary hazard analysis to:
       - Document the hazards of each design concept or operation you are considering.
       - Use lessons learned from past experience.
       - Define safety requirements for the project.
       - Help you select which design concepts or operations to choose.
       - Plan future safety efforts. These could include what other hazard analyses you should do and what techniques you should use such as subsystem hazard analyses operation and support hazard analyses, fault tree analyses, or hazard operability studies.

c. Use hazard analyses to support trade-off studies of different design and operational concepts during each phase of the project.

d. Decide which hazard controls to use. Eliminate hazards with design measures as much as possible. Use other controls for those you can't eliminate by design.

e. Analyze your system's proposed operation for hazards. Consider all phases of your system's operation such as test, startup, operation, maintenance, and disposal.

f. Decide what risk is acceptable to your project.

g. Assess and accept the risks of the system or its operation after you have controlled the hazards by:

   - Using the most effective hazard controls that will be cost effective and will assure mission success.
   - Looking at the risk each hazard poses and decide if it is acceptable or if you should do more to control it and lower the risk.

h. Have the right level of management accept risks.

i. Document all risk decisions and their rationale.

j. Send copies of safety analysis reports and hazard analyses to NASA Headquarters as requested.

19. A hazard analysis must contain at least the following information:

a. The system's name and location

b. The hazards of the system and their causes, including hazards from human factors

c. The consequence of each hazard if it were to cause a mishap (for example, death, major injury, minor injury, or estimated property damage and dollar amount)

d. Any existing engineering or administrative controls for each hazard

e. Proposed engineering or administrative controls for each hazard, if the existing controls are inadequate

f. Consequences if the engineering or administrative controls failed

g. A qualitative evaluation of the possible safety and health effects before and after the controls are in place

h. A list of hazard analysis team members

i. The date on which the system was last analyzed

j. A qualitative evaluation of the risk before and after the hazard controls are in place (This is the risk that management will have to accept.)

20. A risk assessment code (RAC) matrix must be used to assess the risk of each hazard. JSC uses this system to make sure that risk assessments are consistent. To use this matrix:

   a. Find the "severity" or the worst-case outcome of a mishap from the hazard along the left side of the matrix.
   b. Find the "frequency" that you expect the mishap to occur across the top of the matrix.
   c. Find the RAC in the box where the "severity" and "frequency" cross.

Sample RAC Matrix

		PROBABILITY ESTIMATE (FREQUENCY)			
		A Frequent Likely to occur one or more times a year.	**B Probable** Likely to occur once in 1 - 2 years.	**C Occasional** May occur once in 2 - 5 years.	**D Remote** Unlikely to occur, but possible within 5 years to end of system life.
	I Catastrophic Death, several serious injuries or illnesses, or damage over $1,000,000	1	1	2	3
S E V E R	**II Critical** Serious injury or illness, several lost workdays, or Damage between $250,000 - $1,000,000	1	2	3	3
I T Y	**III Marginal** Lost workday, several minor injuries, or Damage between $25,000 - $250,000	2	3	4	4

	IV Negligible Minor injury or damage less than $25,000	3	3	4	4

21. The table below tells you what action you must take for each RAC.

If RAC is	*risk is .*
1	Unacceptable – Correct within 24 hours using permanent or temporary engineering or administrative controls to reduce the hazard to a RAC 3 or 4. Or use engineering or administrative controls to reduce the hazard to a RAC 3 or 4 before the system goes into operation. All operations must cease immediately until the hazard is corrected or until temporary controls are in place and permanent controls are in work. A safety professional should stay at the scene at least until temporary controls are in place. RAC 1 hazards have the highest priority for hazard controls.
2	Undesirable – Correct within 3 working days using engineering or administrative controls to reduce the hazard to a RAC 3 or 4 or less. Use engineering or administrative controls to reduce the hazard to a RAC 3 or 4 before the system goes into operation. All operations must cease immediately until the hazard is corrected or until temporary controls are in place and permanent controls are in work. RAC 2 hazards are next in priority after RAC 1 hazards for control. Program Manager or Center Director may accept the risk with adequate justification.
3	Acceptable with controls – Correct hazard within 30 days and verify that documented procedures and controls are in place. Or correct hazard before system goes into operation. Organizational Director or equivalent management may accept the risk with adequate justification.
4	Acceptable with controls – Correct hazard within 90 days or before system goes into operation. Division Chief or equivalent management may accept the risk with adequate justification.

22. Use the following steps to decide what corrective action to take for any hazard found during your analysis. Take the following actions in the order below to control a hazard. Go to the next step only if the present step or previous steps aren't feasible or are too costly:

    a. Change the design so you eliminate or reduce the hazard. For example, use a less hazardous material or lower voltage, if possible.
    b. Install safety devices or guards. For example, use safety interlocks, machine guards, or relief valves, if possible.
    c. Install caution and warning devices. For example, use oxygen monitors or alarms, if possible.
    d. Use administrative controls, such as special work procedures, training, administrative barriers, and signs.
    e. Use personal protective equipment.

23. All hazards are to be controlled. To do this, you must track each hazard and keep it "open" until one of the above actions has occurred.

NASA Mishap Report

Part A: Mishap Details

MASTER FILE NO.

NOTE: FILL IN ALL KNOWN UNSHADED BLOCKS WITHIN 24 HOURS.

DETAILS

1. DATE OF INCIDENT	2. TIME OF INCIDENT	3. GENERAL LOCATION *(Building, Area, Facility, etc.)*	4. EXACT LOCATION *(street, floor, room, etc.)*
1/28/2003			

5. RESPONSIBLE ORGANIZATION	6. CONTRACT NUMBER	7. ORG. FILE NUMBER	8. ORGANIZATION POINT OF CONTACT	9. MAIL CODE	10. PHONE

11. MISSION AFFECTED, IF KNOWN	12. PROGRAM IMPACT, IF KNOWN (Describe impact in terms of delay, cost adjustment, etc.)

13. INCIDENT DESCRIPTION *(Do not use actual names, include in the description the sequence of events, extent of injury or property damage, cause, etc., if known.)*

IMPACT SUMMARY

14. CHECK ALL OUTCOMES FROM THIS EVENT THAT ARE KNOWN FACTS *(Do not check any box that indicates any future potential or outcome.)*

- ☐ FATALITY
- ☐ PERMANENT DISABILITY
- ☐ 3 OR MORE PEOPLE HOSPITALIZED
- ☐ 1 OR 2 PEOPLE HOSPITALIZED
- ☐ LOSS OF CONSCIOUSNESS
- ☐ FULL LOST WORKDAY(S)
- ☐ RESTRICTED WORKDAY(S)
- ☐ MEDICATION OR MEDICAL TREATMENT ADMINISTERED
- ☐ INJURY OR ILLNESS
- ☐ FIRST AID ONLY WAS ADMINISTERED
- ☐ SERIOUS DAMAGE TO AIRCRAFT OR SPACE HARDWARE
- ☐ SERIOUS DAMAGE TO FLIGHT OR GROUND SUPPORT HARDWARE
- ☐ UNEXPECTED DAMAGE DUE TO TEST FAILURE
- ☐ DAMAGE ESTIMATE OVER $1,000,000
- ☐ DAMAGE ESTIMATE BETWEEN $250K AND $1M
- ☐ DAMAGE ESTIMATE BETWEEN $25K AND $250K
- ☐ DAMAGE ESTIMATE BETWEEN $1K AND $25K
- ☐ DAMAGE ESTIMATE UNDER $1K
- ☐ AFFECTED PRIMARY OBJECTIVE(S) OF MISSION
- ☐ SIGNIFICANT PROGRAM IMPACT
- ☐ HIGH VISIBILITY (*internal or external to NASA*)
- ☐ CLOSE CALL

15. LEVEL OF POTENTIAL FOR THIS EVENT OR CLOSE CALL *(Using reasonable judgment, check the boxes which you believe have a HIGH probability of occurring under similar conditions.)*

- ☐ FATALITY
- ☐ PERMANENT DISABILITY
- ☐ 3 OR MORE PEOPLE HOSPITALIZED
- ☐ FULL LOST WORKDAY(S)
- ☐ POTENTIAL DAMAGE ESTIMATE OVER $250,000
- ☐ POTENTIAL DAMAGE ESTIMATE UNDER $250,000
- ☐ SERIOUS DAMAGE TO AIRCRAFT OR SPACE HARDWARE
- ☐ SERIOUS DAMAGE TO FLIGHT OR GROUND SUPPORT HARDWARE
- ☐ UNEXPECTED DAMAGE DUE TO TEST FAILURE
- ☐ AFFECT PRIMARY OBJECTIVE(S) OF MISSION
- ☐ SIGNIFICANT PROGRAM IMPACT
- ☐ HIGH VISIBILITY (*internal or external to NASA*)

PERSON INVOLVED IN INJURY OR ILLNESS

16. NAME *(Last, First MI)*	17. ORGANIZATION	18. CONTRACT NUMBER	19. JOB TITLE/OCCUPATION

20. SUPERVISOR'S NAME *(Full Name)*	21. SUPERVISOR'S ORGANIZATION	22. SUPERVISOR'S MAIL CODE	23. SUPERVISOR'S PHONE

24. AGE	25. SEX	26. SHIFT WORKED	27. CONTINUOUS DUTY HOURS	28. YEARS OF EXPERIENCE
	☐ Male ☐ Female	☐1st ☐ 2nd ☐ 3rd		☐ Under 1 ☐ Under 5 ☐ Under 10 ☐ Over 10

29. INJURY OR ILLNESS	30. FROM PRE-EXISTING	31. FATALITY?	32. DATE OF DEATH	33. PERMANENT DISABILITY?	34. # OF FULL LOST WORKDAYS	35. # OF RESTRICTED WORKDAYS
☐ INJURY ☐ ILLNESS	☐ YES ☐ NO	☐		☐		

36. INJURY TYPE(S) *(e.g., Abrasion, Burn, Concussion, Laceration, etc.)*	37. AFFECTED BODY PART(S) OR BODY SYSTEM(S)

38. BRIEF MEDICAL DIAGNOSIS

39. MEDICAL TREATMENT ADMINISTERED

- ☐ TREATMENT OF INFECTION
- ☐ APPLICATION OF ANTISEPTIC
- ☐ 2ND OR 3RD DEGREE BURN(S)
- ☐ CUT AWAY DEAD SKIN
- ☐ POSITIVE X-RAY DIAGNOSIS
- ☐ APPLICATION OF SUTURES
- ☐ USE OF BUTTERFLY ADHESIVE
- ☐ REMOVAL OF FOREIGN OBJECT(S)
- ☐ USE OF HEAT THERAPY
- ☐ ADMISSION TO HOSPITAL FOR MORE THAN OBSERVATION
- ☐ REMOVAL OF OBJECT IN WOUND
- ☐ USE OF PRESCRIPTION MEDICATION
- ☐ HOT OR COLD SOAKING/COMPRESS THERAPY
- ☐ USE OF WHIRLPOOL BATH THERAPY
- ☐ FIRST AID ONLY

40. OTHER MEDICAL TREATMENT ADMINISTERED

EQUIPMENT/PROPERTY DAMAGED

41. CLASS OF EQUIPMENT/PROPERTY DAMAGED

- ☐ FLIGHT HARDWARE
- ☐ GROUND SUPPORT EQUIPMENT
- ☐ FACILITY
- ☐ PRESSURE VESSEL
- ☐ MOTOR VEHICLE
- ☐ AIRCRAFT
- ☐ OTHER

42. ESTIMATED COST OF ALL DAMAGED ITEMS

- ☐ OVER $1,000,000
- ☐ BETWEEN $250K AND $1M
- ☐ BETWEEN $25K AND $250K
- ☐ BETWEEN $1K AND $25K
- ☐ UNDER $1,000

43. # OF ITEMS DAMAGED

____

43. SPECIFIC ITEM(S) DAMAGED

SUBMITTER

44. SUBMITTED BY *(Full Name)*	45. ORGANIZATION	46. MAIL CODE	47. PHONE	48. DATE	49. TIME

NASA Mishap Report

Part B: Causes and Corrective Action

MASTER FILE NO.

CAUSES

50. WHAT WAS THE DIRECT CAUSE(S)	51. WHAT OBJECTS OR SUBSTANCES WERE INVOLVED	52. WHAT ACTIVITIES OR UNSAFE ACTS WERE IN PROGRESS

INITIAL CORRECTIVE ACTION

53. **INITIAL** ACTION TAKEN *(Summarize all corrective action taken)*

54. DATE INITIATED	55. DATE COMPLETED	56. PERSON TAKING ACTION *(Full Name)*	57. ORGANIZATION	58. MAIL CODE	59. PHONE

PLANNED CORRECTIVE ACTION

60. **PROPOSED** ACTION TO BE TAKEN *(Summarize any future action to be taken.)*

61. EST. START DATE	62. EST. COMPL.	63. PERSON TAKING ACTION *(Full Name)*	64. ORGANIZATION	65. MAIL CODE	66. PHONE

67. **PROPOSED** ACTION TO BE TAKEN *(Summarize any future action to be taken.)*

68. EST. START DATE	69. EST. COMPL.	70. PERSON TAKING ACTION *(Full Name)*	71. ORGANIZATION	72. MAIL CODE	73. PHONE

NF 1627 MAR 2001 PREVIOUS EDITIONS ARE OBSOLETE.

Instructions

Complete the initial incident report (unshaded portions) and submit to your local NASA Safety Office within 24 hours of the incident occurrence. Complete and submit the follow-up report (with shaded areas) within ten working days of the incident. Retain a copy for your own files.

Working With This Form

This electronic document is a form. It has fields where you can enter information. You can use the mouse or TAB key to move between fields. The TAB key moves to the next field and SHIFT-TAB moves backwards. Some fields control the types of data that you can enter.
You should fill in this form electronically and send it to your local NASA Safety Office by electronic mail.

DETAILS

1. DATE OF INCIDENT - Enter date of the incident in MM/DD/YYYY format. Example: 6/1/2001.
2. TIME OF INCIDENT - Enter time of the incident using 24-hour clock. Examples: 09:30 for 9:30 AM or 14:15 for 2:15 PM.
3. GENERAL LOCATION - Identify the building, area, or facility where the incident occurred.
4. EXACT LOCATION - Describe the location of the incident. Example: Third floor, far west corridor.
5. RESPONSIBLE ORGANIZATION - Enter complete name of organization reporting the incident.
6. CONTRACT NUMBER - When the organization is a contractor, enter the contract number.
7. ORGANIZATION FILE NUMBER - Assign file number using your organization's unique four-character code, the mishap number (sequential) using four digits, and the fiscal year using two digits. Example: EGB1-0001-89.

8 - 10. ORGANIZATION POINT OF CONTACT, MAIL CODE, PHONE - Identify the person to contact at the organization.

11. MISSION AFFECTED - Enter the name or number of the mission, program, or project affected by the mishap. Examples: STS-32; Delta 181.
12. PROGRAM IMPACT - Describe the effect on the mission, program, or project in terms of delay or significant cost adjustment. Example: Two-week launch delay.
13. INCIDENT DESCRIPTION - Describe the event including information about the extent of damage and/or injury, conditions that led to the mishap, and cause if known at this time. Specify location of facility where medical treatment was provided. DO NOT include names of persons.

IMPACT SUMMARY

14. ACTUAL OUTCOMES - Mark every checkbox that represents current facts about the incident.
15. LEVEL OF POTENTIAL - Mark every checkbox that represents likely outcomes for the incident.

PERSONNEL INVOLVED IN INJURY OR ILLNESS

(If more than one person was injured, then attach a NASA Mishap Report (NF 1627) with only this section completed for each additional person.)

16. NAME - Self-explanatory.
17. ORGANIZATION - Identify the organization of the person involved.
18. CONTRACT NUMBER - When the organization is a contractor, enter the contract number.
19. JOB TITLE/OCCUPATION - Describe the job position of the person involved. Example: Technician

20-23. SUPERVISOR'S NAME, ORGANIZATION, MAIL CODE, & PHONE - Provide identifying information about the supervisor of the person involved.

24. AGE - (of the person involved) Self-explanatory.
25. SEX - Check as appropriate.
26. SHIFT WORKED - Check as appropriate.
27. CONTINUOUS DUTY HOURS - Self-explanatory.
28. YEARS OF EXPERIENCE - Check as appropriate.

29. INJURY OR ILLNESS - Check as appropriate.
30. FROM PRE-EXISTING - Check as appropriate.
31. FATALITY? -
32. DATE OF DEATH -
33. PERMANENT DISABILITY?
34. # OF FULL LOST WORKDAYS -
35. # OF RESTRICTED WORKDAYS -
36. INJURY TYPE(S) - Choose one or more items from the list. (See instructions below.)
37. AFFECTED BODY PART(S) or BODY SYSTEM(S) - Choose one or more items from the list. (See instructions below.)
38. BRIEF MEDICAL DIAGNOSIS -
39. MEDICAL TREATMENT ADMINISTERED - Mark every checkbox that represents treatment administered to the person involved. Mark the checkbox for "First Aid Only" if only First Aid treatment was administered to the individual.
40. MEDICAL TREATMENT ADMINISTERED - Describe any treatment not included in box #39.

EQUIPMENT/PROPERTY DAMAGE

41. CLASS OF EQUIPMENT/PROPERTY DAMAGED - Mark checkbox that represents type of damaged.
42. ESTIMATED COST OF ALL DAMAGED ITEMS - Mark one checkbox that represents the initially estimated cost of the damage. Provide Final Cost in follow-up report.
43. # OF ITEMS DAMAGED -
43. SPECIFIC ITEM(S) DAMAGED - Identify or describe the damaged items from box #41. Example: If the class indicated in box #41 is Flight Hardware, then the specific item could be "Orbiter/Avionics."

SUBMITTER

44-47. SUBMITTED BY, ORGANIZATION, MAIL CODE, & PHONE - Provide identifying information about the person filling in this form.
48-49. DATE & TIME - Enter the date and time when the form is filled in.

CAUSES

50. DIRECT CAUSE(S) - Choose one or more items from the list. (See instructions below.)
51. OBJECTS OR SUBSTANCES INVOLVED - Choose one or more items from the list. (See instructions below.)
52. ACTIVITIES OR UNSAFE ACTS IN PROGRESS - Choose one or more items from the list. (See instructions below.)

INITIAL CORRECTIVE ACTION

53. INITIAL ACTION TAKEN -
54. DATE INITIATED -
55. DATE COMPLETED -
56-59. PERSON TAKING ACTION, ORGANIZATION, MAIL CODE, & PHONE - Identify information about the person taking the initial corrective action.

PLANNED CORRECTIVE ACTION

60. PLANNED ACTION TO BE TAKEN -
61. ESTIMATED START DATE -
62. ESTIMATED COMPLETION -
63-66. PERSON TAKING ACTION, ORGANIZATION, MAIL CODE, & PHONE – Identify information about the person taking the planned corrective action.
67. PLANNED ACTION TO BE TAKEN -
68. ESTIMATED START DATE -
69. ESTIMATED COMPLETION -
70-73. PERSON TAKING ACTION, ORGANIZATION, MAIL CODE, & PHONE - Provide identifying information about the person taking the planned corrective action.

Choosing items from a list

The list appears when you move the insertion point to this field. If the field already has data, then clicking with the mouse might not display the list again. In this case, click in an earlier field and use the TAB key to move forward and display the list.

To choose an item from the list first highlight the item you want. You can use the arrow keys or the mouse to highlight the proper item. Then either press the ENTER key, click the Ok button, or double click the item.

The list of items you have chosen is displayed at the top of the window. You can add many items to the list. To remove any item, you must edit the list with the DELETE or BACKSPACE keys. You can edit the list in the list window or you can edit the field on the form.

APPENDIX S

Guidelines for Use of Experimental Animals During Preflight Training Activities

These guidelines specifically address the training activities at the home institutions, e.g., medical centers/universities, of the Principal Investigator conducting experiment-specific training and similar training activities at pertinent NASA facilities. Guidelines relative to animal standards and procedures for training simulations utilizing the flight habitats, chamber simulations (closed environments, and actual space flight are the Animal Enclosure Module (AEM), the Advanced Animal Habitat for Centrifuge (A^2HC) addressed in Appendix V.

All animal holding facilities and/or breeding colonies will generally adhere to the guidelines and recommendations of the Guide for Care and Use of Laboratory Animals, National Academy Press, 1996 and the Association for Assessment and Accreditation of Laboratory Animal Care, Int. (AAALAC. Int.).

Rodents

A. The NASA Flight Quality (NFQ) criteria for rodents are given in Table 1. In addition to certification that their animals are free of these pathogens, commercial vendors must supply a current health status report for the specific room where the animals selected for the investigation were raised. This report must indicate that the animals are completely free of any known or suspected pathogenic microorganisms or parasites using currently accepted screening technology for murine pathogens. After animals enter the user facility, daily inspection of the animals for clinical signs of illness by animal handlers is required. Should animals become clinically ill, they must be excluded from the colony and all reasonable attempts made to establish an etiologic diagnosis. In these circumstances, the remaining animals must be re-certified pathogen-free, or, alternatively, a new supply secured from the vendor.

B. For training with rodents or mice at the above facilities, minimally acceptable laboratory attire is street clothing, a clean laboratory coat and gloves for terminal procedures. When animals are to be returned to the general SPF assured population, proper attire is required. This includes clean coveralls, booties, mask, cap, gloves or the requirements of the facility housing the animals.

Monkeys

NFQ certification will be valid for a period of 6 months although tuberculin skin testing at 3-month interval is recommended. Should hands-on training with monkeys be required at any of the above facilities, the NFQ criteria for space flight animals shall apply (Appendix U). Attire appropriate for personnel protection shall be worn by all individuals who have direct contact with nonhuman primates (scrub suit, lab coat,

mask, gloves, booties, and eye protection (to be consistent with CDC/NIOSH requirements).

Amphibians

The risk of amphibian zoonosis is minimal for colony reared animals. Frogs and other amphibians have the potential to carry *Salmonella* sp. Minimal laboratory attire is street clothing and a laboratory coat and gloves. Individual facilities may have more stringent requirements for animal dress which will be followed.

Other Species

Other animal species will be considered by the JSC CPHS on an individual basis. Animals which are not colony or captive reared, may carry a greater variety of pathogens some of which may have undetermined zoonotic potential. The use of feral or non colony born animals is discouraged.

TABLE 1. NFQ CRITERIA FOR RODENTS/MICE

Agent	Syndrome	Detection
LCMV	Lymphocytic choriomeningitis	Serology (ELISA)
Hantavirus	hemorrhagic syndrome	Serology (ELISA)
TMEV	viral encephalitis	Serology (ELISA)
Salmonella sp.	Enteritis	Fecal culture onto selective media
Leptospira sp.	nephritis or hepatitis	Darkfield urine exam; serology
Giardia muris	Enteritis	Exam wet mount; cecal contents
Rodenolepis nana	enteric helminths	Exam of small intestine
Ornithonyssus bacoti	blood feeding mite	Exam of pelage
Cheyletiella parasitovorax	opportunistic mite	Exam of pelage
Microsporum sp.	fungal infection; hair/skin	Culture pelage on selective media
Trichophyton mentagrophytes	fungal infection; hair/skin	Culture pelage on selective media

TABLE 2. NFQ CRITERIA FOR *Xenopus laevis*

Agent	Syndrome	Detection
Salmonella sp.	enteritis; inapparent carrier	Fecal culture;culture water
Mycobacterium group IV (*M.xenopi, M. marinum*)	atypical mycobacteriosis	Culture water; selective media and conditions
Chlamydia psittaci	Acute hepatitis/death in Xenopus	Necropsy and liver histopathology of representative animals

TABLE 3. NFQ CRITERIA FOR SQUIRREL MONKEYS

Agent	Syndrome	Detection
Campylobacter		Fecal culture
Mycobacterium tuberculosis		Skin test and chest X-ray
Salmonella sp.		Fecal culture
Shigella sp.		Fecal culture
Entamoeba histolytica		Microscopic exam of feces
Hemoprotozoa		Microscopic exam of blood
Strongyloides		Microscopic exam of feces
Trichomonas		Microscopic exam; Oral/feces
Microsporum sp.		Clinical exam of skin
Trichophyton sp.		Clinical exam of skin
Herpes tamarinus		Serology (ELISA)
Herpesvirus salmiri		Serology (ELISA)
Lymphocytic choriomeningitis virus		Serology (ELISA)

TABLE 4. NFQ CRITERIA FOR MACAQUES

Agent	Syndrome	Detection
Campylobacter jejuni		Fecal culture
Mycobacterium tuberculosis		Skin test/chest X-ray; (Cohost group must be negative on 3 successive tuberculin skin tests conducted at 2-week intervals)
Salmonella sp.		Fecal culture
Shigella sp.		Fecal culture
Yersinia enterocolitica		Fecal culture
Yersinia pseudotuberculosis		Fecal culture
Microsporum sp.		Culture pelage; In suspect skin lesions on selective media
Trichophyton sp.		Culture pelage; In suspect skin lesions on selective media
Ascaris lumbricoides		Microscopic exam; fecal
Balantidium coli		Microscopic exam; fecal
Entamoeba histolytica		Microscopic exam; fecal
Enterobius hominis		Microscopic exam; fecal
Trichuris sp.		Microscopic exam; fecal
Glardia sp.		Microscopic exam; fecal
Hymenolepis nana		Microscopic exam; fecal
Strongyloides sp.		Microscopic exam; fecal
Trichomonas hominis		Microscopic exam; fecal
Leptospira sp.		Urine culture
Ebolavirus		Serology (ELISA)
Herpesvirus simiae (B virus)		Serology (ELISA)
SIV		Serology (ELISA)
Lymphocytic choriomeningitis		Serology (ELISA)
Monkeypox		Serology (ELISA)
Rabies		
Rubeola (Measles)		Serology (ELISA)
SRV-1, SRV-2		Serology (ELISA)
Tanapox virus group		Serology (ELISA)
Yaba		Serology (ELISA)

APPENDIX T

Guidelines for Use of Experimental Animals During Training Simulations Utilizing the Flight Research Animal Holding Facility (RAHF), General Purpose Work Station (GPWS), Chamber Simulations (Closed Environments), and Space Flight

This guideline summarizes the JSC CPHS current requirements and recommendations regarding subject experimental animal standards and procedures as viewed in the context of past advisory group meetings on this and related topics.

1. All animal holding facilities and/or breeding colonies must adhere to the guidelines and recommendations of the Guide for Care and Use of Laboratory Animals, National Academy Press, 1996 and the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC, Int.).

2. Only NASA Flight Quality (NFQ) rodents and monkeys shall be utilized for crewmember training and flight activities. The NFQ criteria for rodents are given in Table 1 (Appendix U), for Amphibians in Table 2 (Appendix V). Table 3, (Appendix U) describes the NFQ criteria for squirrel monkeys and Table 4 (Appendix U) for macaques. Fish shall be obtained from colony-bred sources. The use of feral animals for flight or training is discouraged.

3. Other animal species proposed for flight experiments shall be considered by the JSC CPHS on an individual basis. Other animal species will be considered by the JSC CPHS on an individual basis. Animals which are not colony or captive reared, may carry a greater variety of pathogens some of which may have undetermined zoonotic potential. The use of feral or non- colony born animals is discouraged.

4. The following general guidelines shall be followed where applicable:

A. STANDARD MICROBIOLOGICAL PRACTICES

1. Work surfaces shall be decontaminated with a suitable disinfectant before and after use.

2. All waste liquids, solids, tissues, syringes and needles shall be placed in durable, leak proof, puncture-resistant, sealed containers for eventual autoclaving, incineration, or other appropriate decontamination/disposal procedure post-training, post-simulation or postflight. Such materials will not be transported between the animal investigation area and crew living quarters.

3. Hypodermic needles and syringes shall be used only for the parenteral injection or aspiration of fluids from laboratory animals and diaphragm

bottles. Only needle-locking syringes or disposable needle syringe units (i.e., the needle is integral to the syringe) are to be used for the injection or aspiration of fluids. Needles should not be bent, sheared or removed from the syringe following use except if an aspirate is to be transported within a syringe. The needle shall be removed and appropriately discarded and the syringe tip shall be appropriately capped. Needles should not be replaced in the plastic sheath or guard prior to disposal. Needle and syringe should be promptly placed in puncture-proof container for eventual decontamination, preferably by autoclaving, before final discard.

4. Personnel shall use appropriate antiseptic wet wipes or other available means for cleaning hands after handling animals, when departing the laboratory, and especially before eating.

5. Street clothing, a laboratory coat (or equivalent) and latex or similar gloves shall be worn when animals are handled. Facilities may have more stringent requirements for attire when working with or around laboratory animals; these standards shall apply within those facilities. Shorts, sandals or open toed shoes may not be worn under a laboratory coat in the Animal Care Facility.

B. ANIMAL CERTIFICATION

1. Animals will be certified NFQ by the supplier for the proscribed organisms listed in Tables 1, 2, 3, and 4. Rodents or mice will be housed appropriately in filtered cages. A minimum of 5% of animal populations destined for potential crew contact or actual space flight will be sampled for microbial culture screening by oral swab and fecal sample for those organisms on the SPF list 72 hours prior to crew contact. Presumptive results must be available in 24 hours and definitive results in 72 hours. The crew will not be exposed to animals if the sampled animal cultures are positive for a proscribe organism. Rodent viral serology will be completed two weeks prior to crew exposure according to established protocols.

2. Monkeys shall be screened for proscribed organisms at six-month intervals. The flight animals selected will have viral serology screening completed one month before use; will be cultured for proscribed bacteria and undergo intra palpebral tuberculin using mammalian old tuberculin (MOT) testing 96 hours prior to crew contact. All microbiological and tuberculin skin test results will be forwarded to the JSC IRB as part of the Operational Readiness Review (ORR).

3. NFQ certified squirrel monkeys will at all times be housed in isolation apart from other non-certified non-human primates. The isolation quarters will

be provided with a nonrecirculating type ventilation system to preclude contamination from other animals. Room entry will require shoe covers in addition to the standard outerwear (scrub suits, lab coat, mask and gloves as defined by CDC/NIOSH).

C. ANIMAL ENCLOSURE MODULE (AEM), ADVANCED ANIMAL HABITAT for CENTRIFUGE, (A^2HC), ANIMAL TRANSFER MODULE (ATM) AND GENERAL PURPOSE WORK STATION (GPWS) IN-FLIGHT GUIDELINES

1. With the improved integrity of animal enclosures and associated flight procedures, THE ROUTINE USE OF LABORATORY ATTIRE IS NOT REQUIRED.

If anomalous situations should develop which produce free contaminants, all crewmembers will use suitable protective measures (viz., NIOSH-approved respirator) until the particular experiment or procedure is terminated and the contaminant is satisfactorily removed from the spacecraft. This precaution is necessary in the closed microgravity environment, since contamination does not remain localized in the continuous atmosphere of spacecraft.

Particular care should be exercised during the following procedures:

a. Rodents/Mice: Waste tray and food canister changeout; cage removal; condensate bottle changeout; GPWS operations involving animals.

b. Squirrel monkeys: Waste tray changeout; urine canister changeout; food canister changeout; blood sample collection.

2. High Efficiency Particulate Air (HEPA) filtration system of the RAHF and GWPS will remove more than 99% of all particles greater than 0.3 micrometers.

3. Biological samples from animals shall not contaminate the spacecraft or crew at any time during collection, transport and storage procedure.

4. Animals transported between the AEM, ATM, and A^2HC and GPWS must be enclosed in a carrier.

5. Equipment and procedures for the housing, transport, and experimental protocol must preclude any possibility of animal escape into the spacecraft.

SPECIFIC PATHOGEN FREE (SPF) LIST FOR RAT/MICE

Agent	Syndrome	Detection
Sendai virus	pneumonitis	Serology (ELISA)
Mouse adenovirus	clinically inapparent	Serology (ELISA)
K virus	clinically inapparent	Serology (ELISA)
Pneumonia virus of mice	clinically inapparent	Serology (ELISA)
Citrobacter freundii	enteritis	Culture of cecal contents
Mouse parvoviruses (MVM,OPV)	clinically inapparent	Serology (ELISA)
LDH elevating virus	elevated LDH	serum enzyme assay
Mousepox (ectromelia)	mouse pox	Serology (ELISA)
Mouse cytomegalovirus	clinically inapparent	Serology (ELISA)
Mouse rotavirus	enteritis in newborns	Serology (ELISA)
Mouse hepatitis virus	hepatitis, enteritis	Serology (ELISA)
Mouse polyoma virus	clinically inapparent	Serology (ELISA)
Rat coronavirus	sialoadenitis, dacryoadenitis	Serology (ELISA)
Rat rotavirus	enteritis in newborns	Serology (ELISA)
Reovirus 3	clinically inapparent	Serology (ELISA)
Rat parvoviruses (H1,KRV,OPV)	clinically inapparent	Serology (ELISA)
Rat cytomegalovirus	clinically inapparent	Serology (ELISA)
Myobia musculi	fur mite	Direct exam of pelage
Mycoplasma pulmonis	pneumonia, other	Serology (ELISA)
CAR bacillus	pneumonia	Serology (ELISA)
Clostridium piliforme	Tyzzor's disease	Serology (ELISA)
Corynebacterium kutscheri	pneumonia	Nasopharyngeal culture
Pasteurella pneumotropica	opportunistic	Nasopharyngeal culture
Streptococcus pneumoniae	opportunistic	Nasopharyngeal culture
Streptococcus sp.	opportunistic	Nasopharyngeal culture
Bordetella bronchiseptica	opportunistic	Nasopharyngeal culture
Klebsiella pneumoniae	opportunistic	Culture of cecal contents/feces
Pseudomonas aeruginosa	opportunistic	Culture of cecal contents/feces
Hymenolepis diminuta	enteric helminths	Direct exam of small intestine/feces
Aspicularis tetraptera	enteric helminths	Direct exam of proximal colon/feces
Syphacia obvelata	enteric helminths	Direct exam of cecum/feces
Pneumocystis carinii	immunodefic rodents	Lung histology; silver stain
Spironucleus muris	enteritis	Exam wet mount cecal contents/feces
Entamoeba muris	enteritis	Exam wet mount cecal contents/feces

SPECIFIC PATHOGEN FREE (SPF) LIST FOR RAT/MICE
(CONTINUED)

Agent	Syndrome	Detection
Tritrichomonas muris	inapparent	Exam wet mount cecal content/feces
Encephalitozoon cuniculi	nephritis or inapparent	Serology (ELISA)
Trichosomoides crassicaudata	urinary tract helminth	Urinary bladder histology
Syphacia muris	enteric helminths	Direct exam of cecum/feces
Capillaria muris	enteric helminths	Direct exam of small intestine/feces
Trichuris muris	enteric helminths	Direct exam of small intestine/feces
Radfordia ensifera	fur mite	Direct exam of pelage
Radfordia affinis	fur mite	Direct exam of pelage
Myocoptes musculinus	fur mite	Direct exam of pelage
Psorergates simplex	burrowing mite	Direct exam; skin histology of lesions

SPECIFIC PATHOGEN FREE (SPF) LIST FOR *Xenopus laevis*

Agent	Syndrome	Detection
Aeromonas hydrophila	Septicemic syndrome	Culture of lesions or water sample
Alaria sp.	Monogenetic trematodes	Fecal floation in 10% sucrose solution; Histopathology of representative animals

SPECIFIC PATHOGEN FREE (SPF) LIST
(NASA REQUESTED FOR
UNIQUE BASIS)

Agent	Syndrome	Detection
Staphylococcus aureus	opportunistic	Nasopharyngel culture
Klebsiella oxytoca	opportunistic	Culture of cecal contents/feces

APPENDIX U

CPHS Guidelines for In-flight Electrical Standards Associated with Bioinstrumentation for In-flight Investigative Monitoring of Crewmembers

Bioinstrumentation systems shall be designed to limit, to safe levels, electrical shock currents that could flow through an instrumented crewmember as a result of contact with available voltage sources in crew bays, power cords, and extravehicular activity umbilicals or failures within the bioinstrumentation itself.

For voltage sources or power supplies using frequencies from D.C. to 1kHz, nominal subject leakage currents for bioinstrumentation systems utilizing indwelling catheters shall not exceed 10μA. There is insufficient data in the literature to indicate a Critical Hazard level with respect to indwelling catheters. Electric currents in excess of 20μA, conducted via an indwelling catheter, shall be considered a Catastrophic Hazard and shall be controlled as such. For voltage sources or power supplies using frequencies above 1kHz, these values shall be multiplied by the numerical value of the frequency (in kilohertz), but may not exceed 1000μA.

For voltage sources or power supplies using frequencies from D.C. to 1kHz, nominal subject leakage currents for bioinstrumentation systems utilizing body surface electrodes (ECG, EMG, EOG, etc.) shall not exceed 100μA (A.C. or D.C.). Electric currents in excess of 500μA, applied externally, shall be considered a Critical Hazard and shall be controlled as such. Electric currents in excess of 1000μA, applied externally, shall be considered a Catastrophic Hazard and shall be controlled as such. For voltage sources or power supplies using frequencies greater than 1kHz, these values shall be multiplied by the numerical value of the frequency (in kilohertz), but may not exceed 5000μA.

Bioinstrumentation intended to apply electrical currents to crewmembers (e.g., neuromuscular stimulators etc.) shall be evaluated for maximum applied electric current on a case by case basis.

In cases where a crewmember will be instrumented with multiple biomedical instrumentation systems, consideration shall be given to possible interaction, nominal or in the event of failures, between the different instruments such that these requirements are not exceeded by the interaction.

RECOMMENDATION NOTES:

(1) The 10μA current limit for isolated patient connections, as set by ANSI/AAMI includes a safety factor of 2 with respect to a minimum fibrillation threshold of 20μA for canines. Based on a human study reported in the Medical Journal of Australia (Watson et al., 1976), “It is unlikely that ventricular fibrillation will

be induced with currents of much less than 60μA A as the lower 99% confidence limit was above 65μA."

(2) Increased nominal subject leakage current limits for frequencies above 1kHz are consistent with ANSI/AAMI, NFPA 99, and IEC 601-1.

(3) In some cases where surface electrodes were worn for long periods of time, an electrolytic reaction between low levels of D.C. electrical current and skin may have caused irritation and/or mild blistering of the skin. 100μA is the allowable value of patient leakage current under no-fault conditions according to the IEC 601-1. The 50μA risk current limit designated by ANSI/AAMI includes a safety factor of 10 with respect to the minimum threshold of perception (500μA) for large contact areas of dry intact skin and a factor of two with respect to the threshold of perception (100μA) for breached skin or mucus membrane.

(4) Although 500μA may be perceptible, a study performed by Underwriters Laboratories Inc. (Stevenson, 1969) indicated that 500μA was not likely to cause a hazardous startle reaction. A Canadian study has shown that 500μA applied to chest electrodes caused enough irritation that the subjects wearing the electrodes eventually removed them. 500μA is the maximum allowable level of current, given a single fault condition, according to the International Electrotechnical Commission (IEC 601-1).

(5) 1000μA is well below the level of electric current required to cause a thermal burn, respiratory arrest, or cardiac fibrillation; however, this level of current may be high enough to startle an instrumented crewmember and possibly cause a secondary injury. "Thresholds of (cardiac) stimulation with a large-area chest electrode were measured typically between 40 and 70mA with a minimum value of 20mA in test of humans" (Zoll et al., 1985). "60Hz fibrillation thresholds for 200-mm sq chest on dogs averaged 68mA" (Roy et al., 1986).

(6) In situations where a crewmember is wearing bioinstrumentation and operating in a captive environment (i.e., EMU suit or LES), long-term exposure to skin irritation or mild blistering of the skin may impair a crewmember's ability to perform his/her in-flight functions. In light of this possibility, 500μA shall be considered a catastrophic hazard for situations in which a crewmember is operating in a captive environment.

Summary Table

EQUIPMENT TYPE	FREQUENCY BAND	
INDWELLING CATHETERS	d.c. $< f \leq$ 1kHz	1kHz $< f$
Nominal Current Limit (1nom) Critical Current Limit (1crt) Catastrophic Current Limit (1cat)	10μA N/A 20μA	1nom = f(kHz) x 10 ≤1000μA N/A 1cat = f(kHz) x 20 ≤ 1000μA
SURFACE ELECTRODES	d.c. $< f \leq$ 1kHz	1kHz $< f$
Nominal Current Limit (1non) Critical Current Limit (1crt) Catastrophic Current Limit (1cat) Catastrophic Current Limit (Captive Environment)	100μA 500μ 1000μA 500μA	1nom = f(kHz) x 100 ≤ 5000μA 1crt = f(kHz) x 500 ≤ 5000μA 1cat = f(kHz) x 1000 ≤ 5000μA 1cat = f(kHz) x 500 ≤ 5000μA

APPENDIX V

JSC Committee for the Protection of Human Subjects (CPHS)

Page Change Notice (PCN)

Title of Investigation: _____

_____

Principal Investigator:_____
Type of Investigation (Space Flight, KC-135, Ground-based):_____
Phase of Investigation (Pre-, In-, Postflight):_____
PCN Revision Date: _____

Describe below the summary of changes (i.e., page(s), section(s), appendices) applicable to the investigation. Attachments should also be included. Denote all changes by placing bars in the margins:

_____

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_____

APPENDIX W

JSC-COMMITTEE for the PROTECTION of HUMAN SUBJECTS (CPHS) PROTOCOL ACTION ITEM RESPONSE(S)

To: Chairman, JSC-CPHS
NASA Lyndon B. Johnson Space Center
Houston, TX 77058

From: Principal Investigator/Mail Code
Address
City, State and Zip Code

Subject: JSC-CPHS Protocol Action Item Response(s) Associated with [Title of Research Investigation]

A review of the above named proposal was conducted by the JSC-CPHS on _____ with actions and/or recommendations assigned. Written responses to address the JSC-CPHS concerns are hereby submitted for review and formal closure.

JSC-CPHS Recommendation #1

Provide a brief explanation of the JSC-CPHS recommendation.

Investigator Response

Provide a brief explanation replying to CPHS protocol action(s). Include supportive attachments or enclosures.

JSC-CPHS Recommendation #2

Provide a brief explanation of the JSC-CPHS recommendation.

Investigator Response

Provide a brief explanation replying to CPHS protocol action(s). Include supportive attachments or enclosures.

APPENDIX X

21 CFR Part 640
ADDITIONAL STANDARDS FOR HUMAN BLOOD AND BLOOD PRODUCTS

Revision Date - April 1, 2002

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Subpart A – Whole Blood

§ 640.3 Suitability of donor.

A. Method of determining. The suitability of a donor as a source of Whole Blood shall be determined by a qualified physician or by persons under his supervision and trained in determining suitability. Such determination shall be made on the day of collection from the donor by means of medical history, a test for hemoglobin level, and such physical examination as appears necessary to a physician who shall be present on the premises when examinations are made, except that the suitability of donors may be determined when a physician is not present on the premises, provided the establishment (1) maintains on the premises, and files with the Center for Biologics Evaluation and Research, a manual of standard procedures and methods, approved by the Director of the Center for Biologics Evaluation and Research, that shall be followed by employees who determine suitability of donors, and (2) maintains records indicating the name and qualifications of the person immediately in charge of the employees who determine the suitability of donors when a physician is not present on the premises.

B. Qualifications of donor; general. Except as provided in paragraph (f), a person may not serve as a source of Whole Blood more than once in 8 weeks. In addition, donors shall be in good health, as indicated in part by:

(1) Normal temperature;

(2) Demonstration that systolic and diastolic blood pressures are within normal limits, unless the examining physician is satisfied that an individual with blood pressures outside these limits is an otherwise qualified donor under the provisions of this section;

(3) For allogenic donors, a blood hemoglobin level which shall be demonstrated to be no less than 12.5 grams (g) of hemoglobin per 100 milliliters (mL) of blood or a hematocrit value of 38 percent, and for autologous donors, a blood hemoglobin level which shall be demonstrated to be no less than 11.0 g of hemoglobin per 100 mL of blood or a hematocrit value of 33 percent;

(4) Freedom from acute respiratory diseases;

(5) Freedom from any infectious skin disease at the site of phlebotomy and from any such disease generalized to such an extent as to create a risk of contamination of the blood;

(6) Freedom from any disease transmissible by blood transfusion, insofar as can be determined by history and examinations indicated above; and

(7) Freedom of the arms and forearms from skin punctures or scars indicative of addiction to self-injected narcotics.

C. Additional qualifications of donor; viral hepatitis. No individual shall be used as a source of Whole Blood if he has:

(1) A history of viral hepatitis after the 11th birthday;

(2) A history of close contact within 12 months of donation with an individual having viral hepatitis;

(3) A history of having received within 12 months human blood, or any derivative of human blood which the Food and Drug Administration has advised the blood establishment is a possible source of viral hepatitis.

D. Therapeutic bleedings. Blood withdrawn in order to promote the health of a donor otherwise qualified under the provisions of this section, shall not be used as a source of Whole Blood unless the container label conspicuously indicates the donor's disease that necessitated withdrawal of blood.

E. [reserved]

F. Qualifications; donations within less than 8 weeks. A person may serve as a source of Whole Blood more than once in 8 weeks only if at the time of donation the person is examined and certified by a physician to be in good health, as indicated in part in paragraph (b) of this section.

APPENDIX Y

Human Research Multilateral Review Board (HRMRB) Charter

1.0 BACKGROUND

The Human Research Multilateral Review Board (HRMRB) is established to ensure that research involving human subjects on the International Space Station (ISS) will not endanger the health, safety, or well-being of the subjects, and further, that all experiment operations are conducted in an ethical manner. The establishment of the HRMRB is in accordance with Article 11.5 of the Memoranda of Understanding (MOU) between the National Aeronautics and Space Administration (NASA) and the Canadian Space Agency (CSA), NASA and the European Space Agency (ESA), NASA and the Government of Japan (GOJ), and NASA and the Russian Space Agency (currently referred to as the Russian Aviation and Space Agency, or Rosaviakosmos).

The charter for the HRMRB will be approved by the ISS Multilateral Coordination Board (MCB) in accordance with its responsibility to ensure coordination of the activities of CSA, ESA, GOJ, NASA, and Rosaviakosmos (hereinafter "the partners", or where appropriate "the partner" or "each partner"), related to operation and utilization of the Space Station.

The HRMRB is recognized as the ultimate decision-making authority within the scope of its responsibilities. The authority of the HRMRB is limited to the area of its responsibilities and is independent of the MCB or any other ISS management body.

Relevant international agreements concerning human subject research will serve as the basic ethical standards governing decisions by the HRMRB. Specifically, all deliberations and actions of the HRMRB will be in accordance with the Nuremberg Code and the Declaration of Helsinki. A common set of ethical guidelines, building upon existing guidelines, will be developed for use by the Partners to ensure safe and ethical conduct of human research.

HRMRB decisions will be determined by the principle of consensus. If consensus cannot be achieved, the proposed research plan will be returned to the submitting organization with a request for modifications designed to meet the objectives of safe, ethical human research.

2.0 PURPOSE

The HRMRB Charter defines the organizational relationships and responsibilities of the Board and specifies its basic operating principles.

3.0 RESPONSIBILITIES OF THE BOARD

3.1 Each partner will initially conduct its own review of its individual experiments through appropriate national Institutional Review Boards (IRBs) or equivalents.

3.2 Protocols that have been approved by the appropriate national IRBs or equivalents will be submitted to the HRMRB. HRMRB approval of these proposals is required on two occasions:

3.2.1 Prior to each experiment baseline data collection.

3.2.2 Following the total integration of the experimental program for each mission increment. In other words, when the final integrated crew activity schedule for the mission is established.

3.3 Protocols, which are assigned to multiple ISS increments, must be reviewed and approved by the HRMRB for each increment, or every two years.

3.4 The HRMRB may call medical, technical, or other consultants as required, to conduct its proceedings and assure the proper fulfillment of its responsibilities.

4.0 MEMBERSHIP AND DUTIES OF MEMBERS

4.1 Each partner will appoint one member and one alternate to the HRMRB. The appointed members and alternates shall possess broad knowledge in space medicine, biology, and physiology, as well as issues related to the safe and ethical conduct of human research. Furthermore, each member or alternate will be an active participant in his/her national IRB or its equivalent. Appropriate selection of members will ensure that each can represent the full breadth of matters brought before the HRMRB. Each member or alternate will attend and participate in all deliberations.

4.2 Each member will have the authority to represent a partner on all matters within the scope of responsibility of the HRMRB.

4.3 Each partner must be represented at any HRMRB meeting at which a consensus decision involving that partner is required. However, members are encouraged to attend all meetings.

5.0 DUTIES OF THE CHAIRPERSON

5.1 Responsibility for chairing each HRMRB meeting will be rotated among HRMRB members.

5.2 The Chairperson will facilitate the meeting and will seek consensus of all HRMRB members for all decisions and actions to be taken by the board.

6.0 MEETINGS

6.1 Meetings will be held twice per year or more frequently to assure timely resolution of HRMRB issues. Any HRMRB Member may call for a special meeting if warranted by circumstances.

6.2 Meetings will nominally be held via videoconference/audio teleconference with no single host location, but they may occur at a Partner's location with members physically present.

6.3 Meetings will be held only when a quorum participates. A quorum requires at least three HRMRB members.

6.4 Written records will be maintained to document all HRMRB actions. These records may include other documentation, electronic or paper generated as a result of HRMRB meetings, and/or activities conducted in response to HRMRB actions.

7.0 ADMINISTRATIVE SECRETARY

7.1 NASA will provide an Administrative Secretary.

7.2 The duties of the Administrative Secretary include:

- Scheduling meetings
- Coordinating development and distribution of meeting agendas and pertinent documentation
- Carrying out functions related to meeting organization and facilitation
- Recording, publishing, and distributing minutes of HRMRB meetings and other appropriate records of HRMRB actions.
- Maintaining official records of HRMRB.

8.0 MODIFICATION

Upon establishment of this charter, the HRMRB members and approval by the MCB will make modifications only upon consensus recommendation.

APPENDIX Z

POLICY REGARDING HUMAN RESEARCH DATA

Contractors and recipients of grants, for those contracts or grants that involve human research, are required to timely deliver to the Government all reports and other items of data specifically identified in the contract or grant for delivery. In addition, the Contracting Officer or the Grants Officer, at any time during performance of such contract or grant or within a period of three (3) years after acceptance of all items (including data) to be delivered under the contract or grant, may order any data first produced or specifically used in the performance of the contract or grant. The term "data" means recorded information, regardless of form, the media on which it may be recorded, or the method of recording. The term includes, but is not limited to, data of a scientific or technical nature, and any copyrightable work in which the contractor or grant recipient asserts copyright, or for which copyright ownership was purchased.

The Government shall have unlimited rights in all such data. "Unlimited rights," as used in this clause, means the right of the Government to use, disclose, reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, in any manner and for any purpose, and to have or permit others to do so.

Notwithstanding the Government's unlimited rights as set forth in the paragraph immediately above, the Government shall, unless otherwise authorized in writing by the principal investigator, withhold such data from public disclosure or distribution for a period of one year following the conclusion or termination of the experiment or investigation in order to provide the principal investigator adequate opportunity to first publish the results in an appropriate scientific or technical journal as he or she may select.

To the extent authorized in the applicable contract or grant, the contractor or grant recipient may assert copyright subsisting in scientific and technical articles based on or containing data first produced in the performance of the contract or grant and published in academic, technical, or professional journals, symposia proceedings, or similar works. When such assertion of copyright is made, the contractor or grant recipient shall affix the applicable copyright notices of 17 U.S.C. 401 or 402 and acknowledgment of Government sponsorship (including contract or grant number) to the data when such data are delivered to the Government as well as when the data are published or deposited for registration as a published work in the U.S. Copyright Office. The contractor or grant recipient grants to the Government and others acting on its behalf, a paid-up, nonexclusive, irrevocable worldwide license in such copyrighted data to reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, by or on behalf of the Government.

APPENDIX AA

Aerospace Support and Dive Medicine Board

JSC Aerospace Support and Dive Medicine Board Implementation Plan

Space Medicine and Health Care Systems Office
Occupational Health and Human Test Support Office

May 2002

National Aeronautics and Space Administration
Lyndon B. Johnson Space Center
Houston, Texas 77058

REVISION AND HISTORY PAGE

Revision	DESCRIPTION	Publication Date
A	Baseline document	

Signature Page

Submitted by:

Charles E. Ross, DO
Chief, Occupational Medicine and Human Test Support

Approved by:

Craig Fischer, MD
Chairperson, JSC Aerospace Medicine Board

ACRONYM LIST

AMB	Aerospace Medicine Board
ASDMB	Aerospace Support and Dive Medicine Board
HIMS	Health Information Management System
JMI	JSC Management Instruction
JSC	Johnson Space Center
MPB	Medical Policy Board
NASA	National Aeronautics and Space Administration
NBL	Neutral Buoyancy Laboratory
NPC	NASA Policy Charter

1. Purpose

1.1 This document establishes the Lyndon B. Johnson Space Center (JSC) Aerospace Support and Dive Medicine Board (ASDMB) as a sub-board of the Aerospace Medicine Board (AMB).

1.2 This document provides for a consistent approach to the review and medical certification of flight controllers, personnel who participate in underwater diving operations at the Neutral Bouyancy Laboratory (NBL), personnel participating in hypobaric or hyperbaric chamber operations, research aircraft flight participants (investigators and others), and human test subjects.

1.3 The ASDMB will serve as the primary medical review body for diving and hyperbaric medicine issues promoting timely review, by subject matter experts, of the subset of AMB cases specific to these areas.

2. Applicability/Scope

This AMB document is applicable to the operation of the Lyndon B. Johnson Space Center Aerospace Support and Dive Medicine Board (ASDMB), which has the responsibility to support medical operations conducted at Johnson Space Center and its affiliated facilities, including the Neutral Buoyancy Laboratory (NBL), Sonny Carter Training Facility, Ellington Field, and the El Paso Forward Operating Location.

3. Authority

3.1 The Aerospace Medicine Board's authority is established by NASA Policy Charter Directive (NPC 1152.59) "NASA Medical Boards in Support of Space Flight Operations" and 42 U.S.C. 2473 (c) (1), Section 203 (c) (1) of the National Aeronautics and Space Act of 1958, as amended.

3.2 The document, "JSC Aerospace Medicine Board Procedures," outlines AMB authority, responsibility, composition, and functioning. The AMB delegates the authority for specific functions to the Aerospace Support and Dive Medicine Board, but the AMB retains medical oversight responsibility and waiver authority for standards, in accordance with NASA Policy Charter Directive NPC 1152.59.

4. Aerospace Support and Dive Medicine Board Responsibilities

4.1 The ASDMB will establish, review, and modify medical standards for the selection and retention of personnel performing critical operations as members of space flight control teams (flight controllers) and personnel performing duties in special operational environments, including aircraft and chambers.

4.2 The ASDMB will review and act on waiver requests for individuals participating in diving operations at the NBL, NASA flight controllers, individuals involved in KC-135 microgravity flights, altitude/hyperbaric chamber training or testing, research subjects, and similar activities.

4.3 The ASDMB will determine divers' medical fitness for duty and consider waivers for divers who fail to meet applicable medical standards for diving.

The ASDMB functions as the medical review authority for NASA employees, contractors, and others who participate in diving operations at the JSC Neutral Buoyancy Laboratory.

4.4 The ASDMB will periodically review and update, at a minimum of every 3 years, the applicable standards for divers at the NBL.

4.5 The ASDMB will not review or act on waiver requests for astronauts, astronaut candidates, payload specialists, space flight participants, NASA pilots, KC 135 microgravity flight crew, and other aircrew members. The AMB remains the sole forum for medical disqualifications and waivers for astronauts and NASA personnel on flying status.

4.6 At the request of a crew surgeon or the AMB, the ASDMB may serve in a consultative role to determine medical qualifications of astronauts, payload specialists, pilots, and other spaceflight or aviation personnel, when a waiver is considered for medical conditions that result from, or may be affected by, diving or operations in hyperbaric environments.

5. Composition of the JSC ASDMB

5.1 Officers

5.1.1 The Chief, Occupational Health & Human Test Support serves as the chairperson of the ASDMB. If the individual in this position is not a physician, a senior JSC affiliated physician will be appointed by the Chairperson of the AMB.

5.1.2 For the purpose of ASDMB appointment, a senior JSC affiliated physician is defined as an individual with: a degree as doctor of medicine or doctor of osteopathy, a valid license to practice medicine, and at least one year of service as a member of the AMB or ASDMB. Appointment of any acting or regular officers of the ASDMB is to be done with the concurrence of the chairperson of the AMB. There is no limitation on tenure.

5.1.3 An ASDMB officer will be responsible for preparation of a written report that summarizes pertinent findings of the Board, presents the medical dispositions in sufficient detail to permit review, and identifies specific actions for implementation by the chairperson or others. ASDMB minutes, waivers, and actions must be submitted to the AMB chairperson within 30 days for review and concurrence.

5.2 Voting Members

5.2.1 Regular Members

5.2.1.1 Appointment. Members of the ASDMB are appointed by written notice from the chairperson. Composition of the Board must include at least three members in addition to the chairperson. Board members may not be added or deleted to alter Board membership for the reason of influencing a discussion or decision of the Board.

5.2.1.2 Eligibility. Members must have a doctor of medicine or doctor of osteopathy degree, a valid license to practice medicine in the United States, must be a JSC affiliated physician (civil service, Department of Defense, contractor physicians, NSBRI, etc.). Board membership generally will include all physicians providing medical support to the NBL, physicians who previously worked at the NBL and have been reassigned at JSC, and the Manager, Human Test Support Group.

5.2.1.3 An AMB member may request appointment to the ASDMB. There is no limit to the number of regular members of the Board.

5.2.1.4 All members of the ASDMB have the following rights: to attend meetings; to make motions and speak in debate; and to vote (or abstain from voting).

5.2.1.5 Participation in scheduled meetings is a responsibility of ASDMB membership. Members are obligated to comply with the procedures of the Board and any other applicable policies, regulations, or statutes.

5.3 Non-voting Participants of the ASDMB

5.3.1 Ad hoc Participants

Other physicians employed as contractors providing services to the JSC Bioastronautics Office, international partner flight surgeons, and aerospace medicine residents assigned to JSC may be appointed as ad hoc participants of the Board. Appointment of ad hoc participants requires approval of the Chairperson, ASDMB. Ad hoc participants of the ASDMB may present issues and participate in discussion, but may not vote. The chairperson may require ad hoc participants to leave the meeting during a vote.

5.3.2 Consultants

The chairperson of the ASDMB may enlist the participation of specialist consultants from medical or scientific disciplines, as required to address issues before the Board. Invited consultants do not vote. The chairperson may require the consultants to leave the meeting during a vote.

5.3.3 Guests

Individuals affected by ASDMB deliberation generally do not attend meetings. They may attend selected meetings of the ASDMB, at the invitation of the chairperson. Guests' participation in discussions is by invitation only. Guests do not vote and will not be present for the vote. The chairperson may exclude guests from all or part of an ASDMB meeting.

6. Conduct of Meetings

6.1 Scheduling

6.1.1 The ASDMB will meet at least once quarterly, but may meet more frequently.

6.1.2 An officer of the Board, or authorized designee, shall provide proper notice of meetings of the ASDMB, including the time, place, and agenda, to all members of the Board. Notice of regular meetings will be distributed in

advance. For urgent matters, the chairperson may convene a meeting without prior notice.

6.1.3 Members and consultants may participate in ASDMB meetings by teleconference, if necessary.

6.2 Quorum Requirements

6.2.1 A quorum must be present to do business. Three members (including the chairperson) constitute a quorum for the ASDMB.

6.2.2 Absent a quorum, the ASDMB may receive reports (but no action may be taken on them). Emergency action can be taken absent a quorum, but these actions must be reviewed at the next scheduled ASDMB meeting. Emergency actions are defined as those requiring an immediate response to protect health or safety.

6.3 Order of Business

6.3.1 As a general rule, the conduct of the meetings shall assure that majority rule shall prevail. All those in attendance shall give control of the meeting to the chairperson whether the chairperson has invoked formal or informal procedures.

6.3.2 Voting by the members may be by secret ballot or voice vote. Any voting member of the board may request a secret ballot vote in the form of a motion.

6.3.3 The minority opinion shall be made a permanent part of the record of the board meeting when requested by any voting member of the board.

6.3.4 Majority rules. The minority has the right to be heard, but once a decision has been reached by a majority of the ASDMB members present and voting, the minority must then respect and abide by the decision.

6.3.5 A member can request that the minutes of the meeting record his or her vote or abstention.

6.4 Preparation and Presentation of Materials for ASDMB Review

6.4.1 Any Board member may submit items for consideration by the ASDMB.

6.4.2 Requests for medical certification, decertification, and issuance of waivers will be submitted in writing by the examining medical officer. A general format for presentations includes:

- Individual's name and classification.
- Medical history addressing significant issues.
- Occupational and diving history to include training, experience, and other work-related illnesses or injuries.
- Medical examination results including consultation(s) and test(s).
- Diagnosis.

- Prognosis.
- Treatment, if any.
- Summary of the current medical literature, with appropriate references, applicable to the case under consideration.
- Report on consultations with medical experts in the military or other organizations, and notes on how they handle similar cases.
- The possibility of sudden incapacitation, the examinee's ability to perform required duties, the risk to other personnel, the potential for disruption/early termination of operations or training, and the risk to the examinee by exposure to, or work in, the operational environment should be addressed.
- Follow up recommended.
- Medical officer's recommendations regarding medical certification for fitness to perform duties, noting specific medical standards not met, presented in the form of a motion to the Board.

6.5 Discussion

6.5.1 The chairperson will moderate discussion of issues before the ASDMB.

6.5.2 Individual members must feel free to express opinions and concerns without fear of career repercussions.

7.0 Management of Medical Information

7.1 Privacy Act of 1974

7.1.1 Medical and other personal information are reviewed by the ASDMB and are summarized in the Board's reports. These records, as well as other information considered in their preparation, are parts of a system of medical records that are subject to the Privacy Act of 1974, as amended 5 U.S.C. 522 (a) and are a part of the official NASA system of medical records subject to 10 Health Information Management Systems (HIMS). These records and reports may not be disclosed to any person, or to another agency, except pursuant to a written request by, or with the written consent of, the individual to whom the records pertain. Intra-agency disclosure of records is otherwise permitted only as necessary for official purposes, or in accordance with specific exceptions allowed by law. As a general rule, meeting handouts containing medical and other personal information will be collected at the end of the meeting and shredded.

7.1.2 Supporting and other relevant NASA regulations and rules include: 14 C.F.R. Part 1212, "Privacy Act—NASA Regulations;" NMI 1382.17, Privacy Act—NASA Regulations;" JMI 1382.8, "Privacy Act of 1974;" JMI 1382.5, "Maintaining Privacy of Biomedical Data;" JPD 7170.3, "Disposition and Reporting of Anomalous Human Research Data;' and JSC 20483, "JSC Institutional Review Board—Guidelines for Investigators Proposing Human Research for Space Flight and Related Investigations."

7.2 Special Considerations for Sensitive Information

Any written notes of ASDMB proceedings must be maintained in accord with the Privacy Act of 1974. It is forbidden to discuss or disclose medical information presented at the ASDMB, except with: the patient (or those authorized by the patient to receive this information), JSC or consultant medical staff who are participating in the patient's medical care or evaluation, AMB members, the chairperson, Medical Policy Board, or others who have a need to know as determined by the chairperson of the ASDMB or AMB.

7.3 Reports and Actions

7.3.1 The ASDMB chairperson is responsible for preparation of the official written reports of the ASDMB meetings. These reports will summarize pertinent findings, present the disposition in sufficient detail to permit AMB review, and will identify specific actions for implementation. Each ASDMB meeting report will be submitted for review and approval by the Chairperson of the AMB.

7.3.2 Administrative tasks associated with preparation and submission of ASDMB minutes and reports may be assigned by the Chairperson to another board member or support staff.

7.3.3 All decisions of the ASDMB will be forwarded to the Chairperson of the AMB for review and concurrence. Reports will include sufficient information to permit independent review:

a. Individual's name and classification.
b. Diagnosis and prognosis.
c. Copy of the waiver memorandum, noting specific medical standards being waived, signed by the Chairperson, ASDMB noting any restrictions, duration and the follow-up required.

7.3.4 Board actions pertaining to individuals will be communicated to the affected person within 7 days. Board recommendations for additional evaluation, treatment, counseling, or other actions will be incorporated into the individual's permanent medical record.

7.3.5 Decisions of the Board that do not include individuals' medical information may be discussed or disclosed, as required by JSC operational needs. Specific details of the Board's discussion, including any information that identifies statements or positions attributable to specific Board members, are considered confidential.

8. Waivers

8.1 General Considerations

8.1.1 If the examining physician finds a disqualifying condition, the individual is denied medical certification until the ASDMB reviews the findings.

8.1.2 The waiver process is the formal relinquishing of a standard. The NASA JSC Aerospace Medicine Board waiver system is designed to provide maximum benefit to NASA by providing flexibility over standards for physical qualification. This waiver authority is delegated to the ASDMB for specific categories of personnel, not to include astronauts or rated flying personnel. Waiver decisions are biased in favor of safety and mission effectiveness, with consideration given to investment and value of trained and experienced personnel, or those who have uniquely valuable skills.

8.1.3 The Board will consider all aspects of the medical issues. These include, but are not limited to, safety, the present and future health of individual, the potential impact of a medical problem on the individual, and the interests of NASA programs.

8.2 Granting Authority and Precedence of Actions

8.2.1 The NASA JSC Aerospace Medicine Board specifically delegates to the ASDMB the authority granting of waivers for divers, flight controllers, and selected non-aircrew members. The AMB Chairperson, or an authorized delegate, must review all waivers.

8.2.2 If after review, there is not concurrence from the AMB Chairperson, the case will be reviewed by the AMB in a regular meeting. The AMB will then assume the responsibility for action on the case.

8.2.3 Any ASDMB action may be nullified by written notice from the AMB Chairperson, but all such nullifications must have concurrence from a majority of the voting members at the next regular AMB meeting.

8.2.4 Actions and decisions of the AMB have precedence over those of the ASDMB.

8.3 Categories of Waivers

8.3.1 Unconditional Waivers

8.3.1.1 An unconditional waiver will be granted when the Board determines that there is no need for the Board to reconsider the waiver on a regular basis. An unconditional waiver is granted without restriction. No additional medical evaluation, operational testing, monitoring, or treatment is required.

8.3.1.2 During subsequent medical evaluations, the examining medical officer will specifically document the current status of the condition. If there has been no change, no additional report to the Board is required.

8.3.2 Conditional Waivers

8.3.2.1 A conditional waiver may be granted if the Board determines that there is a need for treatment, medical surveillance, or duty restrictions.

8.3.2.2 The specified treatment, surveillance regimen, or restrictions may be communicated in writing to the individual's physician. The presenting physician will brief the individual about waiver requirements. A conditional

waiver will be valid only if the individual agrees to and complies with the conditions of the waiver.

8.3.2.3 The Board must review conditional waivers at least annually.

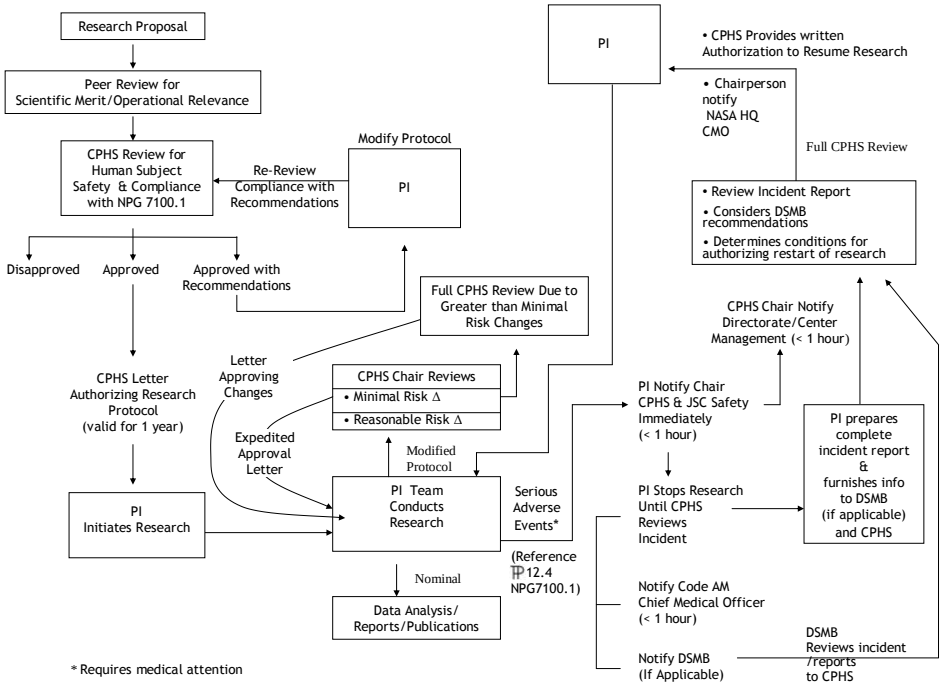
8.4 Reconsideration or appeal of a waiver request

8.4.1 A waiver request, once denied, may be again presented to the Board if there has been a change in the individual's medical condition, a change in the medical standard or requirement, or if significant new information relevant to the issue has become available. This new information may include the results of additional clinical evaluation or diagnostic testing, information about the operational requirements, or information supporting modification of the relevant standard.

8.4.2 A denial of a waiver by the ASDMB may be appealed to the AMB.

8.4.3 Once the intent to appeal is made to the ASDMB by the individual or management, the ASDMB chairperson will notify the AMB chairperson. The AMB chairperson will then review the case to determine whether or not it merits review by the full AMB. If the AMB chairperson determines the case does not merit review by the full AMB, the original findings of the ASDMB stand. If the case merits full review by the AMB the case will be formally heard by the AMB.

APPENDIX BB


Research Proposal
Peer Review for Scientific Merit/Operational Relevance
CPHS Review for Human Subject Safety & Compliance with NPG 7100.1
Re-Review Compliance with Recommendations
Modify Protocol
PI
Disapproved
Approved
Approved with Recommendations
Full CPHS Review Due to Greater than Minimal Risk Changes
CPHS Letter Authorizing Research Protocol (valid for 1 year)
Letter Approving Changes
CPHS Chair Reviews
• Minimal Risk Δ
• Reasonable Risk Δ
Expedited Approval Letter
Modified Protocol
PI Team Conducts Research
PI Initiates Research
Serious Adverse Events*
(Reference ₱12.4 NPG7100.1)
Nominal
Data Analysis/ Reports/Publications
* Requires medical attention
PI
• CPHS Provides written Authorization to Resume Research
• Chairperson notify NASA HQ CMO
Full CPHS Review
• Review Incident Report
• Considers DSMB recommendations
• Determines conditions for authorizing restart of research
CPHS Chair Notify Directorate/Center Management (< 1 hour)
PI Notify Chair CPHS & JSC Safety Immediately (< 1 hour)
PI prepares complete incident report & furnishes info to DSMB (if applicable) and CPHS
PI Stops Research Until CPHS Reviews Incident
Notify Code AM Chief Medical Officer (< 1 hour)
Notify DSMB (If Applicable)
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