The Jackson Laboratory
Human Research Protection Program
Policies

September 2023

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THE JACKSON LABORATORY HUMAN RESEARCH PROTECTION PROGRAM

1.0 PURPOSE AND SCOPE

The Jackson Laboratory ("Laboratory") Human Research Protection Program ("HRPP") is responsible for the protection of the rights and welfare of Human Subjects participating in research; for the development and provision of training and policies for researchers; for coordinating Interactions with potential and enrolled participants; for the conduct of quality improvement and assurance activities; and for supporting the compliance responsibilities of the institution and of Laboratory investigators conducting Human Subjects Research.

The HRPP has jurisdiction over all Human Subjects Research conducted by Laboratory investigators in connection with their institutional roles or responsibilities or in which the Laboratory is otherwise engaged, regardless of the location of the research or the source of funding.

The Laboratory is engaged in non-exempt Human Subjects Research when its employees, faculty, or students for the purpose of the research project obtain: (1) data about the participants of the research through Intervention or Interaction with them; (2) Identifiable Private Information about the participants or identifiable biospecimens for research purposes or (3) the informed consent of Human Subjects for the research. The Laboratory is also engaged in Human Subjects Research whenever a direct award from the Department of Health and Human Services ("HHS") to support Human Subjects Research is received, even for studies in which all activities involving Human Subjects are carried out by employees or agents of another institution.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel will adhere to the HRPP guidelines in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The mission of the HRPP is to protect the rights, dignity, welfare, and privacy of Human Subjects participating in research performed by or on behalf of the Laboratory, in accordance with federal requirements and ethical guidelines. This includes research that is conducted or sponsored by the Laboratory or in which the Laboratory is otherwise engaged, regardless of funding. The HRPP fosters a culture of compliance with the highest legal and ethical standards

for Human Subjects protection across the institution and among its investigators and all members of the research community.

3.1 ETHICAL PRINCIPLES

The ethical principles that guide Laboratory research is outlined in the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, generally known as the "Belmont Report."

Organizational officials, the Institutional Official ("IO"), faculty, researchers, and research staff (including students), Laboratory Institutional Review Board ("IRB") members and all Laboratory employees have the ethical obligation to protect Human Subjects participating in research in which the Laboratory is engaged in accordance with legal requirements and ethical guidelines.

3.2 APPLICABLE LAWS

Laws, regulations, and other policies relevant to the HRPP include guidance pertaining explicitly to research and Human Subjects protections and rules that are not specific to research but that may affect its conduct or oversight. Key laws and regulations include the following, but are not limited to:

- 42 U.S.C. 241(d) (Certificates of Confidentiality)
- Pub. L. No. 104-191, 110 Stat. 1936 (HIPAA)
- Pub. L. No. 111-5, 123 Stat. 226 (HITECH)
- 42 CFR Part 50 (Research Integrity: Objectivity in Research – Financial Conflicts of Interest)
- 45 CFR Part 46 (Protection of Human Subjects)
- 45 CFR Part 160 (Security and Privacy)
- 45 CFR Part 164 (Breach Reporting)
- 21 CFR Part 11 (Electronic Records; Electronic Signatures)
- 21 CFR Part 50 (Protection of Human Subjects)
- 21 CFR Part 54 (Financial Disclosure by Clinical Investigators)
- 21 CFR Part 56 (Institutional Review Boards)
- 21 CFR Part 312 (Investigational New Drug Application)
- 21 CFR Part 610 (Biological Products)
- 21 CFR Part 812 (Investigational Device Exemptions)
- Applicable Maine, California, and Connecticut laws
- For research conducted or supported by governmental entities, entity regulations and requirements as applicable (e.g., U.S. Department of Defense, U.S. Department of Justice)

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3.3 GOVERNANCE

Governance of the HRPP is a function of the IO, Human Protections Administrator, IRB Chair, IRB members and the Office of General Counsel.

The IO executes and provides assurance that the Laboratory IRB, designated in the Federalwide Assurance ("FWA"), is knowledgeable about the local research context and complies with the terms of the FWA. The Laboratory has an approved FWA with the Office of Human Research Protections ("OHRP"). The FWA number is FWA00000323 and is renewed every five years.

3.4 HUMAN RESEARCH PROTECTION PROGRAM ORGANIZATIONAL STRUCTURE

3.4.1 INSTITUTIONAL OFFICIAL

The Institutional Official ("IO") understands the institution's responsibilities under the FWA, assures the protection of Human Subjects in Research, and assures that the IRB is knowledgeable about the local research context and complies with the terms of the FWA. The IO ensures that the IRB (or appropriately designated IRB with whom the Laboratory has a reliance agreement) is the sole entity that can grant approval for non-exempt research activities involving Human Subjects. The IO may delegate the performance of certain oversight and operational duties to appropriate and qualified individuals.

The IO is responsible for and has the authority to:

- "Set the tone" for an institutional culture of respect and conscience, so that the ethical conduct of Human Subjects Research is supported at the highest levels of the organization.
- Ensure effective institution-wide communication and guidance on Human Subjects Research issues.
- Ensure that investigators fulfill their responsibilities.
- Facilitate participation in Human Subject protection education activities.
- Serve as a knowledgeable point of contact for OHRP, the Office of Research Integrity ("ORI") and other relevant federal and state agencies.
- Ensure required reporting to OHRP, ORI and other relevant federal and state agencies.

Administratively, the IO is responsible for:

- Providing the Laboratory IRB and HRPP with the necessary local resources.
- Supporting the authority and decisions of the IRB.

3.4.2 THE INSTITUTIONAL REVIEW BOARD

The Laboratory IRB is registered with OHRP and the Food and Drug Administration ("FDA"). The IRB exercises responsibility for protection of human research subjects with independence of decision-making. Only the designated IRB may grant approval for any non-exempt research activity involving Human Subjects. Human Subjects Research

approved by the IRB may be subject to further institutional review and approval; however, no one within the institution may approve non-exempt Human Subjects Research that has not been approved by the IRB.

When further institutional review and approval is required, the IRB Administrator is responsible for coordinating review and verifying approval of the research by the applicable ancillary committees (e.g., Institutional Biosafety Committee, Information Security, etc.).

3.4.3 HUMAN RESEARCH PROTECTION PROGRAM DIRECTOR/HUMAN PROTECTIONS ADMINISTRATOR

The Director has responsibility for oversight of the institution's HRPP and serves as the Human Protections Administrator of the FWA. The Director provides guidance regarding the interpretation of regulations, laws and policies to the institution's IRB, faculty, and staff on key matters regarding research with Human Subjects.

The Director is responsible for and has the authority to:

- Ensure that the FWA is maintained and ensure compliance with the terms, as well as with Laboratory policies and procedures, federal regulations, and state and local laws relative to the conduct of human research studies.
- In conjunction with the IO, ensure that requirements regarding reporting to federal agencies are satisfied.
- Develop and implement Laboratory HRPP and procedures.
- Determine the selection of the Single IRB ("sIRB") for Laboratory cooperative or multi-site research protocols.
- Assist the IO with recruitment of the IRB.
- Conduct or delegate review of requests for determination of whether an activity qualifies as research, research not involving Human Subjects, or research exempt from IRB oversight.
- Ensure human research protection education and training are available and completed by investigators, key study personnel, the IO, the IRB, and all Laboratory staff who participate in Human Subjects Research.
- Oversee the quality assurance monitoring of the HRPP, including research protocols and investigation of matters of non-compliance.
- Ensure implementation of corrective action, as needed, in accordance with Laboratory policies and IRB policies and procedures.

3.4.4 HUMAN RESEARCH PROTECTION PROGRAM QUALITY ASSURANCE PROGRAM

The Quality Assurance ("QA") program is responsible for assisting the institution and investigators in fulfilling their Human Subjects Research responsibilities through compliance with federal regulations and Laboratory policies governing Human Subjects Research. It is also responsible for promoting an environment for the conduct of Human Subjects Research according to the highest legal and ethical standards. The QA program accomplishes these goals through on-site assessments and educational activities conducted both prior to and during active conduct of the research.

The QA program is responsible for and has the authority to:

- Conduct routine (not-for-cause) audits that focus on compliance with all relevant regulations. These audits may be conducted on any study that has been approved by the IRB or designated IRB or determined exempt by the IRB.
- Conduct directed (for-cause) audits at the request of the IRB or the IO.
- Assist investigators in study start-up activities, such as creating study management documents, data collection tools, and study activation visits.
- Provide practical and specific educational in-service training programs for investigators and research teams.
- Assist investigators in understanding and complying with clinical trials registration and reporting requirements.

3.4.5 THE OFFICE OF GENERAL COUNSEL

Within the Legal Department, the designated counsel to the IRB advises on Human Subjects Research issues, policies, and legal requirements; research compliance matters; research integrity and related misconduct investigations; conflicts of interest; intellectual property; technology transfer and licensing; clinical trial agreements; HIPAA-related concerns (for Laboratory Covered Entity areas) and general research affairs. Work relating to Human Subjects protection includes, for example, reviewing IRB and other institutional policies, reviewing consent form language and other templates, advising on project-specific issues (e.g., informed consent, confidentiality), counseling on privacy requirements, assisting in investigations of alleged noncompliance, advising on liability issues, and general interpretation and guidance on new and existing legal requirements and conflicts between applicable laws.

The Legal Department has a close working relationship with the IRB and the HRPP. Frequent conversations, meetings, and email exchanges take place on a wide range of research issues. In addition, the Legal Department closely advises researchers, innovators, and research leadership across the Laboratory.

3.4.6 PRINCIPAL INVESTIGATORS

Primary responsibility for protecting the rights and welfare of Human Subjects participating in research rests with the Principal Investigator ("PI"). PIs may not commence Human Subjects Research prior to obtaining IRB approval and, as appropriate, other institutional approval of their research activities. The PI may not be a research fellow or other trainee. For each research activity submitted to the IRB for approval, the PI must certify that s/he accepts responsibility for assuring adherence to applicable federal and state research regulations and Laboratory policies relative to the protection of the rights and welfare of participants enrolled in the research.

PIs must be qualified by training and experience to conduct the research and must be in compliance with the institutional policies on investigator financial conflicts of interest (POL.RES.017), PI responsibilities (POL.RES.009) and education and training requirements (POL.RES.011).

The PI must review all study documents to be submitted and sign applications for any research that involves an Intervention or Interaction with Human Subjects, Identifiable Private Information about the participants of the research (i.e., the identity of the participant is or may readily be ascertained by the investigator or associated with the information) or obtains the informed consent of Human Subjects for the research prior to submission to the IRB.

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Research cannot begin until written approval has been received from the IRB, and if applicable, an activation visit by Clinical and Translational Research Support personnel has been conducted. Refer to the activation of research policy (POL.RES.055).

3.4.7 CO-INVESTIGATORS AND RESEARCH STAFF

PIs may delegate responsibilities to appropriately qualified co-investigators and research staff. However, co-investigators and research staff must be qualified by training and experience to perform these responsibilities. Additionally, co-investigators and research staff must be in compliance with the policy on investigator financial conflicts of interest (POL.RES.017), education and training (POL.RES.011) and study staff/collaborator responsibilities (POL.RES.013). The PI remains responsible for the conduct of all persons to whom s/he delegates tasks.

All investigators and research staff must have current Collaborative Institutional Training Initiative ("CITI") Biomedical Research, Social and Behavioral Research, or Computational Scientist Human Subjects Protection Training, and Conflict of Interest Training , or an equivalent program accepted by the Laboratory, in order to participate in the conduct of Human Subjects Research.

Investigators and research staff must be listed on the IRB Application for any protocol in which they are involved as study personnel. For each protocol to which they are added as study staff, investigators and research staff must certify that they:

1. Have completed the Human Subjects protection training requirements.
2. Understand Laboratory policy on conflicts of interest, declare any conflicts that they may have with the research, and be in compliance with the policy at all times during the course of the research.
3. Accept the obligation to comply with all applicable federal regulations, institutional HRPP policies and procedures, and the requirements and determinations of the IRB with respect to the research.

3.4.8 SPONSORED RESEARCH CONFLICT OF INTEREST COMMITTEE

The term "conflict of interest in research" refers to situations in which financial or other personal considerations may compromise or have the appearance of compromising a researcher's professional judgment in conducting or reporting research.

In situations where a financial interest and possible conflict of interest are disclosed by the PI or other member of the study team at the time of IRB review, each situation is reviewed by an independent substantive review committee, known as the Sponsored Research Conflict of Interest Committee (see POL.RES.017 and POL.RES.003).

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4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **FDA:** Food and Drug Administration
- **FWA:** Federalwide Assurance
- **HHS:** Health and Human Services
- **HRPP:** Human Research Protection Program
- **Human Subject (FDA):** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be a healthy individual or a patient.
- **Human Subject (HHS):** A living individual about whom an investigator (whether professional or student) conducting research: (i) obtains information or biospecimens through Intervention or Interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates Identifiable Private Information or identifiable biospecimens.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *Human Subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *Human Subject* or *subject* as defined by FDA.
- **Identifiable Private Information:** Private Information for which the identity of the participant is or may readily be ascertained by the investigator or associated with the information.
- **Interaction:** Includes communication or interpersonal contact between investigator and participant.
- **Intervention:** Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.
- **IO:** Institutional Official
- **IRB:** Institutional Review Board
- **OHRP:** Office of Human Research Protection
- **PI:** Principal Investigator
- **Private Information:** Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- **QA:** Quality Assurance
- **Research (HHS):** A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for

purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

- **Research (FDA) or Clinical Investigation:** Any experiment that involves a test article and one or more Human Subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
- **Single IRB (sIRB):** Selected IRB of record that conducts the ethical review for participating sites of the multi-site or collaborative study.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
Notice Number: NOT-OD-16-094	Final NIH policy on the use of a single institutional review board for multi-Site research
POL.RES.003	Objectivity in sponsored research: Financial conflicts of interest
POL.RES.011	Human Subjects Research: Education and training requirements
POL.RES.017	IRB review of financial conflicts of interest
POL.RES.055	Activation of a research study after IRB approval

IRB AUTHORITY, RESPONSIBILITY AND OPERATING PROCEDURES

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PURPOSE AND SCOPE

The Jackson Laboratory (Laboratory) Institutional Review Board (IRB) provides ethical review and continuing oversight of human subjects research, as further described herein, so as to protect the rights and welfare of the participants in the research. The Laboratory IRB operates in full compliance with all applicable federal, state, and local laws and regulations, with the Federalwide Assurance (FWA) held by the Laboratory, and the incorporated "Terms of the Federalwide Assurance for Institutions within the United States." The responsibility for the protection of the rights and welfare of human subjects is shared both by the institution and the investigators conducting the research.

POLICY STATEMENT

ETHICAL PRINCIPALS

The ethical principles to guide research for which the IRB has overall responsibility, including those protocols that are exempt from the federal regulations, are outlined in the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, generally known as the "Belmont Report."

Organizational officials, the Institutional Official (IO), faculty, researchers and research staff (including students), IRB members and all other Laboratory employees have the obligation to protect human subjects participating in research in which the Laboratory is engaged in accordance with legal requirements and ethical guidelines.

IRB AUTHORITY, RESPONSIBILITY AND OPERATING PROCEDURES

HHS regulations (45 CFR 46) require an assurance, known as the Federalwide Assurance (FWA) from the institution. FDA regulations (21 CFR 50,56,312,812) generally require assurances from either or both the sponsor of the research and the investigator.

The Federal Policy for the Protection of Human Subjects, known as the "Common Rule", updated in 2018, is followed by 20 federal agencies, including HHS. The Food and Drug Administration (FDA), who regulates clinical investigations of drugs, biologics and medical devices, is not considered a "Common Rule Agency" because they have their own set of federal regulations that differ from the Common Rule. FDA is required to harmonize with the Common Rule whenever permitted by law, based upon the 21st Century Cures Act. When a research project is supported by HHS and involves an FDA-regulation product, then the project is subject to both 45 CFR 46 and 21 CFR parts 50 and 56.

AUTHORITY AND INDEPENDENCE

The IRB is authorized by the Laboratory to review and oversee non-exempt human subjects research that is conducted by Laboratory employees or faculty in connection with their institutional responsibilities, regardless of the location of the research or source of funding, in accordance with federal, state, and local laws and regulations.

To fulfill these responsibilities, the IRB has the authority to:

- Determine whether a research activity involves human subjects, or if the institution is engaged in human subjects research as defined by the Department of Health and Human Services (HHS) [45 CFR 46.103], the U.S. Food and Drug Administration (FDA) [21 CFR 50.103] or other applicable federal regulations.
- Determine whether a research activity involving human subjects is exempt from the regulation per 45 CFR 46.104 or 21 CFR 56.104.
- Review and approve, require modifications to (to secure approval), or disapprove all research activities [45 CFR 46.109(a)][21 CFR 56.109(a)], including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption.
- Suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects [45 CFR 46.113][21 CFR 56.113].
- Observe, or have a third party observe the consent process and the conduct of the research [45 CFR 46.109(g)][21 CFR 56.109(f)].
- Act as the HIPAA Privacy Board for research activities involving the Laboratory Covered Entity or a relying external Covered Entity (RECE) when Laboratory IRB serves as single IRB.
- Determine which research studies require review more than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review [45 CFR 46.108(3)(ii)][21 CFR 56.108(a)(2)].

IRB AUTHORITY, RESPONSIBILITY AND OPERATING PROCEDURES

- Conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year, *except* as described in 45 CFR 46.109(f).
- For research subject to FDA regulations, the IRB is required to conduct continuing review at intervals appropriate to the degree of risk, but not less than once per year [21 CFR 56.109(f)].
- Ensure prompt reporting of proposed changes in a research activity, and for ensuring that investigators will conduct the research activity in accordance with the terms of the IRB approval until any proposed changes have been reviewed and approved by the IRB, except when necessary to eliminate apparent immediate hazards to the subject [45 CFR 46.108(3)(iii)][21 CFR 56.108(a)(3) and (4)];
- Ensure prompt reporting of any unanticipated problems involving risks to subjects or others, any serious or continuing noncompliance with federal regulations or the requirements or determinations of the IRB, or of any suspension or termination of IRB approval to the IRB, appropriate institutional officials, the department or agency head, and OHRP [45 CFR 46.108 (4)][21 CFR 56.108(b)];
- Place restrictions on a research activity;
- Request a directed audit, review, or inquiry as needed to obtain information for the fulfillment of human research protection responsibilities;
- Otherwise investigate, address, remedy and, when required or appropriate, report on incidences of noncompliance with legal, regulatory, or IRB requirements or determinations.

In exercising its authority, the IRB communicates its decisions regarding human subjects research to investigators and to the institution through written communications delivered by institutional email.

The IRB has the empowerment, flexibility and discretion to raise the standards of protection above those afforded to research participants in 45 CFR 46, 21 CFR 50 and 21 CFR 56 as it deems appropriate and necessary in particular cases, although it may not lower the protections below those afforded by the regulations.

The IRB exercises independence as the entity authorized to review and oversee non-exempt human subjects research for the Laboratory. Consistent with federal regulations, no one within the institution may approve such human subjects research that has not been approved by the IRB [45 CFR 46.112][21 CFR 56.112]. However, research approved by the IRB may be subject to further institutional review and approval or disapproval.

In the event of undue influence (e.g., someone outside of the IRB seeks to influence the outcome of IRB review of a research activity), the IRB Chair and human protections administrator works with the IO, as necessary, to remedy any concern. Responses to such a concern preserve the IRB's independence.

IRB AUTHORITY, RESPONSIBILITY AND OPERATING PROCEDURES

SCOPE OF RESPONSIBILITY

The IRB is responsible for the review and oversight of all non-exempt human subjects research that is conducted by faculty, employees and students in connection with their institutional responsibilities, regardless of the location of the research or source of funding, except for:

- Research involving prisoners, since the IRB does not have a prisoner representative member.
- Research reviewed by another institution or entity's IRB through an IRB authorization or single-IRB agreement.

At the request of the investigator or other institutional representatives, the IRB may provide guidance on—or review—any research activity that involves human materials, but that does not meet the definition of human subjects research.

IRB members are responsible for initial and continuing ethical and scientific review of all research activities involving human subjects, review of proposed changes in approved research, review of unanticipated problems involving risks to subjects or others, and review of reports of serious or continuing non-compliance. In the course of reviewing such research activities, members are responsible for the following considerations:

- Risks to subjects are minimized: (i) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (ii) Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
- Selection of subjects is equitable.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by, 45 CFR 46.116 or 21 CFR 50.20 (FDA regulated research allows IRBs to waive or alter consent in a few circumstances, 21 CFR 50.24).
- Informed consent will be appropriately documented, or appropriately waived in accordance with, 45 CFR 46.117 or 21 CFR 50.27.
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

IRB AUTHORITY, RESPONSIBILITY AND OPERATING PROCEDURES

REVIEW OF RESEARCH

The IRB has the authority and responsibility to determine whether a research activity submitted to the IRB is human subjects research within the parameters of 45 CFR 46, 21 CFR 50, 56 and 812. When the research activity is human subjects research, the IRB determines whether non-FDA regulated research is exempt in accordance with 45 CFR 46.104(d)(1-8).

The IRB conducts initial and continuing ethical review of non-exempt human subjects research at intervals appropriate to the degree of risk and, when federally funded or otherwise subject to federal regulation, not less than once per year, except as described in 45 CFR 46.109(f) and 21 CFR 56.109. The IRB reviews proposed changes in approved research during the period of IRB approval either at a convened meeting of the IRB or, when applicable, by use of the expedited review procedure as described in 45 CFR 46.110 or 21 CFR 56.110. The IRB determines that all of the requirements for approval of human subjects research in 45 CFR 46.111 or 21 CFR 56.111 are satisfied (see POL.RES.021 and POL.RES.022).

Non-exempt human subjects research cannot be approved by any other institutional body or individual(s) if the research has not been approved by the IRB. Investigators may submit an appeal to a disapproval decision of the IRB in writing directly to the IRB Chair, who will then review the appeal and bring to the convened IRB. The investigator is given the opportunity to appeal the decision of the IRB in person at the convened meeting.

Research submitted and approved prior to January 21, 2019 will be reviewed according to the “pre-2018” Code of Federal Regulations for the lifespan of the research, unless deemed otherwise by the IRB. All research submitted on or after January 21, 2019 will be reviewed according to the “2018” Code of Federal Regulations.

CONFIDENTIALITY

IRB review proceedings and records of review activities are considered confidential and protected from external access. IRB members or others with access to these proceedings or records must not use them for any purpose other than to carry out their IRB responsibilities and must not disclose them to others who are not authorized under these procedures to have access. Such protection is essential to encourage open discussion by the IRB in review of proposed research, maintain the integrity of the deliberative process, safeguard the privacy and confidentiality of participants in research, and to avoid disclosure of information that is proprietary to the Laboratory, research sponsor or other third party and for which the institution may be contractually obligated to keep confidential.

IRB AUTHORITY, RESPONSIBILITY AND OPERATING PROCEDURES

INCIDENT REPORTING

Consistent with the federal regulations, the IO will report to OHRP, FDA , or the appropriate Federal department or agency, any unanticipated problems involving risks to subjects or others or any serious or continuing non-compliance with HHS or FDA regulations, as well as any suspension or termination of IRB approval for federally-funded research only.

PROCEDURE

N/A

DEFINITIONS AND ACRONYMS

- **Human Subject (HHS):** A living individual about whom an investigator (whether professional or student) conducting research (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- **Human Subject (FDA):** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be a healthy individual or a patient.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.
- **Intervention:** Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction:** Includes communication or interpersonal contact between investigator and subject.
- **Private Information:** Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- **Research (HHS):** A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definitions constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
    - Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of

information, that focus directly on the specific individuals about whom the information is collected.

- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products).
- Collections and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

- **Research (FDA) or "Clinical Investigation":** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these section of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

REFERENCES

- 45 CFR 46
- 21 CFR 50
- 21 CFR 56
- 21 CFR 312
- 21 CFR 812
- POL.RES.021
- POL.RES.022

RESEARCH INVOLVING HUMAN SUBJECTS

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PURPOSE AND SCOPE

This policy defines the applicability of the definitions of *research* and *human subject* found in 45 CFR 46 and *clinical investigation*, *human subject* and *subject* found in 21 CFR 50, 56 and 812 to activities overseen and conducted by employees, faculty or students of The Jackson Laboratory (Laboratory). It details the procedures that investigators and the Laboratory's Institutional Review Board (IRB) follow when making such determinations. All activities that meet the HHS definition of *research* and involve a *human subject* or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA are subject to IRB review and approval.

POLICY STATEMENT

The IRB is responsible for review, approval and oversight of research activities involving human subjects when:

- Research is conducted by or under the direction of any Laboratory employee, faculty or student.
- Research is performed at a Laboratory facility.
- The Laboratory is engaged in the research.

All research involving human subjects will be reviewed by the IRB unless either:

A. The research is determined to be exempt (see POL.RES.020), or
B. The research is reviewed by an external IRB as single IRB or IRB review has been ceded to another institution per an institutional authorization agreement (reliance agreement).

RESEARCH INVOLVING HUMAN SUBJECTS

Laboratory investigators and staff should consider whether their project includes activities that might be considered human subjects research, as defined in HHS regulations 45 CFR 46 or FDA regulations 21 CFR 50 and 56, and if so, consult with the IRB.

Research restricted to commercially available human cell lines is not human subjects research and does not require IRB review or approval. For research using de-identified human data, specimens, cells or other materials that does not involve human subjects or use of commercial cell lines, a Determination of Human Subjects Research (DHSR) application should be submitted in the IRBManager system prior to research use of these materials. By registering the research via the Determination of Human Subjects form, secure genomic data storage may be authorized and provisioned and the need for Institutional Certification of the Genomic Data Sharing plan for federally-funded research assessed to meet institutional responsibilities. Documentation describing the research activity in sufficient detail should accompany this DHSR submission to allow the IRB office to make the required determinations. Supporting documentation could include, as applicable:

- The grant application or proposal for funding.
- Lists of specimens, cells, data or other human materials that will be used in the research.
- Protocol or scope of work.
- Materials transfer or collaboration agreements, and/or data use agreements and
- The informed consent document(s) from original specimen or data collection (if applicable).

If it is determined that the research involves human subjects, investigators should complete either an *Initial IRB Review Application* or a *Request for Exempt Review* form and submit through IRBManager.

Research initially submitted and approved prior to January 21, 2019 will be reviewed according to the "Pre-2018" Federal Regulations for the lifespan of the research, unless deemed otherwise by the IRB. All research initially submitted on or after January 21, 2019 will be reviewed according to the "2018" Code of Federal Regulations.

PROCEDURE

NOT HUMAN SUBJECTS RESEARCH DETERMINATION

After submitting the *Determination of Human Subjects Research* (DHSR) form, the IRB Chair or designee may request additional written information to make the determination. This review is an institutional requirement; it is not required by federal regulations.

- For HHS-regulated research: Determine whether the activity meets the HHS definition of *research*, and if so, determine whether the activity involves *human subjects* as defined by HHS. If the research does not meet this definition, then the project may be conducted without IRB review or exemption.
- For FDA-regulated research: Determine whether the activity meets the FDA definition of *clinical investigation*, and if so, determine whether the activity involves *human subjects* or *subject* as

defined by FDA. If the research does not meet this definition, then the project may be conducted without IRB review or exemption.

- A determination of "Not Human Subjects Research" (NHSR) will be communicated via letter emailed to the investigator.

HUMAN SUBJECTS RESEARCH

After submitting the *Initial IRB Review Application*, the IRB Chair or designee may request additional written information to make the determination.

IRB review of the research will be done via expedited review (see POL.RES.021) or through convened IRB review (see POL.RES.022). After the review, the decisions of the IRB will be communicated to the investigator via IRBManager or email.

EXEMPT RESEARCH

If the research is determined to be exempt from IRB review (i.e., activities in which the involvement of human subjects will be in one or more of the categories described in 45 CFR 46.104 and 21 CFR 56.104), then the investigator will be asked to complete a *Request for Exempt Review* form within IRBManager.

Review will be conducted by a designated reviewer and the decisions will be communicated to the investigator via IRBManager or email.

RECORD RETENTION

Records of determinations about whether an activity is research involving human subjects, including materials submitted and related correspondence, are retained by the Laboratory's Human Research Protection Program in accordance to the policy IRB recordkeeping (POL.RES.058).

In addition, records of IRB submission and review are also maintained in accordance to the same policy (POL.RES.058). Investigator record retention is maintained according to POL.RES.015.

DEFINITIONS AND ACRONYMS

- **Human Subject (HHS):** A living individual about whom an investigator (whether professional or student) conducting research: (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- **Human Subject (FDA):** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be a healthy individual or a patient.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the FDA definitions of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.

- **Identifiable Private Information:** Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- **Interaction:** Includes communication or interpersonal contact between investigator and subject.
- **Intervention:** Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Private Information:** Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- **Research (HHS):** A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
    - Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
    - Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
    - Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
    - Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.
- **Research (FDA) or "Clinical Investigation":** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

REFERENCES

- 45 CFR 46
- 21 CFR 50
- 21 CFR 56
- 21 CFR 812
- POL.RES.015
- POL.RES.020
- POL.RES.021
- POL.RES.022
- POL.RES.058

HUMAN SUBJECTS IN RESEARCH: CASE REPORTING

1.0 PURPOSE AND SCOPE

Clinical experiences are often the genesis of research questions and the design and development of clinical research protocols. In an academic institution, it is not unusual for unique and interesting clinical cases to be written up as case reports for publication in medical journals or for presentation at medical or scientific meetings. This Policy is designed to provide guidance on when publication/presentation of case report(s) constitutes human subjects research and requires prospective approval of The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB").

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to and including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 WHAT DOES NOT CONSTITUTE HUMAN SUBJECTS RESEARCH: RETROSPECTIVE REVIEW OF MEDICAL RECORDS FOR PUBLICATION

In general, the review of medical records for publication of "case reports" of typically three or fewer patients is NOT considered human-subject research and does NOT typically require IRB review and approval. This is because case reporting on a small series of patients does not involve the formulation of a research hypothesis that is subsequently systematically investigated for publication or presentation. Reporting or publication is not typically envisioned when one interacts clinically with the subject. In contrast, when larger series of patients are being reported, investigators usually begin to ask specific research questions and formal systematic collection of data occurs, moving these activities closer to systematically designed research.

3.2 WHAT DOES CONSTITUTE HUMAN SUBJECTS RESEARCH: FORMAL RESEARCH INVOLVING RETROSPECTIVE REVIEW OF MEDICAL RECORDS

Formal, systematic medical records review to answer specific research questions DOES constitute research on identifiable human subjects and DOES require IRB review and approval. Federal regulations state that if data is abstracted without retaining any link to specific individuals, some medical records research may be considered exempt from IRB review. The IRB, not the investigator, must make this determination.

HUMAN SUBJECTS IN RESEARCH: CASE REPORTING

The boundaries between case reporting and formal medical records research may be unclear. Laboratory researchers are thus advised to consult with the IRB or submit larger case series reports for IRB review when uncertainty exists about whether formal and systematic collection of human subjects research data is occurring.

3.3 CONFIDENTIALITY

Patient confidentiality should be respected in all clinical situations involving identifiable medical information from patients. All Laboratory researchers and collaborating clinicians are reminded of the following points:

- The names, dates of birth, social security numbers, and other "codes" or combinations of identifiers, which might easily allow someone to identify a subject, should never be used in publications or external presentations.
- Unique family trees or pedigrees should be masked or disguised when such information could identify individuals or kindreds.
- Photographs should be appropriately masked to preclude identification of subjects and should only be obtained when necessary for meeting aims of the research.
- Laboratory researchers and collaborating clinicians should be sensitive to the "small cell count problem" (see HHS De-identification Guidance): the existence of individuals with such unique or unusual diagnoses or illnesses, that it might be possible for others (or patients and families themselves) to identify the individuals in case reports or medical text books based upon limited information, such as state or city of residence, age, and diagnosis.

Investigators are reminded that they should abstract and retain only the minimum relevant clinical information. Investigators should discard links to human subjects when the research has been completed and published, or when relevant research goals requiring links to individuals are accomplished. Institutional and governmental policies on the duration of retention of research records vary. The Laboratory's record retention policy is stated in POL.RES.015.

Links to identifiable subjects may be maintained to comply with these policies, but should not, be retained indefinitely.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **IRB:** Institutional Review Board
- **Medical Case Report:** A detailed report of the signs, symptoms, diagnosis, follow-up and treatment of an individual patient. Case reports usually describe an unusual or novel occurrence and may contain the demographic profile of the patient.

HUMAN SUBJECTS IN RESEARCH: CASE REPORTING

- **Medical Case Reporting:** The reporting of small numbers of patients (i.e., three patients or less) based on previous clinical interactions.
- **Research (HHS):** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
    - Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
    - Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
    - Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
    - Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.
- **Research (FDA) "Clinical Investigation":** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
US Health and Human Services (HHS), Health Information Policy	Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.
POL.RES.015	Human Subjects Research: Recordkeeping and Record Retention

HUMAN SUBJECTS IN RESEARCH: REVIEW OF QUALITY MEASUREMENT INITIATIVES

1.0 PURPOSE AND SCOPE

Federal regulations require the review and approval of all activities that involve the systematic collection of information about living individuals if the collection may contribute to generalizable knowledge and if the information is recorded in any way that allows the individuals, directly or indirectly, to be identified. This Policy describes the procedures for review and approval of such activities, i.e., quality measurement initiatives or institutional databases with the intent to conduct or support research on human subjects, by The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB").

The Laboratory requires that any quality measurement initiative or database of human subject information whose intent is to conduct or support research (i.e., internal or external analyses of identifiable clinical information for a generalizable purpose, such as a scientific publication) be reviewed and approved by the IRB. Alternatively, if the only purpose of a quality measurement initiative or database is quality improvement (including publication of benchmarking analyses or reports), then no formal submission to the IRB is required, though submission to IRBManager for Determination of Human Subjects Research is recommended.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 EXAMPLES OF INITIATIVES THAT DO NOT NEED TO BE SUBMITTED FOR REVIEW

- Initiatives in which the Laboratory submits identifiable (including coded) clinical data to a database maintained by an outside entity that will aggregate the data with information from other institutions and report benchmarking standards to participating institutions. If this is the sole purpose of the database, and the database will not be used by anyone (whether inside or outside the Laboratory) for research projects, then the initiative/database does not need review.

- Initiatives (whether for benchmarking or other purposes) that use anonymized information (i.e., there is no way for anyone, anywhere to link the information back to a specific individual).
- Initiatives that are required by state or federal law, if the identifiable data collected will be used solely for quality measurement purposes. For example, if the Centers for Disease Control and Prevention ("CDC") mandates that institutions report to the agency or to a database maintained by a third party all incidences of a specific infectious disease, that reporting effort does not require IRB review if the information will be used only for quality assurance or improvement purposes.

3.2 EXAMPLES OF INITIATIVES THAT SHOULD SUBMITTED FOR IRB REVIEW

- An initiative in which a Laboratory investigator proposes to collect and/or study a set of identifiable (including coded) clinical data, analyze the data for general trends, and publish a paper in a scientific or other professional journal based on his or her work.
- An initiative in which the Laboratory submits identifiable (including coded) clinical data to a database maintained by an outside entity that will use and/or share the data for research purposes in addition to providing any benchmarking analyses to participating institutions.
- An initiative that is required by law, but in which the institution, the relevant state or federal agency/government body, and/or a third party will be using or sharing the data for research purposes in addition to quality measurement purposes.

If at some point the purpose of such an initiative or database changes to include research conducted by someone at or outside the Laboratory, then the initiative/database must be submitted for IRB review at that time.

In situations when IRB review is required, the IRB will review protocols on an expedited basis under guidelines permitting expedited review for minimal-risk research involving identifiable data collected solely for non-research purposes. When more than one research project is to be performed through one database, and the projects are sufficiently similar and involve a similar level of risk to participants, the IRB will generally require only one protocol to be submitted for the database.

3.3 TIPS FOR SUBMITTING COMPLIANT QUALITY MEASUREMENT PROTOCOLS

As noted above, IRB review may be sought for each database rather than for each separate research project to be performed through the database. To the extent that the submission demonstrates that the projects to be performed through the database are sufficiently similar to one another and involve a similar level of risk to participants, all of them may be covered by the same protocol and IRB review.

If a project involves data of a sensitive personal nature (e.g., abortions, sexually transmitted diseases, or elder or child abuse) or otherwise presents more than minimal risk to patients (e.g., alterations in standard confidentiality precautions or coding practices or potential for contact of patients), then a separate protocol encompassing that project should be submitted for IRB review.

HUMAN SUBJECTS IN RESEARCH: REVIEW OF QUALITY MEASUREMENT INITIATIVES

To the extent that a database involves clinical data from more than source, the use of cooperative IRB agreements (Reliance Agreements) between the Laboratory and another institution may permit the review and approval of the project by one institution's IRB.

If it is not clear based upon this Policy whether a particular quality measurement initiative should be submitted for IRB review, contact the IRB for guidance.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Director, Clinical and Translational Research Support.

5.0 DEFINITIONS AND ACRONYMS

- **CDC:** Centers for Disease Control and Prevention
- **IRB:** Institutional Review Board

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
N/A	N/A

HUMAN SUBJECTS IN RESEARCH: PRINCIPAL INVESTIGATOR RESPONSIBILITIES

1.0 PURPOSE AND SCOPE

This policy outlines the responsibilities of the Principal Investigator ("PI") conducting human subjects research at The Jackson Laboratory (the "Laboratory"). The Laboratory may be the primary site of the research, or the PI could be a collaborator with an external PI in which only part of the research will be conducted at the Laboratory. The PI responsibilities remain the same regardless of whether the Laboratory's Institutional Review Board ("IRB") or another IRB is serving as single IRB for the PI's institution per an executed reliance agreement (IAA).

The PI is personally responsible for conducting or supervising the conduct of human subjects research and for protecting the rights, safety, and welfare of the subjects enrolled in the research. The PI must ensure that all human subjects research is conducted in an ethical manner and in accordance with all federal, state, and local laws and regulations, institutional policies, and requirements or determinations of the IRB.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITIES OF THE PI FOR CONDUCT OF HUMAN SUBJECTS RESEARCH

The PI is responsible for designing and conducting research in a manner than minimizes risks, uses sound research design and accepted scientific and scholarly standards. In addition, the PI ensures;

- IRB approval for the research is obtained at the Laboratory and at collaborating institutions prior to initiation of the research at each institution;
- Research is conducted in accordance with the IRB-approved protocol, including, when applicable, the approved recruitment and consent procedures;
- When required, informed consent is obtained prior to the initiation of any study-related procedures;
- When required, written informed consent is obtained and documented using the current IRB-approved research consent form;
- When drugs, biological products, and devices are being investigated or used, they are managed and controlled as required by institutional policy and by FDA regulations 21 CFR 312 and 21 CFR 812;
- Changes to the IRB-approved protocol and/or the research consent form are not initiated without prospective IRB approval unless necessary to eliminate apparent immediate hazards to the subject;
- Unanticipated problems involving risks to subjects or others (including adverse events) are reported promptly to the IRB in accordance with the event reporting policy (POL.RES.029);
- Continuing review, as required, is conducted for protocols prior to expiration of IRB approval in accordance with IRB submission policy (POL.RES.057);

- When applicable, Data and Safety Monitoring Board/Data Monitoring Committee or other monitoring group reports are submitted promptly to the IRB for review;
- Research procedures stop if the IRB approval lapses until the IRB re-approves the research or until special permission is obtained from the IRB;
- Submit a study closure form to the IRB when the research has been completed or is being terminated;
- Adequate and accurate research records are kept and retained as required by the IRB and if applicable, by the sponsor or FDA;
- Research records are made available to the IRB, HRPP Quality Assurance, the sponsor, and when applicable, the Office for Human Research Protections ("OHRP"), and the Food and Drug Administration ("FDA") for monitoring and oversight of the research.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 QUALIFICATIONS TO SERVE AS A PI

A PI is an individual designated by the institution as having the appropriate background, training (see POL.RES.11), professional qualifications, and level of authority for the proper conduct of research. When the Laboratory submits grant proposals and accepts awards for extramurally funded sponsored projects, the institution assumes significant financial and legal obligations. Although sponsors fund projects based on the professional expertise of the PI submitting the proposal, the formal award is made to the Laboratory. Under the general oversight and authority of the institution, the PI of a sponsored project bears primary responsibility for the ethical conduct of research, fiscal stewardship of sponsor funds and for compliance with federal regulations, applicable state and local laws and institution policies.

PI status is confirmed by the IRB at the time of submission, and can be revoked at any time by the institution.

3.2 DELEGATION OF STUDY-RELATED TASKS TO STUDY STAFF

The PI can delegate certain study-related tasks to co-investigators and study staff. Co-investigators and study staff must receive adequate training on how to conduct the study tasks and procedures. This training should be documented in a Training Log and maintained in the Regulatory Binder. In addition, task delegation by the PI must be documented with the appropriate study team member and maintained in the Delegation of Authority/Responsibility Log. The PI must ensure that co-investigators and study staff:

- Have a specific understanding of the details of the protocol relevant to the tasks they will be performing;
- Are aware of regulatory requirements and acceptable standards for the conduct of human subjects research;
- Are competent and credentialed to perform the delegated tasks; and
- Are informed of any pertinent changes to the protocol during the conduct of the study and are given additional training as appropriate.

HUMAN SUBJECTS IN RESEARCH: PRINCIPAL INVESTIGATOR RESPONSIBILITIES

3.3 FELLOWS, STUDENTS AND TRAINEES CONDUCTING RESEARCH

Students and trainees conducting research as employees or agents of the Laboratory must follow the same requirements for IRB review of research as other investigators and research staff if their activities constitute engagement in human subjects research. This includes interns, residents, fellows, and postdoctoral scholars. Research must be conducted under the supervision of a qualified PI either at the Laboratory or at the institution where the interface with human subjects is occurring.

3.4 OVERSIGHT OF THE CONDUCT OF HUMAN SUBJECTS RESEARCH

The PI should have a plan for supervision and oversight of the research. The intensity of the supervision should take into consideration the study personnel conducting the research, the nature of the research and the subject population. When supervising the conduct of human subjects research, the PI must ensure that the study personnel:

- Are qualified by training and experience to perform the assigned study-related tasks (see POL.RES.011);
- Have an adequate understanding of the research; and
- Follow the IRB-approved protocol, including the recruitment and consent procedures described in the protocol.

3.5 KNOWLEDGE OF HUMAN SUBJECTS RESEARCH PROTECTION STANDARDS

When protecting the rights, safety, and welfare of research subjects, the PI must ensure that:

- All investigators and study staff will adhere to the principles outlined in the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research report, entitled *Ethical Principals and Guidelines for the Protection of Human Subjects of* Research ("Belmont Report");
- All investigators and study staff conduct research according to all applicable HRPP policies, the institution's FWA, as well as federal, state, and local laws for the protection of human subjects in research;
- Adhere to the terms and conditions of any additional research agreements (e.g., material transfer agreements, data access requests, etc.);
- Study subjects can be referred for reasonable medical care for any adverse events related to the research;
- Key personnel are available to answer questions for participants during the conduct of the research; and
- Study staff adhere closely to the research plan, such as inclusion/exclusion criteria, safety assessments, safety monitoring and reporting of unanticipated problems, and procedures to protect privacy of subjects and confidentiality of identifiable data, in order to minimize risks to subjects.

The PI should not commence the research without adequate resources to protect human subjects and should stop the research if the resources necessary to protect subjects become unavailable.

HUMAN SUBJECTS IN RESEARCH: PRINCIPAL INVESTIGATOR RESPONSIBILITIES

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Investigator:** An individual performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, generating, studying, interpreting or analyzing identifiable private information for research purposes, and communicating with the IRB.
- **PI:** Principal Investigator; Individual who is responsible and accountable for conducting the human subjects research. The PI assumes full responsibility for the protection of human subjects, compliance with regulations, and for the integrity of the research data and results.
- **Study Staff:** Individuals to whom the PI has assigned study-specific roles and responsibilities and includes, among others, co-investigators, research nurses, research coordinators, and research assistants. Study staff are individuals who intervene or interact with subjects, obtain consent or access identifiable private information about the subjects of the research for the purposes of research.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.011	Human subjects in research: education and training requirements
POL.RES.029	Reporting unanticipated problems involving risks to subjects, or others, adverse events and other problems in human subjects research
POL.RES.057	IRB submission
45 CFR 46	HHS/OHRP Protection of Human Subjects regulations
21 CFR 50	FDA Protection of Human Subjects regulations
21 CFR 56	FDA Institutional Review Boards regulations
21 CFR 312	FDA Investigational New Drug Application regulations
21 CFR 812	FDA Investigational Device Exemptions regulations
The Belmont Report	Ethical principles and guidelines for the protection of human subjects of research

HUMAN SUBJECTS IN RESEARCH: EDUCATION AND TRAINING REQUIREMENTS

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PURPOSE AND SCOPE

The Jackson Laboratory (Laboratory) has a legal and ethical responsibility to protect the rights and welfare of human subjects participating in research conducted or sponsored by the Laboratory or in which the Laboratory is otherwise engaged regardless of the location of the research or source of funding. Consistent with these responsibilities, the Laboratory requires every individual engaged in all human subjects research to complete the web-based Collaborative Institutional Training Initiative (CITI) human subjects protections and the conflict of interest courses prior to their involvement in the research. A continuing education/refresher course is required in human subjects protections every three years and in conflict of interest every four years after the initial courses. The IRB may accept an equivalent human subjects protection education course on a case-by-case basis. Notwithstanding this policy, the IRB may require an investigator to fulfill additional education and training requirements based on the type of research or as part of remedial education.

POLICY STATEMENT

The required human subjects protection training is provided through the CITI program. Laboratory researchers need to select one of the following learner groups based upon the type of research or role in the research 1) Biomedical Research 2) Social/Behavioral/Educational Research 3) Computational Scientist. The Computational Scientist course may only be selected by those in the data analyst, bioinformatics, computational scientist or genomic data analyst roles.

New research involving human subjects will not be approved by the IRB until all of the study staff contacts have completed the human subject protection education requirements (i.e., the CITI program courses listed above). Completion of the CITI education programs is monitored and recorded by the appropriate clinical research support staff at the Laboratory, including the human protections administrator and regulatory coordinator.

HUMAN SUBJECTS IN RESEARCH: EDUCATION AND TRAINING REQUIREMENTS

The addition of new study staff to a research protocol will not be approved by the Laboratory IRB unless the individuals being added have completed the human subject protection education requirements (i.e., the CITI courses).

If research is eligible for continuing review the research will not be re-approved by the IRB unless all of the study staff listed on the protocol have completed the human subject protection education requirements (i.e., the CITI courses) including, when applicable, continuing education requirements.

The Principal Investigator (PI) may elect to remove individuals from the study staff who have not completed the education requirements so that the study may be re-approved; these individuals may not continue to function as part of the study staff unless and until they have completed the education requirements and an amendment to add them to the study staff has been submitted and approved by the IRB.

PIs are responsible for ensuring that the study staff listed on their protocols complete their continuing education requirements every three years. Study staff education requirements will be reviewed at the annual administrative review for those studies that do not receive continuing review. Study staff that fail to comply with the human subject protection continuing education requirements will be considered non-compliant with Laboratory policies and procedures.

As part of human subject research training, investigators and study staff should be familiar with the principles of the Belmont Report and with the policies and procedures of the Laboratory's Human Research Protection Program. Additional training may be required depending on the sponsor.

PROCEDURE

N/A

DEFINITIONS AND ACRONYMS

N/A

REFERENCES

- CITI Program
- Belmont Report

HUMAN SUBJECTS RESEARCH: STUDY STAFF/COLLABORATOR RESPONSIBILITIES

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PURPOSE AND SCOPE

Principal investigators (PI) are ultimately responsible for the ethical conduct of human subjects research and for compliance with federal regulations, applicable state and local laws, and The Jackson Laboratory (Laboratory) Human Research Protection Program (HRPP) policies. PIs can delegate certain study-related tasks to co-investigators and study staff. The purpose of this policy is to outline institutional expectations of study staff in the conduct of human subjects research at the Laboratory.

Non-Laboratory individuals who perform Laboratory research activities or exercise institutionally delegated authority or responsibility for research, are acting as "agents" of the Laboratory. Therefore, these individuals are considered co-investigators or key personnel and must be appropriately credentialed and trained to perform the research-related responsibilities delegated to them by the PI. These individuals must be approved by the IRB through an IRB submission review (see the IRB submission policy POL.RES.057).

When research conducted by non-Laboratory employees is to be carried out at their home institution, such individuals are considered to be collaborators. In these situations, collaborators are acting as employees of their own institution and must get their own IRB approval or when appropriate, may rely on a single IRB, with an executed IRB Authorization Agreement (IAA) with the Laboratory and others if applicable.

When research conducted by non-Laboratory employees is carried out independent of their home institution, an Individual Investigator Agreement must be executed to allow the Laboratory IRB review to extend to the collaborating investigator.

HUMAN SUBJECTS RESEARCH: STUDY STAFF/COLLABORATOR RESPONSIBILITIES

POLICY STATEMENT

QUALIFICATIONS OF KEY PERSONNEL

Individuals, regardless of employment status, who assist the Laboratory PI or other co-investigator(s) with the conduct of human subjects research must be listed as key study personnel (co-investigators or study staff) with the IRB prior to engaging in study activities. Key study personnel do any of the following research-related activities:

- Obtain informed consent;
- Perform invasive or noninvasive procedures or tests specifically for research purposes;
- Conduct interviews or administer questionnaires, psychological instruments or surveys specifically for research purposes;
- Review health/medical information that is individually identifiable in original source documents (hospital, practice-based or clinical laboratory health/medical records);
- Enter individually identifiable data (data linked by code to an individual subject when a key to the code exists and is held by an investigator on the project) into the study database.

Individuals, such as laboratory technologists/technicians, radiological technologists/technicians, phlebotomists, patient care services staff, or interviewers, who provide standard clinical services or perform routine clinical tests in the course of carrying out their usual non-research-related responsibilities are not considered study staff.

EXPECTATIONS OF CO-INVESTIGATORS AND KEY PERSONNEL

Co-investigators are typically individuals who contribute to the scientific development or execution of a study in a substantive, measurable way.

The expectations of both the co-investigator(s) and key study personnel are as follows;

1. Are qualified by training and/or experience to perform study-related tasks;
2. Have completed CITI training (or equivalent) on human subjects research protections;
3. Have a signed Laboratory project-specific COI disclosure on file;
4. Have adequate understanding of the research; and
5. Follow the IRB-approved protocol, including the recruitment and consent procedures, data and sample handling, as described in the protocol.

PROCEDURE

N/A

HUMAN SUBJECTS RESEARCH: STUDY STAFF/COLLABORATOR RESPONSIBILITIES

DEFINITIONS AND ACRONYMS

- **Collaborator**: Non-Laboratory employees who are engaged in some aspect of the human research but perform all of the research activities 1) at their own institution as part of their institutional responsibilities or 2) separate from their own institutional responsibilities as an individual investigator.
- **Individual Investigator Agreement:** An agreement that binds independent investigators or investigators at institutions that do not already have agreements with the federal government through a (FWA) to have their human subjects research reviewed by an IRB.
- **Investigator:** An individual performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, studying, interpreting or analyzing identifiable private information for research purposes, and communicating with the IRB.
- **Principal Investigator (PI):** The individual who is responsible and accountable for conducting the human subjects research. The PI assumes full responsibility for the protection of human subjects, compliance with regulations, and for the integrity of the research data and results.
- **Study Staff:** Individuals to whom the PI has assigned study-specific roles and responsibilities and includes, among others, co-investigators, research nurses, research coordinators, and research assistants. Study staff are individuals who intervene or interact with subjects, obtain consent or access identifiable private information about the subjects of the research for the purposes of research.

REFERENCES

- POL.RES.057

HUMAN SUBJECTS IN RESEARCH: SINGLE IRB REVIEW IN MULTI-SITE COLLABORATIONS

1.0 PURPOSE AND SCOPE

The purpose of this Policy is to define the requirements and procedures The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") follows for review of multi-site, collaborative, non-exempt human subjects research conducted by Laboratory investigators.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The Laboratory IRB may enter into a formal agreement, known as a Reliance Agreement, with other institutions to serve either as the reviewing IRB or to rely on another institution's IRB for research conducted by Laboratory investigators. The designated single IRB, or sIRB, may be one of the collaborating institutions, or a central IRB.

The Office of Human Research Protections ("OHRP") guidance documents (Guidance on Engagement of Institutions in Human Subjects Research (2008) and Determining When Institutions are Engaged in Research (January 13, 2009)) will be used as the basis for determining engagement in human subjects research. Such determinations will be made in collaboration and consultation with authorized representatives of the collaborating institution and/or the Collaborating Individual Investigators, as applicable.

"Multi-site" is the term used by the National Institutes of Health ("NIH") to describe human subjects research involving more than one institution participating in the same research protocol. This typically involves a lead site that receives the grant directly from the funding agency and establishes sub-awards to the other Participating Sites.

HUMAN SUBJECTS IN RESEARCH: SINGLE IRB REVIEW IN MULTI-SITE COLLABORATIONS

3.1 SINGLE IRB REQUIREMENTS

The NIH Single IRB policy (effective 1/25/2018) requires the use of a sIRB for the review of NIH-funded multi-site studies where each site is conducting the same protocol for non-exempt human subjects research.

The Revised Common Rule (effective 1/20/2020) established the requirements for federally-funded cooperative non-exempt human subjects research conducted at domestic sites to utilize a sIRB for review and approval of studies. The use of a sIRB avoids duplicative review by multiple institutional review boards. The conduct and reporting of the research remain the study team's responsibility.

Both the collaborating institution and the Laboratory must have an active/approved Federalwide Assurance ("FWA").

3.2 RELIANCE AGREEMENTS

A Reliance Agreement, also known as an IRB Authorization Agreement ("IAA"), is a document that permits the Laboratory IRB to cede review to an external IRB for a particular study involving human subjects. In some cases, the external IRB will cede review to the Laboratory IRB. For either case, an agreement must be in place to determine the roles and responsibilities of the involved parties.

The reliance agreement may be for one particular study, or it may pertain to multiple studies (Master Reliance Agreement). Both OHRP and the FDA provide the IRB with the option to rely on the review of another IRB. These agreements are required for federally funded cooperative/multi-site research. The Laboratory IRB allows reliance for studies upon request.

3.2.1 SMART IRB

SMART IRB is a platform designed to provide organization, communication and documentation for institutions implementing sIRB review. The Laboratory is a signatory to the SMART IRB master Reliance Agreement. Implementation of the SMART IRB Online Reliance System is the preferred method to document the reliance. Documentation of the reliance is handled through the SMART IRB platform or through use of SMART IRB forms sent by mail or email between reviewing and relying on IRBs; however, the research project details will be documented in the Laboratory IRBManager system.

3.2.2 MASTER AGREEMENTS

The Laboratory has executed Master Reliance Agreements with several local institutions (UConn Health Center, UConn Storrs, Hartford Healthcare, and CT Children's Medical Center) in order to facilitate IRB review.

3.2.3 INDIVIDUAL IRB RELIANCE AGREEMENTS

For institutions that have not signed onto the SMART IRB system, the Laboratory may use an IRB Reliance/IAA to establish and document the reliance relationship with an external institution for individual research protocols.

HUMAN SUBJECTS IN RESEARCH: SINGLE IRB REVIEW IN MULTI-SITE COLLABORATIONS

3.2.4 SIGNATORY AUTHORITY

The Laboratory Institutional Official ("IO") has delegated the authority to the Director of the Human Research Protection Program to make ongoing determinations about IRB reliance arrangements under the SMART IRB or other agreements.

Factors considered when deciding whether a proposed Reliance Agreement is appropriate:

- Regulatory requirements or funding policies mandate the use of Reliance Agreements.
- Whether collaborating IRB policies and procedures meet the Laboratory standards. Accreditation by the Association for the Accreditation of Human Research Protections Program ("AAHRPP") or lack of does not itself suffice as a basis for the decision.
- Whether Single IRB is mandated.
- Source of funding and which institution in the prime awardee.
- Location of the human research activities and the personnel involved.
- IRB expertise.

3.3 RELYING ON A COLLABORATING INSTITUTION'S IRB

The Laboratory may rely on the IRB of a collaborating institution when all or the majority of the human subjects research is being conducted at the collaborating institution or when the collaborating institution's IRB has more relevant or specialized expertise and/or knowledge of the site where the research will be conducted. The approved protocol and consent are required before making any decisions about relying on another IRB, however exceptions may be made based upon the nature of the research, level of engagement in the research, the funding agency, time sensitivity, and as necessary to collaborate with the other IRB's office procedures.

3.4 SERVING AS THE REVIEWING IRB

The Laboratory may serve as the Reviewing IRB for the research project conducted with a collaborating institution. The Laboratory IRB will not serve as the IRB of record for an institution outside of the United States. That institution must independently obtain IRB or Ethics Committee approval and forward a copy of the approval to the Laboratory Principal Investigator. When a Principal Investigator requests the Laboratory IRB serve as the reviewing sIRB, the IRB must first review and approve the study protocol before Relying Sites submissions are reviewed and approved to be added to the study. Relying Site submissions may be approved using an administrative review process but may also be referred to the IRB as necessary. Initial and subsequent IRB reviews are completed per applicable IRB policies.

3.5 COLLABORATING INDIVIDUAL INVESTIGATORS

When a Collaborating Individual Investigator, whether an independent investigator or an institutional investigator, is engaged in non-exempt human subjects research, the Laboratory may choose to extend its FWA to cover the Collaborating Individual Investigator. In such cases, an Individual Investigator Agreement ("IIA") outlining the terms and conditions of this arrangement must be executed by both parties.

HUMAN SUBJECTS IN RESEARCH: SINGLE IRB REVIEW IN MULTI-SITE COLLABORATIONS

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **AAHRPP:** Association for the Accreditation of Human Research Protections Program
- **Collaborating Individual Investigator:** An investigator who is: 1) not otherwise an employee or agent of the Laboratory; 2) conducting collaborative research activities whether at the Laboratory or off-site and 3) not acting as an employee of any institution with respect to his/her involvement in the research being conducted at the Laboratory (independent investigator) OR acting as an employee or agent of an institution that does not hold an OHRP-approved FWA and does not routinely conduct human-subjects research (institutional investigator).
- **Collaborator:** For the purposes of this policy and for completing IRB submission forms, "Collaborators" are defined as non-Laboratory employees who are engaged in some aspect of the human research but perform all of the research activities 1) at their own institution as part of their institutional responsibilities or 2) separate from their own institutional responsibilities as an individual investigator. In such cases, Collaborators engaged in human research must obtain IRB approval 1) from their own institution or 2) through extension of The Jackson Laboratory FWA to include the individual investigator through execution of an Individual Investigator Agreement.
- **Cooperative Research:** Projects covered by 45 CFR 46 that involve more than one institution.
- **Employees or Agents:** Members of the applicable Laboratory workforce who: 1) act on behalf of the institution; 2) exercise institutional authority or responsibility or 3) perform institutionally designated activities. Employees and Agents include faculty, students/interns, contractors, and volunteers, among others, regardless of whether the individual is being paid by the Laboratory.
- **FWA:** Federalwide Assurance
- **HRPP:** Human Research Protection Program
- **IAA:** IRB Authorization Agreement
- **IIA:** Individual Investigator Agreement
- **IO:** Institutional Official
- **IRB:** Institutional Review Board
- **Multi-site Study:** The same protocol is used to conduct non-exempt human subjects research at more than one site.
- **NIH:** National Institutes of Health
- **OHRP:** Office of Human Research Protections

HUMAN SUBJECTS IN RESEARCH: SINGLE IRB REVIEW IN MULTI-SITE COLLABORATIONS

- **Participating Site (Relying Site):** Will rely on (cede review to) the sIRB to carry out the site's initial and continuing IRB review of human subjects research for the Multi-site Study. Participating Sites are responsible for meeting other regulatory obligations, such as providing local context, obtaining informed consent, overseeing the implementation of the approved protocol, and reporting unanticipated problems and study progress to the sIRB. Participating Sites are expected to rely on the sIRB to satisfy the regulatory requirements relevant to the ethical review.
- **Reliance Agreement (IRB Authorization Agreement):** The agreement that documents respective authorities, roles, responsibilities, and communication between an institution/organization/independent IRB providing the ethical review and a Participating Site relying on the sIRB. An institutional official or designee must agree with and approve any Authorization Agreement.
- **Single IRB (Reviewing IRB, IRB of Record, sIRB):** Selected IRB of record that conducts the ethical review for Participating Sites of the multi-site or collaborative study.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	Basic HHS Policy for Protection of Human Subjects
Extending an FWA to Cover Collaborating Investigators	OHRP Guidance on Extension of an FWA to Cover Collaborating Individual Investigators and Introduction Individual Investigator Agreement
Engagement of Institutions in Human Subjects Research	OHRP Guidance on Engagement of Institutions in Human Subjects Research (2008)
Determining When Institutions are Engaged in Research	OHRP Guidance on Determining When Institutions are Engaged in Research (January 13, 2009)
OHRP Guidance on Coded Private Information or Specimens Use in Research	
NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research	
Boston Children's Hospital IRB Policies & Procedures Manual – Single IRB Review	
SMART IRB	Platform designed to ease common challenges associated with initiating multisite research and to provide a roadmap for institutions to implement the NIH Single IRB Review policy

HUMAN SUBJECTS RESEARCH: RECORDKEEPING AND RECORD RETENTION

1.0 PURPOSE AND SCOPE

Principal Investigators ("PI"), collaborators and Study Staff are required to document and maintain records of their human subjects research activities. The purpose of this policy is to provide guidance regarding the requirements of The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") for maintaining, storing, and safeguarding records containing human subject data obtained in the course of human subjects research.

Complete records are essential for verifying the quality of study data produced and demonstrating investigator compliance with good clinical practice guidelines and applicable regulatory requirements. In general, investigators should establish three sets of files for each study:

1. Regulatory documents (Regulatory Binder)
2. Identified individual subject documents (i.e., consent forms, or other documents that contain signatures and other direct identifiers)
3. Coded individual subject documents (i.e., coded eligibility confirmation forms, coded data collection sheets, coded case report forms)

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

REGULATORY DOCUMENTS

Regulatory documents must be maintained for all studies, regardless of sponsor/funding source, dependent upon the nature of the involvement of human subjects and applicable regulations (e.g., Health and Human Services, Food and Drug Administration ("FDA")). These documents are typically organized within a regulatory binder, which can be maintained either online or in hard copy. Electronic regulatory binders must be stored on a Laboratory server with

limited access file share. Regulatory documents cannot be stored on individual hard drives. It is recommended to maintain a hard copy note to file describing the electronic storage location of the Regulatory Binder.

The Regulatory binder should contain the essential documents listed below. Some documents that may be common to more than one study, such as CVs and professional licenses, may be filed centrally.

The binder must be updated throughout the course of the study and may include any or all of the following, when applicable:

- Grant application and approvals/subcontract/subaward agreements/ progress reports
- Documentation of single IRB or IRB of record that will be reviewing the research
- Study protocol, all versions numbered and dated
- IRB-approved informed consent form(s), all versions and dated
- IRB approval letter or notifications of IRB decisions; investigator responses to IRB notifications
- IRB-approved recruitment materials
- Study information distributed to subjects
- IRB correspondence
- Other committee reviews or approvals
- Correspondence with study sponsor/funding agency
- Blank copies of all case report forms, data collection sheets, and/or questionnaires
- Any applicable study logs (i.e., sample receipt, enrollment, screening, adverse event)
- Data/safety monitoring board reports or data safety and monitoring plan reviews
- Material transfer agreement/data use agreement
- Protocol-specific financial disclosure forms (SFI) for all study personnel
- Delegation of authority/responsibility log
- Monitoring log and letters/reports
- Deviation log
- Notes to file
- Lab information (i.e., lab certification, lab director's CV, and normal lab/reference values)
- Training logs (i.e., human subjects/CITI, study initiation, IT security)
- Signed and dated CVs for PI and co-investigators (NIH bio sketches are also acceptable)
- Valid licenses and certifications for all professional Study Staff performing study procedures

Studies that involve FDA regulation of drugs/biologics or medical devices should also include the following:

- Product information:
    - FDA approved drugs/biologics or approved medical devices
        - Drug package insert
        - Device manual/instructions for use
    - IND drugs/biologics or IDE medical devices
        - Investigator's Brochure ("IB")
        - Device information/Report of prior investigations

HUMAN SUBJECTS RESEARCH: RECORDKEEPING AND RECORD RETENTION

- FDA forms, Submissions and Correspondence:
    - IND/IDE Clinical Investigators (IND/IDE held by sponsor)
        - Form FDA 1572/Statement of Investigator (IND Investigator)
        - Investigator's Agreement (IDE Investigator)
    - Sponsor-Investigator (IND/IDE held by Investigator)
        - IND/IDE Submission
        - IND protocol amendments/IDE supplements
        - IND/IDE safety reports
        - IND/IDE annual reports
        - IDE updated list of investigators
        - Form FDA 1571/IND application
        - Form FDA 3455/Disclosure: Financial Interests and Arrangements of Clinical Investigators
        - Form FDA 3674/Certificate of Compliance, with Requirements of ClinicalTrials.gov
- Drug/Device accountability, records of (when not maintained by research pharmacy, this must be maintained by the PI):
        - Shipping and receipt
        - Dispensing to subjects
        - Return of drug/medical device by subject
        - Return of drug/medical device to sponsor
        - Destruction of drug/medical device (if destroyed at site)

IDENTIFIED INDIVIDUAL SUBJECT DOCUMENTS

All documents that contain direct subject identifiers (i.e., name, social security number, address, birthdate) must be filed and stored separately from the Regulatory Binder and coded case report forms for each participant enrolled or screened for the study.

The following documents are to be placed in the identified file:

a. Screening log: Captures all potential subjects who have been screened for the study.
b. Enrollment log: Captures all subjects who have signed an IRB-approved consent form or, with IRB approval, have given verbal consent or have waived informed consent.
c. Informed consent forms: All documents with subject name, birthdate, or other direct identifiers should be stored with the consent forms. All coded data forms should be stored together separate from the identified information. Names should not be written on coded forms and research codes should not be written on forms with names or signatures.
d. Documentation of informed consent when written consent has been waived.
e. Copies of source documents, if applicable, should be retained to corroborate entries on the case report forms or data collection sheets. If identified, they should be stored with the consent form.

HUMAN SUBJECTS RESEARCH: RECORDKEEPING AND RECORD RETENTION

Individual files are not needed for studies limited to review of health/medical records, use of discarded human material, secondary use, or a data/tissue repository.

CODED INDIVIDUAL SUBJECT DOCUMENTS

This file includes all required documentation of the research that is labeled with a research ID code rather than the individual's name or other direct identifier. Coded data includes:

a. Documentation of subject eligibility. Specific inclusion/exclusion criteria should be labeled with participant research code and signed/dated by the person determining eligibility.
b. Individual case report forms, data collection forms, questionnaires, and/or subject diaries used to capture all data required by protocol for each subject. All primary data must be promptly recorded in clear, adequate, original, and permanent form.

RECORD RETENTION

Research records must be retained for at least three years from the time the study has been completed or longer as required by the sponsor [45 CFR 46.115(b)][21 CFR 56.115(b)]. For federally funded research, the minimum record retention period is three years, but individual granting agencies can require longer periods of up to seven years. If the research records include a HIPAA Authorization, the records must be kept for six years from the last access to the protected health information at the clinical site. For FDA regulated studies conducted under an IND/IDE, the sponsor of the IND/IDE is responsible for informing investigators when the study records can be destroyed. Storage and retention of the documents must be consistent with what is stated in the consent forms. The same record retention timeline applies to electronic files and paper files.

All permanent records must remain at the Laboratory upon departure of the investigator from the institution. Alternative arrangements for copies of records to be kept at the Laboratory, instead of original records, must be reviewed and approved by the Laboratory IRB. Study documentation must be available for internal audits, external monitoring and inspection by regulatory agencies.

STORAGE OF RESEARCH DOCUMENTS

Physical paper records should be stored in a secure area which can be locked. Paper records may be stored off-site; a plan for storage must be reviewed by the HRPP and approved by the Laboratory's Facility Administrative Services (See Records Retention & Management Overview).

When necessary, it is acceptable to create certified electronic copies of source documents (including consent documents and PHI). Certified copies are those in which the investigator or designee has verified that the scanned electronic version of the paper document is an exact copy, having all the same attributes as the original. It is recommended that investigators create a standard operating procedure describing how source documents will be scanned, named, certified, and stored. The PI is responsible for maintaining adequate records and should ensure the standard operating procedure is followed. Electronic files must be stored on a Laboratory Research IT-approved secure

file space, either hosted by Laboratory servers, Laboratory cloud storage or an off-site contracted server. Research study documents may not be stored on desktops, laptops or local PCs that are not backed up by the Laboratory's IT support system. Paper documents may be destroyed after they are scanned, certified, and saved on Laboratory-approved secure file space.

IRB approval is not required to convert paper study documents to an electronic format. There should be three study personnel, including the PI, who have access to the files. Documentation of the files transferred, the location of the files and the certification process should be maintained on-site.

FDA-regulated research has additional requirements on electronic documentation, systems, and processes to comply with 21 CFR Part 11.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **FDA:** Food and Drug Administration
- **IRB:** Institutional Review Board
- **Study Staff:** The Study Staff is made up of the individuals to whom the PI has assigned study-specific roles and responsibilities and includes, among others, co-investigators, research nurses, research coordinators, and research assistants. Study Staff are individuals who intervene or interact with subjects, obtain consent, access or generate identifiable private information about the subjects of the research for the purposes of research.
- **Principal Investigator (PI):** The PI is the individual who is responsible and accountable for conducting the human subjects research. The PI assumes full responsibility for the protection of human subjects, compliance with regulations, and for the integrity of the research data and results.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
21 CFR 56	FDA Institutional Review Board regulations
45 CFR 46	HHS Protection of Human Subjects regulations

HUMAN SUBJECTS IN RESEARCH: PRINCIPAL INVESTIGATOR LEAVE OF ABSENCE, SABBATICAL, TRANSFER OR SEPARATION

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PURPOSE AND SCOPE

This policy provides guidance for Principal Investigators (PIs) actively engaged in human subjects research at The Jackson Laboratory ("Laboratory') who wish to take leave of absence or sabbatical from their positions at the Laboratory, or for PIs moving to another institution or otherwise separating from the Laboratory.

PIs are responsible for timely closure of studies or transfer of PI responsibilities in the event of their absence for medical or family leave, sabbatical, transfer to another institution or separation from the Laboratory.

POLICY STATEMENT

TEMPORARY ABSENCES AND SABBATICALS

In the event of a temporary absence; for example, a six-week medical leave where a complete return to duties is expected, it is acceptable to indicate that a co-investigator will take over PI responsibilities in the interim, without a formal change of PI.

In the event of a leave of absence for three months or longer, such as a sabbatical, a qualified on-site PI must be formally appointed by amendment to the project. The new PI must be willing to assume all PI responsibilities and a formal amendment must be submitted to the Institutional Review Board (IRB). Conflicts of interest and conflicts of commitment should be considered. The Sponsored Research Administration (SRA) office must also be contacted because NIH also mandates an interim or new PI for absences of three months or longer. The Laboratory's Legal Department must be consulted if the study

is funded by industry to determine if an amendment to the agreement or formal notification in writing is needed.

TRANSFER TO ANOTHER INSTITUTION/SEPARATION FROM THE JACKSON LABORATORY

When a PI is leaving the Laboratory, s/he is required to arrange timely transfer of responsibilities to the new institution, or, if relevant, to another investigator within the Laboratory. If this is not feasible, a new PI should be named to complete the study at its original study site. It may occasionally be necessary to stop subjects' participation in the research study. The interests and activities of the subjects' participation should be taken first into consideration and completed before the PI transfers to the other institution.

PIs are encouraged to contact the IRB directly for advice related to specific protocols in situations where the PI may be absent from the institution. Investigators should also work with SRA on the appropriate transfer of research records and funds. When applicable, they may also need to work with Research IT and IT Security for the safe transfer of any data files.

Prior to separation from the Laboratory, the PI will be contacted to assess data and sample security as well as regulatory documentation for all ongoing IRB-approved research projects. This is arranged with the Clinical Research Quality Assurance Specialist.

When research staff who are involved with human subjects research leave the Laboratory, the PI should submit an amendment to the IRB to remove the employee from the study. In addition, privileges to IRBManager will be removed once the employee leaves the Laboratory.

PROCEDURE

N/A

DEFINITIONS AND ACRONYMS

N/A

REFERENCES

N/A

IRB REVIEW OF FINANCIAL CONFLICTS OF INTEREST

1.0 PURPOSE AND SCOPE

The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") ensures the objectivity of human subjects research at the Laboratory by addressing actual or perceived conflicts of interest in research. This is accomplished by providing guidance on what is and is not a Significant Financial Interest ("SFI") and by documenting any existing or anticipated SFI(s) related to human subjects research. The purpose of this Policy is to describe how the IRB oversees the SFI(s) of an investigator that may affect the human subjects research in which he/she is involved.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

This Policy harmonizes with the institutional policy regarding disclosure and management of Financial Conflict of Interest ("FCOI") among investigators conducting sponsored research (POL.RES.003). A *Project-Specific Significant Financial Interest Disclosure Form* is required by the IRB for all investigators and Key Personnel at initial study review and then at subsequent reviews until the study is closed by the IRB. This is in addition to the annual online FCOI reporting to Sponsored Research Administration and to the online reporting at the time of grant proposal submissions.

3.1 IRB PROJECT-SPECIFIC DISCLOSURE PROTOCOL

The Principal Investigator ("PI"), co-investigator(s) and other Key Personnel that participate in the design, conduct or reporting of the research study must complete the IRB *Project-Specific Significant Financial Interest Disclosure Form*. This form is required in the initial IRB submission package, and then at subsequent reviews (continuing IRB review or annual administrative review). If an investigator or other Key Personnel is added to an approved study in the interim, the form, completed by the individual being added, must be included in the study modification materials submitted to the IRB. The IRB refers any disclosed SFI to the Sponsored Research Conflict of Interest Committee for management per Laboratory policy (POL.RES.003).

IRB REVIEW OF FINANCIAL CONFLICTS OF INTEREST

3.2 ROLE OF THE INSTITUTIONAL REVIEW BOARD

3.2.1 REVIEW OF POTENTIAL CONFLICTS OF INTEREST PRIOR TO INITIAL APPROVAL

When a potential SFI has been identified, the IRB communicates closely with the Sponsored Research COI Committee and the investigator throughout the review process. When appropriate, a plan or strategy to adequately eliminate, mitigate, or manage the conflict must be developed by the Sponsored Research COI Committee and accepted by the IRB. The IRB has the final authority to decide whether the potential conflict of interest and its management, if any, allows the research to be approved.

When there are non-substantive outstanding FCOI matters, the protocol may be approved contingent upon the matters being resolved (e.g., requiring that the investigator modify the informed consent document to include specified language).

When there are substantive outstanding FCOI matters, the protocol is either tabled or precluded from possible approval until matters are resolved. When FCOI matters are completely addressed, the protocol approval letter may be generated by the IRB.

3.2.2 REVIEW OF CONFLICTS OF INTEREST DISCLOSED AFTER IRB APPROVAL OF THE RESEARCH

When a potential FCOI arises after the IRB has reviewed and approved a protocol, the PI should immediately notify the IRB of the potential conflict, who then forwards the completed disclosure to the Sponsored Research COI Committee. If applicable, study enrollment and protocol procedures should be stopped, with consideration to subject safety, until the conflict has been reviewed and resolved by the Sponsored Research COI Committee. The Sponsored Research COI Committee final determination and resolution plan is provided to the IRB.

When an undisclosed potential FCOI is discovered by the IRB or others after approval, the PI needs to file the completed disclosure as described above. The IRB may also request the PI to disclose the FCOI to research participants, among other possible actions.

3.2.3 RECORDKEEPING

Records on all FCOI disclosures and all management plans are maintained for three (3) years from the date of disclosure. This information is available to the Department of Health and Human Services (“HHS”) upon request, while maintaining the confidentiality of all records of financial interest.

3.2.4 HANDLING OF NON-COMPLIANCE BY THE IRB

When an investigator has been found to have violated POL.RES.003 or the terms of the management plan, the Sponsored Research COI Committee reports the violation to the IRB, which determines at a convened board meeting whether (1) the violation represents non-compliance or serious non-compliance and (2) the violation is reportable to federal agencies in the event federal funding was received for the research (see POL.RES.026).

IRB REVIEW OF FINANCIAL CONFLICTS OF INTEREST

Actions of the IRB in response to a determination of non-compliance or serious non-compliance for FCOI violations in IRB-approved research include:

- Suspension or termination of the protocol; or
- Requirement for PI to notify current participants of the FCOI (when such information may relate to participants' willingness to continue to take part in the research).

3.2.5 OTHER POSSIBLE IRB ACTIONS INCLUDE BUT ARE NOT LIMITED TO THE FOLLOWING:

- Monitoring of the research or of the consent process.
- Referral to other organizational entities (e.g., legal counsel, Institutional Official).).
- Modification of the research protocol.
- Modification of the information disclosed during the consent process.
- Provision of providing additional information to past participants.
- Requiring re-consent of current participants to continue participation.
- Modification of the continuing review schedule, if applicable.
- Additional training or education for research team members or the PI.
- When appropriate, applying any corrective action to all similar protocols.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Financial Conflict of Interest (FCOI):** A financial interest that could directly and significantly affect the design, conduct or reporting of research.
- **HHS**: Department of Health and Human Services
- **Institutional Responsibilities:** An investigator's professional responsibilities on behalf of the Laboratory, including research, research consultation, teaching, professional practice, institutional committee membership and service on panels such as IRBs and safety monitoring boards.
- **Investigator:** An individual performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, studying, interpreting, or analyzing identifiable private information for research purposes, and communicating with the IRB. Investigators are responsible for the design, conduct and reporting of research.
- **IRB:** Institutional Review Board
- **Key Personnel**: Research personnel who are directly involved in conducting research with human subjects through an interaction or intervention for research purposes. This includes participating in the consent process or being directly involved with recording or processing identifiable private information of the research

participants. This definition extends to the handling of coded information if a key to the data exists and is accessible to investigator(s) collaborating in the research.

- **PI**: Principal Investigator
- **Significant Financial Interest (SFI):** The financial interest of the investigator, spouse, and dependent children, which appears to be related to the investigator's Institutional Responsibilities. Specific details of the interests that fall under this definition are provided within the Laboratory's FCOI policy (POL.RES.003).
- **Sponsored Research:** A systematic investigation, study or experiment designed to develop or contribute to generalizable knowledge supported by a grant, cooperative agreement, sponsored research agreement, internal award, or Public Health Service (PHS) funded research contract. The term encompasses basic, applied human subjects research and product development.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	Protection of human subjects
21 CFR 54	Financial disclosure by clinical investigators
21 CFR 56	Institutional Review Boards
POL.RES.003	Objectivity in Sponsored Research: FCOI
POL.RES.026	Human Subjects Research: Noncompliance
Project-Specific Significant Financial Interest Disclosure Form	

IRB FINANCIAL CONFLICTS OF INTEREST: BONUS PAYMENTS IN CLINICAL TRIAL AGREEMENTS

1.0 PURPOSE AND SCOPE

The responsible conduct of clinical trials requires that research is performed in a manner that does not create inappropriate risk for study subjects; including the risk to subjects from the existence of a financial conflict of interest related to the research. Of particular concern are payment structures that may provide an inappropriate incentive for the recruitment of subjects. Any financial arrangements that could influence, or reasonably be perceived as influencing, the way that study investigators recruit and otherwise interact with study subjects are not acceptable.

This policy addresses clinical trial payment structures between The Jackson Laboratory (the "Laboratory") as a study sponsor (funder) and the institutions conducting the trial that may create inappropriate conflicts of interest. Fully executed clinical trial agreements must be provided and reviewed by the Laboratory's Institutional Review Board ("IRB") prior to issuance of the IRB approval letter.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Payments by the Laboratory for a clinical trial must be directly based upon the cost of the study, including the total costs for the infrastructure, personnel and equipment necessary to recruit, screen and enroll subjects in the trial.

Any extra payment or increase in payment that is not attributable to an increase in actual costs to implement the study is considered to be a "bonus payment" and is not acceptable.

3.1 EXAMPLES OF ACCEPTABLE AND UNACCEPTABLE PAYMENT STRUCTURES

While payment structures for clinical trials vary, typically a sponsor pays on a per-subject basis in order to reimburse costs proportionally. Examples of acceptable and unacceptable structures are provided below. The IRB may develop further guidelines and make decisions in individual cases that do not clearly fall into "acceptable" guidelines.

IRB FINANCIAL CONFLICTS OF INTEREST: BONUS PAYMENTS IN CLINICAL TRIAL AGREEMENTS

3.1.1 GENERALLY ACCEPTABLE PAYMENT SCHEDULES

These include:

1. Payment schedules that provide for unvarying per-subject payments, or payments which are to be made at fixed times, with no contingencies, and that are based upon the actual cost of the study, including recruitment, screening and enrollment, absent unusual circumstances (e.g., unusually high per-participant payments).
2. Payment schedules that provide for increasing per-participant payments over the course of a trial may be acceptable if both of the following conditions are met:
    a. The increased payments are based on increased costs associated with the additional participants, for which costs do not accrue unless and until those additional participants are enrolled (e.g., costs of additional staff that will not be needed unless a certain number of participants are enrolled); and
    b. The IRB reviews and approves the payment schedule.
3. In the foregoing examples, reasonable mark-ups from actual costs are generally acceptable when tied to fair market value of the work performed.
4. Increased payments that are not provided for or anticipated in the initial budget may be acceptable during the course of a study if the increased payment is based on past expenses having been higher than anticipated, or on unanticipated increases in future costs.

3.1.2 UNACCEPTABLE PAYMENT SCHEDULES

Payment structures that create an incentive to hasten or complete enrollment of subjects are unacceptable. Examples include:

1. A per-subject payment schedule that increases after the enrollment of a specified number of subjects (e.g., $100 per subject for the first 10 subjects and $150 per subject for the next 10 subjects, etc.), unless such increase is based on a clear increase in costs (see above).
2. Additional “bonus” payments upon the completion of a specified number of participants.
3. Payments that are made only if a specified number of subjects are recruited (i.e., no payments for 48 subjects, but full payment for 50, or payments made only if 50 subjects are enrolled by a certain date). These payment schemes could influence, or reasonably be perceived as influencing, the way the last few subjects may be recruited.

3.2 INCENTIVE PAYMENTS TO INDIVIDUALS INVOLVED IN CLINICAL STUDIES

This policy addresses payment structures to the institution, and not payment structures that may be offered to investigators and other individuals involved in clinical studies. Such payments are already addressed by other institutional policies including the policies on conflicts of interest (POL.RES.003 and POL.RES.017) and the recruitment of research subjects (POL.RES.040). This existing guidance prohibits, among other things, incentive payments to physicians for referrals of patients to studies and prohibits any incentive payments to investigators to accelerate enrollment of study subjects.

IRB FINANCIAL CONFLICTS OF INTEREST: BONUS PAYMENTS IN CLINICAL TRIAL AGREEMENTS

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **FCOI:** Financial Conflict of Interest; A financial interest that could directly and significantly affect the design, conduct or reporting of research.
- **Investigator:** An individual performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, studying, interpreting, or analyzing identifiable private information for research purposes, and communicating with the IRB. Investigators are responsible for the design, conduct, and reporting of the research.
- **SFI:** Significant Financial Interest; The financial interest of the investigator, spouse, and dependent children, which appears to be related to the investigator's institutional responsibilities. Specific details of the interests that fall under this definition are provided within the Laboratory policy (POL.RES.003).

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.003	Objectivity in Sponsored Research: financial conflicts of interest
POL.RES.017	IRB review of financial conflicts of interest
POL.RES.040	Recruitment of research subjects

IRB MEMBER AND CONSULTANT CONFLICTS OF INTEREST

1.0 PURPOSE AND SCOPE

To ensure the objectivity of human subjects research and clinical investigations, and to avoid actual or perceived Conflicts of Interests ("COI") in the review of such research, this policy defines the process for identifying and managing COI among members of The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB"). This Policy applies to all members of the IRB and *ad hoc* consultants, who are not IRB members but are asked to attend or contribute to an IRB review to provide expertise about aspects of a study or study population not represented in the expertise of IRB members.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Annually, IRB members disclose all financial and non-financial interests with respect to any research being conducted at the Laboratory by completing an *IRB Members Annual Financial Disclosure Form*. In addition, when assigned to review a research protocol, members must notify the IRB Administrator if they could potentially have a conflicting interest [45 CFR 46.107 (d)][21 CFR 56.107(e)]. In such a case, the review of the protocol will be assigned to another IRB member. Conflicts are to be declared prior to the relevant IRB meeting, but if that is not possible, declaration of conflicts should be reported at the beginning of the meeting where any such protocols are being reviewed.

An IRB member or consultant or an Immediate Family Member is automatically deemed to have a conflict of interest with respect to a research protocol if they:

- Are involved in the design, conduct, analysis or reporting of the research.
- Have equity interests related to the research.
- Have compensation related to the research (other than Laboratory salary if member is an employee).
- Have any intellectual property related to the research.
- Are a participant in the research.

IRB MEMBER AND CONSULTANT CONFLICTS OF INTEREST

All IRB members are regularly notified and reminded of this policy and their responsibilities described in IRB composition policy (POL.RES.056). Members are directed to the policy in preparation for each meeting, a summary of which appears on IRB members' agenda documents (included with meeting materials and protocols).

When IRB members receive materials before a meeting, they will be asked to review the list of protocols and identify any of their financial or Non-financial Interests (including any that may be permitted by the sponsored research policy POL.RES.003) pertaining to the project. Any such conflicts must be disclosed to the Chair or their designee. The member will be recused from discussion and vote at a convened meeting and will not be permitted to perform expedited review or make determinations of exemption for that protocol. An IRB member who has been determined to have a COI may provide information to the IRB, at the IRB's request. An IRB member may not consult, with or without compensation, for a business to assist it in shepherding a project through the IRB process when the project is performed within the Laboratory.

When performing expedited review, the IRB reviewer must promptly report any financial and Non-financial Interests with the project to the IRB Administrator. The IRB Administrator will confer with the Chair, who will determine the extent of a conflict, and as needed, the protocol will be reassigned to another reviewer.

Any IRB member or consultant who has a conflict of interest in a project (including any such interest that is attributable to a family member) must leave the room during the discussion of the project and the related vote. The meeting minutes will document the recusal (i.e., the temporary absence of the IRB member during the deliberation and vote on the project with respect to which the member has a conflict).

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **COI:** Conflicts of Interest
- **Financial Conflict of Interest:** A financial interest that could directly and significantly affect the design, conduct or reporting of the research.
- **Immediate Family Member:** A spouse or domestic partner, minor/dependent children or other persons living in the same household.
- **IRB:** Institutional Review Board
- **Non-financial Interest:** Relationships that may impair or influence the judgment of the member. Examples include being a direct supervisor or trainee of the researcher(s); being related to a researcher whose protocol is under consideration; having a prominent role in a directly competing research team or product; having a close personal relationship with a researcher; or for other reasons the member feels unable to render a fair and unbiased review.

IRB MEMBER AND CONSULTANT CONFLICTS OF INTEREST

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46.107 (d)	
21 CFR 56.107 (e)	
POL.RES.003	Objectivity in sponsored research: Financial conflict of interest
POL.RES.056	IRB composition

HUMAN SUBJECTS RESEARCH: EXEMPT RESEARCH

1.0 PURPOSE AND SCOPE

Research involving human subjects may be exempt from federal regulations (as defined in 45 CFR 46.104 and 21 CFR 56.104) requiring Institutional Review Board ("IRB") review. The Jackson Laboratory (the "Laboratory") investigators within the organization may NOT make exemption determinations (see policy POL.RES.019) because of the potential for conflict of interest. The Laboratory IRB has the designated sole responsibility for determining whether a research activity at the Laboratory is exempt from 45 CFR 46 and/or 21 CFR 56.

The purpose of this Policy is to define the applicability of 45 CFR 46.104 and/or 21 CFR 56.104 for the determination of human subjects research that is exempt from IRB review and the procedures followed by the IRB staff when conducting the review of exempt human subjects research. Investigators performing exempt research must still comply with the requirements and policies of the Laboratory's Human Research Protection Program ("HRPP").

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to and including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 SUBMISSION AND REVIEW PROCESS

Investigators are required to complete the Exempt Review Application in IRBManager and provide all required documents as described in the instructions provided on the form. The IRB Administrator then reviews the submission for completeness and accuracy. Principal Investigator requirements for investigator qualifications, CITI training, and COI disclosure also apply to Exempt research, as it is human subjects research.

HUMAN SUBJECTS RESEARCH: EXEMPT RESEARCH

During the ethical review of Exempt research, the designated reviewer is responsible for determining that the research only involves human subjects in the categories described in federal regulations 45 CFR 46.104 and/or 21 CFR 56.104.

3.1.1 UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES ("HHS")-REGULATED RESEARCH

Involves research activities in which the only involvement of human subjects will be in one or more of the following categories per federal regulations 45 CFR 46.104:

1. Research conducted in established or commonly accepted educational settings that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:
    i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.
    ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
    iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).
3. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
    i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.
    ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
    iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).
    iv. For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

v. If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
   i. The identifiable private information or identifiable biospecimens are publicly available.
   ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects.
   iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
   iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.
5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.
   i. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.
6. Taste and food quality evaluation and consumer acceptance studies:
   i. If wholesome foods without additives are consumed, or
   ii. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and

Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

7. Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).
8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:
   i. Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §46.116(a)(1) through (4), (a)(6), and (d).
   ii. Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117.
   iii. An IRB conducts a limited IRB review and makes the determination required by §46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section; and
   iv. The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

NOTE: The Laboratory IRB does not use the Revised Common Rule (2018 Requirements) Exempt Category 7 or 8.

3.1.2 FOOD AND DRUG ADMINISTRATION ("FDA")-REGULATED RESEARCH

Involves the following categories of clinical investigations that are exempt from the requirements of IRB review per federal regulations 45 CFR 56.104(c) and (d):

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. (Note: this exemption does not apply to human subjects research regulated by HHS)
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

Any other research subject to FDA regulation cannot be Exempt. Research is subject to FDA regulations if it involves a drug, medical device, food, or other product regulated by the FDA. **NOTE:** FDA-regulated research determined to be exempt from 21 CFR 56 IRB requirements is subject to 21 CFR 50, Informed Consent of Human Subjects.

3.1.3 IRB REVIEW OF EXEMPT RESEARCH

When providing the review of exempt research, the designated reviewer is responsible for determining that the research meets the institution's ethical principles for human subject protection, as outlined in *Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (the "Belmont Report") and when applicable, the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

The reviewer is also responsible for determining that (1) the research presents not greater than minimal risk to subjects; (2) the selection of subjects is equitable; and (3) when applicable, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of identifiable data.

When exempt research involves an interaction with participants, informed consent will be obtained (1) by a process that discloses adequate information; (2) informs that the activity involves research; (3) participation is voluntary; (4) given a description of the research procedures; and (5) provided with investigator name and contact information.

Upon review, the designated reviewer will make one of the following determinations:

- The submission does not meet the federal definitions for research involving human subjects (determined Not Human Subjects Research).
- The proposed research involves human subjects, qualifies as exempt, and may be conducted without IRB review.
- The proposed research involves human subjects and qualifies as exempt with limited IRB review to protect privacy of the subject and confidentiality of the research data.
- The research involves human subjects, is not exempt and must be submitted for IRB review, expedited (POL.RES.021) or convened (POL.RES.022).

3.2 MODIFICATIONS OR CHANGES TO THE RESEARCH

No changes may be made to the research activity without first submitting the changes to the IRB to ensure that the research remains within the parameters of exemption. The Principal Investigator should submit a "Request to Amend/Modify a Protocol" form in IRBManager and provide the required information. The reviewer may request additional information from the Principal Investigator to make the determination or to request changes in the research to meet the institution's ethical principles for human subject protection and HIPAA requirements, if applicable.

If the research no longer meets the criteria for exemption, the investigator must resubmit the research for review by the IRB, according to the IRB submission policy (POL.RES.057).

If the changes to the research permit the research to remain exempt, the IRB Administrator will distribute an approval letter to the Principal Investigator.

HUMAN SUBJECTS RESEARCH: EXEMPT RESEARCH

3.3 COMMUNICATING EXEMPT DETERMINATIONS

Exempt research may not begin until the IRB administrator notifies the Principal Investigator in writing that the research is exempt from further IRB review.

In addition, the IRB Administrator distributes a report of all human subjects research activities approved as exempt from requirements of 45 CFR 46 and 21 CFR 56 to the IRB members on a quarterly basis as part of the IRB meeting agenda and minutes. Reports are made available to the Institutional Official (IO) within IRBManager.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Research Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Exempt Research:** Research that involves human subjects that is not subject to regulations requiring IRB review and approval. Categories of research activities that may be determined to be exempt from review by the IRB are defined by federal regulations, 45 CFR 46 and 21 CFR 56.
- **FDA:** Food and Drug Administration
- **HHS:** United States Department of Health and Human Services
- **HRPP:** Human Research Protection Program
- **IRB:** Institutional Review Board

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46.104	HHS Exempt Research regulations
21 CFR 56.104	FDA Exempt Research regulations
21 CFR 50	FDA informed consent regulations
POL.RES.019	IRB member and consultant conflicts of interest
POL.RES.021	Human subjects research: Expedited review
POL.RES.022	Human subjects research: Convened IRB review
POL.RES.057	IRB submission

HUMAN SUBJECTS RESEARCH: EXPEDITED REVIEW

1.0 PURPOSE AND SCOPE

This Policy complies with the regulatory requirements in the Code of Federal Regulations [45 CFR 46.108(3)] and [21 CFR 56.108(a)(1)] requiring Institutional Review Boards ("IRBs") to establish and follow written procedures for conducting initial and continuing review of research, and for reporting its findings and actions to the investigator and to the institution. In addition, this Policy complies with the regulations that specify Expedited IRB Review requirements and regulatory criteria for IRB approval of research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program (HRPP) policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 ELIGIBLE RESEARCH

The IRB Chair, Vice Chair, or other experienced IRB members designated by the IRB Chair may use expedited review procedures to approve specific non-exempt research activities involving human subjects. Expedited review procedures may be used for the following:

1. Research activities listed in one or more of the categories in *Categories of Research That May be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure* unless that IRB reviewer determines that the study involves more than Minimal Risk [45 CFR 46.110][21 CFR 56.110].
2. Continuing review of research previously approved by the convened IRB, under specified circumstances, such as;
    a. The research is permanently closed to enrollment, all participants have completed all research-related intervention, and the research remain active only for long-term follow-up.
    b. No participants have been enrolled and no additional risks have been identified.
    c. The remaining research activities are limited to data analysis.
3. Review of minor changes to previously approved research, when initial and continuing review of research was approved by expedited or convened review.

4. Research eligible for review according to §46.118 (to document for a grant (institutional or training), cooperative agreement, or contract when the specific activities of the research involving human subjects have not yet been determined).
5. Research for which limited IRB review is a condition of exemption under §46.104(d).
6. Review of Reportable Events that do not meet the definition of an unanticipated problem involving risks to subjects or others.
7. Review of Study Closure submissions.
8. Application for Extramural Institutional Certification of human genomic data sharing plans.

The expedited procedure may not be used to review research in which identification of the participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are not greater than minimal.

The expedited review procedure may not be used for classified research involving human subjects.

3.2 SUBMISSION PROCESS

3.2.1 INITIAL AND CONTINUING REVIEW

Principal Investigators ("PI") relying on the IRB for review of human subjects research are required to complete the *Initial IRB Review Application* or *Continuing IRB Review Form* and submit all required information and documents through IRBManager. Initial review may be conducted through expedited process if the research meets the criteria as defined above.

Continuing review of research is required at least annually for research reviewed under the pre-2018 Common Rule (submitted and approved prior to 1/21/19), until the research has been completed. For research initially approved by the expedited review process after 1/21/19, continuing review is not required.

All required forms and documents submitted by the PI are pre-reviewed by the IRB Administrator for completeness, consistency, and confirmation that the protocol meets the criteria for expedited review. Once screened, the IRB Administration will assign the submission to a designated IRB reviewer.

3.2.2 MINOR CHANGES IN IRB APPROVED RESEARCH

If minor changes are required in the research, investigators relying on the IRB for review of human subjects research are required to complete the *Request to Amend/Modify a Protocol* form and submit all required information and documents through IRBManager.

All forms and documents submitted by the investigator are pre-reviewed by the IRB Administrator for completeness and consistency, and when accepted, are assigned to the designated IRB reviewer. The IRB reviewer is responsible for determining whether the proposed modification is minor. If the change is minor, the reviewer will review and approve or request additional information from the investigator.

The proposed change is considered minor when the research meets all of the following criteria:

- The proposed change does **not** significantly alter the risk to benefit assessment the IRB relied upon to approve the research.
- The proposed change does **not** significantly affect the safety of subjects.
- The proposed change does **not** involve the addition of procedures, interactions or interventions that add significant medical, social, or psychological risks.
- The proposed change does **not** involve the addition of a vulnerable population in research not otherwise eligible for expedited review.

3.2.3 118 DETERMINATION

The regulations of 45 CFR 46.118 recognize that certain research applications may be submitted to a sponsoring agency with the knowledge that human subjects will be involved during the period of support, but definite plans for this involvement cannot be described in the application. This is referred to as "delayed onset human subjects research." As such, an investigator may submit a *118 Determination Form* for review in order to receive applicable funds. This determination is valid for one year. The investigator will need to submit either an *Initial IRB Review Application* or *Request for Exempt Review Application* for the review of the involvement of human subjects in the research.

The 118 determination is not applicable to non-federally funded research, but the IRB will follow this process if required from a private funder or organization.

3.2.4 LIMITED REVIEW AS A CONDITION OF EXEMPTION

Certain categories of exempt research [categories 2(iii) and 3(i)(C)] submitted on or after January 21, 2019 (under the new 2018 Common Rule) require a limited IRB review of the research to ensure that the information obtained by the investigator is recorded and maintained in a manner that protects the participant's privacy and maintains the confidentiality of the research data.

The PI should complete and submit the *Request for Exempt Review* form along with associated study documents through IRBManager. All submissions are pre-reviewed by the IRB Administrator for completeness and consistency, and when accepted, are assigned to the designated IRB reviewer. The IRB reviewer is responsible for reviewing and assessing the provisions are adequate to protect the privacy of subjects and to maintain the confidentiality of the data.

3.2.5 REPORTABLE EVENTS

Reportable events that do not meet the definition of "unanticipated event involving risks to subjects or others" or reports of noncompliance may be reviewed by expedited review. The requirements are defined in the event reporting of unanticipated problems involving risks to subjects, or others, adverse events and other problems policy (POL.RES.029).

The PI completes and submits the *Reportable Event* form along with associated relevant study documents through IRBManager. All submissions are pre-reviewed by the IRB Administrator for completeness and consistency, and when accepted, are assigned to the designated IRB reviewer when the event qualifies for expedited review.

3.2.6 STUDY CLOSURE

To close a research protocol, the PI submits the *Closure of Research Study* form in IRBManager. For multi-site research, the research may be considered completed or may be closed prior to completion when the Laboratory PI is no longer obtaining, using, or analyzing identifiable data. The IRB Administrator will review the submission and close the study in the IRBManager system.

3.2.7 EXTRAMURAL INSTITUTIONAL CERTIFICATION

PIs that plan to submit large-scale human genomic data to NIH-designated repositories must obtain institutional certification that the data sharing plans are consistent with the NIH Genomic Data Sharing ("GDS") policy. The IRB is responsible for reviewing the genomic data sharing plans and consent forms to verify that NIH certification requirements have been met. The PI should complete and submit the *Institutional Certification* form along with any associated study documents in IRBManager.

Upon review, the IRB will assure that the data sharing plan is consistent with the informed consent of the participants from whom the data was obtained to determine any data use restrictions; consideration was given to the risks to individuals/families associated with the data submitted and shared; and the plan for de-identification of the data is consistent with the NIH GDS policy. The PI and the Institutional Signing Official must both sign the completed Certification.

Provisional Institutional Certification may be obtained in order to accompany the Just in Time submission when study documents are not yet available for review. This serves as commitment to complete the final Institutional Certification when the documents are available.

3.3 REVIEW PROCESS

The IRB Administrator will assign expedited reviews to one or more IRB members from the pool of designated experienced members. Assignments consider scientific or scholarly expertise, reviewer experience, reviewer workload, and potential conflicts of interest (both financial or personal/professional as defined in the IRB member conflict of interest policy (POL.RES.019).

The IRB reviewer is responsible for determining whether the research is eligible for expedited review. The IRB reviewer utilizes a checklist that includes requirements for the applicability of expedited review and the categories of research eligible for expedited review. The reviewer documents:

- The research is eligible for expedited review.
- The research is of no more than Minimal Risk.
- The research activities fall within one or more of the research categories eligible for expedited review as defined in 45 CFR 46.110(a).
- The consent form includes the basic elements of informed consent or that a waiver or alteration of informed consent is submitted for review.

HUMAN SUBJECTS RESEARCH: EXPEDITED REVIEW

If the proposed research is not eligible for review using the expedited review procedure, the IRB Administrator will add the study to the meeting agenda for a convened board review and inform the investigator of the IRB meeting when the study will be reviewed.

The IRB reviewer may approve, approve with contingencies (to secure approval), or defer (pending receipt of additional information from the PI). The Expedited IRB Reviewer may not disapprove research; if the reviewer cannot approve the research it must be referred to a convened IRB meeting for review.

The IRB reviewer may consult another IRB member(s) or an outside consultant with specific scientific or scholarly expertise; however, the IRB reviewer is ultimately responsible for the review and decisions about approval of the research. When a consultant is used, a member of the HRPP team will verify that the consultant does not have a conflict of interest using the "Consultant or Meeting Guest Conflict of Interest and Confidentiality Form" as defined in the IRB member and consultant conflict of interest policy (POL.RES.019).

If the IRB reviewer approves with contingencies for specific modifications required for approval or defers action pending receipt of additional information or substantive modifications to the research, the IRB Administrator notifies the PI in writing of the required modifications or additional information required before the review process can continue. The PI is asked to submit a point-by-point response and revised documents to the IRB via IRBManager.

When received, the IRB reviewer determines whether the modification requirements have been met as requested and the research can be approved. The IRB reviewer may request additional modifications or information until the research meets the approval criteria or may refer for full board review.

When the expedited review procedure is used, the IRB reviewer is responsible for determining that all requirements for IRB approval set forth in 45 CFR 46.111 and, when applicable, 21 CFR 56.111 are satisfied.

Research may be forwarded to the convened IRB for review when the expedited reviewer cannot determine that the research meets the criteria for expedited review or cannot approve the research or require modification in the research to secure approval.

Independent verification of information provided at initial or continuing review, or for review of proposed changes in research during the period of approval, may be requested by the IRB reviewer in the course of conducting the review. Such independent verification may be considered in the following situations:

- The research is being conducted by persons who previously failed to comply with all regulations or requirements of the IRB.
- Research conduct has been called into question as a result of information provided at continuing review.
- Substantial segments of the research are conducted off-site by Laboratory investigators or non-Laboratory collaborators.

Independent verification may include, but is not limited to the following sources of information:

- Audit by Human Research Protection Program ("HRPP") staff.
- Communication with the sponsor, collaborating institutions, coordinating centers, or regulatory agencies.

- Communication with any monitoring group (e.g., Data Safety Monitoring Board or Data Monitoring Committee).
- NIH communications and reviews; and/or
- Communication with collaborating IRBs.

3.4 COMMUNICATING EXPEDITED REVIEW ACTIONS

The IRB Administrator will notify the PI in writing of the IRB action and any modifications required as a condition for IRB approval. Notifications of IRB approval by expedited procedures include the category(s) under which the research qualifies and the approval period. More information is found in IRB action and communication policy POL.RES.059.

IRB members are notified of all human subjects research approved using the expedited review procedure. Reports are distributed to the convened IRB on a quarterly basis. The Institutional Official may access Expedited IRB Reviews and approvals through IRBManager or the HRPP regulatory file share.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Expedited IRB Reviewer:** The IRB Chair, Vice Chair and those experienced IRB members designated by the IRB Chair who may perform some or all types of expedited review.
- **Expedited IRB Review:** Process by which designated IRB members, on behalf of the full IRB, approve a limited class of research activities through reviews conducted outside of the convened IRB meeting.
- **Minimal Risk:** 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.
- **PI:** Principal Investigator

HUMAN SUBJECTS RESEARCH: EXPEDITED REVIEW

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	Common Rule
21 CFR 56	Institutional review boards
Categories of Research That May Be Reviewed by the Institutional Review Board Through an Expedited Review Procedure	
Prior NIH Approval of Human Subjects Research in Active Awards Initially Submitted without Definitive Plans for Human Subjects Involvement (Delayed Onset Awards): Updated Notice (July 30, 2015)	
POL.RES.019	IRB member and consultant COI
POL.RES.022	Human subjects research: Convened IRB review
POL.RES.029	Human subjects research: Event reporting of unanticipated problems involving risks to subjects, or others, adverse events, and other problems
POL.RES.057	IRB submission
POL.RES.059	IRB actions and communications
NIH Genomic Data Sharing Policy	The National Institutes of Health (NIH) announces the final Genomic Data Sharing (GDS) Policy that promotes sharing, for research purposes, of large-scale human and non-human genomic data generated from NIH-funded research
Institutional Review Board; Management and Function, Third Edition. Public Responsibility in Medicine & Research (PRIM&R); Elizabeth A. Bankert, MA; Bruce G. Gordon, MD; Elisa A. Hurley, PhD; Sharon P. Shriver, PhD. Jones and Bartlett (2022), ISBN: 9781284181159.	

HUMAN SUBJECTS RESEARCH: CONVENED IRB REVIEW

1.0 PURPOSE AND SCOPE

This Policy is established to comply in part with the regulatory requirement in 45 CFR 46.108(a)(3) and 21 CFR 56.108(a)(1) requiring Institutional Review Boards ("IRB") to establish and follow written procedures for conducting its initial and continuing review of research, and for reporting its findings and actions to the investigator and the institution.

The Policy defines the procedures that The Jackson Laboratory (the "Laboratory") IRB follows when conducting initial review, continuing review of applicable studies, and review of proposed changes to human subjects research by a convened board.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The IRB must review all non-exempt human subjects research at a convened meeting at which more than half the members, including at least one non-scientific member, are present, unless the research is eligible for review using the expedited review procedure. All research involving human subjects reviewed by the convened IRB must be evaluated for issues that may affect the rights and welfare of the participants.

3.1 MEETING DATES

IRB meetings are scheduled quarterly (i.e., once every three months). *Ad hoc* meetings may be scheduled between quarterly meetings to review investigator responses to contingencies for approval or modifications to research that require full board review, to allow resubmission of IRB-deferred projects, to meet sponsor deadlines that fall between scheduled IRB meetings, to review Reportable Events (POL.RES.029) and other issues that require discussion and decision of the convened board.

HUMAN SUBJECTS RESEARCH: CONVENED IRB REVIEW

3.2 AGENDA, ATTENDANCE AND ASSIGNING REVIEWERS

Confirmation of member attendance is done prior to each convened meeting to determine whether the requirement for Quorum will be met and that members with the appropriate scientific or scholarly expertise will be in attendance.

The IRB Administrator assigns primary and secondary reviewers to each protocol based on expertise, experience, conflict of interest status and workload. Protocols are scheduled for review by receipt date; however, the IRB reserves the right to reschedule protocols for review based on other factors, such as the experience and expertise of the members planning to attend the IRB meeting, to request the use of a consultant to supplement the review, or the expiration date of IRB approval.

All IRB reviewers and consultants are subject to the IRB member conflict of interest policy (POL.RES.019).

When the agenda includes protocols that involve vulnerable populations, the IRB Administrator is responsible for ensuring that at least one member attending the meeting has knowledge of and/or experience in working with the study population.

The primary reviewer is typically a physician-scientist or other scientific member with experience in working with the population being studied and/or expertise in the type of research under consideration, although this is not an absolute requirement, depending upon the type of study.

The secondary reviewer is typically an individual who can provide another perspective, for example, a layperson, or a member with expertise in genetics. The secondary reviewer, therefore, complements the scientific or scholarly expertise of the primary reviewer.

Both the primary and secondary reviewers are responsible for performing an in-depth review of all aspects of the protocol, consent form and associated materials.

Reviewers are encouraged, although not required, to contact the PI prior to the meeting if they have questions about the study, particularly if they have significant concerns about the study or believe additional information is needed for the IRB to be able to assess the risks and anticipated benefits, if any, to participants and the importance of the knowledge that may be expected to result from the research.

The agenda and materials related to the human subjects research scheduled for review at the meeting is provided to members at least five days in advance of the meeting to allow sufficient time for review.

3.3 USE OF CONSULTANTS TO INFORM THE IRB REVIEW PROCESS

Consultants may be used to supplement or provide expertise not available on the IRB. When, in the opinion of the IRB Chair or Vice Chair, the IRB membership lacks the expertise needed to review the protocol, potential expert consultants may be identified.

Consultants are also subject to the IRB member conflict of interest policy (POL.RES.019) and must confirm in writing that they have no project specific conflict of interest. The consultant is provided access to all the forms and documents submitted to the IRB for review. Consultants can attend the meeting in person or via phone or teleconference to

present their findings relative to the scientific merits of the study, the risks, and potential benefits to participants, and alternative treatments or procedures, and to answer questions. If the consultant is unavailable to attend the meeting in person, s/he may provide written comments for distribution or communication to the IRB members. Consultants are not voting members, and their attendance is recorded in the Minutes as "guests (consultant)."

3.4 DISTRIBUTION OF MATERIALS AND REVIEW BY IRB MEMBERS

At least five days prior to the meeting, all members are provided access to the following via the IRBManager electronic submission system/email:

- Meeting agenda
- IRB applications and other documents
- Links to guidance documents for the regulatory criteria for approval
- Regulatory requirements for informed consent

Primary and secondary reviewers are also provided with:

- Full Board IRB Reviewer Form
- Initial or Continuing Review Summary Template form
- Informed Consent Checklist (for studies submitting a Laboratory Informed Consent Form)

3.5 CONFLICTS OF INTEREST

IRB members are subject to the IRB member conflicts of interest policy (POL.RES.019) and every agenda includes a reminder about the conflicts of interest policy. Any member with a conflict of interest is asked to recuse him/herself and leave the room while the protocol is being reviewed. If necessary, he/she can answer questions or provide information to the IRB before leaving the meeting. The member with a conflict may not be involved in the discussion or vote of the protocol, and this is recorded in the minutes. Recused members are not counted towards the Quorum requirement; therefore, if Quorum of the membership is not present for the review of any protocol, no vote is taken, and the protocol is held for review at the next meeting of the convened board.

3.6 DISCUSSION AND VOTING PROCESS

The IRB Administrator takes attendance at the meeting and records voting members present and absent for each review. Late arrivals, early departures and individuals recused or out of the room during the discussion and vote on each protocol are also recorded in the minutes.

The IRB Chair or Vice Chair and assigned reviewers lead the discussion of each new protocol, continuing review or amendment listed on the meeting agenda.

The primary reviewer presents a brief synopsis of the research protocol, with the expectation that the other members have reviewed the protocol materials. The primary reviewer is responsible for covering:

- The scientific background and rationale, study design, and how the research differs from and compares to standard healthcare.

- The appropriateness of the study population and the inclusion/exclusion criteria.
- The risks and potential benefits to participants.
- Alternative treatments or procedures.
- The criteria for IRB approval.
- When applicable, additional protections for human fetuses and neonates; children; employees; and individuals with impaired decision-making capacity.
- Primary reviewers may have particular insight into clinical standards within the community, or routine care for the conditions under study, and it is expected that these are also part of the presentation to the IRB.
- Secondary reviewers are asked to present any additional clarifications or commentary on the study plan and any questions, concerns, or modifications s/he would require for approval.
- Both the primary and secondary reviewers are expected to provide an in-depth review of the consent form and identify missing required elements and when applicable, additional elements for informed consent.
- Reviewers are encouraged to provide written comments to ensure that the IRB records convey the modifications required and/or questions and concerns raised by the IRB completely, accurately, and precisely.
- After the primary and secondary reviewers have presented the study and their comments, the IRB Chair opens the protocol for discussion. The IRB members may direct specific questions to the assigned reviewers or to other members with specific expertise or viewpoints (e.g., a layperson, or other member who may bring a different perspective to the discussion).
- At the end of the discussion, one of the reviewers or another member makes a motion to approve, approve with contingencies (to secure approval), defer action on (pending receipt of additional information), or disapprove the protocol (see POL.RES.059). A vote on the motion is taken (for, against, or abstain) by a show of hands and/or a voice vote and is recorded in the minutes. All motions are decided by majority vote of the eligible members present for the review. A Quorum of the members of the IRB (more than one-half the members, including one non-scientific member) must be present in order for the IRB to take a vote.

3.7 QUORUM

The presence of more than half the voting membership with on non-scientific member in attendance constitutes a Quorum. Quorum is maintained for the discussion and vote on each research activity on the agenda. Members not present for the discussion or recused from the discussion and vote due to a conflict of interest, are not counted towards the Quorum. Abstaining members do count for the Quorum. The IRB does not vote on any research activity when a Quorum of the membership is not present for the vote. The IRB Administrator or designee is responsible for ensuring that at least one nonscientist member is in attendance and that Quorum is achieved before the meeting begins and is maintained throughout the meeting when each research activity on the agenda is reviewed.

3.8 GUESTS

IRB meetings are closed to the public, although on occasion and at the discretion of the IRB, individuals (such as consultants or others) may attend IRB meetings as guests. In such cases, guests are reminded that the discussions that take place at the meeting are confidential and must not be disclosed to others. Guests are not members of the IRB by virtue of their attendance and are not eligible to vote. Their presence is recorded in the meeting minutes.

HUMAN SUBJECTS RESEARCH: CONVENED IRB REVIEW

3.9 MINUTES

The minutes of the meeting are maintained by the IRB Administrator and include the following:

- Primary voting members present and absent
- Staff and guests, including consultants, present
- Date, start and end time of the meeting

For each human subjects research activity/submission reviewed at the meeting, the minutes include:

- Action taken by the IRB.
- Separate deliberations for each action.
- Number of votes for each protocol as numbers for, against, or abstaining (documentation of Quorum).
- Members attending the meeting but not present for the discussion and vote.
- Recusals of voting members due to conflicts of interest.
- Period of IRB approval, (e.g., one year or less).
- When applicable, summary of information provided by consultant(s).
- Required regulatory determinations of the IRB and protocol-specific findings justifying those determinations including, when applicable: waiver or alteration of the consent process; additional protections for pregnant women, fetuses, and neonates; additional protections for children and additional protections for participants with diminished capacity.
- Summary of the discussion of controverted issues and their resolution, if any.
- When applicable, justification of deletion or substantive modification of information concerning risks or alternative procedures contained in the consent document.
- Modifications required and/or additional information requested by the IRB.
- Basis for requiring changes or disapproving the research.

Minutes are drafted by the IRB Administrator and are sent to the IRB members for review, comments, and approval. A final vote to approve the minutes is conducted at the subsequent IRB meeting. Meeting minutes are saved securely within IRBManager. Minutes are available upon request, when applicable, to authorized representatives of HHS, NIH, and other federal agencies for inspection and copying onsite during normal business hours. Minutes are not ordinarily available to others within or outside the Laboratory unless otherwise required by law. Subpoenas for meeting minutes are handled in consultation with the Legal Department.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

HUMAN SUBJECTS RESEARCH: CONVENED IRB REVIEW

5.0 DEFINITIONS AND ACRONYMS

- **IRB:** Institutional Review Board
- **Minimal Risk:** 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.
- **Quorum:** More than one-half of the voting IRB membership including one non-scientist member present.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	IRB review of research
21 CFR 56	Institutional Review Boards
POL.RES.019	IRB member and consultant conflicts of interest
POL.RES.029	Human subjects research: Event reporting - unanticipated problems involving risks to subjects, or others, adverse events, and other problems
POL.RES.059	IRB actions and communications

HUMAN SUBJECTS RESEARCH: NONCOMPLIANCE

1.0 PURPOSE AND SCOPE

All human subjects research conducted by employees or agents of The Jackson Laboratory (the "Laboratory") shall be conducted in accordance with all applicable federal, state, and local laws and regulations and the highest ethical standards. This Policy outlines the procedures and responsibilities of individuals reporting and investigating observed or apparent Noncompliance in connection with human subjects research.

This Policy is established to comply in part with the regulatory requirement in 45 CFR 46.108(a)(4)(i) and 21 CFR 56.108(b)(2) requiring Institutional Review Boards ("IRBs") to have written procedures which the IRB will follow for ensuring prompt reporting to the IRB, appropriate institutional officials, the Office for Human Research Protections (OHRP), and when applicable, the Food and Drug Administration ("FDA"), of any Serious or Continuing Noncompliance with the regulations or the requirements or determinations of the IRB.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel must adhere to the Human Research Protection Program ("HRPP") policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 REPORTING OBSERVED OR APPARENT NONCOMPLIANCE

Any individual who observes or otherwise becomes aware of apparent Noncompliance with applicable federal, state, and local laws and regulations or the requirements or determinations of the IRB has the duty and responsibility to report the Noncompliance to the IRB. These reports can be associated with or become apparent from protocol deviations, complaints from researchers or participants, or other problems in the research, or from results of audits of the research performed for other reasons.

Observed or apparent Noncompliance should be reported in good faith, and all parties are expected to cooperate with any internal inquiries. The Laboratory intends to protect, to the greatest extent possible, the privacy of an individual who reports Noncompliance on the part of another individual. Such reports will not reflect negatively on the individual reporting the Noncompliance and, when applicable, will not affect his/her employment.

HUMAN SUBJECTS RESEARCH: NONCOMPLIANCE

If an individual is unsure whether there are grounds to suspect Noncompliance, they may call upon the Laboratory Institutional Official ("IO"), IRB Chair and/or Vice Chair to discuss the situation informally and confidentially.

Reports should be made in writing; however, in some cases, reports of Noncompliance may be made orally. When a report of Noncompliance is received orally, the person receiving the report is responsible for creating a written account of the report.

Reports of Noncompliance should include a complete description of the Noncompliance, the observed circumstances, and the names of the individuals involved, if known.

3.2 INVESTIGATING AND PRELIMINARY REPORT OF NONCOMPLIANCE

The IRB and HRPP staff with clinical research quality assurance ("QA") responsibilities will: (1) fully investigate any reports of Noncompliance and any audit results or reports of protocol deviations, complaints, or other problems that it receives that indicate observed or apparent Noncompliance; (2) have a process for determining appropriate actions for any findings of Noncompliance; and (3) for federally funded projects, report any findings of Serious or Continuing Noncompliance as required by HHS regulations. When reviewing reports of Noncompliance, the IRB Chair/Vice Chair and members of the IRB are subject to the IRB conflicts of interest policy (POL.RES.019).

Noncompliance that is associated with or becomes apparent from protocol deviations, complaints from researchers or participants, or other problems in the research may be reported to the IRB as part of any deviation, complaint, or problem report required under the Laboratory's policies on event reporting (POL.RES.029) and the policy on participant questions and complaints (POL.RES.030).

I. *Initial fact-gathering process.* The IRB Chair, Vice Chair and QA staff are responsible for gathering facts to ascertain the nature and scope of the reported Noncompliance. Such fact-gathering shall be concluded within forty-five (45) days of receipt of the report. The fact-gathering process shall include an interview with the affected investigator(s), and other study staff as appropriate. Failure of the investigator(s) to cooperate with such a request or with any other inquiry or process described in this policy shall itself be grounds for IRB action. During this time period, the PI may voluntarily place the research on hold in whole or in part while the Noncompliance investigation is being conducted. Conversely, the IRB Chair or Vice Chair may temporarily suspend (in whole or in part) or may terminate the research. Such suspensions or terminations are reported in accordance with the suspension or termination of human subjects research policy (POL.RES.027).

II. *Preliminary written report and IRB action.* Within fifteen (15) days of the completion of the initial fact-gathering process, a preliminary written report of findings of fact with one of the following determinations:

- No Noncompliance. The facts do not support a finding of Noncompliance as defined in this policy, the report is dismissed, and no further action is taken.
- Minor Noncompliance. The facts support a finding of Minor Noncompliance as defined in this policy, the IRB Chair/Vice Chair approves the research to either continue with no further action required or requires modifications that do not constitute more than a minor change in the research. These modifications are submitted by the investigator in response to the report and reviewed by the IRB.
- Serious or Continuing Noncompliance. The facts support a finding of Serious or Continuing Noncompliance as defined in this policy. The report is referred to the convened IRB for review as described in this policy or,

at the discretion of the IO and IRB Chair/Vice Chair, the IO shall appoint a case-specific Committee on Research Compliance to make recommendations to the IRB with respect to corrective action appropriate to the Noncompliance.

3.3 REVIEW OF SERIOUS OR CONTINUING NONCOMPLIANCE AT A CONVENED IRB MEETING

The IRB members receive a copy of the initial report of Noncompliance, any written reports of findings or audit and determinations and recommendations issued by the IRB Chair/Vice Chair and QA staff. Upon request, the entire protocol file and/or minutes of meetings at which the protocol was discussed previously are made available to members. The IRB Chair or Vice Chair is responsible for presenting the report and determinations to the convened IRB.

By majority vote of a quorum of the membership present at the convened meeting, the IRB makes a determination as to the Noncompliance and takes one or more of the following actions with respect to the research:

- Approve the research to continue with no further action required.
- Defer the decision pending additional information.
- Require modifications in the research, protocol, and/or consent process or form.
- Require participants in the research be re-consented or notified in writing of the Noncompliance.
- Require observation of the consent process by a member of the IRB or support staff.
- Require that participants whose participation has ended be notified in writing of the Noncompliance.
- Suspend IRB approval of this research and other research under the PI.
- Terminate IRB approval of the research.
- Require periodic audits.
- Any other action the IRB deems appropriate to the Noncompliance.

With respect to the affected investigator(s), the convened board may also take one or more of the following actions:

- Require remedial education.
- Require oversight by a senior investigator.
- Restrict or place limitations on the conduct of research or use of research data.
- Restrict research privileges.

The IRB Chair or Vice Chair is responsible for ensuring the description of the Noncompliance and a recording of the findings and actions of the IRB are accurately recorded in the IRB minutes.

The findings and actions of the IRB shall be communicated in writing to the affected investigator(s), IO, and site Scientific Director.

At any point during the investigation, if the IO or IRB Chair/Vice Chair determine that the facts raise issues apart from or in addition to Noncompliance with applicable regulations or the requirements/determinations of the IRB, other institutional authorities (e.g., site scientific director) shall be notified for review or other remedial or corrective actions.

HUMAN SUBJECTS RESEARCH: NONCOMPLIANCE

3.4 INVESTIGATOR APPEALS

As stated in the regulations, any decision of the IRB with respect to research involving human subjects is final. However, the convened IRB may review an investigator's request for reconsideration or appeal to a determination regarding Noncompliance and/or corrective action(s) as warranted by the presentation of new information or unusual circumstances. All investigator petitions must be made within 30 days of his/her notification of the IRB's findings. The IRB will review an investigator's request or appeal within 30 days, and the investigator will be notified in writing of the IRB's decision within 14 days of the review.

3.5 REPORTING SERIOUS OR CONTINUING NONCOMPLIANCE AND, WHEN APPLICABLE, SUSPENSION OR TERMINATION OF THE RESEARCH

The Chair, Vice Chair or designee is responsible for submitting a final report of the Serious or Continuing Noncompliance to the IO and site Scientific Director. When applicable, the Chair or Vice Chair are also responsible for suspending or terminating the research in accordance with the policy on reporting to IOs and regulatory agencies (POL.RES.028).

3.6 RECORD RETENTION

The records of the fact-gathering process and review by the IRB and associated findings of fact and determinations and recommendations are to be maintained within the IRB submission system and/or secure regulatory files for a minimum of three years after completion of the research or any corrective actions (whichever is longer).

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Continuing Noncompliance:** Any Noncompliance that occurs repeatedly after appropriate remedial education or corrective action has been instituted taking into consideration all relevant factors, including, for example: (1) whether the continuing noncompliance was intentional, or (2) whether the investigator collaborated in remedial activity and the continuing noncompliance was not intentional.
- **FDA:** Federal Drug Administration
- **HRPP:** Human Research Protection Program
- **IO:** Institutional Official
- **IRB:** Institutional Review Board
- **Minor Noncompliance:** Any Noncompliance that is not Serious or Continuing Noncompliance. For example, minor Noncompliance might include the following deviations: (1) missing an original signed and dated research consent form, but a copy is available; (2) missing pages of executed research consent forms; (3) obtaining

informed consent using an invalid/outdated research consent form that contains all of the information required by the IRB; or (4) unplanned deviation from the approved protocol where the deviation does not impact the rights and welfare of participants or the integrity of the research.

- **Noncompliance:** Any failure to comply with any regulation that governs human subject research or of any institutional policy for human subjects research. In addition, any violation of any conditions imposed by the IRB on the approval of the study or conduct of the research.
- **QA:** Quality Assurance
- **Serious Noncompliance:** Any Noncompliance that negatively impacts the rights and welfare of participant or compromises the integrity of the study data. For example, serious noncompliance might include, but is not limited to, the following deviations: (1) failure to obtain prospective IRB approval; (2) failure to obtain informed consent of participant(s); (3) missing signature of a participant on an informed consent form; (4) enrollment of participant(s) who do not meet all eligibility criteria; (5) obtaining informed consent using an invalid/outdated research consent form that is missing information that might affect the individual's willingness to participate or continue to participate in the research; (6) failure to perform follow-up as outlined in the protocol where the lack of follow-up places the participant at increased risk of harm; and (7) failure to report a serious unanticipated problem involving risks to participants or others, including adverse events.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	
21 CFR 56	
POL.RES.019	IRB member and consultant conflicts of interest
POL.RES.027	Suspension or termination of human subjects research
POL.RES.028	IRB reporting to institutional officials and regulatory agencies
POL.RES.029	Event reporting: Unanticipated problems involving risks to subjects, or others, adverse events, and other problems
POL.RES.030	Data safety and monitoring plans

REVIEW OF HUMAN SUBJECTS RESEARCH ACTIVITIES: SUSPENSION OR TERMINATION OF HUMAN SUBJECTS RESEARCH

1.0 PURPOSE AND SCOPE

The purpose of this policy is to define the procedures that The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") follows when suspending or terminating IRB–approved Human Subjects Research.

This Policy complies with the regulatory requirements in Department of Health and Human Services ("HHS") Code of Federal Regulations ("CFR") 45 CFR 46.108(a)(4)(ii) and 21 CFR 56.108 (b)(3) that requires IRBs to have written procedures that the IRB will follow for ensuring prompt reporting to the IRB, appropriate institutional officials, Office for Human Research Protections ("OHRP"), and, when applicable, the Food and Drug Administration ("FDA"), of any Suspension or Termination of IRB approval in federally-funded Human Subjects Research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and Termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Consistent with federal regulations, the IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the requirements or determinations of the IRB or that has been associated with unexpected serious harm to subjects. Additionally, the Laboratory's Institutional Official ("IO") may suspend or terminate research approved by the IRB for human subjects protection, administrative, financial, or other reasons.

When the IO suspends or terminates IRB–approved research, s/he is responsible for promptly notifying the Principal Investigator and the IRB of the Suspension or Termination and the reasons for doing so.

REVIEW OF HUMAN SUBJECTS RESEARCH ACTIVITIES: SUSPENSION OR TERMINATION OF HUMAN SUBJECTS RESEARCH

When research approved by the IRB is suspended or terminated, the IRB Chair/Vice Chair considers and determines whether:

- Subjects will be placed at risk of harm by withdrawing them from the study; and
- Subjects must continue to be followed for safety reasons.

3.1 EARLY WITHDRAWAL OF SUBJECTS

When the Suspension or Termination involves withdrawal of subjects from an interventional study, the IRB Chair/Vice Chair considers and determines what, if any, Termination procedures are required for the safety and welfare of those subjects. Termination procedures may include, but are not limited to the following:

- Making a final study visit at which a physical exam and/or laboratory or other tests will be performed; or
- Making arrangements for subjects to receive medical care by their primary care physician or specialist or through referrals to other healthcare providers.

When the IRB determines that the Suspension or Termination will place subjects at risk of harm, the IRB must determine what subjects are to be told and the manner in which they are to be notified (e.g., in writing, in person, or by telephone).

3.2 SUBJECT FOLLOW-UP

When the IRB requires or approves subject follow-up for safety reasons, the investigator is subject to continuing review and requirement to promptly report any unanticipated problems involving risks to subjects or others, including adverse events, to the IRB.

3.3 NOTIFICATION OF SUBJECTS

Depending upon the reasons for the Suspension or Termination and the design of the protocol, the IRB may require that the following subjects be notified of the Suspension or Termination:

- All subjects who have been or are enrolled;
- Subjects currently on protocol; or
- Subjects who participated in a certain aspect of the protocol.

3.4 REPORTING REQUIREMENTS

Whenever the IO or IRB suspends or terminates a research protocol involving human subjects, the IO and IRB Chair/Vice Chair are responsible for submitting a report of the Suspension or Termination of the research in accordance with the policy reporting to institutional officials and regulatory agencies (POL.RES.028).

REVIEW OF HUMAN SUBJECTS RESEARCH ACTIVITIES: SUSPENSION OR TERMINATION OF HUMAN SUBJECTS RESEARCH

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Director, Clinical and Translational Research Support.

5.0 DEFINITIONS AND ACRONYMS

- **CFR:** Code of Federal Regulations
- **FDA:** Food and Drug Administration
- **HHS:** Department of Health and Human Services
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.
- **IO:** Institutional Official
- **IRB:** Institutional Review Board
- **OHRP:** Office for Human Research Protections
- **Suspension:** To cause some aspect of the research to be stopped temporarily or permanently while the research continues under review or an investigation takes place.
- **Termination:** To cause the research to be stopped permanently in its entirety. Expiration and lapse of IRB approval is not considered termination of research.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	HHS Protection of Human Subjects regulations
21 CFR 56	Food and Drug Administration Institutional Review Board regulations
POL.RES.028	IRB reporting to IOs and regulatory agencies

IRB REPORTING TO INSTITUTIONAL OFFICIALS AND REGULATORY AGENCIES

1.0 PURPOSE AND SCOPE

The purpose of this Policy is to comply in part with the regulatory requirement in 45 CFR 46.108(a)(4)(i) and 21 CFR 56.108(b)(2) and to define the procedures The Jackson Laboratory ("Laboratory") Institutional Review Board ("IRB") follows when reporting any unanticipated problem involving risks to subjects or others, serious or Continuing Noncompliance, or any Suspension or Termination of IRB–approved non-exempt Human Subjects Research to the Institutional Official ("IO"), and as required or appropriate, to the Office for Human Research Protections ("OHRP"), the Food and Drug Administration ("FDA") or other applicable regulatory agency.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of Noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and Termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The policies and procedures for an investigator's prompt reporting to the IRB, as well as the review of the reports of Unanticipated Problems, Noncompliance, and Suspensions or Terminations by the IRB are covered in separate policies, which include; event reporting (POL.RES.029), Suspension/Termination of research (POL.RES.027) and Noncompliance (POL.RES.026).

The Laboratory Federalwide Assurance ("FWA") applies to all federally supported human subjects research. The same criteria and process for the conduct and oversight of human subjects research, for determinations about reportable events, and for actions taken in response to such events will apply to all human subjects research at or affiliated with the Laboratory regardless of funding source. However, if such an event involves human subjects research that is not federally conducted or supported, the IRB is not required to report the event to OHRP or other federal department or agency head (reporting to the FDA may still be required, if the research is subject to FDA regulations). All other reporting requirements described below apply regardless of funding source.

IRB REPORTING TO INSTITUTIONAL OFFICIALS AND REGULATORY AGENCIES

The IRB Chair/Vice Chair are responsible for preparing incident reports, which include the following information:

- The nature of the event (e.g., an Unanticipated Problem Involving Risks to Subjects or Others, serious or Continuing Noncompliance, Suspension or Termination of approval of research).
- Name of the institution conducting and collaborating on the research.
- IRB number of the research project and the number of any applicable federal award(s) (e.g., grant, contract, or cooperative agreement).
- A detailed description of the problem including the findings of the IRB and the reasons for the decision.
- Actions the IRB/institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend enrollment, terminate the research, revise the informed consent document, inform enrolled participants, increase monitoring of participants, etc.).
- Plans, if any, to send a follow-up or final report by (1) a specified date or (2) when the research has been completed or a corrective action plan has been implemented.

When the final incident report is approved, it may be sent to (as applicable) the Principal Investigator ("PI"), IRB members and support staff, the Laboratory's Privacy Officer (if the report involves unauthorized use, loss, or disclosure of individually identifiable patient information from the covered entity), Laboratory IO, regulatory agencies and accrediting organizations, including:

1. OHRP (Note: reporting to OHRP is not required for non-federally funded research).
2. FDA, if the research is subject to FDA regulations.
3. Any Federal Agency supporting the research, when applicable.
4. Others, such as IRBs at collaborating research institutions as deemed appropriate by the IO or IRB Chair/Vice Chair.

The IO and IRB Chair/Vice Chair will ensure that all steps of this policy are completed generally within thirty (30) days of the date when the IRB determines that either an incident is an Unanticipated Problem Involving Risks to Subjects or Others, an incident is serious or Continuing Noncompliance with HHS or FDA regulations or the requirements or determinations of the IRB, or the IRB or IO suspends or terminates the research.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

IRB REPORTING TO INSTITUTIONAL OFFICIALS AND REGULATORY AGENCIES

5.0 DEFINITIONS AND ACRONYMS

- **Continuing Noncompliance:** Any Noncompliance that occurs repeatedly after appropriate remedial education or corrective action has been instituted taking into consideration all relevant factors, including, for example: (1) whether the Continuing Noncompliance was intentional, or (2) whether the investigator collaborated in remedial activity and the Continuing Noncompliance was not intentional.
- **FDA:** Food and Drug Administration
- **Federalwide Assurance (FWA):** An assurance of compliance for all U.S. institutions engaged in human subjects research conducted or supported by HHS. Under a Federalwide Assurance, an institution commits to HHS that it will comply with the requirements set forth in 45 CFR 46 as well as the terms of assurance.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by the FDA.
- **IO:** Institutional Official
- **IRB:** Institutional Review Board
- **Minor Noncompliance:** Any Noncompliance that is not serious or Continuing Noncompliance. For example, Minor Noncompliance might include the following deviations: (1) missing an original signed and dated research consent form, but a copy is available; (2) missing pages of executed research consent forms; (3) obtaining informed consent using an invalid/outdated research consent form that contains all of the information required by the IRB; or (4) unplanned deviation from the approved protocol where the deviation does not impact the rights and welfare of research participants or the integrity of the research.
- **Noncompliance:** Any failure to comply with any regulation that governs human subjects research or of any institutional policy for human subjects research. In addition, any violation of any conditions imposed by the IRB on the approval of the study or conduct of the research.
- **OHRP:** Office for Human Research Protections
- **PI:** Principal Investigator
- **Serious Noncompliance**: Any Noncompliance that negatively impacts the rights and welfare of research participants or compromises the integrity of the study data. For example, Serious Noncompliance might include, but is not limited to, the following deviations: (1) failure to obtain prospective IRB approval; (2) failure to obtain informed consent of research participants(s); (3) missing signature of a research participant on an informed consent form; (4) enrollment of participant(s) who do not meet all eligibility criteria; (5) obtaining informed consent using an invalid/outdated research consent form that is missing information that might affect the individual's willingness to participate or continue to participate in the research; (6) failure to perform follow-up as outlined in the protocol where the lack of follow-up places the participant at increased risk of harm; and (7) failure to report a serious Unanticipated Problem Involving Risks to Subjects or Others, including adverse events.
- **Suspension:** To cause some aspect of the research to be stopped temporarily or permanently while the research continues under review or an investigation takes place.

IRB REPORTING TO INSTITUTIONAL OFFICIALS AND REGULATORY AGENCIES

- **Termination:** To cause the research to be stopped permanently in its entirety. Expiration and lapse of IRB approval is not considered termination of research.
- **Unanticipated Problem Involving Risks to Subjects or Others:** Any incident, experience, information, outcome, or other problem that is unexpected and related to the research, and that indicates that the research places participants or others at an increased risk of physical, psychological, economic, legal, or social harm than was previously known or recognized.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
Federalwide Assurance (FWA) for the Protection of Human Subjects	
45 CFR 46	
21 CFR 56	
POL.RES.026	Noncompliance in human subjects research
POL.RES.027	Suspension or termination of human subjects research
POL.RES.029	Event reporting: unanticipated problems involving risks to subjects, or others, adverse events, and other problems

REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS, OR OTHERS, ADVERSE EVENTS AND OTHER PROBLEMS IN HUMAN SUBJECTS RESEARCH

1.0 PURPOSE AND SCOPE

When The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") approves human subjects research, the approval is based on information about how the research will be conducted and the risks and anticipated benefits, if any, to subjects that are known or recognized at the time the research is reviewed. Once the research is approved, however, Unexpected problems may occur, or new information may become available that indicates that the research places subjects or others at an increased risk of harm. The purpose of this Policy is to define the problems and Adverse Events that require prompt reporting to the IRB.

Unexpected problems and new information about risks, anticipated benefits or conduct of the research that increase risk of participation to subjects or others are referred to as *unanticipated problems*. Some unanticipated problems, such as Adverse Events, cause actual harm to subjects. Others may not cause actual harm to subjects but suggest that the research places subjects or others at an increased risk of harm. All such unanticipated problems must be reported promptly to the IRB so that the Committee can consider whether 1) the risks to subjects are still minimized and reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected to result; and 2) any changes to the research or other corrective actions are warranted in order to protect the safety, welfare, or rights of subjects or others.

This Policy complies with the federal regulations 45 CFR 46.108(a)(4) and 21 CFR 56.108(b)(1) that require IRBs to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any unanticipated problems involving risks to subjects or others. This Policy is also consistent with Office for Human Research Protections ("OHRP") guidance on reviewing and reporting unanticipated problems involving risks to subjects or others and Adverse Events.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to and including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS, OR OTHERS, ADVERSE EVENTS AND OTHER PROBLEMS IN HUMAN SUBJECTS RESEARCH

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 REPORTING OF ADVERSE EVENTS AND UNANTICIPATED PROBLEMS

The Principal Investigator ("PI") is required to report to the IRB any of the following problems that occur during the conduct of the study, after study completion, or after subject withdrawal or completion. **Reports are to be submitted within five (5) working days/seven (7) calendar days of the date the investigator first becomes aware of the problem**.

- Internal Adverse Events that are Unexpected, related or possibly related to the research and that indicate there are new or increased risks to subjects.
- External Adverse Events that are serious, Unexpected, related or possibly related to the research and that indicate there are new or increased risks to subjects that require some action (e.g., modification of the protocol, consent process, or informing subjects).
- Unanticipated Adverse Device Effects that are serious and caused by, or associated with, the device.
- Deviation from the approved research protocol or plan without IRB approval in order to eliminate apparent immediate hazard to subjects or harm to others.
- Deviation from the approved research protocol or plan that placed subjects or others at an increased risk of harm regardless of whether there was actual harm to subjects or others.
- Any event that requires prompt reporting according to the research protocol or investigational plan or the sponsor.
- Breach of confidentiality or violation of HIPAA (e.g., lost, or stolen laptop).
- Procedural or laboratory error (e.g., errors in surgical or other procedure, or testing of samples or test results) regardless of whether subjects experienced any harm.
- Interim analysis, safety monitoring report, publication in a peer-reviewed journal, or other finding that indicates that there are new or increased risks to subjects or others or that subjects are less likely to receive any direct benefits from the research.
- Change in FDA labeling, withdrawal from market, manufacturer alert from the sponsor, or recall of an FDA-approved drug, device, or biologic used in the research.
- Complaint by/on behalf of a research subject that indicates that the rights, welfare, or safety of the subject have been adversely affected or that cannot be resolved by the investigator.
- Incarceration of a research subject during participation in research that is not approved for involvement of prisoners as subjects.
- Noncompliance with applicable regulations or requirements or determinations of the IRB identified by the research team or others (e.g., audit, monitoring report, FDA Warning Letter) that indicates that the rights, welfare, or safety of subjects have been adversely affected.

- Suspension or Termination of the research, in whole or in part, based on information that indicates that the research places subjects at an increased risk of harm than previously known or recognized.
- Suspension or disqualification of an investigator by FDA, sponsor, or others.
- Scientific Misconduct.
- Any other problem that indicates that the research places subjects or others at an increased risk of harm or otherwise adversely affect the rights, welfare or safety of subjects or others.

3.2 REPORTING PROTOCOL DEVIATIONS

Unplanned or unintentional Deviations in IRB–approved research may occur during the conduct of a research study or be discovered during routine data monitoring activities of the sponsor, investigators or IRB directed audit. The PI is responsible for reviewing the Deviation log periodically to monitor compliance with the approved research. Unapproved *Major* Deviations must be recorded in a protocol-specific Deviation log and reported to the IRB within five (5) working days of the date the investigator becomes aware of the unapproved Deviation. Unapproved *Minor* Deviations are to be recorded by the investigator in the Deviation log and submitted for IRB review at continuing or annual review.

It is the responsibility of the PI to determine whether an unapproved Deviation from the IRB–approved protocol is major or minor and to ensure proper reporting to the IRB. When making this determination, the PI should consider whether the Deviation negatively affected any of the following: the rights or welfare of the subject; the risk-benefit assessment of their participation in the study; and/or the integrity of the study data and/or the ability to draw conclusions from the study data.

3.3 REPORTING UNANTICIPATED PROBLEMS THAT ARE ADVERSE EVENTS

Any unanticipated, untoward, or unfavorable medical occurrence, including abnormal signs (for example, abnormal physical exam or laboratory finding), symptoms or diseases, that indicates that the research places subjects at increased risk of physical or psychological harm than previously known or recognized are to be submitted to the IRB as an unanticipated problem. The investigator must provide the following information in the "*Reportable New Event Form"* in IRBManager:

a) A detailed description of the Adverse Event.
b) The basis for determining that the event is Unexpected in nature, severity, or frequency.
c) The basis for determining that the event is related or possibly related to the research procedures.
d) The basis for determining that the research places subjects at an increased risk of harm (i.e., a Serious Adverse Event).
e) Whether any changes to the research or other corrective actions are warranted.

REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS, OR OTHERS, ADVERSE EVENTS AND OTHER PROBLEMS IN HUMAN SUBJECTS RESEARCH

3.4 REPORTING UNANTICIPATED PROBLEMS THAT ARE *NOT* ADVERSE EVENTS

All other unanticipated incidents, Deviations, experiences, information, outcomes, or other problems that indicate that the research places subjects at an increased risk of physical, psychological, economic, legal, or social harm than was previously known or recognized are to be submitted to the IRB Office as an unanticipated problem. The investigator must provide the following information in the "*Reportable New Event Form"* in IRBManager:

a) A detailed description of the unanticipated problem.
b) The basis for determining that the problem is Unexpected.
c) The basis for determining that the problem indicates that the research places subjects at an increased risk of harm.
d) Whether any changes to the research or other corrective action are warranted.

3.5 REVIEW PROCESS

Event reports and accompanying information will be screened by the IRB Administrator and additional information may be requested. Reports that meet the requirements for "unanticipated event involving risks to subjects or others" or a report of Noncompliance will be forwarded to the IRB for convened review. Reports that do not meet these requirements will be reviewed by expedited review.

3.5.1 EXPEDITED REVIEW

a) IRB reviewers will have access to the complete protocol file and will determine if the event report raises any new concerns about risks in the study. If necessary, the reviewer may forward to the convened IRB to determine if Suspension or Termination of the protocol is needed.
b) If the event is determined not to be an Unanticipated Problem Involving Risks to Subjects or Others, the reviewer may make any necessary recommendations for action which are then communicated to the PI.
c) IRB members will be informed of these expedited reviews as described in the expedited review procedures (POL.RES.021).

3.5.2 CONVENED REVIEW

a) Copies of the report, all information provided by the PI, current consent documents and any proposed changes will be included in the review materials for each member. Sections of the protocol and any other relevant information will also be provided.
b) The IRB will determine by convened review whether the event is an Unanticipated Problem Involving Risks to Subjects or Others and if the event represents serious and/or continuing Noncompliance. Actions taken will be based on the nature of the event, degree to which research participants are placed at risk, occurrence of problems, etc.

c) The IRB determination and actions, including discussion and vote will be recorded in the meeting minutes. The requirements for quorum apply.
d) Investigators will be notified of convened reviews as described in the convened review policy (POL.RES.022).

3.5.3 IRB ACTIONS

a) Modification(s) to the protocol, procedures, consent process/form.
b) Providing additional information to current or past research participants.
c) Reconfirming consent of current research participants.
d) Monitoring of the research, including audits.
e) Education or mentoring of the PI and/or research staff.
f) Additional reporting or more frequent continuing review.
g) Placing limitations on the PI's research activities or use of research data.
h) Suspending or terminating the research.
i) Referral to other appropriate institutional authorities.

If the IRB determines that an event represents an Unanticipated Problem Involving Risks to Subjects or Others, serious and/or continuing Noncompliance, or if the IRB suspends or terminates approval of the research, the appropriate internal and external persons and/or agencies will be notified according to the IRB reporting to Institutional Official and regulatory agencies policy (POL.RES.028).

3.6 AMENDMENTS BASED ON THE OCCURRENCE OF AN ADVERSE EVENT OR UNANTICIPATED PROBLEM

Investigators should take into consideration whether substantive changes in the research or informed consent document, or other corrective actions may be warranted in order to protect the safety, welfare, or rights of subjects or others. Changes to the protocol and/or the informed consent document are to be submitted to the IRB as an amendment and must be approved by the IRB before they are adopted into the research, except to eliminate an immediate risk to safety of a participant. Examples of substantive changes include:

- Changes to the eligibility criteria
- Changes to safety monitoring procedures
- Changes to the informed consent document to describe newly identified risk

REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS, OR OTHERS, ADVERSE EVENTS AND OTHER PROBLEMS IN HUMAN SUBJECTS RESEARCH

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Adverse Event:** Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (i.e., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.
- **Deviation:** Any alteration/modification to the IRB approved research without prospective IRB approval. The term research encompasses all IRB approved materials and documents including the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study.
- **External Adverse Events:** Adverse events experienced by subjects enrolled at sites that are not relying on the IRB review of the research. In the case of an External Adverse Event, the PI typically becomes aware of the adverse event upon receipt of a report from the sponsor, coordinating center or other monitoring group, such as a Data and Safety Monitoring Board (DSMB)/Data Monitoring Committee (DMC), or collaborating investigator at another site.
- **Internal Adverse Events:** Adverse Events experienced by subjects at sites that are relying on IRB review of the research. In the case of an Internal Adverse Event the PI typically becomes aware of the Adverse Event directly from the subject, co-investigator or other member of the study staff, or the subject's healthcare provider.
- **IRB:** Institutional Review Board
- **Major Deviation:** Any alteration/modification to the IRB–approved research that has the potential to negatively impact subject safety or the integrity of study data (e.g., the ability to draw conclusions from the study data) or affect the subject's willingness to participate in the study.
- **Minor Deviation:** Any deviation from the IRB–approved research that does not have the potential to negatively impact subject safety or the integrity of study data (e.g., the ability to draw conclusions from the study data) or affect subject's willingness to participate in the study.
- **Noncompliance:** Any failure to comply with any applicable federal, state, or local laws and regulations or the requirements or determinations of the IRB, which include IRB and institutional policies related to human subject protection.
- **OHRP:** Office for Human Research Protections
- **PI:** Principal Investigator

REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS, OR OTHERS, ADVERSE EVENTS AND OTHER PROBLEMS IN HUMAN SUBJECTS RESEARCH

- **Possibly Related to the Research:** There is a Reasonable Possibility that the Adverse Event, incident, experience, or outcome may have been caused by the procedures involved in the research.
- **Reasonable Possibility*:*** The event is more likely than not related to participation in the research or, in other words, there is a >50% likelihood that the event is related to the research procedures.
- **Scientific Misconduct:** Any fabrication, falsification, plagiarism, or other practice that seriously deviates from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research.
- **Serious Adverse Event*:*** Any event or reaction temporally associated with the subject's participation in research that meets any of the following criteria; results in death; is life threatening (i.e., places the subject at immediate risk of death from the event as it occurred); requires inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or any other Adverse Event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the outcomes listed above.
- **Suspension:** To cause some aspect of the research to be stopped temporarily or permanently while the research continues under review, or an investigation takes place.
- **Termination:** To cause the research to be stopped permanently in its entirety. Expiration of IRB approval is not considered termination of research.
- **Unanticipated Adverse Device Effect**: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
- **Unanticipated Problem Involving Risks to Subjects or Others:** Any incident, experience, or outcome that is unexpected and related to the research and suggests that the research places subjects or others at a greater risk of physical, psychological, economic, legal, or social harm than was previously known or recognized.
- **Unexpected:** The incident, experience, or outcome is Unexpected (in terms of nature, severity, or frequency) given the (a) research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document and (b) the characteristics of the study population being studied.
- **Unexpected Adverse Event:** Any Adverse Event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with:
  1) The known or foreseeable risk of Adverse Events associated with the procedures involved in the research that are described in the protocol-related documents, such as the IRB-approved research protocol and the current IRB-approved informed consent document, and
  2) The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the Adverse Event and the subject's predisposing risk factor profile for the Adverse Event.

REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS, OR OTHERS, ADVERSE EVENTS AND OTHER PROBLEMS IN HUMAN SUBJECTS RESEARCH

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events	This guidance represents OHRP's current thinking on this topic and should be viewed as recommendations unless specific regulatory requirements are cited.
45 CFR 46	Federal (HHS) Regulations for the Protection of Human Subjects in Research
21 CFR 56	FDA Regulations for IRBs in Clinical Investigations
POL.RES.021	Human Subjects Research: Expedited Review
POL.RES.022	Human Subjects Research: Convened IRB Review
POL.RES.028	IRB Reporting to Institutional Officials and Regulatory Agencies

HUMAN SUBJECTS RESEARCH: QUESTIONS, CONCERNS OR COMPLAINTS FROM SUBJECTS OR FAMILY MEMBERS

1.0 PURPOSE AND SCOPE

The Jackson Laboratory (the "Laboratory") is committed to protecting the rights, safety and welfare of subjects participating in human subjects research. This includes provisions for allowing participants and their family members to raise questions and/or concerns and to have those concerns addressed in a timely manner. This Policy provides an overview of institutional guidelines and expectations for managing such questions, concerns or complaints and the processes for remedial action should such questions, concerns or complaints reflect broader issues of research compliance.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program ("HRPP") policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Participants and their family members are encouraged to ask questions or voice any concerns or complaints they may have about the research or their participation in the research during the consent process and throughout the study period. The Principal Investigator ("PI") is responsible for answering all questions, addressing all concerns, and responding to all complaints raised by participants to the best of his/her ability.

3.1 PARTICIPANT ACCESS TO CONTACT INFORMATION FOR THE PI, RELEVANT STUDY PERSONNEL AND THE INSTITUTIONAL REVIEW BOARD

The Research Informed Consent Form ("ICF") includes a section that addresses whom to contact if participants or family members have questions, concerns, or complaints about the research. This section includes the name of the PI responsible for the research and their contact information, as well as the name and contact information for others on the study team who are available to answer the participant's questions or address any concerns or complaints they might have about the research or their participation in the research. The ICF also includes the telephone number for the reviewing Institutional Review Board ("IRB") should participants wish to discuss their rights, their concerns, or a complaint about the research with someone not involved in the research project.

HUMAN SUBJECTS RESEARCH: QUESTIONS, CONCERNS OR COMPLAINTS FROM SUBJECTS OR FAMILY MEMBERS

If the research study has a waiver of consent or waiver of document of consent, contact information for the PI must be included in a study information sheet or other written statement about the research, or in other written materials used during the recruitment and consent processes.

Participants are encouraged to contact the IRB if they have any concerns that they do not want to discuss with the research staff, e.g., feeling pressured to take part in the research or, after enrollment, to continue to take part in the study.

3.2 COMPLAINTS RECEIVED BY INVESTIGATORS/STUDY STAFF

Prospective participants and participants enrolled in the research may ask questions or voice concerns or complaints directly to the PI responsible for the research or to a member of the study staff, verbally or in writing before, during or after taking part in the research.

PIs are responsible for ensuring that participant complaints are handled in a respectful manner and that participants are not penalized or lose any benefits they are receiving or have a right to receive. Complaints must be resolved thoroughly and in a timely manner.

When, despite their best efforts, the PI is unable to resolve a complaint thoroughly or in a timely manner, the complaint must be referred to the Laboratory's HRPP Director. The HRPP Director will then work with the investigator and the IRB to resolve the complaint. The IRB will address the complaint in a timely manner and communicate its resolution to the complainant, generally within thirty (30) days.

PIs must document all complaints received from participants or family members and their resolution and report them at the Annual Administrative Review with the clinical research quality assurance specialist.

3.3 COMPLAINTS RECEIVED BY THE IRB

Prospective participants and participants enrolled in the research may ask questions or voice concerns or complaints to a representative of the IRB, or HRPP staff, verbally or in writing before, during or after taking part in the research. The investigator is then informed of the complaint and needs to submit a response to the issues raised in the complaint. The privacy of the complainant is maintained during this process.

The HRPP staff, investigator, IRB, and other institutional representatives, as appropriate, work together to resolve the complaint. Investigators and study staff are expected to cooperate with internal efforts to investigate and resolve complaints. The IRB and/or the PI must address the complaint in a timely manner and communicate its resolution to the complainant, generally within thirty (30) days of receipt of the complaint. The IRB maintains records of participants' complaints and their resolution, and a copy is retained in the applicable protocol file.

HUMAN SUBJECTS RESEARCH: QUESTIONS, CONCERNS OR COMPLAINTS FROM SUBJECTS OR FAMILY MEMBERS

3.4 REMEDIAL ACTION, SUSPENSION OR TERMINATION OF RESEARCH AND NONCOMPLIANCE

The IRB is responsible for determining whether remedial action is necessary. Should the complaint result in an allegation of noncompliance or be cause for suspension or termination of the research, the IRB follows the procedures outlined in the noncompliance policy (POL.RES.026) suspension policy (POL.RES.027) and the IRB reporting policy (POL.RES.028).

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **HRPP:** Human Research Protection Program
- **ICF:** Informed Consent Form
- **IRB:** Institutional Review Board
- **PI:** Principal Investigator

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.026	Noncompliance in human subjects research
POL.RES.027	Review of human subjects research activities: Suspension or termination of human subjects research
POL.RES.028	IRB reporting to institutional officials and regulatory agencies

HUMAN SUBJECTS IN RESEARCH: DATA AND SAFETY MONITORING PLANS

1.0 PURPOSE AND SCOPE

This Policy defines the requirements for a data and safety monitoring plan in interventional clinical research protocols submitted to The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") for review and approval. This Policy is established to comply in part with the requirement for IRBs to determine that where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects" [45 CFR 46.111(a)(6)][21 CFR 56.11(a)(6)].

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The IRB requires the inclusion of a Data and Safety Monitoring Plan ("DSMP") in all interventional clinical research protocols that involve more than minimal risk to subjects. The DSMP must be described in sufficient detail for the IRB to determine whether the plan is appropriate for the research. This Policy is established to comply in part with the requirement for IRBs to determine "where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects" [45 CFR 46.111(a)(6) and 21 CFR 56.111(a)(6)]. The following information is provided to assist investigators in establishing an appropriate DSMP for their research.

3.1 ITEMS TO BE INCLUDED IN THE DATA AND SAFETY MONITORING PLAN

1. The type of data or events that are to be captured under the monitoring plan.
2. Who will be responsible for monitoring the data collected, including data related to unanticipated problems and adverse events, and their respective roles (e.g., the investigators, the research sponsor, a coordinating or statistical center, an independent medical monitor, a Data and Safety Monitoring Board ("DSMB") or Data Monitoring Committee ("DMC"), or some other entity).
3. The time frames for reporting adverse events and unanticipated problems to the monitoring entity, such as the research sponsor, coordinating or statistical center, independent medical monitor, or DSMB/DMC.

4. The frequency of assessments of data or events captured by the monitoring plan, such as points in time or after a specific number of participants are enrolled.
5. Definition of specific triggers or stopping rules that will dictate when some action is required. Stopping rules are predetermined guidelines that are used to determine that the study should be altered or stopped, based on review of study related events that occur during the conduct of the study. Stopping rules should be specific about the endpoints that will be used and the decisions that will be made. Studies may be stopped, for example, when there is a greater than expected rate of morbidity or mortality or when the experimental arm of a head-to-head comparison study is shown to be better or worse statistically than the standard-of-care arm.
6. Procedures for communicating to the IRB, the study sponsor, and other appropriate entities the outcome of reviews by the monitoring entity.

3.2 TYPES OF DATA AND SAFETY MONITORING PLANS

A DSMP is tailored to the nature, size, and complexity of the research protocol, the expected risks of the research, and the type of subject population being studied. Appropriate DSMPs may fall anywhere along a continuum from monitoring by the Principal Investigator ("PI") or group of investigators to the establishment of an independent DSMB/DMC.

1. *Principal Investigator–led DSMP.* This type of plan is appropriate when:
    a. the study involves a small number of subjects
    b. the study is conducted only at one site
    c. the range of possible study events that could have an important impact on the risks and benefits of research participants is narrow.

    In such cases, continuous monitoring of events by the PI, and prompt reporting of adverse events to the IRB and, when applicable, the sponsor or others, may be adequate.
2. *Monitor/Monitoring Group DSMP.* A qualified and objective individual or group not directly involved with the design and conduct of the study (e.g., safety officer, designated Medical Monitor or Monitoring Group) could perform this function. These individuals may or may not be employees of the Laboratory. However, conflict of interest is an important consideration when employees of the study sponsor have the primary responsibility for monitoring data from the standpoint of scientific integrity and participant safety.

    This type of plan is often appropriate to monitor data and safety for clinical trials that involve:
    - Endpoints that are not serious irreversible events
    - An intervention (for example, to relieve symptoms) that is not high risk and the effects of which would not generally be so compelling as to ethically warrant early termination for effectiveness
    - Short-term treatments where effects are evaluated over periods of a few days to a few months; and
    - A small number of subjects where the study is completed quickly, and the risk can be adequately assessed through simple comparisons.

    In these studies, valuable secondary objectives such as characterization of the effect (i.e., magnitude, duration, time to response), assessment of the effect in population subsets, comparison of several doses or comparison of the new product to an active control can be ethically pursued even when the conclusion regarding the

primary efficacy outcome is clear. Early termination for effectiveness is rarely appropriate in such studies. First, the study may be essentially completed by the time any interim analysis to evaluate effectiveness could be undertaken. Second, the effectiveness of an intervention, for example, to relieve symptoms, would not generally be so compelling as to override the need to collect the full amount of safety data, or to collect other information of interest and importance that characterizes the effect.

3. *Data and Safety Monitoring Board/Data Monitoring Committee.* A DSMB/DMC is a formal committee that is established specifically to monitor data throughout the life of a study to determine if it is appropriate, from both the scientific and ethical standpoint, to continue the study as planned. In general, an independent DSMB/DMC is the most appropriate way to monitor data and safety for studies that involve:
    - *Large numbers of subjects* where risk may better be assessed through statistical comparisons of treatment groups
    - *Blinded study treatment groups* where the validity and integrity of the study may be adversely affected by having an individual or group associated with the design and conduct of the study break the blind
    - *Multiple clinical sites* where there is a need for investigators to submit reports of adverse events to a central reporting entity, such as a coordinating center or statistical center, responsible for preparing timely summary reports of adverse events for distribution among the clinical sites, and to the IRBs.

3.3 DATA SAFETY AND MONITORING BOARD/DATA MONITORING COMMITTEE MEMBERSHIP, CHARTERS, AND RESPONSIBILITIES

DSMBs/DMCs are typically made up of individuals who have expertise in the field, experience in the conduct of clinical research and trials, and/or statistical knowledge, and who do not have any conflicts of interest, such as financial interests that could be substantially affected by the outcome of the trial, strong views on the relative merits of the interventions under study, or relationship with the sponsor or those in trial leadership positions that could be considered reasonably likely to affect their objectivity.

DSMBs/DMCs typically operate under a written charter that includes well-defined standard operating procedures that address the following:

- Meeting schedule (frequency) and format (in person or by videoconference or telephone).
- Meeting structure and confidentiality (including who will attend all or part of DSMB/DMC meetings and who will have access to interim data).
- Format, method, and timing of interim reports to the DMC.
- Procedures for assessing conflict of interest of potential DSMB/DMC members.
- Other issues relevant to committee operations, such as membership, voting, quorum, and handling of minutes.
- Board/committee Responsibilities.

The DSMB/DMC charter may be drafted by either the sponsor or the DSMB/DMC; however, both must agree to the procedures outlined in the charter.

The responsibilities of DSMBs/DMCs may be broad or narrow in scope, and include some or all of the following responsibilities:

- Monitoring for effectiveness
- Monitoring for safety
- Monitoring study conduct, including:
    - Rates of recruitment, ineligibility, noncompliance, protocol violations and dropouts
    - Completeness and timeliness of the data
    - Degree of concordance between site evaluation of events and centralized review
    - Balance between study arms on important prognostic variables; and
    - Accrual within important subsets.
- Consideration of external data, such as release of results of a related study that may have implications for the design of the ongoing study, or its continuation
- Making recommendations to the sponsor (or other group delegated by the sponsor to make decisions about the study) concerning continuation of the study with or without modifications, temporary suspension of enrollment or intervention, or termination of the study based on review of interim data; and/or
- Maintaining meeting minutes.

3.4 NATIONAL INSTITUTES OF HEALTH-SPONSORED RESEARCH

The NIH has established a policy that requires each of its Institutes and Centers ("IC") to have a system for the appropriate monitoring of the conduct of clinical trials to ensure the safety of participants and the validity and integrity of the data for all NIH-supported or conducted clinical trials. Investigators must comply with monitoring requirements of the relevant funding agency in addition to those of the IRB.

The establishment of DSMBs is required for multi-site clinical trials involving interventions that entail potential risk to the participants.

An IC may require a DSMB to perform monitoring functions. This DSMB would be composed of experts relevant to the study and would regularly assess the trial and offer recommendations to the IC concerning its continuation. For more information on NIH Policy, see: The NIH Policy for Data and Safety Monitoring

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

HUMAN SUBJECTS IN RESEARCH: DATA AND SAFETY MONITORING PLANS

5.0 DEFINITIONS AND ACRONYMS

- **Data and Safety Monitoring:** The process for reviewing accumulated outcome data from an ongoing clinical trial to ensure the continuing safety of current participants and those yet to be enrolled, as well as the continuing validity and scientific merit of the trial.
- **DMC:** Data Monitoring Committee
- **DSMB:** Data and Safety Monitoring Board
- **DSMP:** Data and Safety Monitoring Plan
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve and *human subject* as defined by HHS or meet the definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.
- **IC:** Institutes and Centers
- **Interventional Clinical Research:** A prospective study involving human subjects that is designed to answer specific questions about the clinical effects or impact of a particular biomedical or behavioral intervention (i.e., drugs, devices, treatments or procedures, behavioral or nutritional strategies), or designed to answer specific questions about human physiology.
- **Minimal Risk:** 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.
- **PI:** Principal Investigator

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46.111	Criteria for IRB approval of research (OHRP)
21 CFR 56.111	Criteria for IRB approval of research (FDA)
Data and Safety Monitoring Plans in Human-Subjects Research	Mass General Brigham Human Research Protection Program Policy on Data and Safety Monitoring Plans in Human Subjects Research, 12/01/2020.

RESEARCH IN VULNERABLE POPULATIONS: RESEARCH INVOLVING CHILDREN

1.0 PURPOSE AND SCOPE

The purpose of this Policy is to define the procedures The Jackson Laboratory (the "Laboratory') Institutional Review Board ("IRB") follows when reviewing Human Subjects Research involving Children and wards of the state and procedures the IRB follows when Children reach age 18 while participating in ongoing research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Federal regulations require additional protections for Children involved in research. To the extent that law of the jurisdiction in which the research will be conducted does not specifically address consent of Children with majority status to research, the IRB reviews issues of consent related to enrollment of these Children in research on a case-by-case basis and seeks guidance from the Legal Department as needed. For research conducted in multiple jurisdictions, the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions. The Legal Department provides assistance with regard to the laws in other jurisdictions as needed.

The IRB may approve research that involves Children as subjects of research if regulatory requirements at 45 CFR 46 Subpart D or 21 CFR 50 Subpart D are met, as quoted in part below:

1. Research not involving greater than Minimal Risk [45 CFR 46.404][21 CFR 50.51];
2. Research involving greater than Minimal Risk but presenting the prospect of direct benefit to individual subjects [45 CFR 46.405][21 CFR 50.52].
3. Research involving greater than Minimal Risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition [45 CFR 46.406][21 CFR 50.53].
4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of Children [45 CFR 46.407][21 CFR 50.54]. HHS-funded research in this category must be submitted to the Secretary of HHS for consultation with a panel of experts in

pertinent disciplines and opportunity for public review and comment. When the research is funded by a federal agency other than HHS, the IRB consults with appropriate officials at the relevant federal agency or department funding the research.

The IRB must determine and document whether Permission of one or both Parents must be obtained for participation of the Children in the research.

- When the research is covered by 45 CFR 46.404, 45 CFR 46.405, 21 CFR 50.51 or 21 CFR 50.52, the IRB may determine that Permission of one Parent is sufficient.
- When the research is covered by 45 CFR 46.406, 45 CFR 46.407, 21 CFR 50.53 or 21 CFR 50.54, Permission of both Parents must be obtained unless one Parent is deceased, unknown, incompetent, or not reasonably available or when only one Parent has legal responsibility for the care and custody of the Child.

Principal Investigators (PI) planning research involving Children, other than analysis of specimens and data provided by an external collaborator that obtained consent/Assent external to the Laboratory must complete the appropriate sections on the Initial IRB Review Application in IRBManager to address 45 CFR 46 Subpart D or 21 CFR 50 Subpart D regulations and submit the form to the IRB for review and approval prior to enrollment of Children.

3.1 ASSENT

The IRB must also determine whether Assent of the Children participating in the research is required. When making determinations regarding Assent, the IRB considers the capacity of the Children to Assent, taking into consideration the age, maturity and psychological state of the Children involved. Determinations regarding Assent may be made for all of the Children participating in the research or for each child. When the IRB determines that Assent is required, it is also determined whether Assent will be documented and if so, the process to be used. When the research holds out the prospect of direct benefit that is important to the health or well-being of the Children and is available only in the context of the research, the Assent of the Children is not necessary for proceeding with the research.

3.2 WARDS OF THE STATE

Children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406, 45 CFR 46.407, 21 CFR 50.53 or 21 CFR 50.54 only if the research is:

1. related to their status as wards; or
2. conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of Children involved as subjects are not wards.

If the research is approved based on the paragraph above regarding Children who are wards, the IRB requires appointment of an advocate for each Child who is a ward, in addition to any other individual acting on behalf of the Child as Guardian or in loco parentis. One individual may serve as advocate for more than one Child. The advocate is an individual who has the background and experience to act in, and agrees to act in, the best interest of the Child for the

duration of the Child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the Guardian organization.

3.3 CHILDREN REACHING THE LEGAL AGE OF CONSENT WHILE ENROLLED IN A STUDY

The Office for Human Research Protections ("OHRP") notes that informed consent should be viewed as an ongoing process throughout the duration of a research project. When a Child who was enrolled in research with parental or Guardian Permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of 45 CFR part 46.408 or 21 CFR 50.55 regarding parental or Guardian Permission and subject Assent.

Unless the IRB determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in 45 CFR 46.116 or 21 CFR 50.20, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental Permission and Child Assent are not equivalent to legally effective informed consent for the now-adult subject. However, IRB could approve a waiver of informed consent under 45 CFR 46.116(f), if the IRB finds and documents that the required conditions are met. FDA regulated research does not allow a waiver or alteration of the consent process.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Assent:** A child's affirmative agreement to participate in research.
- **Child/Children:** Person(s) who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. The IRB generally defines children as persons under eighteen years of age. According to the NIH, a child is an individual under the age of 18 years. This definition applies to all NIH applications submitted on or after January 25, 2016.
- **Guardian:** An individual authorized under applicable State or local law to consent on behalf of a Child to general medical care.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.
- **IRB:** Institutional Review Board
- **Minimal Risk:** 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. [45 CFR 46.102(ij)]

RESEARCH IN VULNERABLE POPULATIONS: RESEARCH INVOLVING CHILDREN

- **OHRP:** Office for Human Research Protections
- **Parent:** A Child's biological or adoptive parent.
- **Permission:** The agreement of Parent(s) or Guardian to the participation of their Child or ward in research.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	Protection of human subjects (OHRP 2018 Requirements)
21 CFR 50	Protection of human subjects (FDA)

RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, OR NEONATES

1.0 PURPOSE AND SCOPE

Federal regulations require additional protections for pregnant women, Fetuses, or Neonates involved in research. These requirements include, among other things, that research involving greater than minimal risk is conducted only when benefits are anticipated for the mother and/or Fetus, preclinical and clinical studies have been conducted (where scientifically appropriate) that provide data for assessing potential risks, and informed consent processes describe the reasonably foreseeable risks to the Fetus or Neonate.

The purpose of this policy is to define the procedures The Jackson Laboratory's ("Laboratory") Institutional Review Board ("IRB") follows when reviewing human subjects research involving pregnant women or human Fetuses, Nonviable Neonates, Neonates of uncertain viability, or placenta post-Delivery. The IRB will approve federally-funded human subjects research that include pregnant women or human Fetuses, Nonviable Neonates or Neonates of uncertain viability, only if the IRB finds and documents that the research satisfies the conditions of 45 CFR 46, Subpart B, and applicable state law in the jurisdiction where consent is signed and of the Laboratory site (CA, CT, ME) where specimens are analyzed.

Principal Investigators ("PIs") planning federally-funded research involving pregnant women, Fetuses, non-Viable Neonates, Neonates of uncertain viability or placenta post-Delivery, must complete the questions on the initial review submission within IRBManager to explain the protections provided for the participants.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, OR NEONATES

3.0 POLICY STATEMENT

3.1 ADDITIONAL PROTECTIONS FOR PREGNANT WOMEN AND FETUSES

Pregnant women or Fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies (including studies on pregnant animals) and clinical studies (including studies on non-pregnant women) have been conducted and provide data for assessing potential risk to pregnant women and Fetuses.
2. Regarding the risk(s) of the research, any risk is the least possible for achieving the objectives of the research, and either of the following applies:
    a. The risk to the Fetus is caused solely by interventions or procedures that offer the prospect of direct benefit for the woman or the Fetus.
    b. If there is no expectation of benefit(s), the risk to the Fetus is not greater than minimal and the purpose of the research is the development of important knowledge that cannot be obtained by any other means.
3. Consent of the pregnant woman is obtained and documented as described in the informed consent policy (POL.RES.037) in any of the following circumstances:
    a. The research offers the prospect of direct benefit to the pregnant woman.
    b. The research offers the prospect of a direct benefit to both the pregnant woman and the Fetus.
    c. The research does not offer the prospect of benefit for either the woman or the Fetus, but the risk to the Fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.
4. The consent of both parents must be obtained and documented as described in the informed consent policy (POL.RES.037) for research that holds out the prospect of direct benefit solely to the Fetus, with the following exceptions:
    a. The father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity.
    b. The father’s consent need not be obtained if the Pregnancy resulted from rape or incest.
5. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the Fetus or Neonate.
6. No inducements (monetary or otherwise) will be offered to terminate a Pregnancy.
7. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a Pregnancy.
8. Individuals engaged in the research will have no part in determining the viability of a Neonate.

RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, OR NEONATES

3.2 ADDITIONAL PROTECTIONS FOR NEONATES

Where scientifically appropriate, preclinical, and clinical studies have been conducted and provide data for assessing potential risks to Neonates. Individuals engaged in the research are to have no part in determining the viability of the Neonate.

Nonviable Neonates may be involved in research as described below:

1. Vital functions of the Neonate will not be artificially maintained.
2. The research will not terminate the heartbeat or respiration of the Neonate.
3. There will be no added risk to the Neonate resulting from the research.
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.
5. The consent of both parents must be obtained and documented as described in the informed consent policy (POL.RES.037), with the following exceptions;
    a. If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent is sufficient.
        i. The consent of a legally authorized representative (for either or both of the parents of a Nonviable Neonate) is not sufficient.
        ii. Provisions for waiver or alteration of the consent process are not applicable.
    b. The consent of the father need not be obtained if the Pregnancy resulted from rape or incest.
6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the Neonate.

Neonates of uncertain viability may be involved in research as described below:

1. Regarding the risk(s) of the research, one of the following applies:
    a. The research offers the prospect of enhancing the probability of survival of the Neonate to the point of viability, and any risk is the least possible for achieving that objective.
    b. If the research does not offer the prospect of enhancing the probability of survival, the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means, and there will be no added risk to the Neonate resulting from the research.
2. The consent of either parent is obtained and documented as described by the informed consent policy (POL.RES.037) with the following exceptions:
    a. If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of either parent's legally authorized representative is obtained.
    b. The consent of the father or his legally authorized representative need not be obtained if the Pregnancy resulted from rape or incest.
3. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the Neonate.

RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, OR NEONATES

A Neonate, after Delivery, that has been determined to be Viable, may be included in research only to the extent permitted by and in accord with the requirements of the IRB review process, research involving children (45 CFR 46, Subpart D and if applicable, 21 CFR 50 Subpart D), and policy on research involving children (POL.RES.034).

3.3 RESEARCH INVOLVING, AFTER DELIVERY, THE PLACENTA, THE DEAD FETUS OR FETAL MATERIAL

Research involving, after Delivery, the placenta; the Dead Fetus; macerated fetal material; or cells, tissue, or organs excised from a Dead Fetus, must be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects, and 45 CFR 46 applies.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Dead Fetus:** Fetus which exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord if still attached.
- **Delivery:** The process of giving birth; complete separation of the Fetus from the woman by expulsion, extraction, or any other means.
- **Fetus:** Unborn child; the product of conception from implantation until Delivery.
- **IRB:** Institutional Review Board
- **Neonate:** Newborn.
- **Nonviable Neonate:** A Neonate that (although alive following Delivery) is not capable of surviving to the point of sustaining life independently, even with the support of available medical treatment, as determined by a physician who is not engaged in the research.
- **PI:** Principal Investigator
- **Pregnancy:** Period of time from implantation (of a fertilized egg within the uterus) until expulsion or extraction of the Fetus.
- **Viable Neonate:** Being able to survive, after Delivery, to the point of independently maintaining heartbeat and respiration as determined by a physician who is not engaged in the research (given the benefit of available medical therapy).

RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, OR NEONATES

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46 Subpart B	
Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials Guidance for Industry, Draft Guidance 4/2018	
Embryonic and Fetal Research Laws (2016)	
US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g	
POL.RES.034	Research in children
POL.RES.037	Informed consent of research subjects

RESEARCH IN VULNERABLE POPULATIONS: RESEARCH INVOLVING PRISONERS

1.0 PURPOSE AND SCOPE

Prisoners are considered a particularly vulnerable subject population and require additional protections when participating in human subjects research. This Policy describes Institutional Review Board ("IRB") management of inclusion of Prisoners in research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The federal regulations governing human subjects in research 45 CFR 46, Subpart C provide additional safeguards for the protection of research subjects who are Prisoners because the constraints associated with incarceration may affect the individual's ability to make a truly voluntary and uncoerced decision regarding participation in research. The additional protections apply to research subjects who are Prisoners at the time of enrollment in the research as well as research subjects who become Prisoners after they enroll in the research.

3.1 IRB REVIEW OF RESEARCH INCLUDING PRISONERS AS SUBJECTS

For an IRB to review and approve research that involves Prisoners, the membership of the IRB must include at least one member who is or has been a Prisoner, or a Prisoner representative (someone who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the Prisoner). The Jackson Laboratory IRB does not have Prisoner representation, thus review of research involving Prisoners will not be accepted for review and may not be conducted if the Laboratory IRB is the sole IRB reviewing the research.

RESEARCH IN VULNERABLE POPULATIONS: RESEARCH INVOLVING PRISONERS

3.2 RESEARCH EXEMPT FROM THE REQUIREMENTS OF 45 CFR 46

For research prior to 1/21/2019, the exemptions at 45 CFR 46.104 do not apply to research involving Prisoners.

For research approved after 1/21/2019 under the "Final Rule", the exemptions are allowable if the research is aimed at a broader population and incidentally includes Prisoners. The Final Rule also permits the exempt secondary research of information or biospecimens from subjects who are Prisoners if the research is not seeking to recruit Prisoners or examine Prisoners as a subpopulation.

3.3 WHEN A SUBJECT BECOMES A PRISONER WHILE PARTICIPATING IN AN IRB-APPROVED RESEARCH STUDY

When a subject becomes a Prisoner while participating in a non-exempt research study approved only by the Laboratory IRB, all research interactions, and interventions with the subject and/or collection of identifiable private information about the subject must cease and participation terminated since the Laboratory IRB cannot review research involving Prisoners.

When a subject becomes a Prisoner, the investigator must notify the IRB immediately of the situation for guidance on management based on the specific circumstances of the study.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **IRB:** Institutional Review Board
- **OHRP:** Office for Human Research Protections
- **Prisoner:** Any individual involuntarily confined or detained in a penal institution. Office for Human Research Protections ("OHRP") Guidance extends the definition in *Guidance on Involvement of Prisoners in Research* to "individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing."

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46 Subpart C	Additional protections pertaining to biomedical and behavioral research involving Prisoners as subjects

INFORMED CONSENT OF RESEARCH SUBJECTS

1.0 PURPOSE AND SCOPE

Informed consent is an essential part of ethical human subjects research. Institutional Review Boards ("IRB") and Investigators are responsible for ensuring that research subjects provide informed consent prior to participating in research unless the requirement for informed consent is waived or altered (in non-exempt research) by the IRB. Investigators must educate potential subjects to ensure that they can reach a truly informed decision about whether or not to participate in the research. Their informed consent must be given freely, without Coercion or Undue Influence, based on a clear understanding of what participation involves. This policy defines the requirements for the informed consent process, the elements of consent, and documenting the informed consent of research subjects.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 BACKGROUND

The requirement to obtain the informed consent of individuals before involving them in research is founded on the principle of *Respect for Persons*, one of the three ethical principles governing human subjects research described in the Belmont Report. The process of educating subjects about the study begins during initial contact and continues for the duration of their participation. Thus, information conveyed through advertisements, recruitment letters, pre-screening phone calls, and study description sheets as well as written informed consent documents and discussions must be understandable to the subjects and must contribute to their understanding of the research. Technical and medical terminology should be avoided or explained in "lay" language, and materials should be written at an 8th grade reading level or lower. Non-English speaking subjects must have information presented in a language they understand, refer to POL.RES.038 for guidance. The IRB must approve written and oral information (including recruitment materials) provided to subjects before use.

The entire text of the research consent forms must be approved by the IRB as part of the review process. The effective date of the IRB-approved consent form is added to the consent form by the IRB administrator upon approval. Subjects

must be given and sign the most recently approved version of the research consent form. Out-dated research consent forms must not be used in the consenting process or to document informed consent.

The original signed (including in an electronic format) and dated research consent form must be retained in the research records. A copy of the signed and dated research consent form must be given to the subject unless documentation of consent is waived by the IRB.

To further document the informed consent process, the Investigator should complete a Documentation of Informed Consent form or document in progress notes indicating the version and IRB approval date of the consent form used to explain the study to the subject, that all questions were answered (if any), that the subject agreed to participate and signed/dated the consent form, and that a copy of the consent form signed by the subject and consenter was given to subject.

3.2 CONSENT DISCUSSION

The consent discussion should begin in advance of study-related procedures to allow potential subjects time to reflect on the potential benefits and risks of participation. The following method is preferred by IRB, though it may be tailored to the circumstances of individual studies and may not be appropriate or feasible in all situations.

- First, potential subjects are given general information about the research (e.g., through IRB- approved advertisements, information sheets, letters, or through discussion with their clinicians). If they are interested in learning more about the study, they contact the study staff. Potential subjects may also be referred to the study team by a clinician involved in their clinical care.
- The Investigator or their designee then meets with the potential subject to review and to discuss the details of the research study using the IRB-approved informed consent document as a guide. This discussion must include all of the basic elements of informed consent and additional elements of consent, as applicable to the specific study (Section 3.7).
- Preferably, potential subjects are then given a copy of the informed consent document to review so they can carefully read the document and discuss the research with their family, friends and/or physician and develop questions to ask at their next meeting with the research staff. Please note that subjects must always be given the opportunity to ask questions and have them answered by the Investigator or designee and, whenever possible, to consult with friends/family and/or their physicians prior to consenting to participation.
- If the subject and/or Legally Authorized Representative ("LAR"), as applicable, agrees to participate in the research, they sign and date the informed consent document along with the member of the study team obtaining consent, unless documentation of consent has been waived by the IRB. The subject and/or LAR is provided with a copy of the signed consent form, as applicable.

3.3 TIMING OF INFORMED CONSENT

Special consideration must be given to the timing of the consent process when the subject population includes patients who are seen only at one visit for study presentation, discussion, and consent. Whenever possible, provide potential subjects with a copy of the informed consent form in advance.

INFORMED CONSENT OF RESEARCH SUBJECTS

With few exceptions, the informed consent of subjects, must be obtained and documented in writing before the start of any study-related procedures, including screening tests and exams done solely to determine their eligibility for the study. Refer to the pre-screening policy (POL.RES.043) for guidance. Informed consent is to be obtained directly from each subject, with the exception of children (see below and POL.RES.034) and individuals with impaired decision-making capacity.

3.4 INDIVIDUALS WHO CAN OBTAIN INFORMED CONSENT

IRB-approved study personnel have been trained in the protocol and designated by the Primary Investigator ("PI") to administer the informed consent process. It is the PI's responsibility to ensure that proper informed consent is obtained from every subject according to the procedures approved by the IRB.

3.5 OBTAINING PARENTAL/LEGAL GUARDIAN PERMISSION FOR PARTICIPATION OF CHILDREN

Federal regulations require that permission to participate in research on behalf of a child be provided by a parent or a LAR. In general, a parent is authorized to consent to general medical care on behalf of their child. However, in some circumstances (such as when both parents are deceased), it may be necessary to identify another individual with this authority (for example, a court-appointed guardian). Before an Investigator allows an individual other than a parent to give permission on behalf of a child, the Investigator must document the basis for the individual's authority to act on behalf of the child and place any relevant documentation in the research file. In situations when it is unclear under state law who has the authority to provide consent on behalf of a child, the IRB must consult with the Office of General Counsel, as needed.

When obtained, Assent must be documented in writing using the IRB–approved Assent form. When Assent is not obtained, the Investigator must document his/her rationale in the research records. Refer to POL.RES.034 for more details on institutional policy regarding research involving children.

3.6 USE OF A SUBJECT ADVOCATE

In certain situations, the IRB may require the use of a subject advocate in the consent process. The subject advocate is an individual who has no vested interest in the research and who agrees to act as an impartial third party in the consent process. The subject advocate is expected to act in the best interests of the subject by participating in discussions with the Investigator and in the consent process. The subject advocate is responsible for ensuring that the subject understands the research procedures, the risks and potential benefits of participation and that his/her consent is free and voluntary. When a subject advocate is used, the subject advocate must sign and date the consent form.

3.7 ELEMENTS OF INFORMED CONSENT

In most cases, Investigators must document the Informed Consent process by use of a written IRB approved consent form signed and dated by the subject or their LAR (only when IRB-approved this process) and the Investigator or designated study staff who obtained the subject's consent.

For studies approved under the 2018 Common Rule, the Informed Consent must begin with a concise and focused presentation of the key information that is most likely to assist a subject or LAR in understanding the reasons why one might or might not want to participate in the research. The information should be provided in sufficient detail, organized, and presented in a way that facilitates comprehension.

INFORMED CONSENT OF RESEARCH SUBJECTS

At minimum, the research consent form must include the following basic elements of Informed Consent [45 CFR 46.116(b)][21 CFR 50.25(a)]:

1. A statement that the study involves research, 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 that are experimental.
2. A description of any reasonably foreseeable risks or discomforts to the subject.
3. A description of any benefits to the subject or to others that may reasonably be expected from the research.
4. A disclosure of appropriate alternative 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. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
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.
8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and
9. For studies approved under the 2018 Rule, one of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens must be included [45 CFR 46.116 (b)(9)]:
    a. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future studies or distributed to another Investigator for future research studies without additional Informed Consent From the subject or the LAR, if this might be a possibility; or
    b. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

When appropriate, the following additional elements of Informed Consent must be provided to each subject [45 CFR 46.116(c)][21 CFR 50.25 (b)]:

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) that are currently unforeseeable.
2. Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's or LAR's consent.
3. Any additional costs to the subject that may result from participation in the research.
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
5. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject.
6. The approximate number of subjects involved in the study.

7. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit [45 CFR 46.116(c)(7)].
8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions [45 CFR 46.116 (c)(8)].
9. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen) [45 CFR 46.116 (c)(9)].

3.8 BROAD CONSENT

Broad consent is an optional alternative consent process for the storage, maintenance, and secondary use of identifiable private information or identifiable biospecimens for future, yet-to-be-specified research. To use broad consent, the PI responsible for the storage of the data/biospecimens are required to (1) identify the types of research that may be conducted with the data/biospecimens, (2) record and track who has agreed to or refused consent, and (3) track the terms of consent to determine whether proposed future secondary research use falls within the scope of the identified types of research.

The Laboratory's Human Research Protection Program ("HRPP") and IRB will not mandate or implement the institutional use of Broad Consent. Therefore, exemption categories 7 and 8 (see POL.RES.020) will not be available to researchers. PIs seeking subject permission for the collection and storage of identifiable private information or biospecimens for future secondary use can do so using study-specific consent or an IRB waiver of consent (as eligible) or de-identification to remove applicability of IRB review.

If the Laboratory is collaborating with an institute where broad consent was obtained for biospecimens to be used at the Laboratory, the IRB must confirm that the conditions of broad consent were maintained in the transfer of the materials.

3.9 CLINICAL TRIALS

When seeking Informed Consent for applicable NIH-funded clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement must be provided to each clinical trial subject, *"A description of this clinical trial will be available on http://ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time."*

3.10 EXCULPATORY LANGUAGE

Any Informed Consent, whether written or oral, must not include Exculpatory Language such that the subject is made to waive, or appear to waive, any of his or her legal rights or to release the institutions or its agents, the Investigators, from liability or negligence.

Examples of Exculpatory Language:

- By agreeing to this use, you give up all claim to personal benefit from commercial or other use of these substances.
- I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.

- By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
- I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

3.11 PHONE CONSENT

Consent by phone may be considered on a case-by-case basis and should be appropriate for the study. Consent discussions may take place by phone in situations where it is not possible for the participants to meet with the Investigator/study staff in person. The phone consent process must be approved by the IRB.

3.12 ELECTRONIC CONSENT

Electronic systems and processes, such as websites, email, audio, and video may be used to convey information related to the study and to obtain and document Informed Consent. The electronic system may supplement or replace traditional consent mechanisms, however, participants must have the option to use the traditional paper form or the electronic system.

The IRB should review all methods used to gauge subject comprehension of key study elements, the usability of the electronic materials to ensure that they are easy to navigate, and the contents of any hyperlinks used to convey study related information. Full content of any hyperlinks included in the e-consent must be provided to potential participants that choose the traditional paper form consent process.

The electronic consent form must include contact information for the PI and the study team for the potential participant to connect to ask questions and to discuss participation in the study prior to consent and at any time during the conduct of the research.

Digital signatures can be (1) actual signatures on tablets or computers (where the individual uses a stylus or finger to make a signature) or (2) validated electronic signatures on platforms with password control. Both forms of digital signature can be used in minimal risk research consent forms. The participant signing the electronic consent must confirm that they are the study participant and that the signature entered on the electronic consent form is their signature. Scanned signatures that are copied and pasted into a document are not acceptable digital signatures unless they are applied per (2) above.

3.13 SPECIAL CONSIDERATIONS IN INFORMED CONSENT

The consent process must provide potential participants sufficient opportunity to consider whether to participate and must minimize the possibility of Coercion or Undue Influence. When some or all of the participants are likely to be vulnerable to Coercion or Undue Influence, such as pregnant women, prisoners, children, students, employees, or individuals with impaired decision-making capacity, economically or educationally disadvantaged persons, additional safeguards are required to protect the rights and welfare of these participants. Additional requirements for obtaining Informed Consent (or Assent) in specific populations are described in the following policies:

- Research Involving Pregnant Women, Fetuses, or Neonates (POL.RES.035)
- Research Involving Prisoners (POL.RES.036)

- Research Involving Children (POL.RES.034)
- Collection of Biological Specimens from the Laboratory's Employees (POL.RES.051)
- Obtaining and Documenting Informed Consent of Subjects who don't Speak English (POL.RES.038)

3.14 DOCUMENTATION OF WRITTEN CONSENT

In almost all cases, Investigators must document the Informed Consent process by use of a written consent document signed and dated by the subject (or his/her LAR, when IRB approved to do so) and the Investigator (or study staff) who obtained the subject's consent. Subjects must be given a signed copy of the most recently approved version of the consent form.

Digital signatures may be accepted as documentation of written consent. The technology and process for obtaining digital signatures must be approved by the IRB.

3.15 ALTERATION OR WAIVER OF ELEMENTS OF INFORMED CONSENT

The IRB can approve a consent process that does not include, or that alters, some or all of the elements of Informed Consent or can waive the requirement to obtain Informed Consent provided that the research is not subject to FDA regulations and the IRB finds and documents that the research meets all of the following requirements:

1. The research involves no more than minimal risk to the subjects.
2. The research could not practicably be carried out without the requested waiver or alteration.
3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects.
5. Whenever appropriate, the subjects or LAR will be provided with additional pertinent information after participation.

In addition, for studies approved under the 2018 rule, use of identifiable information/biospecimens to identify potential subjects (i.e., screening for recruitment purposes) is allowed without Informed Consent under certain circumstances [45 CFR 46.116(g)]. A waiver of consent is no longer needed for these screening activities; however, HIPAA requirements still apply.

Requests for alterations or a waiver of Informed Consent requirements should be made in the IRB application in IRBManager and address each of these requirements.

3.16 WAIVER OF WRITTEN DOCUMENTATION OF INFORMED CONSENT

The IRB may waive the requirement for the Investigator to obtain a signed Informed Consent form for some or all of the subjects, when the research is not regulated by the FDA, if it finds any of the following:

1. That the only recording linking the subject and the research would be the Informed Consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or LAR) will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern;

2. That the research present no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or
3. If the subjects or LAR are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that Informed Consent was obtained.

If the IRB approves a waiver of written documentation of Informed Consent, Investigators must fully inform prospective subjects about the study, answer their questions, and obtain their verbal Informed Consent. The IRB must review a written description of the information that will be provided to prospective subjects to ensure that the required elements of consent are included in the consent discussion. The IRB may require the Investigator to provide subjects with a written statement regarding the research.

3.17 OBTAINING NEW CONSENT AND/OR NOTIFYING SUBJECTS OF MAJOR CHANGES TO THE INFORMED CONSENT FORM

When subjects are actively engaged in the research and there have been major changes to any component of the consent form (e.g., study procedures, risks and discomforts, benefits, and alternatives), they should be asked for new consent and sign a revised, IRB-approved consent form. This is paramount if knowledge of the new information might affect subjects' willingness to continue participation.

As part of the review of amendments to the protocol and/or Informed Consent document, the IRB determines whether the change(s) requires obtaining new consent from subjects enrolled in the study.

An example of when a subject should be asked for new consent in writing is when the research has been revised to include a new procedure that the subject will be asked to undergo (e.g., genetic testing, biopsy, etc.). An Investigator may not perform a procedure on a subject without new consent if the procedure was not mentioned in the original consent process and form.

Subjects should be given the revised information in a timely manner so that they can make a fully informed decision about whether they wish to continue their participation.

The IRB may approve a letter being sent to notify the subject of the change(s) without signing a new consent form in the following circumstances:

- The PI has and/or the contact telephone number have changed.
- The study contacts and/or the contact telephone numbers have changed.
- The subject has completed the study interventions and is in the follow-up phase of the study or in some cases has completed the study, and the information is such that learning it would not materially affect the subject's decision to continue participation in follow-up.

INFORMED CONSENT OF RESEARCH SUBJECTS

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Assent:** An affirmative agreement to participate in research. Children ages 7 and older should be given an opportunity to provide assent based on capacity of the children, taking into consideration the age, maturity and psychological state of those involved. Generally, oral assent through the use of a script should be obtained from children 7 - 11 years of age. Written assent using a document for the children to sign may be sought for older children. In these instances, assent by the child is suggested and permission of one or both parents, as determined by IRB, is required. Children below the age of 7 years are not deemed capable of providing assent.
- **Coercion:** Persuasion (i.e., of an unwilling person) to do or agree to something by using obvious or implied force or threats.
- **Exculpatory Language:** As it applies to Informed Consent, any written or verbal communication through which a research participant (or his/her LAR) is asked to waive or appear to waive any of the participant's legal rights or to release (or appear to release) the Investigator, sponsor, or institution from liability for negligence.
- **FDA:** US Food and Drug Administration
- **Informed Consent:** the process by which an Investigator obtains permission from a potential subject (or his/her LAR, if IRB approved) before conducting research on that subject. Voluntary agreement by the subject, without Coercion, to participate in the study must be obtained in writing, unless waived by the IRB.
- **Investigator:** An individual performing various tasks related to the conduct of human subjects' research activities, such as obtaining Informed Consent from subjects, interacting with subjects, studying, interpreting, generating or analyzing identifiable private information for research purposes, and communicating with the IRB.
- **IRB:** Institutional Review Board
- **LAR:** Legally Authorized Representative; An individual, judicial, or other body authorized under applicable law to consent on behalf of a prospective subject for participation in the procedure(s) involved in the research.
- **OHRP:** US Dept of Health and Human Services Office for Human Research Protections
- **PI:** Principal Investigator; The individual who is responsible and accountable for conducting the human subjects research. The PI assumes full responsibility for the protection of human subjects, compliance with regulations, and for the integrity of the research data and results.
- **Undue Influence:** Excessive or inappropriate reward or other incentive in which a person is induced to act otherwise than by his/her own free will or without adequate consideration of the consequences.

INFORMED CONSENT OF RESEARCH SUBJECTS

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	HHS Protection of Human Subjects regulations
21 CFR 50	FDA IRB regulations
Belmont Report	Ethical Principles and Guidelines for the Protection of Human Subjects of Research
OHRP FAQ	"Informed Consent Frequently Asked Questions" (revised 07/14/08)
OHRP Guidance	"Informed Consent – Legally Effective and Prospectively Obtained" (OPRR Reports 93-03, 08/12/93)
OHRP Guidance	"Tips on Informed Consent" (OPRR, revised 03/16/93)
FDA Information Sheet	"Informed Consent" Draft Guidance for IRBs, Clinical Investigators, and Sponsors (July 2014)
OHRP & FDA Q&A	Use of Electronic Informed Consent: Questions and Answers (12/2016)
POL.RES.020	Describes Human Subjects Research: Exempt Research
POL.RES.034	Describes Research in Vulnerable Populations: Research Involving Children
POL.RES.035	Describes Research Involving Pregnant Women, Fetuses or Neonates
POL.RES.036	Guidelines for Researching in Vulnerable Populations: Research Involving Prisoners
POL.RES.038	Guidelines for Informed Consent of Non-English Speaking Research Subjects
POL.RES.043	Describes the Recruitment of Research Subjects: Pre-Screening of Research Subjects During Recruitment
POL.RES.051	Guidelines in the Collection of Biological Specimens from Jackson Laboratory Employees

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

1.0 PURPOSE AND SCOPE

Implicit in the definition of informed consent is the expectation that the subject clearly understands the information that is being provided to them. Investigators must carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented, the subject's consent is not truly informed and may not be legally effective. The purpose of this Policy is to define the requirements for obtaining and documenting informed consent of research subjects who do not speak English.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

If an investigator enrolls non-English-speaking subjects, the protocol must reflect the methods for assuring full understanding, possibly with the assistance of an interpreter and/or by using translated informed consent forms or Short Form Consent forms. When the investigator anticipates enrolling non-English-speaking subjects, the Institutional Review Board ("IRB") reviews and approves a translated version of the informed consent document or approves use of a Short Form Consent process per 45 CFR 46.117(b)(2).

The Department of Health and Human Services ("HHS") regulations 45 CFR 46.116 and 45 CFR 46.117 require that informed consent information be presented in a language understandable to the subject, and in most situations, that informed consent be documented in writing. Investigators may encounter non-English-speaking patients who are interested in participating in a research study. It is neither ethically justifiable to exclude potential subjects in a research study solely on the basis of language spoken nor ethically justifiable to obtain consent of subjects who do not have a clear understanding of the consent document or who do not have the opportunity to freely ask and receive answers to their questions. In order to address these considerations, when enrolling subjects who do not speak English in research, the subject must be provided with BOTH:

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

- A written consent document in a language understandable to them, AND
- An interpreter fluent in both English and the subject's spoken language

Depending upon the research, the written consent document can be either:

- A written translation, in the subject's language, of the entire English version of the consent form approved by the IRB, or
- A written translation of a "short form" consent document.

The short form consent document should generally only be used when the research involves no more than minimal risk to subjects or, if more than minimal risk, presents the prospect of direct benefit to individual subjects, at the present time or in the future.

3.1 USE OF A WRITTEN TRANSLATION OF THE ENTIRE ENGLISH VERSION OF THE IRB-APPROVED CONSENT DOCUMENT

When investigators can reasonably expect that more than an incidental number of subjects speaking the same non-English language will be enrolled (for example, if the research is targeting a specific non-English-speaking group), the use of a written translation of the *entire* English version of the consent form is required. The IRB must approve all written translated versions of the consent form and recommends that the written translation be performed by a professional translation service or other qualified person or service.

Two methods of translation are acceptable to the IRB. One method is that the document is translated by a professional translation service that attests to the accuracy of the translation. The second is the use of back-translation into English. In this scenario:

1. The English version of the consent form is translated into the foreign language.
2. The name and credentials of the individual who did the translation are provided to the IRB via the Investigator.
3. Another individual who has not seen the English version of the consent document translates the foreign language document back into English.
4. This individual provides his/her name, credentials, and a statement that s/he has not seen the original English version to the IRB via the investigator.
5. Both English versions and the foreign language version are submitted to the IRB for review.
6. The IRB compares both English versions and if the IRB determines the translation is accurate the foreign language document is stamped with approval.

Investigators must also arrange for a medical interpreter fluent in both English and the subject's spoken language to be present, or available by phone or videoconference, during the consent process.

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

3.2 USE OF A WRITTEN TRANSLATION OF THE SHORT FORM CONSENT DOCUMENT

Although it is always preferable, and in some cases required by the IRB, to use a written translation of the entire IRB-approved English version of the consent form (see above), a translated version of a short form consent document can be used to document informed consent when a non-English-speaking individual is encountered, and a written translation of the IRB-approved consent form is not available. The short form must be IRB-approved before use. The short form attests that the elements of consent have been presented orally. When the short form is used to document informed consent, the consent process must include oral presentation of the English version of the consent form in a language understandable to the potential subject. An interpreter must be physically present to interpret, in the subject's language, the researcher's oral presentation of the English version of the consent form.

The consent process for enrolling subjects using the short form consent document is outlined below.

ALL of the following requirements must be completed:

1. The Principal Investigator ("PI") (or other member of the study staff with PI-delegated responsibility for obtaining informed consent) must present the IRB–approved English version of the consent form orally to the subject through an interpreter physically present and fluent in English and the language understandable to the subject.
2. The subject must be given a written translation of the short form consent document in the language understandable to him/her to read.
3. The entire consent process must be witnessed by an individual who is fluent in both English and the language understandable to the subject. The interpreter may serve as the witness to the consent process (which must include presentation of the information in the consent form in the language understandable to the subject and the opportunity to ask and receive answers to questions).
4. The IRB-approved English versions of the full consent form and the English short form must be signed by the investigator obtaining informed consent **and** the witness to the consent process.
5. The IRB-approved written translation of the short form in the native language of the subject must be signed by the subject **and** the witness to the consent process.
6. The subject must be given signed copies of **both** the IRB-approved English full version of the consent form **and** the written translation of the short form consent document.
7. The original signed English version of the consent form with the original signed written translation of the short form document attached should be placed in the subject's research record.

The IRB must review and approve all foreign language versions of the short form document as a condition of approval [see 46.117(b)(2)]. Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been IRB-approved.

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

3.3 GUIDANCE FOR ENROLLING SUBJECTS WITH SOME ENGLISH COMPREHENSION OR ILLITERATE ENGLISH-SPEAKING SUBJECTS

Sometimes a subject whose first language is foreign understands English but does not read or write English. An impartial witness should document that the subject understands the study and the consent process and consented to participate. This witness should also sign and date the consent form. The subject must be provided with a copy of the signed document (making a mark will suffice if the subject is unable to sign).

3.4 AFTER INITIAL CONSENT

Because informed consent is an ongoing process, issues related to the subject's ability to understand and ask questions should continue to be considered throughout the study, and not just at the time of initial consent. For example, it is recommended to arrange for an interpreter to be available at subsequent study visits to ensure that subjects have an opportunity to ask questions and receive relevant study information.

3.5 FREQUENTLY ASKED QUESTIONS

When must a written translation of the entire English version of the consent form be used to obtain and document informed consent?

When investigators can reasonably expect that more than an incidental number of subjects speaking the same non–English language will be enrolled (for example, if the research is targeting a specific non–English speaking group), the use of a written translation of the entire English version of the consent form is required. Investigators are also generally expected to use a written translation of the entire English version of the consent form for research that involves more than minimal risk and no direct medical benefit to subjects.

Is an interpreter required for the consent discussion when a written translation of the entire English consent form is used?

Yes. Because the consent process involves more than simply reading the consent form, an interpreter must be in attendance, either physically or by phone or videoconference so that the subject can ask and receive answers to any questions they might have about the research from the member of the study team administering the informed consent process.

When can the short form written consent document be used to obtain and document informed consent of a subject who does not speak English?

An IRB approved translated version of a short form written consent document can be used to document informed consent when a non-English-speaking individual is encountered and a written translation of the entire Jackson Laboratory (the "Laboratory") IRB–approved consent form is not available in the participant's language. The short form written consent document should generally only be used when the research involves no more than minimal risk to subjects or, if the research involves more than minimal risk, presents the prospect of direct benefit to individual subjects.

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

Can a family member serve as the interpreter when using the short form written consent document or the translated version of the entire English consent form?

Generally, no. Family members may not be impartial or possess knowledge of medical terminology or the confidence to ask for clarification, and subjects may not feel comfortable revealing certain sensitive personal or medical information through family members. Also, rather than interpret, family members often tend to speak for the subject, removing the subject from the decision-making process. Consequently, misunderstandings may inadvertently occur. Professional medical interpreters or bilingual medical personnel should perform this important task.

Can a bilingual investigator*obtain informed consent using the short form written consent document or a translated version of the entire English consent form?

Yes. When the investigator is truly fluent in the language understood by the subject AND English, s/he may obtain informed consent. When a bilingual investigator obtains informed consent using the short form written consent document, there must ALSO be an independent witness to the presentation who is fluent in English and the language understood by the subject. **NOTE:** Investigator refers to a member of the study staff approved by the IRB to obtain informed consent.

Will the Laboratory or the IRB cover the cost of using medical interpreter services or obtaining written translations of study documents?

No. These funds should be built into research proposal budgets. Consider asking the sponsor for additional funds to cover this important service, which is necessary to enroll subjects from diverse populations.

In the short form consent process, will the interpreter perform a sight translation of the English version of the consent form?

No. The investigator is responsible for presenting the information in the English version of the consent form orally to the subject. The interpreter interprets the investigator's presentation. The investigator should direct his/her presentation to the subject, not to the interpreter.

In the short form consent process, must the investigator present the entire English version of the consent form to the subject?

Yes. The investigator must present all of the information in the English version of the consent form. Investigators should present the information in simple lay terms and should encourage questions from subjects and family members.

Should the use of an interpreter/bilingual investigator during the consent process be documented anywhere in addition to the signed consent documents?

Yes. To further document and facilitate clarification of any future questions regarding the consenting process, the investigator should include the following information in the research record:

- That **XX** study was presented orally to the subject in **[specify language]** through a medical interpreter (bilingual medical professional) OR by me because I am fluent in **[specify language]** and English.
- The subject's questions were answered (if any).
- The subject agreed to participate and signed the short form written consent document.
- A copy of the English version of the consent form signed by the investigator and interpreter/witness was given to the subject; AND
- A copy of the translated short form written consent document signed by the subject and the interpreter/witness was given to subject. This note should be signed and dated by the person obtaining consent.

When the short form written consent document is used to obtain informed consent, which consent document does the subject sign?

The subject signs the short form written consent document (in their language).

When the short form written consent document is used to obtain informed consent, which consent document does the investigator obtaining informed consent sign?

The investigator obtaining informed consent signs the English versions of the full consent form and short form.

When the short form written consent document is used to obtain informed consent, which consent documents are signed by the medical interpreter or the witness fluent in both English and the language understood by the subject?

The interpreter signs the statement specific to witness in the English version of the full consent form AND the interpreter (witness) line in the short form written consent documents both in English and the language of the participant. When a bilingual investigator obtains informed consent, the witness fluent in both English and the language understood by the subject signs the witness statement in the English version of the consent form AND the witness line in the short form written consent document.

When the short form written consent document is used to obtain informed consent, copies of which of the signed consent documents are given to subjects?

The subject must be given signed copies of BOTH the Laboratory IRB–approved English version of the consent form AND the written translation of the short form consent document.

When the short form written consent document is used to obtain informed consent, which of the original signed consent documents are retained in the subject's research records?

The original signed English version of the consent form WITH the original signed written translation of the short form document attached should be placed in the subject's research record.

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

When informed consent is obtained by a bilingual investigator using the short form consent document, should the bilingual investigator sign the short form written consent document?

No. The investigator should sign the English version of the full consent form and the witness should sign the short form written consent document AND the English version of the full consent form as witness.

When the entire English version of the consent form is translated into the language understood by the subject, do both the subject and investigator sign the translated consent form?

Yes. The translated consent form must be signed by both the subject AND investigator obtaining informed consent. A witness signature is not required; however, an interpreter must be available to interpret the consent discussion/questions and answers about the research. Participation by the interpreter in the consent process should be documented in the translated consent document and by a note in the research record.

Can informed consent be obtained from a non-English-speaking subject if there is a medical interpreter present BUT there is no short form written consent document translated into the language understood by the subject?

No. In order to obtain and document informed consent of subjects who do not speak English, you must have a short form written consent document in the subject's language that has been approved by IRB. The short form explains that informed consent is being obtained for research and that the basic and, when applicable, addition elements of informed consent will be described to them orally and that their participation is voluntary.

Can a family member who speaks English provide informed consent for a non-English-speaking subject who is legally competent to give informed consent to participate in research?

No. When a subject is legally competent to give informed consent to participate in research, s/he must give his/her own consent.

Must a medical interpreter be used for study visits or follow-up phone calls? Yes. You will need to enlist the services of interpreters in these settings.

When you think about enrolling someone who does not speak English, consider carefully whether you can accomplish this throughout the study. On occasion, safety issues may preclude enrolling non–English speakers.

Must study questionnaires/instruments, information sheets, and other study documents be translated into the subject's language?

Generally, yes. Investigators are expected to provide subjects with a written translation of all study documents that are given to subjects to ensure that they can follow study directions and participate safely in the study.

INFORMED CONSENT OF NON-ENGLISH SPEAKING RESEARCH SUBJECTS

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **HHS:** Department of Health and Human Services
- **Informed Consent:** The process by which an investigator obtains permission from a potential subject (or his/her legally authorized representative) before conducting research on that subject. Voluntary agreement of the subject, without coercion, to participate in the study must be obtained in writing on an IRB-approved form, unless waived by IRB.
- **Investigator:** An individual performing various tasks related to the conduct of human subjects research activities, such as obtaining informed consent from subjects, interacting with subjects, studying, interpreting, or analyzing identifiable private information for research purposes, and communicating with the IRB. Investigators are responsible for the design, conduct and reporting of the research.
- **IRB:** Institutional Review Board
- **PI:** Principal Investigator; the individual who is responsible and accountable for conducting the human subjects research. The PI assumes full responsibility for the protection of human subjects, compliance with regulations, and for the integrity of the research data and results.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46.116	General requirements for Informed Consent
45 CFR 46.117	Documentation of Informed Consent
POL.RES.037	Informed Consent of research subjects

RECRUITMENT OF RESEARCH SUBJECTS

1.0 PURPOSE AND SCOPE

In line with the basic ethical principles for the protection of human subjects, 45 CFR Part 46, investigators, and the Institutional Review Board ("IRB") must consider the ethical nature of a proposed recruitment strategy. A given recruitment strategy must i) respect an individual's reasonable expectations for privacy, ii) allow subjects ample time to consider participating in the study, and iii) provide accurate, balanced, and unbiased information as appropriate for each stage of recruitment. This policy provides guidance to investigators on the principles of sound recruitment strategies and institutional policy for review and approval of recruitment strategies.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Under Federal regulations, the IRB must review and approve methods used to recruit subjects to ensure that the methods are not coercive and that the confidentiality and privacy of potential subjects are protected. If a research study is recruiting participants, the protocol must include a recruitment section that clearly describes:

- How potential subjects are identified.
- How and by whom subjects are approached about participation.
- When consent is obtained in relation to the start of the study procedures.
- Whether third parties (calling centers/centralized screening centers) will assist with recruitment of subjects.

Recruitment methods depend on how the potential subject is initially identified. Potential subjects can be identified through one of four venues:

I. Through private medical information about individuals who are NOT patients of the investigator(s) (e.g., through referring physicians).
II. From among the patients of the investigator(s), if applicable.
III. By advertisements in various media.
IV. From among the employees/students of the investigator(s), if applicable.

RECRUITMENT OF RESEARCH SUBJECTS

3.1 RECRUITING SUBJECTS IDENTIFIED THROUGH PRIVATE MEDICAL INFORMATION

Recruitment efforts frequently target individuals known to have a specific medical or genetic condition. Medical records, patient registries, clinical databases, and referrals from treating physicians can be useful resources to identify potential subjects; however, it is essential to take special precautions to ensure that patient privacy is protected and that the individual patient is appropriate to participate in the research. It is not appropriate for investigators to make the first contact with potential subjects identified through their private health information. Rather, active participation by the patient's primary/specialist health care provider in the recruitment process ensures that consideration is given to the appropriateness of an individual patient's participation in the research prior to recruitment and that the patient's privacy is respected.

The primary/specialist health care provider, usually a physician, who is known to the potential subject and has first-hand knowledge of the patient's medical history must 1) give approval for his/her patient to be contacted for research purposes, 2) initially introduce the study to the patient, AND 3) obtain the patient's permission to be contacted by study staff.

The primary/specialist health care provider can introduce the study and obtain the patient's permission to be contacted by study staff either; 1) verbally during the course of providing medical care, OR 2) through the use of a recruitment letter (refer to guidelines for use of recruitment letters below).

When the Principal Investigator (“PI”) asks colleagues to refer patients, the PI must include information about study design, risks, and benefits so that the study can be reasonably presented to their patients. Notices to clinical colleagues seeking study referrals, such as letters, electronic postings and other notices require IRB approval.

3.1.1 GUIDELINES FOR THE USE OF RECRUITMENT LETTERS

Although recruitment letters sent to potential participants are frequently prepared by the study staff, they must be signed by the patient's physician, or the patient's physician and the investigator, but not the investigator alone. In some cases, it may be appropriate for a physician representative on behalf of an entire practice/clinic staff to sign the letter rather than the potential subject's primary/specialist physician. It is never appropriate for recruitment letters to come from study staff, such as Research Assistants or Data Managers.

In the letter, the primary/specialist physician should indicate that one of his/her colleagues is conducting a research study. The letter should explain the purpose of the research, and provide a brief description of the nature and extent of involvement, e.g., duration of participation and study procedures.

Potential subjects must be allowed to "opt out" or "opt in", depending upon the nature of the research. When the research involves sensitive or personal information, such as illegal behavior, drug or alcohol use, mental illness, sexual behavior or other sensitive issues, the IRB may require that the more stringent "opt in" procedure be followed.

OPT OUT Procedure: The recruitment letter must include a telephone number, secure website/email to contact or a postcard to return if the subject is *not* interested in participating in the study. If no telephone call is received or postcard returned, the subject may then be contacted by the investigator to determine whether or not the subject is interested in learning more about and/or participating in the study.

OPT IN Procedure: The recruitment letter must include a telephone number, secure website/email to contact or a postcard to return if the subject *is* interested in learning more about and/or participating in the study. The investigator may not contact subjects who have not called/emailed or returned a postcard indicating interest in learning more about the study.

In either case, take care to ensure that letters are properly addressed to avoid delivery to an incorrect party, and return postcards must not contain information regarding the patient's medical condition, medication, or diagnosis.

Recruitment letters must be submitted for review and approval by the IRB before use.

3.2 RECRUITING SUBJECTS THROUGH ADVERTISING

All direct advertising for research subjects, i.e., advertising that is intended to be seen or heard by prospective participants, must be reviewed, and approved by the IRB prior to distribution, posting, publication, or broadcasting. Direct advertising includes, but is not limited to newspaper, radio, TV, bulletin boards and the internet. See the policy POL.RES.041 for detailed guidance.

Unlike potential subjects identified through private medical information, those responding to advertisements have initiated the first contact and therefore, have implicitly given their permission to be contacted by study staff.

3.3 RECRUITING EMPLOYEES OR STUDENTS WITHIN AN INVESTIGATOR'S DEPARTMENT

Studies of volunteers who are directly supervised by the investigator(s) or who are the investigator's students must be approached cautiously as there could be confidentiality problems and issues of coercion or obligation (either real or perceived). It is acceptable to advertise for volunteers in approved areas in the investigator's department and allow individuals who are not directly supervised by the investigator(s) to participate in research studies, see POL.RES.051 for guidance on the collection of biospecimens from employees.

3.3.1 ALTERNATIVE RECRUITMENT APPROACHES

The guidelines listed above may not be applicable to every situation that arises in the research process. Carefully justified alternative approaches are considered on a case- by-case basis. The IRB offers guidance to investigators upon request.

3.3.2 INCENTIVES AND REWARDS FOR RECRUITING PATIENTS AND REFERRAL TO CLINICAL INVESTIGATORS

Timely enrollment of patients into approved studies is desirable, but care must be taken to ensure that the interests of participants are not jeopardized during the recruitment process. Cash payments or other financial or non-monetary incentives to physicians for referral of patients, otherwise known as "finder's fees", pose a conflict of interest and are not permissible. Financial incentives to physician-investigators to accelerate enrollment of their own patients in their own clinical trials pose a similar conflict of interest and are not acceptable. The IRB requires full disclosure of any financial arrangements that may encourage investigators to recruit subjects for research participation that may not be in the subject's best interests. In some special circumstances, physician investigators who are not formally listed on the protocol may be performing specific research-related activities (such as conducting screening examinations or tests, or

participating in the consent process), but solely in the role of service providers. These physicians may be reasonably compensated for their time and effort. Such arrangements should be clearly detailed and justified in the research protocol.

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **IRB:** Institutional Review Board
- **PI:** Principal Investigator

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.041	Recruitment of research subjects: Guidelines for recruitment materials and advertising
POL.RES.051	Collection of biological specimens from Jackson Laboratory employees

RECRUITMENT OF RESEARCH SUBJECTS: GUIDELINES FOR RECRUITMENT MATERIALS AND ADVERTISING

1.0 PURPOSE AND SCOPE

Under Federal regulations, the Institutional Review Board ("IRB") must review and approve methods and materials used to recruit participants to research studies.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 RECRUITMENT OF SUBJECTS THROUGH ADVERTISING

Direct advertising for research subjects, i.e., advertising that is intended to be seen or heard by prospective subjects, must be reviewed and approved by the IRB prior to distribution, posting, publication, or broadcasting. Direct advertising includes, but is not limited to, notices aimed at recruiting research subjects that investigators intend to place in newspaper, radio, TV, bulletin boards and websites. In addition, notices directed to clinical colleagues seeking study referrals require IRB approval. These include, but are not limited to, letters, electronic and other postings, or notices in professional publications.

Direct advertising for study subjects is the start of the informed consent and subject selection process. Generally, advertisements should be reviewed and approved by the IRB as part of the package for initial review. The IRB reviews the advertising to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. This is especially critical when a study may involve subjects who are likely to be vulnerable to undue influence.

When direct advertising is to be used, the IRB reviews the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting subjects is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

RECRUITMENT OF RESEARCH SUBJECTS: GUIDELINES FOR RECRUITMENT MATERIALS AND ADVERTISING

The IRB must review and approve the final copy of text of print advertisements, as the ad will appear in print in the newspaper or other media so the reviewer can assess the visual impact, emphasis, and graphic message. Similarly, the IRB must review and approve the final copy of the script of the audio/video tape that will be broadcast on radio or television.

Advertisements should include:

- Name of research facility and of the Principal Investigator;
- Purpose of the research;
- Eligibility criteria (briefly stated);
- Benefits of participation (if any);
- Duration of study and number of visits;
- Payment, if any, for participation;
- Contact person for more information; and
- The word "research" somewhere prominent in the advertisement.

Do:

- Use the word "Research" in the advertisement. The term "Study" does not convey the same message.
- Provide information prospective subjects need to determine interest, such as eligibility, significant study procedures, and time commitment.
- Use the term "healthy volunteers" instead of "normal volunteers".
- Use simple lay language without acronyms or abbreviations unless these are well known to the public or to the special patient group targeted, e.g., patients with ALS or women with PMS.
- Provide simple symptom complexes if seeking subjects who do not already carry the diagnosis.
- Provide basic exclusion criteria whenever possible to reduce unnecessary calls.
- Use the words "at no cost" rather than "free" where relevant.
- Specify amount of monetary compensation.
- Use the words "up to" if compensation is pro-rated.

Do not:

- Feature monetary compensation as a lead-in before the description of study purpose and procedures.
- Bold, italicize, underline or enlarge fonts on type describing monetary compensation.
- Provide detailed lists of risks and benefits (this should be done in person).
- "Hype" the study with overly optimistic or effusive language implying benefit (commercially designed radio ads occasionally do this).

RECRUITMENT OF RESEARCH SUBJECTS: GUIDELINES FOR RECRUITMENT MATERIALS AND ADVERTISING

3.2 NOTICES OR LETTERS SENT TO OTHER HEALTH CARE PROVIDERS

When seeking assistance of physicians in referring patients to the study, include additional information about study design, risks, and benefits. Provide enough information for physicians to reasonably present a study to their patients.

3.3 POSTING STUDY INFORMATION TO CLINICAL TRIALS REGISTRY WEBSITES

Clinical trial websites that provide only directory listings with basic descriptive information about clinical trials in general do not need to be reviewed by the IRB. Examples of clinical trial listing services that do not need IRB review and approval include the National Library of Medicine ClinicalTrials.gov website, the NIH National Cancer Institute's cancer clinical trials search, and the government-sponsored AIDS Clinical Trials Information Service ("ACTIS").

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **ACTIS:** AIDS Clinical Trials Information Service
- **IRB:** Institutional Review Board
- **NIH:** National Institutes of Health

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
HHS Guidance on IRB Review of Clinical Trial Websites	
POL.RES.040	Recruitment of research subjects
POL.RES.042	Recruitment of research subjects: subject compensation

RECRUITMENT OF RESEARCH SUBJECTS: SUBJECT COMPENSATION

1.0 PURPOSE AND SCOPE

Recruitment methods, including subject Compensation arrangements, may affect the equitable selection of participants and the consent process, and therefore relate to a key criterion for Institutional Review Board ("IRB") approval. The purpose of this Policy is to outline institutionally acceptable practices that pertain to payment of participants in human subjects research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Jackson Laboratory Employees and IRB members must adhere to this Policy in order to appropriately compensate human test subjects.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

A research study may have fair selection criteria but use payment arrangements that lead to inequitable selection. For example, payment arrangements that target economically disadvantaged participants can lead to unfair selection of participants despite reasonable selection criteria. Therefore, the IRB evaluates whether payment arrangements affect the equitable selection of participants.

Payment arrangements also represent a part of the consent process. Payments for participation are provided to reimburse participants for their time, effort, or other expenses. Payment arrangements that are misleading, inaccurate, exculpatory, coercive, or unduly influential (excessive) violate the regulatory requirements for consent. Therefore, the IRB should review proposed recruitment processes and advertising materials to determine whether they fulfill the regulatory requirements for consent.

Federal regulations provide no clear guidance on the level of Compensation that should be offered to research subjects. However, the regulations do require that researchers seek consent only under circumstances that minimize the possibility of Coercion or Undue Influence [45 CFR 46.116][21 CFR 50.20]. Research incentives may limit the ability of the research subject to provide truly voluntary informed consent. Subjects should be able to make informed decisions to participate based on the real risks and benefits of participation, not on Compensation. Subject Compensation should be equitable, and the confidentiality of information related to payments should be protected. Thus, the IRB reviews

protocol plans for subject Compensation with these goals in mind, and researchers should be cognizant of the related issues, as described below.

3.1 PROTOCOL AND CONSENT CONSIDERATIONS

The IRB application must fully describe the plan for compensating subjects as well as the reasoning behind the amount, method, and terms of Compensation proposed. The informed consent document must disclose all information concerning payment, including the total amount, schedule/form of payment, and any plans for prorating payment if a subject withdraws.

Compensation is **not** a benefit to subject participation and is not considered when the IRB weighs the risks and benefits of the research. Therefore, this information must be stated separately from the discussion of benefits in both the protocol and consent document.

It is also appropriate to disclose possible Compensation in recruitment/advertising materials. In general, payment information should not be any more prominent than the other elements of the recruitment materials (e.g., purpose, procedures, inclusion criteria, etc.).

3.2 ETHICAL CONSIDERATIONS

3.2.1 AMOUNT OF PAYMENT

Compensation should be appropriate for the time and effort subjects devote to participation. The level of payment should not be high enough to cause subjects to accept risks that they would not otherwise accept or participate in activities to which they would otherwise strongly object based on personal values or beliefs. Excessive incentives may also be of concern since they could induce subjects to lie or conceal information that would disqualify them from the study in order to receive payment. This could in turn undermine the scientific integrity of the study or compromise the safety of the subject.

On the other hand, if subjects are being asked to undergo a certain amount of risk, discomfort or inconvenience with no direct benefit, and no Compensation of any kind will be offered, the IRB may ask the Investigators to justify this. The same is true if it is proposed to compensate subjects at a rate that is substantially lower than average local Compensation for such activity, or to compensate subjects in one group less than another, even though subjects in both groups will carry out the same procedures. The IRB will consider individual circumstances, including funding or lack thereof, for such studies.

Many researchers base the payment amount on the acceptable average wage in the location where the research is conducted or for the specific study population. This is often an acceptable level of payment that does not exert Undue Influence. When hourly payments are not suitable or feasible, Compensation may be task- or procedure-specific (for example, some studies pay subjects per sample collection or survey). In general, all subjects completing the same tasks in a single research project should be compensated at equivalent rates. In some cases, distinct subject populations may

be compensated at different rates, but clear justification for this is needed. For example, a research study with several international sites may have different payment levels depending on the average local wage.

Whenever possible, subjects should be *reimbursed* for costs incurred as a result of study participation (e.g., parking and transportation costs, meals, etc.). These payments should be differentiated from Compensation in the study protocol.

3.2.2 TIMING AND FORM OF PAYMENTS

Consideration should also be given to timing of payment. Making payment conditional on completing a multi-session study could unduly influence a subject's decision to exercise his/her right to withdraw at any time. For studies that require extended time or multiple interactions/interventions, it is recommended that payment be prorated for the time of participation in the study rather than delayed until study completion. However, it would be acceptable to compensate subjects who withdraw early from a study at the time they would have completed it.

While total Compensation should not be contingent on completion of the entire study, it is acceptable to offer an additional incentive or completion bonus to subjects that remain for the duration of the study. For example, a researcher might offer a small bonus percentage of total Compensation if subjects complete all sessions in a study. If offered, these amounts should be reasonable so as not to unduly influence subjects to stay in the study when they otherwise would have withdrawn.

Alternative forms of Compensation (such as gift cards, certificates, or other tangible gifts) are acceptable forms of payment and are considered by the IRB in the amount of their cash equivalent.

Compensation can also take the form of being entered in a drawing. If using a drawing, researchers must ensure that there is a fair method of selecting winners and that the consent document includes a description of the possible prizes, the odds of winning, the timing of the drawing/payment, and how subjects will be notified. **NOTE:** The term "drawing" rather than "lottery" or "raffle" should be used, since the latter terms imply purchase of tickets by participants.

3.2.3 COMPENSATION OF MINORS AND OTHER VULNERABLE POPULATIONS

Federal regulations stipulate that additional safeguards must be included in the study to protect the rights and welfare of subjects vulnerable to Coercion or Undue Influence. Subjects vulnerable to such influence would include children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons [45 CFR 46.111 (b)][21 CFR 56.111(b)].

Researchers including such vulnerable populations should pay special attention to the Compensation scheme proposed in the protocol and subjects' economic status and resources. For example, researchers involving minors as participants will need to consider the ways children of different ages view the value of payment and ensure that the amount and method is age-appropriate and does not present Undue Influence. For younger children, a small gift/toy may be suitable, but for older adolescents/teens, a gift card or other form of payment may be more appropriate.

In addition, researchers should consider whether payment will be made to the parent(s) or the child, or both. Parents may receive Compensation to defray expenses/inconvenience associated with their child's participation in the research.

However, use caution as parents have the authority to permit a child's participation in research, an excessive payment could cloud the parent's judgment or cause the parent to exert pressure on the child's decision to participate. This would negatively impact the rights and welfare of these subjects.

3.2.4 IRS REPORTING AND COLLECTION OF SOCIAL SECURITY NUMBERS ("SSNS")

It is the responsibility of the Principal Investigator ("PI") to maintain accurate payment records. In addition, the IRS requires that whoever is paying research participants for participation report payments in excess of $600. If a PI anticipates a subject may reach this threshold in a calendar year, s/he should consult the Laboratory's Accounting Department regarding this requirement to ensure the appropriate paperwork is filed.

Because of the sensitive data associated with SSNs, these should generally be collected for research payment *only when necessary to comply with IRS reporting requirements* (i.e., only if it is anticipated that individual subjects will receive $600 or more in a calendar year). For projects that involve collection of SSNs, this may be explained in the protocol. The protocol should indicate that these data will be collected separately from the research records and should describe security measures that will be used to protect subject confidentiality. In addition, the consent form should indicate that subjects will be asked for their SSNs, why this information will be collected, and how it will be protected.

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Coercion:** Persuasion (i.e., of an unwilling person) to do or agree to something by using obvious or implied force of threats.
- **Compensation:** Payment or non-monetary reward to subjects as remuneration for time and inconvenience of participation, as well as an incentive to participate. Compensation can include monetary (cash, gift cards, vouchers, etc.) and/or non-monetary (gifts/promotional items, course credit, extra credit, etc.) remuneration.
- **FDA:** US Food and Drug Administration
- **HHS:** US Department of Health and Human Services
- **IRB:** Institutional Review Board
- **PI:** Principal Investigator
- **SSN:** Social Security Number
- **Undue Influence:** Excessive or inappropriate reward or other incentive in which a person is induced to act otherwise that by his/her own free will or without adequate consideration of the consequences.

RECRUITMENT OF RESEARCH SUBJECTS: SUBJECT COMPENSATION

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
21 CFR 56	FDA Institutional Review Boards regulation
21 CFR 50	FDA Protection of Human Subjects regulation
45 CFR 46	HHS/OHRP Protection of Human Subjects regulation
POL.RES.040	Guidelines for the recruitment of research subjects
POL.RES.041	Describes recruitment materials and advertising

RECRUITMENT OF RESEARCH SUBJECTS: PRE-SCREENING OF RESEARCH SUBJECTS DURING RECRUITMENT

1.0 PURPOSE AND SCOPE

Screening activities start when an Investigator obtains information about a prospective participant to determine if they are eligible for the research project. Pre-screening of research subjects during recruitment to determine eligibility may involve obtaining private information and is therefore considered human subjects research and must be conducted in accordance with the federal regulations and with The Jackson Laboratory's (the "Laboratory") Institutional Review Board ("IRB") policies. The purpose of this policy is to outline acceptable practices that pertain to pre-screening of research subjects and to ensure that personal subject information collection is minimized during the pre-screening process.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Pre-screening of potential subjects over the telephone, through electronic surveys or in person to determine their initial eligibility for and interest in a study is a common strategy in the recruitment process. An IRB may approve a proposal to obtain information or biospecimens to recruit, screen or to determine eligibility of a prospective subject for a research study without informed consent if certain conditions are met; (1) the Investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or (2) the Investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens [45 CFR 46.116(g)].

Investigators should adhere to the following guidelines to protect the privacy of the potential subject and the confidentiality of information collected about them.

1. The Investigator must have IRB approval for pre-screening of research subjects. The IRB may waive the requirement for Health Insurance Portability and Accountability Act ("HIPAA") Authorization for the pre-screening activities.

RECRUITMENT OF RESEARCH SUBJECTS: PRE-SCREENING OF RESEARCH SUBJECTS DURING RECRUITMENT

2. Obtain potential subject's permission to be contacted. The potential subject's permission to be contacted must be obtained prior to direct contact by study staff. Subjects who respond to advertisements or recruitment letters have implicitly given their permission to be contacted. Refer to the policy on recruitment of research subjects (POL.RES.040) for other acceptable methods of obtaining an individual's permission to be contacted, particularly those who have been identified through their clinician.
3. Acceptable Information to gather during Pre-screening: Questions appropriate for pre-screening address the specific inclusion/exclusion criteria for the study and other issues of practicability and suitability. It is not appropriate at this point in the process (i.e., prior to obtaining informed consent/enrollment) to gather information that is not directly related to assessing eligibility and suitability (e.g., obtaining complete medical histories).
4. Conducting Pre-screening over the telephone: At the beginning of a phone pre-screening conversation, potential subjects should be informed of the nature and sensitivity of the questions, asked whether this is an appropriate time for them to answer these questions, and told how long the phone call is expected to take. The questionnaires or screening tools that will be used must be submitted to IRB and approved prior to use. Subjects should be offered the option of completing the pre-screening in person if they wish and if it is feasible.
5. In the interests of confidentiality, the researcher should not record identifiers at the beginning of the screening conversation; explain to the subject that s/he will be asked a set of questions to determine eligibility and that at the end, only if s/he appears to be eligible and is interested in pursuing the study, will s/he be asked to provide contact/identifying information (e.g., last name, address, birth date, address, etc.). By following this procedure, identifiable personal information is only created for those persons who likely meet eligibility criteria. For persons who do not meet entry criteria, only non-identifiable health information is recorded.
6. Conducting Pre-screening in person: Investigators may conduct pre-screening in person if potential subjects are finding out about research during a routine clinical care visit or while in the hospital. All of the questionnaire and screening checklists that would be used during phone pre-screening are appropriate in this setting as well. Complete medical histories are not acceptable and should only be conducted after the subject provides informed consent.
7. Retaining Information from Individuals who are pre-screened but not Enrolled: It is acceptable to retain non-identifying information about individuals who are pre-screened for a study, but do not actually pursue the study or enroll. In fact, this is often desirable or even requested at publication to provide information about the entire pool of individuals interested or potentially eligible for the study from which the study sample was selected. Pre-screening forms from individuals who did not provide identifying information can be retained with no further action. Pre-screening forms with identifying information gathered prior to signing of informed consent form may also be retained in research files but must have segments containing identifiable information blacked out or cut off as soon as it is clear that the individual will not be enrolled.

RECRUITMENT OF RESEARCH SUBJECTS: PRE-SCREENING OF RESEARCH SUBJECTS DURING RECRUITMENT

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **HHS:** US Department of Health and Human Services
- **OHRP:** Office of Human Research Protections
- **IRB:** Institutional Review Board
- **HIPAA:** Health Insurance Portability and Accountability Act

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.040	Describes the recruitment of research subjects
https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.116	HHS/OHRP Protection of Human Subjects regulation, "Screening, recruiting, or determining eligibility."
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/screening-tests-prior-study-enrollment	Screening guidance for Institutional Review Boards and Clinical Investigators
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recruiting-study-subjects	Recruiting guidance for Institutional Review Boards and Clinical Investigators

RESEARCH INVOLVING BIOSPECIMENS

1.0 PURPOSE AND SCOPE

The study of biological materials and clinical data derived from Human Subjects is critical in furthering biomedical research and education, and thereby advancing the prevention, diagnosis, and treatment of disease. This Policy provides guidance on the use of human Biospecimens at The Jackson Laboratory ("the Laboratory") and the institutional requirements for Institutional Review Board ("IRB") review of research using human Biospecimens.

Depending on the specific types of samples being used, research conducted using human Biospecimens may or may not be considered Human Subjects Research or may be Human Subjects Research that qualifies for exemption from the requirements for IRB review. Investigators are strongly urged to consult with IRB and institutional guidance documents, including Office for Human Research Protections ("OHRP") Decision Charts and National Institutes of Health ("NIH") Decision Flowchart when planning their research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel will adhere to the Human Research Protection Program ("HRPP") policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 RESEARCH SUBJECT TO FDA REGULATIONS

Some activities listed below that do not require IRB approval under U.S. Department of Health and Human Services ("HHS") regulations must still receive IRB approval if the activities are subject to U.S. Food and Drug Administration ("FDA") regulations (e.g., involving FDA-regulated products or submission of data/results to the FDA). Research with data and/or specimens defined by FDA as "research involving human subjects" includes the testing of *in vitro* diagnostic devices using biological specimens.

3.2 RESEARCH ON BIOSPECIMENS THAT DOES NOT REQUIRE IRB REVIEW

3.2.1 COMMERCIALLY AVAILABLE BIOSPECIMENS, HUMAN CELLS OR CELL LINES

Research restricted to commercially available human cell lines is not Human Subjects Research and does not require IRB review or approval. However, some vendors may require IRB approval or exemption for use of their products in research. In addition, some journals may also require justification for use of the samples by an IRB review process. In this case, a "*Determination of Human Subjects Research*" form must be submitted, and a letter of determination received before research using these materials is initiated. This review is an institutional IRB administrative requirement rather than an IRB review of the research.

Investigators are reminded to review the vendor's contract carefully to ensure that the planned use of the biospecimen will be in accordance with the terms and conditions outlined in the contract.

3.2.2 BIOSPECIMENS OBTAINED FROM IRB-APPROVED LABORATORY REPOSITORY

IRB review is not required for research on (1) non-identifiable Biospecimens or (2) coded Biospecimens that are provided without linked identifiable information, when the Tissue is obtained from IRB–approved repository or bank within the Laboratory. In such cases, the IRB has approved the repository's policies and procedures for distribution of non-identifiable Tissue or coded Tissue without linked identifiable information to investigators. Any Laboratory repository is responsible for complying with the Research Tissue Banks and Repository policy (POL.RES.045).

3.2.3 CELLS OR CELL LINES DERIVED FROM PDX MODELS

Patient-Derived Xenografts ("PDX") are models of cancer where the Tissue or cells from a human are implanted into a mouse. Once the human cells are integrated within the mouse, the model no longer has normal human Tissue. Research using cells or derived tumor cell lines from PDX models are about the PDX tumor and not about the patient whose Biospecimens were used to create the PDX model. This is not Human Subjects Research.

3.3 RESEARCH ON BIOSPECIMENS THAT DOES REQUIRE IRB REVIEW

3.3.1 BIOSPECIMENS OBTAINED PROSPECTIVELY, EXPLICITLY AND SOLELY FOR RESEARCH

IRB approval is required for the collection and research use of human Biospecimens obtained from individuals explicitly for research purposes; for example, blood samples drawn, or extra blood taken at the time of a clinical blood draw specifically for a research project, or additional Tissue biopsies performed solely for research purposes during a clinically indicated endoscopic procedure. The IRB requires written consent of each research participant prior to collection or use of the biospecimen in the research.

3.3.2 EXCESS CLINICAL SAMPLES OBTAINED FROM THE LABORATORY'S CLINICAL LABORATORY

IRB review is required for any proposed research use of excess clinical samples obtained from the CLIA-certified Clinical Laboratory. The IRB determines whether the proposed research is:

- Human Subjects Research, as defined by federal research regulations.
- Human Subjects Research exempt from the requirements outlined in 45 CFR 46.
- Research that presents no more than minimal risk to Human Subjects and involves procedures in one or more of the categories of research that may be reviewed by an IRB through an expedited review procedure; or
- Research that requires review by the IRB at a convened meeting (full board review).

These determinations are based upon the nature of the research, the source of the Biospecimens, use and/or disclosure of identifiable health information, privacy, and confidentiality protections, and whether informed consent/authorization of subjects should be required, among other factors.

Investigators who wish to make a preliminary determination of whether their research falls under the definition of Human Subjects Research may consult the OHRP Decision Charts and NIH Decision Flowchart. Investigators are reminded that the official determination may only be made by the IRB. Investigators must fill out and submit a "*Determination of Human Subjects Research*" form and receive an IRB letter of the determination before they are permitted to proceed with non-human-subjects research.

3.3.3 BIOSPECIMENS OBTAINED FROM COLLABORATORS OUTSIDE OF THE LABORATORY

IRB review is required for any research limited to laboratory investigation of human materials provided to Laboratory investigators by outside collaborators. The IRB determines whether the proposed research is:

- Human Subjects Research, as defined by federal research regulations.
- Human Subjects Research exempt from the IRB review requirements outlined in 45 CFR 46.
- Research that presents no more than minimal risk to Human Subjects and involves procedures in one or more of the categories of research that may be reviewed by an IRB through an expedited review procedure; or
- Research that requires review by the IRB at a convened meeting (full board review).

These determinations are based upon the nature of the research, the source of the Biospecimens, use and/or disclosure of identifiable health information, privacy, and confidentiality protections, and whether informed consent of participants should be required, among other factors.

Investigators who wish to make a preliminary determination of whether their research falls under the definition of Human Subjects Research may consult the OHRP Decision Charts and NIH Decision Flowchart. Investigators are reminded that the official determination may only be made by the IRB.

If the planned research is identified as Human Subjects Research by the investigator through use of the decision charts, and the level of IRB review (Exempt, Expedited or Full Board review) has also been identified, the investigator may proceed to preparation of the IRB submission materials for the level of review indicated. The final determination of the required level of review lies with the IRB.

3.3.4 SECONDARY USE OF PREVIOUSLY COLLECTED RESEARCH SAMPLES

IRB review is required for any proposed secondary use of existing samples collected previously for research. The IRB determines whether the proposed research is:

- Human Subjects Research, as defined by federal research regulations.
- Human Subjects Research exempt from the requirements outlined in 45 CFR 46.
- Research that presents no more than minimal risk to Human Subjects and involves procedures in one or more of the categories of research that may be reviewed by an IRB through an expedited review procedure; or
- Research that requires review by the IRB at a convened meeting (full board review).

These determinations are based upon the nature of the research, the source of the Biospecimens, use and/or disclosure of identifiable health information, privacy, and confidentiality protections, and whether informed consent/authorization of participants should be required, among other factors. The IRB takes into consideration the scope/intent of the original research project, as well as the informed consent from participants when the sample was provided for the initial research use. If consent was not obtained (e.g., Biospecimens obtained for non-research purposes) or the original consent does not adequately include the proposed secondary use, specific informed consent for the new research may be required. De-identification or coding of Biospecimens should not be used as a means for circumventing the original terms of consent. Material Transfer Agreements ("MTAs") are required for sharing Biospecimens with non-Laboratory collaborators.

Investigators who wish to make a preliminary determination of whether their research falls under the definition of Human Subjects Research may consult the OHRP Decision Charts and NIH Decision Flowchart. Investigators are reminded that the official determination may only be made by the IRB.

3.4 SPECIAL SAMPLES FOR CONSIDERATION

3.4.1 HUMAN EMBRYONIC STEM CELLS (HESCS)

In Connecticut, Stem Cell Research Oversight ("SCRO") review and approval through UCONN Health is required for research on existing hESC lines and for the derivation of new hESC lines. This is not required for research performed in Maine, unless there is a collaboration with a Connecticut researcher. SCRO review is arranged through the IRB.

3.4.2 FETAL TISSUES

Depending on how the fetal Tissue will be used determines the type of ethical oversight of the research. If the fetal Tissue is being used for research only, then IRB review is required. If cell lines will be derived from fetal Tissue, then SCRO review, and approval is needed. For the purpose of this Policy, cord blood or materials derived from a placenta are not considered fetal Tissue.

There are state and federal laws that govern research use of fetal Tissue. Investigators must indicate in their IRB submission why the fetal material is required for the research and why other materials cannot be substituted for the fetal material, as well as specify the source of materials. Generally, the IRB will not approve the retention of any code or link to the identity of the woman from whom the fetal Tissue originated.

3.4.3 AUTOPSY SPECIMENS/SPECIMEN FROM DECEASED INDIVIDUALS

Deceased individuals do not meet the definition of a Human Subject. However, if there are ethical considerations remaining, the Laboratory IRB will review the research involving specimens from deceased individuals. A "*Determination of Human Subjects Research*" form must be submitted to IRBManager, reviewed, and a Determination Letter must be received by the investigator before research using these materials is initiated.

3.5 LABELING OF HUMAN SAMPLES

Biospecimens retained in research laboratories must be labeled with an alphanumeric code rather than the participant's name, initials, medical record number, date of birth, or Social Security number in order to protect the participant's privacy and confidentiality. When the IRB approves the retention of a link, such as a code key that could be used to identify the participant from whom the biospecimen was derived, the link/code key must be kept in another secure location. Specific measures taken to protect the privacy and confidentiality of the Biospecimens/data must be described in the submission to the IRB and, whenever relevant, addressed in the research consent document. Generally, Biospecimens/data sent outside the Laboratory must not be labeled with names, birth dates, or medical record or social security numbers.

3.6 TRANSFER OF SAMPLES TO RESEARCH COLLABORATORS OUTSIDE THE LABORATORY

The IRB must review any plan to transfer Biospecimens to outside collaborators for research. Exception: The transfer of non-identifiable Biospecimens from an IRB-approved research biospecimen bank to another investigator, as specified by policies and procedures of the Tissue bank, does NOT require separate IRB review and approval (see also 3.2.2, above). Separate approval is not needed because the IRB will have already reviewed and approved the operating policies and procedures of the bank, which describes such transfers. For more information, refer to Research Tissue Banks and Repositories (POL.RES.045).

Investigators are asked to address in submissions to the IRB when there are plans to transfer Biospecimens outside the Laboratory. Whenever plans to transfer Biospecimens outside the Laboratory arise after initial IRB approval, an amendment to the protocol should be submitted to the IRB for approval. Exception: When the IRB determines that the research is not Human Subjects Research or is exempt from the requirements of 45 CFR 46, if the planned transfer of Biospecimens alters the circumstances of the project and may change the IRB determination, an amendment must be submitted to the IRB for approval. The investigator must follow all other requirements outlined below.

3.7 MATERIALS TRANSFER AGREEMENTS

Investigators are reminded that an MTA may be required for the transfer of human Biospecimens to a recipient entity.

3.7.1 TRANSFER OF BIOSPECIMENS TO FOR-PROFIT OR COMMERCIAL ENTITIES OR COLLABORATORS.

In addition to IRB approval, the Legal Department must negotiate an MTA on behalf of the Laboratory investigator with the recipient when the recipient is a for-profit or commercial entity. When Biospecimens are being transferred for purposes other than genuine research collaborations, the proposed transfer will require additional institutional review in accordance with institutional policy. Contact the Laboratory's Legal Department for questions.

3.7.2 TRANSFER OF BIOSPECIMENS TO AN ACADEMIC OR NON-PROFIT ENTITY OR COLLABORATOR.

An MTA is required to transfer Biospecimens to an academic or non-profit entity or collaborator. Biospecimens that are in any way "encumbered" by past, existing, or planned collaborations with corporate entities may not be transferable. Contact the Laboratory's Legal Department for questions.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Biospecimen (see also Tissue):** Any biological specimen obtained from patients, decedents, or human research subjects. This includes, for example, fixed, frozen, or fresh pathology or autopsy Tissue; blood; urine; stool; saliva; cerebrospinal fluid; semen; breast milk or other biological material. It also includes any purified human DNA, RNA, proteins, cell lines or clones. The terms *biological materials*, *Tissue*, *Biospecimens*, and *samples* are used interchangeably in this Policy.
- **FDA:** U.S. Food and Drug Administration
- **hESC:** Human Embryonic Stem Cell
- **HHS:** U.S. Department of Health and Human Services
- **HRPP:** Human Research Protection Program
- **Human Subject (HHS):** A living individual about whom an investigator (whether professional or student) conducting research; (i) obtains information or Biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimen; or (ii) obtains, uses, studies, analyzes, or generates identifiable Private Information or identifiable Biospecimens.
- **Human Subject (FDA):** An individual who is or who becomes a participant in research, either as a recipient of the test article or as a control. A participant may be a healthy individual or a patient.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *Human Subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *Human Subject* or *subject* as defined by FDA.
- **IRB:** Institutional Review Board
- **MTA:** Material Transfer Agreement
- **NIH:** National Institutes of Health
- **OHRP:** Office for Human Research Protections
- **PDX:** Patient-Derived Xenografts
- **Private Information:** Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

- **Research Tissue Bank (or Repository):** An entity involved in procuring, processing, storing and/or distributing Biospecimens expressly for use in research.
- **Research (HHS):** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this Policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
    - Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
    - Public health surveillance activities, including the collection and testing of information or Biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
    - Collection and analysis of information, Biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
    - Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.
- **Research (FDA) or "Clinical Investigation":** Any experiment that involves a test article and one or more Human Subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
- **SCRO:** Stem Cell Research Oversight
- **Secondary Research:** Study of existing information or materials (e.g., data or Biospecimens) that have been previously collected for a purpose (including non-research purposes) other than the currently proposed activity.
- **Tissue (see also Biospecimen):** Any biological specimen obtained from patients, decedents, or human research subjects. This includes, for example, fixed, frozen, or fresh pathology or autopsy specimens; blood; urine; stool; saliva; cerebrospinal fluid; semen; breast milk or other biological material. It also includes any purified human DNA, RNA, proteins, cell lines or clones. The terms *Tissue*, *Biospecimens*, and *samples* are used interchangeably in this Policy.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	HHS Policy for Protection of Human Subjects
21 CFR 56	FDA Policy for Institutional Review Boards
POL.RES.045	Research Tissue Banks and Repositories
OHRP Decision Charts	Human Subject Regulations Decision Charts: 2018 Requirements
NIH Decision Flowchart	Research Involving Private Information or Biospecimens – June 25, 2019
FDA Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable	
OHRP Guidance on Research Involving Coded Private Information or Biological Specimens	

RESEARCH TISSUE BANKS AND REPOSITORIES

1.0 PURPOSE AND SCOPE

The study of human materials—including tissue, DNA, blood, serum, microbiome, and excreta as well as research and clinical data—derived from research participants and patients is critical in furthering biomedical research and education, and thereby advancing the prevention, diagnosis, and treatment of disease. Scientists at The Jackson Laboratory (the "Laboratory") spend increasing time and effort on studies that require access to human specimens and data, including for future research through the creation of tissue banks and repositories.

The purpose of this Policy is to define the requirement for Institutional Review Board ("IRB") review and approval of Research Tissue Banks and Repositories, and of the research use of identifiable tissue obtained from established Research Tissue Banks and Repositories.

This Policy applies to Research Tissue Banks and Repositories and data associated with those tissues established by Laboratory investigators for the purpose of storing tissue for future research use. It also applies to Laboratory-affiliated investigators who obtain tissue for research use from established Research Tissue Banks and Repositories.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The IRB must review and approve all research involving Human Tissue collection and use. This includes;

1. The *establishment* of Research Tissue Banks and Repositories for research;
2. The research use of identifiable tissue obtained from established Research Tissue Banks and Repositories; and
3. The research use of banked tissue that is not consistent with the scope of research (nature and purpose) described in the tissue bank consent form.

Note that IRB review of the tissue repository will include a review of the procedures for placing tissues into the bank and the procedures for release of stored tissues to investigators.

RESEARCH TISSUE BANKS AND REPOSITORIES

Avoid use of the terms “anonymous” or “anonymized” when describing the status of tissue or data as these terms are interpreted differently by different investigators. The IRB considers “anonymous” samples to be “non-identifiable” as defined in Section 5.0 of this policy. If a key to the code linking the sample to the tissue donors exists anywhere, the samples are not anonymous.

3.1 ESTABLISHING A TISSUE BANK OR REPOSITORY

Investigators must submit an application for initial review of research to the IRB for review and approval.
The collection and storage of tissue samples becomes a Research Tissue Bank when:

i) the specimens collected prospectively or retrospectively will be shared by multiple investigators; disbursed to other non-collaborating investigators; used repeatedly; or stored for future research use; or

ii) excess research samples collected as part of an IRB–approved protocol will be stored for multiple future research uses or by multiple investigators.

The prospective collection and storage of samples for defined research purposes as part of a single IRB-approved protocol is not considered a Research Tissue Bank.

Informed consent/authorization is required for the collection and storage of directly or Indirectly Identifiable Excess Clinical samples AND samples obtained solely for research (research samples). In such cases, the responsible principal investigator or tissue bank director/designee must obtain informed consent/authorization from each tissue specimen donor or their authorized representative. In general, tissue specimen donors whose samples were collected when they were minors must be approached for consent when they turn 18. If the individual cannot be located, the sample may be rendered non-identifiable and continue to be used in ways consistent with consent provided by parents or guardians. This approach should be described in the consent form for parents. Generally, the IRB will NOT grant waivers of consent/authorization for prospective collection of directly or Indirectly Identifiable samples in tissue banks.

3.2 ACCESSING TISSUE FROM THE TISSUE BANK/REPOSITORY

The tissue bank can only release tissue with identifiable information to researchers who have obtained separate IRB approval for a specific research protocol. As part of that review, the IRB must determine whether the original consent/authorization signed by the subject covers the proposed use.

If the original informed consent/authorization does not cover the scope of research (nature and purpose), the IRB may require the researchers to obtain separate informed consent/authorization for this new study or may waive the requirement for informed consent/authorization depending on the specific circumstances. In general, the IRB recommends seeking consent for future use at the outset, when tissues are collected, for the expected research. Although re-contact of subjects for new consent is not impossible, nor prohibited, it may be impractical and bothersome if frequent. Advance planning and description of research plans at the time of initial consent may obviate these difficulties.

RESEARCH TISSUE BANKS AND REPOSITORIES

If a researcher requests coded tissue with no identifiable information (Indirectly Identifiable Tissue), the tissue bank may release tissue that retains a link (code) to identifiable information about the tissue donor without additional IRB review if the following conditions are met:

1. The recipient researcher will not be given Individually Identifiable information linked to the tissue and agrees in writing not to access identifiers or attempt to ascertain the tissue donor's identity; and
2. The proposed research is consistent with the scope of research described in the consent/authorization signed by the tissue donor.

If these conditions are not met, the requirements for release of tissue with identifiable information must be followed.

NOTE: The tissue bank can release information, such as diagnosis, age, or gender, if the information released cannot be used to readily ascertain the identity of the individual from whom the tissue was obtained.

If a researcher requests tissue with no identifiers or codes (Non-identifiable Tissue), the tissue bank can release Non-identifiable Tissue (i.e., tissue that never retained a link to the tissue donor OR is fully anonymized by the tissue bank before release such that no link to the tissue donor will exist) to the recipient researcher without IRB review and approval. However, if the tissue was initially collected under a research informed consent/authorization, the tissue can only be used for the scope of research described in the consent/authorization signed by the tissue donor.

3.3 TRANSFERRING TISSUES TO OTHER INSTITUTIONS FOR RESEARCH

If tissue will be sent to a non-profit, for-profit or commercial collaborator outside of the Laboratory, a materials transfer agreement is required. See the Human Tissue policy on research use and requirement for IRB review (POL.RES.044) and consult with the IRB Office and the Legal Department as needed for further guidance.

3.4 USE OF OLD OR "GRANDFATHERED" SPECIMENS FOR RESEARCH

The IRB recognizes that identifiable, existing, and sometimes very old and valuable tissue may have been collected prior to more recent federal guidance on requirements in this area. New informed consent/authorization may not be required for existing tissue collected prior to recent changes to federal regulations. The IRB will consider requests for a waiver of informed consent/ authorization for existing, archival research specimen collections, i.e., "grandfathering" of existing samples collected in the distant past.

Investigators must submit an application for IRB approval of existing collections of samples that were obtained and stored for future research use prior to the establishment of this policy (i.e., "historical" collections). Investigators may wish to build upon existing specimen collections by prospectively adding more samples. This may be accomplished by establishing a Tissue Bank that includes both the existing specimens and those added prospectively.

3.5 CONSENT FOR LARGE-SCALE GENOMIC RESEARCH AND/OR GENOME-WIDE ASSOCIATION STUDIES

Since many investigators perform genome-wide association studies or large-scale gene sequencing on samples and send resulting data and samples to National Institutes of Health ("NIH")-sponsored or other central repositories, the tissue bank consent form should include the possibility of performing whole-genome analysis and sending the results and samples to central repositories where they may be used by other researchers for genetic links to many diseases or conditions.

Since January 25, 2015, investigators conducting new or ongoing NIH-funded research that generates or uses subsequent research large-scale human or non-human genomic data must include language in the consent form that addresses future research uses and broad sharing. Refer to the NIH Genomic Data Sharing policy for more information.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Directly Identifiable Tissue:** Tissue that is labeled or released to researchers with Personal Identifiers; for example, name, medical record number, social security number, laboratory accession number, etc.
- **Excess Clinical/Research Tissue Samples:** Tissue that was collected for clinical or research purposes and is no longer needed for the original purpose.
- **HHS:** U.S. Department of Health and Human Services
- **Human Tissue:** Any biological specimen or by-product obtained from living or deceased individuals. This includes, for example, fixed, frozen, or fresh pathology or autopsy specimens; blood; urine; stool; saliva; cerebrospinal fluid; semen; breast milk, microbiome, or other biological material. It also includes any purified human DNA, RNA, proteins, cell lines or clones. The terms *tissue, specimens*, and *samples* are used interchangeably in this policy.
- **Indirectly Identifiable (Coded) Tissue**: Tissue that retains a link (or code) to information about the tissue donor that includes any of the 18 HIPAA Personal Identifiers.
- **Individually Identifiable:** Private information that the identity of the subject is or may readily be ascertained by the investigator(s) or associated with the information.
- **IRB:** Institutional Review Board
- **NIH:** National Institutes of Health
- **Non-identifiable Tissue***:* Tissue that cannot be linked to a specific individual either because the existing link (such as a code key) to the identity of the individual was destroyed or because a link was never created or retained. Non-identifiable tissue lacks all of the 18 Personal Identifiers specified by HIPAA. Information that cannot be used to identify the individual, such as diagnosis, age, and gender, may be recorded with or linked to the tissue.

- **OHRP:** Office of Human Research Protections
- **Personal Identifiers:** Any of the 18 personal identifiers specified under HIPAA. While HIPAA regulations do not apply to tissue samples, they do apply to health information linked to the tissue. Of note, use of any part of an identifier, e.g., patient initials, in combination with code numbers, is also considered an identifier under HIPAA.
- **Protected Health Information:** Individually Identifiable health information, including demographic information, which relates to i) the individual's past, present, or future physical or mental health or condition; ii) the provision of health care to the individual, or iii) the past, present, or future payment for the provision of health care to the individual, and that identifies the individual or for which there is a reasonable basis to believe can be used to identify the individual. Protected health information includes common identifiers (e.g., name, address, birth date, Social Security Number) when they can be associated with the health information listed above. Laboratory research activities are not subject to the HIPAA Privacy Rule, with the exception of research occurring in the Clinical Laboratory, which is the designated health care component of the Laboratory under the HIPAA Privacy Rule.
- **Research Tissue Bank (or repository):** An entity involved in procuring, processing, storing and/or distributing tissue expressly for use in research.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.044	Research involving biospecimens
Health Insurance Portability and Accountability Act of 1996 (HIPAA)	HHS Health Information Privacy information for professionals and individuals
OHRP Guidance on Research Involving Coded Private Information or Biological Specimens	
NIH Genomic Data Sharing policy	

REVIEW OF HUMAN SUBJECTS RESEARCH CONDUCTED OFF-SITE

1.0 PURPOSE AND SCOPE

This Policy defines the requirements and procedures the Institutional Review Board ("IRB") follows for review of non-exempt human subjects research conducted by employees or agents of The Jackson Laboratory (the "Laboratory") at sites other than those owned or controlled by the Laboratory (i.e., off-site research).

Human subjects research conducted by employees or agents of the Laboratory at sites other than those owned or controlled by the Laboratory (i.e., off-site research) must be conducted in compliance with applicable international, federal, state, and local laws and regulations as well as any requirements of the performance site's institution or entity.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Investigators must specify in the IRB submission the places where employees or agents of the Laboratory will conduct the research, including any off-site locations. These sites may be institutions, facilities, or external health care entities; private physician or group practices; rehabilitation, nursing, or assisted living facilities; private or public primary schools, colleges, or universities; and community or other activity-based centers in the U.S. or any foreign country.

3.1 REVIEW OF PERFORMANCE SITE

When reviewing human subjects research that takes place off-site, the IRB obtains and considers information about the performance site and study population. The review may include some or all of the following information:

- The scope of the research activities that will take place at the site.
- The size and complexity of the institution/facility/entity.
- Standards of professional conduct and practice.
- Policies and procedures of site.
- Applicable local laws and regulations.

- The types of subject populations likely to be involved.
- Language(s) understood by prospective subjects.
- Method for equitable selection of subjects.
- Method for minimizing the possibility of coercion or undue influence.
- Method for protection of privacy of subjects.
- Method for maintenance of confidentiality of data; and
- Safeguards to protect the rights and welfare of vulnerable subjects.

3.1.1 DOMESTIC PERFORMANCE SITES IN STATES OTHER THAN MAINE, CONNECTICUT, OR CALIFORNIA

When the performance site is in a state other than Maine, Connecticut or California, representatives from the site are asked to provide information about the site and confirm that local applicable laws and requirements will be met. In addition, the IRB may consult with the Office of General Counsel about applicable state law.

When research is conducted in other states, the IRB ensures the participants are afforded protections that are at least equivalent to those provided in the Laboratory IRB policies and the ethical standards outlined in the Belmont Report.

3.1.2 INTERNATIONAL PERFORMANCE SITES

When the performance site is outside the United States or its territories, consultants at the international site or within the United States are asked to provide information about the researchers, site, and applicable laws. Consultants in this context are individuals with personal knowledge of the local research context, such knowledge having been obtained through extended, direct experience with the research institution, the subject populations, and the surrounding communities. The IRB must confirm the qualifications of the investigators and research staff and consider the cultural, economic, and political conditions of the country.

Research conducted outside the United States, or its territories are subject to approval of a local IRB or Ethics Committee ("EC") and/or governmental officials. When reviewing the research, the IRB takes into consideration the local IRB or EC review of the qualifications of the investigators and research staff, the recruitment and consent procedures, as well as language and other culturally based issues. When the research is federally funded, IRB/EC approval must be obtained from an institution/entity in that country that has a current approved FWA and a registered IRB/EC. The IRB requires documentation of the site's IRB approval and Federalwide Assurance ("FWA")/IRB registration status. A database of registered international IRBs searchable by country can be found on the Office for Human Research Protections ("OHRP") website at http://ohrp.cit.nih.gov/search/. In addition, OHRP has compiled a listing of the laws, regulations and guidelines that govern human subjects research in many countries around the world (see The International Compilation of Human Subject Research Protections).

When research is conducted outside the United States or its territories, the IRB ensures the participants are afforded protections that are at least equivalent to those provided by IRB policies and the ethical standards outlined in the Belmont Report. Specifically, research overseen by the IRB and conducted outside the United States, or its territories is

subject to IRB policies and procedures including: (1) initial and continuing review; (2) review of changes in approved research; (3) reporting and handling of complaints; (4) unanticipated problems involving risks to subjects or others and noncompliance; and (5) post-IRB approval monitoring. When the research is also subject to review of the local IRB or EC, the IRB requires documentation of review and approval throughout the project. When unanticipated problems or noncompliance are reported to the IRB, the IRB requires documentation of local IRB/EC review and, when appropriate, will communicate directly with the local IRB/EC. Post-approval monitoring will be coordinated with the local IRB/EC when required and as needed.

3.2 ENGAGEMENT OF PERFORMANCE SITES IN HUMAN SUBJECTS RESEARCH

As part of its review, the IRB considers whether the performance sites listed in the application are engaged in human subjects research and what, if any, additional IRB approvals are needed. OHRP's *Guidance on Engagement of Institutions in Human Subjects Research* is used as the basis for determining engagement in human subjects research. Such determinations will be made in collaboration and consultation with authorized representatives of the performance site. When the performance site is engaged in human subjects research, refer to the multi-site collaboration policy (POL.RES.014).

When the research is conducted off-site at a performance site that is *not* engaged in human subjects research, the IRB may require written documentation of permission (e.g., letter of support) to use the facilities for research signed by the institution/facility/entity's legally authorized representative.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Employees or Agents:** Members of applicable Laboratory workforce who: (1) act on behalf of the institution; (2) exercise institutional authority or responsibility; or (3) perform institutionally designated activities. Employees and agents include faculty, professional staff, students/interns, contractors, and volunteers, among others, regardless of whether the individual is being paid by the Laboratory.
- **EC:** Ethics Committee
- **FWA:** Federalwide Assurance
- **IRB:** Institutional Review Board
- **OHRP:** Office for Human Research Protections
- **The Belmont Report:** Published in 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, outlines the basic ethical principles in research for the protection of

human research participants. The three principles; Respect for Persons, Beneficence; and Justice form the basis for United States federal regulations on human subjects research .

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
OHRP *Guidance on Engagement of Institutions in Human Subjects Research*	
The Belmont Report	
OHRP Database of registered international IRBs searchable by country	
OHRP International Compilation of Human Subject Research Protections	
POL.RES.014	Guidelines for human subjects in research: single IRB review in multi-site collaborations

COLLECTION OF BIOLOGICAL SPECIMENS FROM JACKSON LABORATORY EMPLOYEES

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PURPOSE AND SCOPE

The Jackson Laboratory (Laboratory) employees may enroll as research subjects, although they may be at heightened risk of feeling pressured to participate in research than are volunteers from outside the Laboratory. This risk diminishes their ability to make an autonomous decision to participate, which runs counter to the legal and ethical principles of the Belmont Report. The Laboratory is aware of these risks and has taken additional measures designed to protect its employees from coercion or undue influence while preserving opportunities for employees to positively contribute to the research endeavor and quality assurance activities at the Laboratory.

The purpose of this policy is therefore to provide guidance on how human subjects research and other prospective collection of human biological specimens from employees may be conducted at the Laboratory.

POLICY STATEMENT

Employees may be recruited for research participation; however, an employee may not be required to participate in research as a condition of employment. Employees should also not be selected solely on the basis of convenience when they would not otherwise be appropriate for inclusion into research. The IRB must be vigilant about minimizing the possibility for coercion and undue influence. Both must be actively considered by the IRB when making a determination that collection of human biological specimens involving employees is or is not human subjects research, as well as when a project involving

COLLECTION OF BIOLOGICAL SPECIMENS FROM JACKSON LABORATORY EMPLOYEES

employees will be reviewed by IRB. It is important to note that investigators must not make the determination of whether their activities involving employees is human subjects research on their own, and that only the IRB may make this determination. Investigators contemplating the use of employees for any potential research, quality assurance or other activities that will obtain biological specimens from Laboratory employees are required to contact the IRB for guidance before any employee specimen or data collection may begin.

OBTAINING BIOLOGICAL SPECIMENS FROM EMPLOYEES THAT DOES NOT QUALIFY AS HUMAN SUBJECTS RESEARCH

While collection of biological samples from employees may not always meet the federal definition of research (POL.RES.006), all proposed collection of specimens from Laboratory employees must be reviewed by IRB in advance. This requirement is to ensure that current regulations, laws and policies are considered by IRB in review of planned collection of biological specimens from Laboratory employees. The IRB will issue a letter that applies to the currently proposed activity only and provides evidence of the determination in writing to the requester for their records. Please keep in mind that human specimen collection that does not constitute human subjects research, but involves Laboratory employees, must nonetheless conform to ethical standards described in the Laboratory's code of conduct policy (POL.ORG.038), federal, state and local laws. This is particularly relevant when supervisors/managers in a research laboratory are inviting their staff members to participate in a biological specimen collection activity that does not meet the federal definition of research.

OBTAINING BIOLOGICAL SPECIMENS FROM EMPLOYEES THAT DOES QUALIFY AS HUMAN SUBJECTS RESEARCH

The principal investigator (PI) must submit an IRB application through IRBManager for exempt (POL.RES.020), expedited or full board review (POL.RES.021 and POL.RES.022).

RECRUITMENT METHODS

The IRB strongly encourages PIs to devise recruitment methods that minimize direct interface between the PI or study staff and the potential employee subject. Laboratory-wide emails and flyers are the preferred recruitment materials; conversely, verbal recruitment methods are discouraged. All recruitment materials must conform to the Laboratory policy on advertisement for recruiting human subjects for research (POL.RES.041) and must be included in the application materials.

Obtaining human biological specimens from employees who are directly supervised by the investigator(s) should be avoided and will usually be disapproved by the IRB. In this setting, there are confidentiality problems and issues of coercion or obligation (either real or perceived) that are best avoided entirely. It is acceptable to advertise for volunteers in approved areas in the investigator's

COLLECTION OF BIOLOGICAL SPECIMENS FROM JACKSON LABORATORY EMPLOYEES

department and allow individuals who are not directly supervised by the investigator(s) to participate in research studies.

INFORMED CONSENT AND ENROLLMENT

Protection of privacy and confidentiality is a special consideration for Laboratory employees at all stages of the human subjects research process and employee biological specimen collections. When possible, it is preferred to limit participation to a single visit to obtain informed consent and samples. Additional considerations to keep in mind:

- Use of a private room at the Laboratory to obtain informed consent and samples.
- For blood samples, it is expected that a trained phlebotomist will perform the blood draw. Other types of samples (skin swabs, buccal swabs) should be obtained by individuals with proper training.
- Explanation of the study and details of the informed consent form, and written signed consent, must be obtained before detailed eligibility screening can begin and relevant medical history obtained.

COMPENSATION

Compensation for participation is permissible provided it conforms to the guidelines set forth in the Laboratory's policy on remuneration for participation in human subjects research (POL.RES.042). Compensation should be commensurate with the time and effort required by the subject to participate in the research.

RETURN OF RESULTS TO PARTICIPANTS WHO ARE LABORATORY EMPLOYEES

Research results may be shared with participants in the aggregate, i.e., at the cohort level. However, individual results may not be returned to participants at any time unless testing was performed in a CLIA certified laboratory using validated procedures for clinical use and the employee-participant agreed to receive or have their physician receive the results as part of the informed consent process.

PROCEDURE

N/A

DEFINITIONS AND ACRONYMS

- **Coercion:** Persuasion (i.e., of an unwilling person) to do or agree to something by using obvious or implied force or threats.
- **Employees or Agents of The Jackson Laboratory:** Members of The Jackson Laboratory workforce who: 1) act on behalf of the institution; 2) exercise institutional authority or

responsibility; or 3) perform institutionally designated activities. Employees and agents include faculty, professional staff, students/interns, contractors and volunteers, among others, regardless of whether the individual is being paid by the Laboratory.

- **Undue Influence**: Excessive or inappropriate reward or other incentive in which a person is induced to act otherwise than by his/her own free will or without adequate consideration of the consequences. (i.e., employees are encouraged to participate with the expectation or hope of "entitlements" as a result of their participation; employee feels pressure to participate when all of their colleagues are doing so.)

REFERENCES

- POL.ORG.038
- POL.RES.006
- POL.RES.020
- POL.RES.021
- POL.RES.022
- POL.RES.041
- POL.RES.042

AUDIO/VIDEO RECORDING OF HUMAN SUBJECTS

1.0 PURPOSE AND SCOPE

Audio, video, digital or any other recording of human research participants during research participation may affect the privacy of participants and confidentiality of their personal information relating to key criteria for Institutional Review Board ("IRB") approval. The purpose of this Policy is to outline institutionally acceptable practices for creating and/or storing audio, video, or digital recordings of Human Subjects obtained during participation in research overseen by The Jackson Laboratory IRB.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Recording the voice and/or image of an individual creates a record that requires unique handling and storage, particularly if the content may be sensitive. As with all research procedures, the dignity of participants must be respected. Therefore, the scope and content of the recording must be limited to what is necessary for the purpose of the study. Research participants must be informed prospectively that such recording will occur, and the informed consent process will include providing the participant with information about the storage, confidentiality, and future use of the recording.

If a research protocol involves the recording of research participants, the principal investigator must include the following elements in his/her protocol and informed consent form (FRM.EXT.022) for submission to and review by the IRB:

- The type of recording that will be utilized.
- The specific identifiers that will be recorded (e.g., partial facial features, full facial features, participant's name).
- The people who will have access to the recording(s).
- The mechanisms in place to protect the confidentiality of the person(s) being recorded.
- A clear indication of when the recording(s) will be destroyed or that recording(s) will be kept indefinitely.

- The use(s) of the recording(s), including educational or commercial purposes, analysis by the research team; or future unspecified use.
- The compensation, if any, to participants for allowing themselves to be recorded.

If the recording is an integral part of the research and not an optional procedure, a separate informed consent document is not required. However, documentation of the considerations listed above must be included within the body of the informed consent document for the overall study. It is important that this information be clearly stated, preferably preceded by a heading, so that it is clear to the participant that a recording will be made.

If the recording is not required as part of the research procedures, then the consent document must include a specific statement indicating that participation in the research study is not contingent upon agreeing to be recorded. A separate consent signature for permission to record is necessary. This permission can be in the form of a consent addendum (FRM.EXT.022), which includes the considerations listed above, or a separate signature line on the informed consent document labeled specifically for permission to record. If a separate signature line is used, the considerations listed above must be included within the body of the informed consent document.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Human Subject (HHS):** A living individual about whom an investigator (whether professional or student) conducting research: (i) obtains information or biospecimens through Intervention or Interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates identifiable Private Information or identifiable biospecimens.
- **Human Subject (FDA):** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be a healthy individual or a patient.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *Human Subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *Human Subject* or *Subject* as defined by FDA.
- **Interaction**: Includes communication or interpersonal contact between investigator and participant.
- **Intervention**: Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the participant or the participant's environment that are performed for research purposes.
- **IRB**: Institutional Review Board

- **Private Information**: Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- **Research (HHS):** A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
    - Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
    - Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
    - Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
    - Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.
- **Research (FDA) or "Clinical Investigation":** Any experiment that involves a test article and one or more Human Subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	
21 CFR 56	
FRM.EXT.022	Audio/video recording addendum to consent form

INFORMED CONSENT FOR SURVEY RESEARCH (PAPER OR INTERNET)

1.0 PURPOSE AND SCOPE

This Policy outlines institutionally acceptable practices for obtaining informed consent from Human Research Subjects participating in survey Research reviewed by The Jackson Laboratory (the "Laboratory") Institutional Review Boards ("IRB").

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

Informed consent standards are the same in survey Research (paper or internet) as for Research that does not involve a survey. Informed consent must contain all elements required by federal regulations whether the participants are required to sign a consent form or if documentation of consent is waived.

The IRB may waive the requirement for the Investigator to obtain a signed consent form for some or all subjects for a survey Research project, if it finds:

1. That the only record linking the subject and the Research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality; or
2. That the Research presents no more than minimal risk of harm to subjects, and involves no procedures, for which written consent is normally required outside of the Research context.

When documentation of consent is waived, the IRB may require the Investigators to provide participants with a brief information sheet which describes the study, contains all required elements of consent, and provides contact information for participant questions or concerns. This information sheet must be Page One of the paper survey (FRM.RES.001). For online surveys, the screen containing consent information should appear before participants have to provide identifiable data so that if they choose not to participate, identifiable data is not transmitted to the Researchers (FRM.RES.002).

INFORMED CONSENT FOR SURVEY RESEARCH (PAPER OR INTERNET)

Internet survey Research presents challenges regarding confidentiality. The information sheet provided with this type of survey must address this challenge and must state that confidentiality during online communications cannot be guaranteed even when every reasonable effort is taken. Clear information regarding which identifying data is kept, such as email or IP addresses, and how and where the data is stored must also be addressed. In addition, if data are transferred to the Researchers with identifiers attached, explain why this is necessary and at what point the Researchers strip identifiers from data. When choosing web-based survey tools, choose a tool that allows you to assure respondents that you won't capture information that they do not voluntarily provide. Investigators conducting internet survey Research must work with the Laboratory's Information Technology Security group to ensure that the proper confidentiality and data security protections are in place prior to commencing with any Research activities.

4.0 QUESTIONS/GUIDANCE

Questions about this policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Human Subject:** A living individual about whom an Investigator (whether professional or student) conducting Research: (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimen; or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *Human Subject*.
- **IRB:** Institutional Review Board
- **Research:** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

INFORMED CONSENT FOR SURVEY RESEARCH (PAPER OR INTERNET)

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
FRM.RES.001	Template for paper survey informed consent for survey research
FRM.RES.002	Template for online survey informed consent for survey research
POL.RES.037	Informed Consent of Research Subjects
https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html	HHS Informed Consent checklist (1998)
https://www.umass.edu/research/guidance/survey-guidelines	UMass Amherst guidance for online survey/survey research, last modified on September 29, 2015
http://www.unh.edu/research/human-subjects	U of New Hampshire, guidelines for conducting web-based survey research
Bankert, Elizabeth A. and Amdur, Robert J., Institutional Review Board Management and Function, 2nd Edition, 2006.	
45 C.F.R. §§46.101(b)(2); 46.116; 46.117	Federal Regulation for the Protection of Human Subjects

HUMAN SUBJECTS RESEARCH: ACTIVATION OF A RESEARCH STUDY AFTER IRB APPROVAL

1.0 PURPOSE AND SCOPE

This Policy outlines institutional practices for activating a research study following The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") or external single IRB approval for the Laboratory. Activation from the Clinical and Translational Research Support ("CTRS") staff is recommended prior to the start of any specimen or data collection. The activation meeting includes a CTRS authorized staff member, the Principal Investigator ("PI") and research study staff.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 GENERAL INFORMATION

The activation procedures have been introduced to ensure the protection of human subjects and the quality and integrity of the data and information collected, generated, and analyzed in the project. The Laboratory has a vested interest in protecting human subjects in research, the quality of the research that is performed at the facility, and in maintaining its reputation as an outstanding research center.

The activation meeting should be scheduled as close as possible to start-up of the research so that information is retained by the staff. If the study is not started within four months of the activation meeting, another session may be required.

A CTRS staff member schedules the activation meeting for the PI and study staff. At a minimum, the PI and study coordinator must attend this meeting; the meeting should also include other applicable study staff who will participate in conduct of the research. The meeting includes a tour of the laboratory, if applicable; review of the regulatory binder (see below); and discussion about the protocol, consent process, sample acquisition and labeling, data transfers and security measures with PI and applicable study staff.

HUMAN SUBJECTS RESEARCH: ACTIVATION OF A RESEARCH STUDY AFTER IRB APPROVAL

The Green Light Activation Checklist (FRM.RES.003) must be completed and signed by the CTRS staff. CTRS provides the PI with a final report and a copy of the checklist that may include action items that need to be completed prior to study activation. Once the checklist is finalized, study activities can be initiated. This document is retained in the regulatory binder.

Goals of the site activation:

1. To orient and train staff on the protocol and study related process at the Laboratory;
2. To ensure all study staff are fully informed of their roles, responsibilities and obligations;
3. To confirm readiness for study implementation, and availability of adequate resources; and
4. To confirm status of regulatory binder.

3.2 REQUIRED TRAINING

Study staff should be trained on all protocol procedures, including inclusion/exclusion criteria, screening tools, data entry/management/transfer, and compliance with regulations, as applicable. All staff must have completed at least one of the Laboratory CITI courses for protection of human subjects in research (i.e., Biomedical Research Investigators, Social-Behavioral-Educational Researchers, Computational Scientists, or IRB Members course).

3.3 REGULATORY BINDER

The regulatory binder/document files serve as a central location for maintaining study management documents to demonstrate compliance with applicable regulations and institutional policies and procedures associated with human subjects research. CTRS staff may assist in the development of the regulatory binder. Afterwards, the PI and study team are responsible for verifying that appropriate study-specific documents are updated and contained in a regulatory binder.

If the regulatory binder is stored electronically, the location should be noted in the Green Light Activation Checklist (FRM.RES.003) and two members of the CTRS team should be granted read-only access to the electronic location.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

HUMAN SUBJECTS RESEARCH: ACTIVATION OF A RESEARCH STUDY AFTER IRB APPROVAL

5.0 DEFINITIONS AND ACRONYMS

- **CTRS:** Clinical and Translational Research Support
- **FDA:** U.S. Food and Drug Administration
- **HHS:** U.S. Department of Health and Human Services
- **Human Subject (HHS):** A living individual about whom an investigator (whether professional or student) conducting research: (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- **Human Subject (FDA):** An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be a healthy individual or a patient.
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.
- **IRB:** Institutional Review Board
- **OHRP:** HHS Office of Human Research Protections
- **PI:** Principal Investigator; The individual who is responsible and accountable for conducting the human subjects research. The PI assumes full responsibility for the protection of human subjects, compliance with regulations, and for the integrity of the research data and results.
- **Research (HHS):** A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research:
    - Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
    - Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
    - Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
    - Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

HUMAN SUBJECTS RESEARCH: ACTIVATION OF A RESEARCH STUDY AFTER IRB APPROVAL

- **Research (FDA) or "Clinical Investigation":** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the FDA under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46	HHS/OHRP Protection of Human Subjects regulation
21 CFR 56	FDA Protection of Human Subjects regulation
FRM.RES.003	Green Light Checklist: Research Involving Human Subjects

HUMAN SUBJECTS RESEARCH: IRB COMPOSITION

1.0 PURPOSE AND SCOPE

The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") must be appropriately constituted for Human Subjects Research to be reviewed in accordance with federal regulations. The IRB provides ethical and continuing oversight of Human Subjects Research at the Laboratory, as further described herein, so as to protect the rights and welfare of the participants in the research. The IRB operates in full compliance with all applicable federal, state, and local laws and regulations, and with the Federalwide Assurance ("FWA") of the Laboratory. The responsibility for the protection of the rights and welfare of human subjects is shared both by the institution and the investigators conducting the research.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 MEMBERSHIP

The Laboratory IRB is composed of at least five (5) members with varying backgrounds to promote complete and adequate review of Human Subjects Research. The membership includes individuals with the necessary experience and scientific or scholarly expertise and knowledge of the local research context to review the scope of biomedical and behavioral research conducted by Laboratory Principal Investigators ("PI"). The membership does not include individuals who have responsibilities for business development or for negotiating grants or contracts. Members include both men and women and each member counts as one vote.

The membership of the IRB panel includes:

- At least one Physician
- Other Scientific members
- At least one member who is Unaffiliated with the Laboratory and who is not part of the Immediate Family of a person who is Affiliated with the Laboratory
- At least one member whose primary concerns are in nonscientific areas

HUMAN SUBJECTS RESEARCH: IRB COMPOSITION

Except when an expedited review procedure is used, reviewing, and approving proposed research at convened meetings needs a majority (more than half) of the IRB members present, also known as "quorum." Quorum must include at least one member whose primary concerns are in nonscientific areas.

3.2 RECRUITMENT AND SELECTION OF MEMBERS

The Institutional Official ("IO") and the Human Research Protections Program ("HRPP") Director recruit both Affiliated and Unaffiliated Physician, Scientific and Nonscientific members. New members are recruited as needed to ensure that the membership of the IRB continues to include individuals with varying backgrounds and the necessary experience and scientific or scholarly expertise to review the scope of biomedical and behavioral research conducted at the Laboratory. In addition, new members are recruited on an as-needed basis to replace the scientific or scholarly expertise of members who resign and, when needed, to provide additional scientific or scholarly expertise to review new research programs.

The membership includes individuals who can represent the perspective of the subjects who participate in research. No qualified individual is rejected from the membership on the basis of race, gender, creed, religion, color, national origin, age, disability, or sexual orientation.

3.3 PERIODIC REVIEW OF THE MEMBERSHIP

Membership of the IRB is reviewed annually to determine if the membership continues to include individuals with varying backgrounds and the experience and scientific or scholarly expertise needed to review the scope of biomedical and behavioral research conducted at the Laboratory.

3.4 APPOINTMENT, REAPPOINTMENT, RESIGNATION, SUSPENSION OR REMOVAL OF MEMBERS

Terms are typically for a one to three-year period and may be renewed indefinitely. When appointed by the IO, prospective members are asked to:

1. Provide a copy of their curriculum vitae or resume.
2. Complete the Collaborative Institutional Training Initiative ("CITI") program IRB Members course.
3. Complete the IRB member orientation training.
4. Complete the IRB Confidentiality Agreement.
5. Complete the IRB Member Annual Financial Disclosure (COI) form
6. Review the conflict of interest policy for IRB members (POL.RES.019) and have a current IRB Member COI Disclosure on file.

All members are expected to attend at least one-half (1/2) of the scheduled IRB meetings in a calendar year.

A member may resign from the IRB at any time with a written resignation submitted to the IO.

The IO and IRB Chair may suspend or remove any member of the IRB, provided that such member is given reasonable notice of the grounds for the suspension or removal and an opportunity to be heard. For this purpose, cause (with respect to a voting member) shall include the failure to attend more than one-half (1/2) of the convened IRB meetings

in a calendar year without excuse or the failure to perform reviews when assigned as a primary or secondary reviewer without prior notice or excuse.

3.5 MEMBERSHIP RECORDS/ROSTER

The HRPP Office maintains a roster of IRB members that includes the following information:

- Name
- Earned degree(s)
- Scientific status (i.e., Scientist, or Nonscientist)
- Experience and expertise, such as board certifications, licenses
- Representative capacity (e.g., children, prisoners, or adults with impaired decision-making capacity)
- Affiliation, if any, with the Laboratory

Assigned HRPP staff is responsible for updating the membership roster and IRB registration information with OHRP as needed when membership changes. IRB rosters are retained for at least three (3) years after completion of research that was reviewed by the IRB members. IRB rosters are made available upon request, when applicable, to authorized representatives of HHS, NIH, and other federal agencies for inspection and copying onsite during normal business hours. Individual membership records are retained by the IRB for at least seven (7) years from date of last service.

To vote at an IRB meeting, a person must be a rostered member of the IRB. This may be a primary member, or an alternate member who replaces a primary member.

3.6 MEMBER ORIENTATION, EDUCATION, TRAINING, AND EVALUATION

New members are provided with access to all IRB policies and relevant federal and state regulations. Members must complete the CITI program IRB Member Course. Prior to attending the first IRB meeting, the member is provided IRB New Member Orientation Training from the HRPP Director.

Ongoing education is provided to IRB members during meetings when regulatory issues are discussed in the context of each review. Additionally, members have the option of completing additional CITI human research protection courses, such as basic Good Clinical Practice (“GCP”) or the related refresher courses. The IRB Administrator provides members with any new IRB policies, guidance, or new and updated guidance documents from OHRP or other governing agencies.

Each year, in January, the performance of the IRB members is evaluated by the IRB Chair and Vice Chair. Some of the criteria in consideration are attendance, number of studies reviewed, ability to apply the ethical principles to the review process, thoroughness of the reviews performed, contribution to the meeting discussions, and overall participation in the IRB. The evaluations are provided to the IO for review.

HUMAN SUBJECTS RESEARCH: IRB COMPOSITION

3.7 IRB MEMBERSHIP ROLES AND RESPONSIBILITIES

3.7.1 IRB CHAIR AND VICE CHAIR

The IO selects and appoints the IRB Chair and Vice Chair. The Chair may be selected from among IRB members, or a Physician may be selected and appointed Chair. Appointments are a one to three-year term that may be renewed with no restriction to length of service. Both the IRB Chair and Vice Chair are voting members of the IRB and have responsibility for the following:

1. Providing leadership to the IRB to help ensure the rights and welfare of human subjects participating in research reviewed by the IRB.
2. Completing the CITI IRB Chair course and the CITI IRB Members course.
3. Determining whether a research activity submitted to the IRB for review is Human Subjects Research as defined by HHS or other applicable regulations.
4. Conducting initial and continuing ethical review of research activities involving human subjects that may be approved using the expedited review procedure.
5. Presiding at convened meetings and reviewing and approving the minutes documenting IRB discussions and findings.
6. Managing conflicts of interest by ensuring that IRB members with conflicts are not present for review of research for which a conflict may exist.
7. Conducting review of initial or continuing of research at convened meetings to secure approval.
8. Conducting review of modifications in research at convened meetings to secure approval and confirming that modifications have been made as required by the IRB.
9. Conducting review of proposed minor changes in approved research during the period of IRB approval.
10. Conducting review of unanticipated problems involving risks to subjects or others, including adverse events that are serious, unexpected, and related to the research.
11. Assisting with investigations and review of reports of alleged serious or continuing noncompliance with human subjects protections according to the noncompliance policy (POL.RES.026).
12. Participating in the development of Human Subjects Research policies and procedures.
13. Administering Board decisions and maintaining the independence of the IRB.
14. Signing correspondence communicating and documenting IRB decisions.
15. Maintaining a current knowledge of and assuring compliance with relevant regulations, laws, and Laboratory policies related to the protection of human subjects.
16. Maintaining continuing education in human subjects protection, including CITI Program courses, attendance at conferences, workshops, seminars, or lectures pertaining to Human Subjects Research.
17. Performing other activities to fulfill IRB responsibilities set forth in 45 CFR 46.110 or at the request of the IO to fulfill institutional responsibilities set forth in the FWA.

HUMAN SUBJECTS RESEARCH: IRB COMPOSITION

3.7.2 IRB MEMBERS

IRB member responsibilities include all of the following:

1. Attending IRB meetings and actively participating in the review of research.
2. Completing CITI IRB Members course prior to voting on any research, with continuing education every three years and as provided.
3. Understanding and applying the principles of the Belmont Report and the federal regulations related to the protection of human subjects.
4. Providing timely written comments on research undergoing IRB review, when required.
5. Annually completing the IRB Member Financial Conflict of Interest Form and disclosing any potential conflicts prior to IRB review of the research for which a conflict may exist.
6. Maintaining confidentiality of IRB-related information in accordance with the terms and conditions of the IRB Member Confidentiality Agreement.
7. Maintaining a current knowledge of and assuring compliance with relevant regulations, laws, and Laboratory policies related to the protection of human subjects.
8. Working with investigators to resolve matters relating to research approval and participating in educational efforts for investigators, research staff, and new IRB members.

3.7.3 ALTERNATES

Federal regulations allow organizations to appoint an alternate(s) to substitute for an IRB member(s) who is unable to attend so that IRB business may move forward in a timely manner. Alternates are appointed by the same process and for the same length of time as IRB members. IRB alternates function as regular board members when they are in attendance. An alternate may substitute for the primary IRB member for an entire meeting or at any time during a meeting. Alternates and IRB members have equal responsibilities in terms of required education, service and time commitments, and participation. When an alternate substitutes for a regular IRB member, the alternate receives and reviews the same materials that the regular member received (or would have received), and IRB minutes document that an alternate replaced a primary member.

3.7.4 CONSULTANTS

The IRB has the authority to use consultants, when needed, to supplement or provide scientific or scholarly expertise. Members of the IRB may vote to defer action and require an expert in the scientific area or discipline to review the research and provide consultation to the IRB. In such cases, the IRB Chair or Vice Chair are responsible for identifying the consultant and for requesting such consultation, which may be provided in writing or orally at a convened meeting. Consultants are not considered members and, as such, do not vote on any IRB submissions. However, consultants are subject to the IRB member conflicts of interest policy (POL.SEC.019). Consultants must be reminded that the discussions that take place at the meeting are confidential, information may not be disclosed to others. and sign a confidentiality agreement. Consultants must complete an HRPP Consultant or Meeting Guest Conflict of Interest and Confidentiality Form before they review IRB documents.

HUMAN SUBJECTS RESEARCH: IRB COMPOSITION

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **Affiliated:** Members, or their Immediate Family Members, who are affiliated with any Laboratory location as individuals who are: part-time employees; current students; members of any governing panel or board of the institution; paid or unpaid consultants; and volunteers working at the institution on business unrelated to the IRB.
- **CITI:** Collaborative Institutional Training Initiative
- **FWA:** Federalwide Assurance
- **GCP:** Good Clinical Practice
- **HRPP:** Human Research Protections Program
- **Human Subjects Research:** Activities that meet the HHS definition of *research* and involve a *human subject* as defined by HHS or meet the FDA definition of *clinical investigation* and involve a *human subject* or *subject* as defined by FDA.
- **Immediate Family Member:** A spouse or domestic partner, minor/dependent children or other persons living in the same household.
- **IO:** Institutional Official
- **IRB:** Institutional Review Board
- **Nonscientists:** Members whose training, background and occupation would not incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are categorized as nonscientists.
- **Other Scientific Members:** Members who are not physicians, but whose training, background and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline are categorized as scientists [45 CFR 46.107(c)].
- **Physicians:** Members who have a medical degree are categorized as physicians and Scientists.
- **PI:** Principal Investigator
- **Unaffiliated:** Members, or their Immediate Family Members, who are not Affiliated with any Laboratory location as defined by having an employment relationship with, a professional relationship with, a paid consultant relationship with, or a trustee/governing board member relationship with, or as being a student or volunteer of the Laboratory.

HUMAN SUBJECTS RESEARCH: IRB COMPOSITION

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
POL.RES.019	IRB member and consultant conflicts of interest
POL.RES.026	Noncompliance in Human Subjects Research

IRB SUBMISSION

1.0 PURPOSE AND SCOPE

The Jackson Laboratory (the "Laboratory") Institutional Review Board ("IRB") must receive sufficient information from investigators to provide adequate review of proposed research and to make the determinations required by regulations for IRB approval. This Policy describes the submission requirements and pre-review process for research requiring IRB review, which is defined in the human subjects research policy (POL.RES.006).

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program ("HRPP") policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

3.1 SUBMISSION REQUIREMENTS

3.1.1 INITIAL REVIEW

Investigators complete an *Initial IRB Review – Expedited and Full Board Review* application within IRBManager and provide all applicable information. In addition to the application, the Principal Investigator ("PI") may upload the following documents, as applicable:

a. Grant application, funding proposal or statement of work
b. Research protocol
c. Consent form(s), assent form(s), permission form(s) and verbal script(s)
d. Data collection forms
e. Recruitment materials (e.g., ads, flyers, telephone scripts, email, bulletins)
f. Instruments (e.g., questionnaires or surveys)
g. Other committee approvals (e.g., collaborating IRB approvals, IT security)
h. Drug manufacturer's approved labeling/investigator's drug brochure
i. Device manufacturer's approved labeling
j. Material Transfer Agreements, Data Transfer Agreements
k. Other supporting documentation and materials

IRB SUBMISSION

3.1.2 CONTINUING REVIEW

The IRB conducts continuing review of the research at intervals appropriate to the degree of risk. FDA regulated research and those studies which are greater than minimal risk must be renewed at least annually. Studies that qualify for Expedited IRB Review or those that have completed subject intervention/interaction and whose activities are limited to long-term follow up and data analysis of identifiable data/biospecimens or involve accessing follow-up clinical data from procedures that subjects undergo as part of clinical care are not required to obtain continuing IRB review, see the Annual Administrative Review section below for more information.

A *Continuing IRB Review* form and applicable protocol-related documents should be submitted in IRBManager at least 30 days before the study approval period ends. The study approval period is valid through midnight on the expiration date. The protocol is then reviewed in accordance with IRB policies and procedures for continuing review either at a convened IRB meeting (POL.RES.022) or using the Expedited IRB Review procedure (POL.RES.021).

3.1.3 ANNUAL ADMINISTRATIVE REVIEW

For any studies approved under the 2018 Common Rule and not regulated by the FDA, continuing review is no longer required when eligible for Expedited IRB Review or when the activity is limited to final analysis of identifiable data/biospecimens or in follow-up clinical care. If the research project does not meet the regulatory requirements for continuing review, annual administrative review will be performed by HRPP Quality Assurance.

Investigators submit an *Annual Administrative Review* form in IRBManager and provide necessary study status information and documents. The Quality Assurance Specialist reviews the submission and verifies human subjects protection training as well as project-specific significant financial interest disclosures (POL.RES.059 and POL.RES.064).

3.1.4 EXPIRATION OF IRB APPROVAL

If IRB approval expires on those studies that require continuing review, the IRB Administrator notifies the PI in writing that IRB approval has lapsed and that all research activities must stop. Research activities include, but are not limited to, recruitment and enrollment of subjects, collection of specimens, research on previously collected specimens, review of medical records or other health information, data analysis, performance of research tests/procedures, and follow-up of previously enrolled subjects.

The IRB may “Administratively Close” a research study when the PI fails to submit a Continuing Review or if the study relies on an external IRB, when the Reviewing IRB does not provide current IRB approval of the study. The PI receives 30- and 60-day notifications prior to the expiration date. The IRB will change the status of the study to “Administrative Hold” and the PI has 90 days to obtain IRB approval by submitting a *Continuing Review IRB Form* or by obtaining approval from the Reviewing IRB. If approvals are not obtained, then the study will be Administratively Closed and no research activities may occur.

If follow-up of subjects is necessary for subject safety and welfare, the PI must request permission of the IRB to continue previously enrolled subjects on study during the lapse period. The IRB Chair/Vice Chair is responsible for considering these requests on a case-by-case basis and for providing the investigator with written documentation of permission, when granted.

IRB SUBMISSION

Expiration of IRB approval is considered a lapse in approval and is not considered suspension or termination of research and is not subject to the suspension or termination of human subjects research policy (POL.RES.027).

3.1.5 AMENDMENTS

Investigators conducting human subjects research approved by the IRB are required to submit proposed changes in approved research, for review and approval prior to initiation of the change except where necessary to eliminate apparent immediate hazards to the subject.

Investigators must submit a *Request to Amend/Modify a Protocol* form in IRBManager. In addition, investigators must upload revised versions of the document(s) being modified with proposed changes underlined (or "tracked changes") within the document(s).

Amendments that add or remove co-investigators or key personnel can be submitted at any time and may be administratively reviewed by the IRB Administrator. However, personnel additions cannot be processed until all study team members have current Collaborative Institutional Training Initiative ("CITI") human subjects protection training (either IRB Member, Biomedical, Social and Behavioral, or Computational Scientist – see POL.RES.011) and Conflict of Interest training completed, as well as submitted project-specific SFI disclosures.

Changes made without IRB approval to eliminate apparent immediate hazards to the subjects must be reported to the IRB as described in the event reporting policy (POL.RES.029).

3.1.6 RESPONSE TO MODIFICATION REQUEST

When the IRB requires modifications to the research, investigator responses will be reviewed to verify that all the conditions for approval have been satisfied. Depending on the nature of the modifications, the subsequent review may be performed by the convened IRB (as described in policy POL.RES.022), or by one of the designated expedited IRB members (as described in the expedited review policy POL.RES.021). If further clarification or changes are needed, the IRB Administrator will communicate with the submitter through email or IRBManager. When conditions for approval have been verified, the approval letter is issued to the investigator.

3.1.7 118 DETERMINATION

The regulations of 45 CFR 46.118 recognize that certain research applications may be submitted to a sponsoring agency with the knowledge that human subjects will be involved during the period of support, but definite plans for this involvement cannot be described in the application. This is referred to as "delayed onset human subjects research." As such, an investigator may submit a *118 Determination* Form to the Laboratory IRB for review in order to receive applicable funds. This determination is valid for one year. At that time, the investigator will need to submit either an *Initial IRB Review* application or *Request for Exempt Review* application for the review of the involvement of human subjects in the research.

The 118 determination is not applicable to non-federally funded research, but the IRB will follow this process if required from a private funder or organization.

3.1.8 STUDY CLOSURE

If the research has been completed or closed at the Laboratory, the PI must complete the *Closure of Research Study* to end IRB oversight of the study. For multi-site research, the research may be considered completed or may be closed prior to completion when the investigator at the Laboratory site is no longer obtaining, using, or analyzing identifiable data.

3.1.9 REPORTABLE EVENT REPORTS

Event reports are submitted by the investigator through IRBManager using the *Reportable New Event* form. All applicable information should be included in a timely manner according to the event reporting of unanticipated problems, adverse events and other problems policy (POL.RES.029).

3.1.10 EXTRAMURAL INSTITUTIONAL CERTIFICATION

PIs that plan to submit genomic data to NIH-designated repositories must obtain institutional certification that the data sharing plans are consistent with the NIH Genomic Data Sharing Policy. The IRB is responsible for reviewing the genomic data sharing plans and consent forms to verify that NIH certification requirements have been met. The PI should complete and submit the *Institutional Certification* form along with any associated study documents in IRBManager.

3.2 PRE-REVIEW AND REVIEWER ASSIGNMENT

Upon receipt of submission for IRB review, the IRB Administrator pre-reviews the material to verify completeness of the application as described above. Submissions deemed incomplete or in need of clarifications will require contact with the PI or study coordinator via IRBManager or email. If no response is received in 60 days, the submission is withdrawn.

Submissions may not be reviewed until all study team members have current Collaborative Institutional Training Initiative (CITI) human subjects protection training (either IRB Member, Biomedical, Social and Behavioral, or Computational Scientist – see POL.RES.011) and Conflict of Interest training completed. In addition, a project specific financial disclosure form must be completed for all study team members.

3.3 REVIEWER ASSIGNMENT

Once the submission is complete, the IRB Administrator determines the review level and assigns reviewers. See the following institutional policies for more information; exempt review (POL.RES.020), expedited review (POL.RES.021), and convened IRB review (POL.RES.022).

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

IRB SUBMISSION

5.0 DEFINITIONS AND ACRONYMS

- **CITI:** Collaborative Institutional Training Initiative
- **Convened IRB Review:** Review of proposed human subjects research by an IRB that meets the membership requirements specified in federal regulation regarding the number, qualifications, diversity, and affiliation of its members, at which a majority of the members are present, including at least one member whose primary concerns are in nonscientific areas.
- **Expedited IRB Review:** Process by which designated IRB members, on behalf of the full IRB, approve a limited class of research activities through reviews conducted outside of the convened IRB meeting.
- **Exempt Research:** Research that involves human subjects that is not subject to regulations requiring IRB review and approval. Categories of research activities that may be determined to be exempt from review by the IRB are defined by federal regulations.
- **IRB:** Institutional Review Board
- **Limited IRB Review:** Research qualifying as exempt under categories 45 CFR 46.104(d)(2)(iii) or 45 CFR 46.104(d)(3)(i)(C) (on or after 1/21/19) which is reviewed by an IRB member by expedited means to document that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.
- **PI:** Principal Investigator

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
45 CFR 46.108, 45 CFR 46.109(e), 45 CFR 46.118	
21 CFR 56.108	
21 CFR 56.109	
Prior NIH Approval of Human Subjects Research in Active Awards Initially Submitted without Definitive Plans for Human Subjects Involvement (Delayed Onset Awards): Updated Notice (July 30, 2015)	
NIH Genomic Data Sharing Policy	
POL.RES.011	Human subjects in research: Education and training requirements
POL.RES.020	Human subjects research: Exempt research
POL.RES.021	Human subjects research: Expedited Review
POL.RES.022	Human subjects research: Convened IRB Review
POL.RES.027	Review of human subjects research activities: Suspension or termination of human subjects research
POL.RES.029	Human subjects research: Event reporting - unanticipated problems involving risks to subjects, or others, adverse events, and other problems
POL.RES.054	Informed consent for survey research (paper or internet)
POL.RES.059	IRB actions and communications

IRB RECORDKEEPING

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PURPOSE AND SCOPE

The Jackson Laboratory (Laboratory) Human Research Protections Program (HRPP) maintains records relating to research, including materials submitted by investigators for Human Subjects Institutional Review Board (IRB) review (or exemption, human subjects research determination, or Institutional Certification of Genomic Sharing Plans), documents of IRB activities, and other required records, such as IRB correspondence, rosters, and policies. All records are retained in a secure manner that allows for a review of the history of IRB actions and for inspection by authorized personnel.

This policy describes recordkeeping and record retention activities for the HRPP and IRB that comply with federal regulations and policies, state and local laws and institutional policy.

POLICY STATEMENT

IRB AGENDA AND MINUTES

The Laboratory IRB meetings are scheduled in advance for the entire calendar year and are posted on the internal Laboratory website. The agenda is finalized by the IRB administrator and is drafted to allow adequate time for discussion by the Committee for each research activity or education presentation.

The agenda will include determinations and findings required for each protocol, links to relevant regulatory guidance, documents or policies, as applicable. The agenda will also remind members of the IRB Member Conflict of Interest policy (POL.RES.017). In addition, the agenda notifies the members of expedited and ceded reviews and approvals as well as exempt determinations made since the last meeting.

IRB RECORDKEEPING

The agenda is provided to the members at least five (5) days in advance of the meeting to allow for sufficient time to review. Members confirm attendance to ensure that a quorum will be met for the meeting.

Convened IRB discussions and decisions are documented by the IRB administrator in the IRB meeting minutes. The minutes include, at a minimum:

- Members in attendance for each action, including their representative capacity, status, affiliation, etc. as well as the presence of any guests or staff.
- Documentation of quorum.
- Names of any IRB members who has a conflicting interest in a research study, and therefore is recused from participation in the review of the study and the and the reason for the recusal.
- Actions taken by the IRB, including numbers of votes for, against or abstained.
- Basis for requiring changes in or disapproving research.
- Summary of the discussion of controverted issues (if any) and their resolution.
- Determination of risk level for initial and continuing review.
- The approval period for initial and continuing review, as applicable.
- Rationale for significant/non-significant risk device determinations, when applicable.
- Determinations required by the regulations and protocol-specific findings justifying those determinations for:
    - Waiver or alteration of the consent process or documentation.
    - Research involving children.
    - Research involving pregnant women, fetuses or neonates.
    - Research involving vulnerable populations.

IRB RECORDS

The IRB maintains individual files of every research activity reviewed by the IRB, whether at a convened meeting or through the use of the expedited review procedure, the exempt research determination or the determination of human subjects research. These records are organized to allow a reconstruction of IRB actions. Included, but not limited to (as applicable):

- All of the documents submitted by investigators, including research protocol, application form, recruitment materials (letters, flyers, advertisements, etc.), consent form(s), ancillary committee/department review, scientific evaluations.
- Grant applications, including cooperative group protocols (for studies reviewed under pre-2018 requirements)
- Written reports from IRB consultants.
- IRB–approved recruitment materials and consent forms.
- IRB reviewer completed checklist/reviewer sheet.
- Progress reports, interim analyses, safety reports, or data safety monitoring board (DSMB)/data monitoring committee (DMC) reports.

- Reports of injuries to subjects, subject complaints and/or adverse events.
- Reports of unanticipated problems involving risk to subjects or others, protocol deviations and non-compliance.
- Records of continuing review activities.
- Amendments to previously approved research.
- All correspondence between the IRB and investigator.

For expedited initial or continuing reviews, records also include the following:

- Specific categories permitting review by expedited procedures.
- Determinations required by the regulations and protocol-specific findings justifying those determinations for the following:
    - Waiver or alteration of the consent process or documentation.
    - Research involving children.
    - Research involving pregnant women, fetuses or neonates.
    - Research involving vulnerable populations.

For exempt research, records also include the following:

- Any associated correspondence between investigators and HRPP staff.
- Exempt determinations, including citations of the specific category(ies) justifying the exemption as described in the exempt research policy (POL.RES.020).

For research determined not to be research involving human subjects, records will include copies of all documents submitted and/or correspondence between investigators and HRPP staff, as well as information documenting the determination.

Other IRB records maintained by HRPP include (but are not limited to) the following:

- IRB rosters and membership information/documentation.
- HRPP and IRB policies. **NOTE:** HRPP and IRB policies are maintained in the Laboratory's Document Control System)
- Institution FWA, IRB registration, Authorization Agreements, and IRB agreements.
- General IRB correspondence (i.e., not related to specific protocols).

RECORDS MAINTENANCE AND RETENTION

Individual files of research activities are retained by the IRB for at least three years from completion of the research or closure of the protocol. Files are maintained in electronic format within the IRB Regulatory file share and/or IRBManager. If applicable, paper records are stored in a locked file cabinet accessible only to IRB staff.

ACCESS TO RECORDS OF REVIEW ACTIVITIES

IRB RECORDKEEPING

Access to individual files of review activities will be provided to the Institutional Official (IO) and to the IRB Chair, IRB Vice Chair, Human Protections Administrator, HRPP staff, and General Counsel to carry out their responsibilities, as needed. Other institutional access to individual files of review activities is limited to those with a legitimate need for access, such as other institutional offices or departments within research compliance areas (e.g., IT Security, Sponsored Research Administration). With respect to parties outside the institution, individual files of review activities are made available upon request to authorized representatives of the sponsor and, when applicable, to authorized representatives of OHRP, NIH and other federal agencies for inspection and copying onsite during normal business hours. Subpoenas for documents or materials maintained in the IRB's files are handled in consultation with the Laboratory's General Counsel.

PROCEDURE

N/A

DEFINITIONS AND ACRONYMS

N/A

REFERENCES

- Written IRB Procedures: OHRP Guidance (05/18)
- POL.RES.017
- POL.RES.020
- POL.RES.021

IRB ACTIONS AND COMMUNICATIONS

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PURPOSE AND SCOPE

The Jackson Laboratory (Laboratory) Institutional Review Board (IRB) is responsible for determining the type of review, approval, and appropriate approval period of a human subjects research study and must notify the Principal Investigator (PI) and institutional officials of its decisions. This policy complies with the regulatory requirement in 45 CFR 46.108 (a)(3) and 21 CFR 56.108 (a)(1) requiring IRBs to have "written procedures for conducting initial and continuing review of research and for reporting its findings and actions to the investigator and the institution."

This policy describes the actions that the IRB may take during review of research and the communication of these actions, as well as the process for review of PI responses to IRB determinations. Convened IRB review of initial and continuing review (for studies reviewed under the pre-2018 Common Rule or those determined to be of greater than minimal risk under the 2018 Common Rule) and review of amendments are conducted as described in the policy POL.RES.022. Review, actions and communications of expedited review are covered in the expedited review policy (POL.RES.021). Exempt and determination of human subjects research are described in exempt research policy (POL.RES.020).

POLICY STATEMENT

ACTIONS OF THE IRB

The convened IRB takes one of the following actions when conducting initial review, continuing review, or review of amendments to previously approved research:

- Approved – Determined that the research involving human subjects is consistent with federal regulations, state and local laws, and institutional policy.

- Approved Contingent (modifications required) – Action that specifies conditions under which research can be approved, pending confirmation of specific understandings by the IRB about how the research will be conducted, submission of additional documentation, and/or precise language changes to the protocol and/or informed consent document(s).
- Deferred - Action taken when the convened IRB cannot fully evaluate the research under review and make the determinations required for approval without substantive modifications to the protocol and/or informed consent document, or submission of clarifications or additional materials prior to reconsideration of the research.
- Disapproved - Action taken when the determinations required for approval of research cannot be made, even with substantive clarifications or modifications to the protocol and/or informed consent process/document.
- Tabled – Action that indicates that review was not initiated or was not completed, resulting in postponement of IRB review, usually due to loss of quorum or other administrative issue.

When research is reviewed by expedited procedures, as described in the expedited review policy (POL.RES.021), the following actions can be taken:

- Approved - Determined that the research involving human subjects is consistent with federal regulations, state and local laws, and institutional policy.
- Approved Contingent (modifications required) – Action that specifies conditions under which research can be approved, pending confirmation of specific understandings by the IRB about how the research will be conducted, submission of additional documentation, and/or precise language changes to the protocol and/or informed consent document(s).
- Deferred - Action taken when the convened IRB cannot fully evaluate the research under review and make the determinations required for approval without substantive modifications to the protocol and/or informed consent document, or submission of clarifications or additional materials prior to reconsideration of the research.

A study may not be disapproved by expedited review. Studies that cannot be approved, approved contingent or deferred by expedited review will be sent to the convened IRB for review.

IRB APPROVAL PERIOD

For all research initially approved under the pre-2018 Common Rule (before 1/21/19), the IRB may approve research for a period of up to one year, unless a shorter review period is specified. For research reviewed under the 2018 Common Rule (on or after 1/21/19), the IRB may approve minimal risk research without a defined approval period and continuing review (45 CFR 46.109(f)(1)). For research that is reviewed by the convened IRB and deemed of greater than minimal risk, the IRB approval period is not less than once per year.

The date that research is approved at initial review, or if modifications are required (to secure approval), the date that the modifications/conditions are met by the PI, is the “start date” for the IRB approval

period. For continuing review, the date that research is re-approved is the "start date" for the approval period. Amendments submitted concurrent with continuing review are approved independent of the continuing review and do not impact the start date for the approval period.

The expiration date is the last date on which the IRB approved research may continue to be performed. The study approval lapses at midnight on the expiration date.

FREQUENCY OF IRB REVIEW

Pre-2018 Common Rule (initial IRB approval before 1/21/19):

The IRB requires continuing review at intervals appropriate to the degree of risk, but not less than once per year. Depending on the research, the interval frequencies may be a specified time period (i.e., annual, semi-annual), after a specific number of subjects enrolled, or another point of time meriting report and review by the IRB. The criteria used to consider whether more frequent review is required includes, but is not limited to, the following:

- High risk research where there is concern about serious adverse events.
- Protocols with complex regulatory requirements, such as involving an IDE.
- Research being conducted in international or other off-site locations when the Laboratory IRB is serving as the IRB of record.
- Research where the PI has a potential conflict of interest that warrants more frequent review and reporting.

2018 Rule (initial IRB approval on or after 1/21/19):

Continuing review of research is only required by the convened IRB at intervals appropriate to the degree of risk, but not less than once per year.

Otherwise, continuing review of research by the IRB is not required when:

- Research is eligible for expedited review.
- Exempt research conditioned on limited IRB review.
- Research that has completed all interventions and now only includes analyzing data, even if the information or biospecimens are identifiable.
- Research that has completed all interventions and now only includes accessing follow-up clinical data from procedures that are part of the clinical care.

The IRB can override this and choose to require continuing review of the research, as long as the IRB documents the decision and the rationale for the decision.

The Laboratory has determined that an administrative annual review (AAR) will be done by the HRPP, in order to assess current study status, to ensure the safety and privacy of the subjects, and for the

protection and confidentiality of the data. Refer to the HRPP quality assurance policy (POL.RES.064) for more information.

REVIEW OF INVESTIGATOR RESPONSES

When the IRB requires modifications to the research to secure approval, the PI is notified in writing of the IRB action and of the IRB-required modifications to the research. The PI is asked to submit a point-by-point response and revised documents to the IRB. Depending on the nature of the modifications, the subsequent review may be performed by the IRB Chair/Vice Chair, a designated IRB member to confirm that all modifications required by the IRB have been made and whether the protocol can be fully approved. When the conditions for approval have not been met, the PI is notified of remaining modifications and needs to submit a subsequent response.

When the research is deferred by convened review, only the convened IRB may reconsider the clarifications and/or modifications to the submission. When possible, the original primary reviewers will be assigned to review.

When the research is disapproved, the PI is notified in writing of the action and the basis for the disapproval. Disapproval means that, as designed, the study cannot be approved. The decision of the IRB to disapprove the research cannot be overruled by any other institutional body or individual(s). The PI must submit a new, revised application to request approval. The convened IRB reviews such applications unless the new research meets the criteria for expedited review, as described in the expedited review policy (POL.RES.021). The PI may appeal the decision of the IRB in writing. The IRB Chair/Vice Chair is responsible for reviewing the appeal and then presenting to the full board for review at a convened IRB meeting.

COMMUNICATION OF IRB ACTIONS

After IRB review is completed for the submitted project, the IRB administrator prepares a notification letter to inform the PI and specified study contacts of the IRB actions. Notification letters include the following, at a minimum:

- Date of review and type of submission reviewed
- IRB action
- Approval and expiration date (when applicable)
- Any associated approvals requiring specific regulatory findings (e.g., waiver of consent)
- Modifications or clarifications required that must be satisfied by the investigator, if any, for IRB approval.
- For initial review, any conditions under which the research may be initiated.
- For continuing review (pre-2018 studies and as applicable for 2018 Common Rule studies) and amendments, any conditions that must be satisfied before a PI can continue research activities.
- For research that is deferred, a statement of the reasons for deferral and a description of how the PI can respond.

- For research that is disapproved, a statement of the reasons for disapproval and a description of how the PI can respond.

IRB meeting minutes including exempt and expedited review summaries are made available to the IRB members and IO in the IRBManager system and HRPP regulatory file share.

PROCEDURE

N/A

DEFINITIONS AND ACRONYMS

- **Approval Date:** The first date that research activities can be performed (following notification from the IRB), consistent with federal regulations, state and local laws, and institutional policy. The approval date is the date that the research is approved by convened or expedited IRB review, or if modifications are required (to secure approval), the date that the modifications/conditions are met by the PI.
- **Approval Period:** For initial review, the interval that begins on the day research is approved by convened or expedited review, or if modifications are required (to secure approval), the date that the modifications/conditions are met by the PI. For continuing review, the interval that begins on the day research is re-approved (by convened or expedited review) or modifications are required. If the modifications are not met prior to the continuing review expiration date, the interval will begin on the date that the modifications/conditions are met by the PI. Note: An approval period for initial or continuing review may not be longer than one year.
- **Expiration Date:** The last date on which the IRB approved research may continue to be performed. The approval lapses at midnight of the expiration date and research can no longer be performed after that point. Note: An expiration date may not be longer than one year from the date the approval period begins.

REFERENCES

- 45 CFR 46.108, 109, 111
- 21 CFR 56
- OHRP Guidance on Approval of Research with Conditions (11/10/10)
- OHRP Guidance on Written IRB Procedures (2018)
- The Ohio State University HRPP Policy #13, IRB Actions and Communications (6/14/16)
- POL.RES.020
- POL.RES.021
- POL.RES.022
- POL.RES.064

HUMAN SUBJECTS RESEARCH: POLICIES AND PROCEDURES

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PURPOSE AND SCOPE

The policies and procedures developed for the Human Research Protection Program (HRPP) are mandated by state and federal regulations, recommended by federal guidance, and/or are reflections of best practices among peer institutions. The scope of the HRPP policies and procedures includes, but is not limited to, human subjects research submission and review criteria, Institutional Review Board (IRB) review and approval procedures, oversight and compliance processes, and quality improvement initiatives.

POLICY STATEMENT

POLICY DEVELOPMENT

Research stakeholders, including Jackson Laboratory faculty, administrators, investigators, research staff, IRB members, and HRPP staff, may make recommendations for new policies or revisions to existing policies. The HRPP staff are responsible for drafting new or revised policies and procedures after review of the regulations, guidance, and best practices at peer institutions and in consultation with the Institutional Official (IO), Human Protections Administrator, and IRB Counsel. Policies reflect available information and are written in sufficient detail to describe the actions that are followed to achieve the intended outcome.

HUMAN SUBJECTS RESEARCH: POLICIES AND PROCEDURES

IMPLEMENTATION

The HRPP Quality Assurance (QA) Specialist is responsible for the implementation and communication of the policies and procedures. When a policy or procedure represents a significant change to existing policy, processes or procedures, the effective date is set to allow communication, including education and planning, for operational changes.

POLICY MAINTENANCE

The QA Specialist is responsible for maintaining HRPP policies and procedures. The existing policies are reviewed at least every three years. In addition, policies and procedures are developed or updated as needs are recognized or change. Research stakeholders also recommend needed revisions or additions.

PROCEDURE

- **Policy:** Formal statement of principles on which action(s) for a specific issue are based.
- **Procedure:** A series of actions conducted in a certain order or manner; operational method by which policy is put into place.

DEFINITIONS AND ACRONYMS

N/A

REFERENCES

N/A

HUMAN RESEARCH PROTECTION PROGRAM QUALITY ASSURANCE PROGRAM

1.0 PURPOSE AND SCOPE

The Jackson Laboratory (the "Laboratory") Human Research Protection Program ("HRPP") Quality Assurance ("QA") program implements quality processes to ensure regulatory compliance and promote human subjects protections through the ethical conduct of research.

The objective of the QA program for human subjects research is to provide investigators and the Institutional Review Board ("IRB") with an internal mechanism for quality improvement in human subjects research. This is accomplished by providing education or assistance as well as practical support in the conduct of human subjects research by optimizing compliance with federal regulations, institutional policies, and the provisions of IRB-approved protocols.

2.0 ADMINISTRATIVE CONTROLS

2.1 ACCOUNTABILITY AND SANCTIONS

You are expected to read and understand this Policy, and to seek answers or clarification whenever needed. Instances of noncompliance or subversion of this Policy may result in disciplinary action up to an including loss of facility and systems access privileges and termination of employment.

2.2 RESPONSIBILITY

All Laboratory personnel shall adhere to the Human Research Protection Program policies in protecting human welfare and rights.

2.3 EXCEPTIONS PROCEDURE

N/A

3.0 POLICY STATEMENT

The QA program focuses on reviewing and monitoring the activities, policies, procedures and records of Laboratory investigators, research staff, the IRB and HRPP staff supporting the IRB. The QA program plan incorporates routine and ad hoc monitoring activities as required to achieve the specific objectives for compliance improvement. The plan is adjusted throughout the year to address input from monitoring and evaluation activities and to respond to changes in federal and state requirements. Activities include:

1. Routine and ad hoc reviews to monitor compliance with HRPP policies and federal regulations. Focus includes roles and responsibilities of research team members, regulatory and IRB compliance, recruitment, consent process, case review for protocol adherence, source documentation and data collection, adverse events, file security and other applicable aspects of the study. For-cause audits are performed when concerns regarding compliance, protocol adherence, or subject safety are brought to the attention of the Clinical and Translational Research Support staff or IRB members.

2. Conduct initiation meetings for research protocol start-up. The goals of the site initiation meeting is to orient and train staff on the protocol and study related activities at the Laboratory to ensure all study staff are fully informed of their roles, responsibilities, and obligations, to confirm readiness for study implementation, and availability of adequate resources and to confirm status of regulatory binder and data security.
3. Identify areas for improvement within HRPP operations based on analysis of regulatory requirements, reviews, and feedback received from Laboratory investigators and staff. The QA specialist develops action plans to correct issues and provides education and outreach to promote effective improvement.
4. Provide education and assistance to investigators, staff, and IRB members. The QA program develops, implements, and hosts educational opportunities for research personnel. All IRB members and IRB staff receive regular, ongoing training and continuing education. Activities may include but are not limited to the following: CITI training, IRB new member training, and general education sessions.

Based on the activities of the QA program, significant changes may result in the HRPP, such as additional policies, changes to policies and procedures, changes to the IRBManager system, and changes to the design and delivery of education for IRB members and the research community. Existing policies are reviewed at least every three years. New policies and procedures will be developed or updated as needs are recognized for change.

Communication is issued about new or revised HRPP policies and QA initiatives through Laboratory communication mechanisms. When a Quality Improvement initiative represents a significant change to existing processes or practices, the effective date is set to allow for communication, including education and planning for operational changes.

4.0 QUESTIONS/GUIDANCE

Questions about this Policy should be directed to documentcontrol@jax.org or the person identified below as responsible for interpretation and administration of this Policy.

The Laboratory employee responsible for interpretation and administration of this Policy is the Human Protections Administrator.

5.0 DEFINITIONS AND ACRONYMS

- **HRPP:** Human Research Protection Program
- **IRB:** Institutional Review Board
- **QA:** Quality Assurance

6.0 REGULATORY AUTHORITY, RELATED POLICIES, PROCEDURES, AND OTHER DOCUMENTS

Citation	Description
N/A	N/A