OKLAHOMA STATE DEPARTMENT OF HEALTH
Oklahoma.gov/Health | 405-426-8000

MEMORANDUM

TO: Keith Reed, Interim Commissioner of Health 4/5/2022

DATE: March 17, 2022

THROUGH: Jan Fox, Deputy Commissioner Health Preparedness JF 4/5/2022

THROUGH: Derek Pate, Director of Center for Health Statistics DP 3/18/2022

FROM: Evaren Page, Director of Science and IRB EP 3/17/2022

RE: Approval Request for Revisions to OSDH IRB Administrative Procedures (AP No. 1-40)

The OSDH IRB is seeking approval for revisions to the OSDH IRB Administrative Policies and Procedures (No. 1-40). These revisions are necessary in order to align with changes which took place at the state and federal level. Revisions were also made in order to reduce the overall length of the procedures and remove unnecessary details which are already outlined in the federal regulations that govern how IRB should operate.

The IRB voted to approve these revisions on March 16, 2022.

A copy of the updated Administrative Procedures is attached for your review and signature.

Please let me know if you have any questions or concerns regarding these revisions.

OKLAHOMA STATE DEPARTMENT OF HEALTH
ADMINISTRATIVE POLICIES AND PROCEDURES

NUMBER: 1-40
TITLE: Institutional Review Board (IRB)
RESPONSIBLE SERVICE: Center for Health Statistics

APPROVED: _____
Keith Reed
Interim Commissioner

I. Purpose

The purpose of this administrative policy and procedure is to inform Oklahoma State Department of Health (OSDH) employees of the agency's dedication to the ethical principles for safeguarding the rights and welfare of the human beings recruited to participate in research activities. The OSDH maintains an Institutional Review Board (IRB) to review human subjects research engaged in by the OSDH in accordance with federal regulations[1] and state law.[2]

The IRB is responsible to assure that the risks of the research are: justified by the potential benefits to the participants and to society; minimized to the extent possible consistent with sound research design; and planned to not fall disproportionately on one group while the potential benefits accrue to another.

This policy applies to any person paid by, under the control of, or affiliated with the OSDH, such as scientists, contractors, trainees, technicians and other staff members, students, fellows, guest researchers, or collaborators. The commissioner of health retains final authority to determine whether a particular activity is subject to this policy.

II. Operations

The IRB assures the researchers respect individual privacy, preserve the confidentiality of private information, engage in a consent process to assure voluntary and knowing consent to participate in research, and provide vulnerable populations with additional protection.

The IRB monitors research to assure the welfare of the participants and to determine that the risks and potential benefits remain unchanged. The IRB may

[1] 45 CFR Part 46
[2] Oklahoma Administrative Code, Title 310, Chapter 2, Subchapter 31

approve, not approve, or require changes to research protocols. It may also suspend or terminate its approval of previously approved research.

Federally and non-federally supported human subject research for which the OSDH IRB provides review and oversight will comply with federal regulations for the protection of human subjects[3] or public health surveillance activities.

The commissioner of health assures the IRB access to meeting space and sufficient staff to support the IRB's review and recordkeeping duties.[4]

Documentation

The IRB administrator maintains: written procedures and guidelines for the IRB activities; current list of the IRB members identified by name, earned degrees, representative capacity, certifications/licenses, and relationship to the institution; protection of human participants in research training certificates for Principal Investigator (PI) and co-PIs; and minutes of each IRB meeting and signs the IRB approved meeting minutes.

Records Retention

The IRB administrator retains for no less than three (3) years after the closing of the study the following records: meeting minutes until three (3) years past the final closure dates of all of the studies reviewed at the meeting, IRB files, budget and accounting records regarding acquisition and expenditure of resources. Records of research involving minor subjects require maintenance for 25 years.

Registration

Federalwide Assurance (FWA) is agreement between the agency and the U.S. Health and Human Services (HHS) to comply with federal regulations and ethical guidelines outlined in the Belmont Report concerning research involving human subjects.

The assurance (FWA 00000183) between this institution (IORG # 0000576) and the federal departments and agencies that provide support for research covered by this policy and 45 CFR 46 must be maintained and on file with the Office of Human Research Protections (OHRP) and approved for federalwide use.

The OSDH IRB (IRB 00000908) is registered with HHS and may review human subjects research conducted or supported by HHS. The OSDH IRB is designated under the OSDH federalwide assurance of compliance by OHRP.

[3] 45 CFR Part 46
[4] 45 CFR 46.108

IRB Composition[5]

The IRB members must be sufficiently qualified through experience, expertise, and diversity to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB ascertains the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice.

To promote complete and adequate review of research activities commonly conducted, the IRB has at least five members that are:

- knowledgeable about and have experience working with the vulnerable subjects involved in research that it regularly reviews and

- inclusive of at least: one member whose primary concerns are in scientific areas, one member whose primary concerns are in nonscientific areas, and one member not affiliated with the OSDH and who is not part of the immediate family of a person affiliated with the OSDH.

No IRB member participates in the initial or continuing review of any research in which the member has a conflicting interest, except to provide information requested by the IRB.

The IRB may invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

The commissioner of health appoints the IRB chair. The IRB chair must be fully capable of managing the IRB and the matters brought before it with fairness and impartiality. The IRB chair can be from within or outside the OSDH.

Meetings

The IRB convenes once monthly on the third Wednesday. The IRB may meet on an emergency or otherwise as needed basis at times other than the regularly scheduled meetings. The IRB administrator prepares the meeting agenda and minutes.

One week prior to the meeting, each IRB member receives the following: meeting agenda, draft minutes of the most recent IRB meeting, and any submitted IRB forms and supporting documentation for each item on the agenda. This includes, but may not be limited to, new applications, reliance agreement requests, proposed modifications, continuing review forms, final closure reports and/or adverse event reports.

[5] 45 CFR 46.107

The meeting agenda details all items approved under the expedited review process and members may initiate discussion on any actions carried out under expedited review for which they have questions or concerns.

IRB members may participate in the convened meeting via telephone conference call providing: the remote member has received all pertinent materials prior to the meeting, can equally participate in the discussion, and meeting minutes clearly document that the participation met the above conditions.

Voting

At convened meetings, the IRB reviews, discusses and votes individually to approve new research, continuing research, changes to currently approved research, continuing review requirements for expedited research, reliance agreements, meeting minutes and to accept adverse events. The vote is documented in the minutes.

The following outline the voting requirements:

- majority of the IRB members present,
- at least one member whose primary concerns are in nonscientific areas is present,
- at least one physician member is present when investigational drug study is reviewed,
- no proxy votes are permitted,
- simple majority of votes cast is needed for approval,
- an IRB member may not vote on his/her own study or on any study where there is a potential conflict of interest,
- any member determined to have a conflict of interest on a study will be excused from IRB discussion and will not vote on the study, and
- majority of the membership must remain intact when any member is excused, as they are no longer eligible to count towards this majority.

Communication of the IRB Decision

The IRB notifies the PI of its decision in writing, within two weeks of the decision.

If the IRB approves the study, the PI will receive: a decision letter, and a copy of the informed consent document with stamped approval date and date of approval expiration from which the PI will generate copies of the document for subject signature, if applicable.

If IRB approval is conditional upon minor and specific changes, the PI will receive: written documentation of the recommended changes or modifications and an opportunity to reject or accept the condition.

The PI may accept conditions and send written modifications to the office of the IRB administrator.

- The IRB administrator reviews the items to ensure the PI made the requested changes in accordance with the original IRB requests as reflected in the meeting minutes.
- The IRB administrator or IRB Chair verifies that the specific changes are complete.
- Once verified, the IRB chair or administrator authorizes approval on behalf of the IRB. Within five (5) working days of verification, the IRB administrator sends an approval letter to the PI.

PI may reject conditions by written response or at the next scheduled meeting for the IRB's reconsideration.

If the IRB requires additional information, the IRB defers the study and sends the PI:

- notice in writing of the reasons for deferral with instructions to provide additional information to address these concerns and
- an opportunity to present the additional information in writing or in person at the next scheduled IRB meeting.

The IRB notifies certain OSDH offices of IRB-approved research which fall under other state and federal laws. For example, studies involving vital statistics, cancer registry, or other identifiable information require additional review, commissioner approval, and/or data use agreements.

The IRB notifies the commissioner of health of the IRB findings and actions on a monthly basis in the form of IRB-approved meeting minutes.

Appeal of IRB Decision

The office of the IRB administrator must receive a request for appeal in writing within ten (10) working days of notification of the original decision.

The IRB considers the appeal at the next regular meeting. In addition to the written request for appeal, the PI may respond in person at the meeting.

In accordance with HHS regulations,[6] no other institutional office or official may approve human subject's research that has not been approved by the IRB.

VIII. Criteria for IRB Approval

[6] 45 CFR 46.112

HHS regulations provide the criteria for approval of research.[7] To approve a research study, the IRB determines that the study meets all the requirements for approval as defined by 45 CFR Part 46.111.

If approved, the IRB determines the appropriate length of the approval, meaning the maximum number of days that the IRB feels is appropriate for this study to continue without another review of the research. Federal regulations do not allow the approval to exceed 365 days except when the research meets 2018 requirements at 45 CFR 46.109(f) and the IRB has determined the elimination of the continuing review requirement is acceptable.

The IRB may require verification from sources other than the PI for some studies. These types of studies do not receive additional outside review, include an extremely high level of risk, or have a PI who has a history of research-related problems. In these circumstances, the IRB works jointly with the appropriate OSDH officials to assure that appropriate monitoring procedures are in place prior to study enrollment and that the IRB receives reports on a regular basis.

Informed Consent

Informed consents should include the elements required in 45 CFR 46.116.

Informed consent should be documented in accordance with 45 CFR 46.117 except when the IRB has waived the requirement for the investigator to obtain a signed informed consent form for some or all subjects. In order to receive a waiver for obtaining signed consent forms, the PI must request in writing consent waiver, modification, or non-documentation. Waivers for non-documentation will only be granted when criteria provided in 45 CFR 46.117(c)(1) has been met.

For clinical trials conducted or supported by a Common Rule department or agency, a copy of an IRB approved consent form which was used to enroll subjects must be posted on a public federal website designated for posting consent forms. A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions to evaluate the effects of the intervention on biomedical or behavioral health-related outcomes. The form must be posted after recruitment closes and no later than 60 days after the last study visit.

Advertising for Research Subjects

If the PI advertises to the public, the IRB reviews the information contained in the advertisement and the mode of its communication to determine that the procedure for recruiting subjects provides adequate and accurate information.

[7] 45 CFR § 46.111 and at subparts B, C, and D of 45 CFR part 46, when applicable

Advertisements may mention payments to subjects, but not the specific amount. Payments cannot be the primary focus of the recruitment tool.

Research not based within the OSDH will not use the name of the health department other than to state the project meets the requirements of the IRB.

Reliance Agreements

The OSDH IRB may enter into a reliance agreement with another institution and its IRB to provide review or cede review of cooperative research on a study-by-study basis. Agreements where OSDH cedes review may only be made with another institution on the condition that it has a current FWA on file with OHRP.

Generally speaking, the OSDH IRB should be the IRB of record on collaborative research projects if any of the following conditions apply:

- OSDH is funding the project either directly or indirectly via grants;
- the PI or co-PI is an OSDH employee, contractor, or intern; or
- the project is being done at the direction of OSDH.

The PI or program area should consult with the OSDH IRB to determine the level of OSDH's involvement in the review process prior to submitting any IRB application(s). The OSDH IRB will vote on proposed reliance agreements on a study-by-study basis when the use of a single IRB is deemed to be appropriate. An acknowledgement letter of the vote will be placed in the study file.

Reliance agreements will be reviewed by a representative from legal and the IRB administrator. The OSDH Commissioner of Health or an individual with signatory authority will provide final approval to establish a reliance agreement. The reliance agreement is not considered in effect until it has been signed by all involved parties.

IV. Review Process

Pre-Review

The IRB administrator or a designated reviewer receives all submissions and conducts pre-reviews to obtain complete documentation, which includes: Human Subjects Research Application form, and applicable supporting documentation including: complete protocol, grant narrative describing planned human subjects research, consent process and forms, study materials, and all audio or visual advertisements for potential research subjects.

Based upon the information gathered during the pre-review process, the PI may receive written feedback to make appropriate revisions to the documentation prior to final submission to the IRB.

The pre-review process also applies to submissions for proposed modifications and continuing review requirements.

Exempt Research

To qualify for exempt status research must fall under one of the federally defined exempt categories as defined by 45 CFR. 46.104(d).

The PI requests determination of exempt status prior to research initiation. The IRB administrator or chair determines the exemption status. The IRB administrator sends a letter to the PI if the study is determined to be exempt from further review. If the research does not meet the exemption criteria,[8] the office of the IRB administrator proceeds with the study review as expedited or by the convened IRB. When Limited IRB review is required as a condition of exemption, procedures for expedited review will be utilized.

While continuing review is not required for exempt research, the IRB requests that the PI submit the Annual Update of Exempt Study form so that the IRB may maintain an accurate census of ongoing research projects.

Limited Review

Limited IRB review is a process which does not require the IRB to consider all of the approval criteria established by 45 CFR 46.111; but instead focuses solely on assuring adequate protections for privacy and data confidentiality. Limited IRB review may be required for granting exempt status in some circumstances.

The OSDH IRB will conduct limited IRB review utilizing the expedited review procedures outlined in this policy when a study meets the criteria as outlined by 45 CFR §46.104(d)(2)(iii), (d)(3)(i)(C), and (d)(7), and (8).

Expedited Review for Non-Exempt Research

The IRB reviews certain research activities through an expedited review process that (1) present no more than minimal risk to human subjects and (2) involve only procedures listed in one or more of defined categories.[9] Please refer to OHRP Expedited Review Categories for detailed information on research activities that may be eligible for expedited review procedures. Expedited review may also be utilized for proposed modifications that constitute minor, non-substantive changes.

The expedited review procedure can be applied to studies where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects if reasonable and

[8] 45 CFR § 46.101
[9] 45 CFR § 46.110 and 21 CFR § 56.110

appropriate protections to reduce the risks of invasion of privacy and breach of confidentiality to no greater than minimal.

Under expedited review, the IRB administrator, IRB chair or designated reviewer exercises all of the authorities of the IRB to approve but not disapprove research. The meeting agenda details items approved under expedited review. Members may ask questions and/or discuss the expedited review items.

Revisions to 45 CFR 46 (also referred to as the revised Common Rule), effective January 21, 2019, eliminated the requirement for continuing review of studies with an expedited initial approval date after the effective date unless the IRB determines otherwise.[10] The convened IRB will vote on continuing review requirements for eligible studies at the next regularly scheduled IRB meeting following expedited approval. If the IRB determines that continuing review is warranted, standard continuing review procedures will be followed. If the IRB determines that continuing review is not necessary, the IRB will request the completion of the an Annual Activity Statement of Expedited Study by the PI to inform the IRB whether or not a study is still active and share any recent results, publications or presentations.

Full Board Review for Non-Exempt Research

Studies that do not meet criteria for exempt, limited, or expedited review, will receive full board review by the convened IRB. The IRB administrator or IRB chair has the discretion to require full board review of any research activities as he or she deems fit.

X. Oversight of Previously Approved Research

The IRB conducts continuing review of research at intervals based on the degree of risk. The IRB has the authority to observe the consent process and the research. The IRB requires reviews of high-risk protocols or protocols with a high risk to benefit ratio on a more frequent basis. The continuing review of research is substantive and meaningful. Criteria must be satisfied when the IRB conducts continuing review of research either at a convened meeting or under an expedited review procedure. These criteria include determinations of risks, potential benefits, informed consent, and additional safeguards for subjects who are likely to be vulnerable to coercion or undue influence.

Procedures for continuing review are subject to the date of the initial study approval. Studies with an initial approval date on or after January 21, 2019 are subject to 2018 requirements. Studies with an initial approval date prior to January 21, 2019 are subject to pre-2018 Requirements. The PI of a study subject to pre-2018 requirements may request transition to 2018 requirements by submitting a Request for Modification.

[10] 45 CFR 46.109(f)(1)(i)

Pre-2018 studies are reviewed when (i) there is active enrollment of subjects or pending enrollment of the first subject, (ii) the research is permanently closed to the enrollment of new subjects, and (iii) all subjects have completed all research related interventions. Continuing review is required as long as the research remains active for long-term follow-up of subjects and involves non-exempt human subjects research. Furthermore, the IRB conducts continuing review when research activities are limited to data analysis of individually identifiable private information.

The 2018 requirements eliminate the continuing review requirement for research initially approved under expedited review unless an IRB determines otherwise. Studies involving the following ***will be*** required to complete an annual PPR:

- Research involving vulnerable populations (children, pregnant women, and prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons);
- Research with the potential to impact other ongoing OSDH activities;
- Research projects or staff with a history of adverse events or non-compliance.

The IRB will vote on all other studies which are eligible for the elimination of continuing review to decide whether or not a PPR will be required. The vote will be documented in IRB meeting minutes. The PI will be notified within 5 business days of outcome of the vote and the study expiration date if applicable. Studies subject to 2018 requirements that are not subject to continuing review will not expire.

Continuing review requirements for 2018 studies that do not receive an initial approval through expedited review are subject to the same continuing review procedures as pre-2018 studies.

Periodic Progress Reports

The office of the IRB administrator sends out a request for the Periodic Progress Report form (PPR)[11] to the PI four weeks prior to the date that the research approval expires. The IRB administrator sends a second notice about two weeks later if the PI was unresponsive to the first notice.

The PI must provide adequate information in the PPR for the IRB to determine if the study is appropriate for continuation. The PI must provide all information requested on the PPR form. Incomplete forms will be returned to the PI for completion.

[11] ODH Form No. 1006

The IRB reviews the current informed consent document(s) to ensure the following:

- the currently approved or proposed consent document is still accurate and complete and
- the PI provides any significant new findings that related to the subject's willingness to continue participation to the subject in accordance with HHS regulations.[12]

The IRB administrator or convened IRB approves the PPR before the expiration date of the approval to comply with federal regulations.

Federal regulations do not allow for any grace period for renewal. For example, if a study's approval period begins on July 15, 2011, the initial approval ends on July 14, 2012. A satisfactory progress report must be received, reviewed, and on the IRB meeting agenda prior to July 14, 2012.

- If the due date approaches and a PPR is not received, the IRB sends a notice to inactivate the study with a final deadline to the PI.
- If the approval date passes with no response, the IRB inactivates the study with letter of notification to the PI stating that research must stop until PPR submission and approval.

Modifications to Previously Approved Research

PIs must promptly report any proposed changes or revisions of approved research to the IRB using the Request for Modification of Approved Research Form.[13] Approval of such changes or revisions are required before implementation of changes or revisions.

PI submits a copy of the protocol, consent forms, attachments, advertisements, and instruments related to the modification with the changes highlighted, preferably using track changes. The PI also includes a clean copy of the items with the proposed modifications.

If the PI feels it is necessary to initiate the revisions immediately to eliminate apparent immediate hazards to the subject, the PI must immediately contact the office of the IRB administrator. The PI provides a reasonable and compelling rationale for the immediate modification with signatures of the PI and a physician not involved with the study, if applicable.

[12] 45 CFR § 46.116(b)(5)
[13] ODH Form No. 1001

Serious, Unanticipated, and Other Adverse Events (AE)

PIs must promptly report any unanticipated problems involving risks to subjects or others to the IRB. The Adverse Event (AE) and Other Unanticipated Problem Report Form[14] captures all adverse events occurring under the jurisdiction of the IRB. The PI completes the form and furnishes it to the office of the IRB administrator within 4 working days of the PI becoming aware of the event. The death of a subject, whether study-related or not must be reported by the next working day by phone or email to IRB@health.ok.gov and the completed form submitted according to the above guidelines.

A *serious* adverse event involves:

- any experience that is immediately life threatening, permanently disabling, or requires (or prolongs) inpatient hospitalization;
- a congenital anomaly or birth defect; or
- a death of a subject, whether study-related or not.

Other adverse events reported on the Adverse Event and Other Unanticipated Problem Report Form include:

- subject's complaints that the researchers put undue pressure to participate,
- subject experienced extreme distress requiring medical treatment or follow-up as a result of research participation,
- compromise of data confidentiality,
- protocol deviations, and
- other serious complaints lodged by subjects or potential subjects.

The IRB chair or administrator makes an immediate and preliminary determination regarding the degree of risk involved and notifies the PI if the study is immediately suspended.

If the IRB chair or administrator does not determine the event requires immediate suspension, the next scheduled IRB meeting holds discussion on the completed report.

- Upon review, the IRB determines if the event was related, possibly related, or unrelated to participation in the study and if it was expected or unexpected.

[14] ODH Form No. 1003

- The IRB votes on whether the study continues, requires modifications, or discontinues. The IRB administrator records the votes in the minutes for each event.[15]

For serious adverse events occurring at outside sites for multi-center trials, the PI submits a copy of the report furnished from the sponsoring institution or other PI, if applicable. The copy must have the OSDH IRB number, OSDH PI, and OSDH PI signature. The IRB chair or administrator reviews the event and reports to the IRB at the next meeting. The IRB chair implements a review process for outside serious adverse events in any situation where he/she feels that the situation warrants such process.

The IRB administrator ensures prompt reporting to institutional officials, relevant department, agency, regulatory body, and the OHRP of any:

- unanticipated problems involving risks to participants or others in any federally supported research;
- serious or continuing noncompliance with federal, institutional, or IRB requirements; or
- suspension or termination of IRB approval for federally supported research.

Final Closure Report

The completion or termination of a study is a change in activity and therefore reported to the IRB. A notice of closure closes the IRB file and provides pertinent information to the IRB in its evaluation and approval of related studies. The PI reports the completion or termination of a study to the IRB on a Final Closure Report[16] or on the PPR if within thirty (30) days of termination of the study

The IRB administrator or chair reviews all reports of study completion and, if needed, requests further information from the PI for clarification of any questions that may arise.

The IRB administrator generates a final closure letter and sends the letter to the PI. A copy of the letter completes the study file.

Annual Updates on Exempt and Expedited Studies

For exempt studies, once each year the IRB administrator requests the PI to submit an Annual Update of Exempt Study.[17] For expedited studied excused

[15] 45 CFR § 46.115(a)(2)
[16] ODH Form No. 1005
[17] ODH Form No. 1004

from continuing review requirements, the IRB administrator requests the PI to submit an Annual Activity Statement.[18]

The PI indicates on these forms if the study is active or terminated and returns the form to the IRB. Upon receipt of the letter from the PI, the IRB processes the letter based upon the response given.

A copy of any submitted Annual Update of Exempt Study or Annual Activity Statement is provided to the IRB at the next month's meeting. The meeting agenda will reflect such submissions.

Monitoring of Studies

The IRB monitors research activities by conducting random detailed reviews of patient charts and patient interviews, as it deems necessary for proper continuing review of research.

- The IRB chair appoints appropriate IRB members and staff to conduct such monitoring activities.
- The IRB monitors studies as often as deemed necessary.
- The PI makes all requested records available to the IRB.
- The PI and IRB receive a report of findings at the conclusion of the review.

Special Considerations

Inclusion of Genders and Minorities

Research reviewed by the IRB shall not routinely exclude a gender, minorities, or any other subset of the population from participation in clinical research. The IRB recognizes that certain research is gender specific and must include only one gender. The PI provides the rationale for the exclusion of a gender, minorities, or any subsets of the population from the research. The rationale must contain strong scientific or practical reasons that clearly justifies such exclusion and establishes to the satisfaction of the IRB that such exclusion is appropriate with respect to the health of the subjects or the purpose of the research. The IRB has discretion to determine the scientific merits of the grounds for exclusion and may require additional information from the sponsor.

When NIH supports the research, each PI is responsible for following the NIH guidelines on the inclusion of women and members of minority groups and their subpopulations.[19] The PI furnishes the IRB with evidence of compliance before IRB approval.

[18] ODH Form No. 1365

Note: Clinical research cannot exclude women of childbearing potential from trials involving investigational drugs/devices simply because of potential teratogenic effects. Women of childbearing potential can be required to use contraception while participating and informed of the known and potential side effects if they become pregnant. Scientifically justified exclusions are allowed.

Inclusion of All Ages in Research

NIH guidelines require the inclusion of individuals of all ages in all research studies unless there is scientific or ethical justification for exclusion. Each PI is responsible for compliance with the guidelines.[20]

Inclusion of Children in Research

When a PI intends to use children as research subjects, he/she must address these issues directly in the protocol in a section entitled "The ethical and regulatory considerations concerning the involvement of children" and identify the research category the study fits into and the rationale for this categorization.

Generally, the law considers any person under 18 years old to be a child. The federal regulations permit four categories of research involving children. The categories reflect the degree of risk and prospect of benefit to the participating child-subject. For any protocol involving children, the IRB, in consultation with the PI, determines the category of research that the study belongs and documents the decision and rationale in the minutes.

The four categories for child involvement are:

1. research that does not involve greater than minimal risk to children;

2. research that involves greater than minimal risk but presents the prospect of direct benefit to the individual child subject;

3. research that involves greater than minimal risk and no prospect of benefit to the individual child subject given that:

    - the risk of the research represents no more than a minor increase over minimal risk,

    - the intervention or procedure presents experiences to the child-subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations, and

    - the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital

[20] Revision NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Research Subjects, NOT-OD-18-116

importance for understanding or the amelioration of the disorder or condition; and

4. research not otherwise approvable under one of the above categories but the IRB determines the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children may be approved under the following procedures.

    - The Commissioner of Health may approve non-HHS funded research if a separate panel of experts determined that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, and that the research is conducted in accordance with sound ethical principles and adequate provisions are in place for soliciting the assent and permission of their parents or guardians as set forth in 45 CFR 46.408.
    - If the research is funded by HHS, approval for the study to proceed must be obtained from HHS.

Children who are wards of the state or any other agency, entity or institution, can be included in approved research if the research relates to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in where the majority of child subjects are not wards.

For each child who is a ward, an advocate is appointed 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 shall be an individual who has the experience and agrees to act in, the best interest of the child for the duration of the child's participation in the research. The advocate is only associated with the research, the PI, or guardian organization with their role as the child advocate.

A minor may consent to research if a lawfully recognized court of law has entered an order specifying the minor can consent to a specific research activity. Additionally, a minor[21] who may consent to health services, may consent to research that is to preserve the child's life or IRB-approved research that relates to the management of reportable diseases.

Assent of children is required unless:

- subject is too immature/incapacitated to be consulted;

[21] Title 63 OS § 2602

- the intervention/procedure involved in the research holds out a 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; or

- the IRB has approved a waiver of assent documentation.

Prisoners as Research Subjects

In accordance with our FWA, the IRB provides additional protection for research subjects that are prisoners, as their incarceration could affect their ability to make voluntary or uncoerced decisions regarding participation as subjects in research. The principal considerations for including prisoners as research subjects are outlined at 45 CFR Part 46.305.

For the review of studies involving the use of prisoners, the IRB will include at least one IRB member who is either a prisoner or a prisoner representative with appropriate background and experience to review any study that involves prisoners as subjects.[22]

Mentally Disabled/Cognitively Impaired

The primary ethical concern in research involving the mentally disabled and cognitively impaired is that their disability may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participation.

Generally, all adults are competent to consent unless there is evidence of serious mental disability that impairs reasoning or judgment. Even those who do have a diagnosed mental disorder may be able to understand the situation of being a research volunteer and capable of consenting or refusing participation.

In the past, institutionalized individuals were research subjects in drug and vaccine tests that were unrelated to their disorders or institutionalization. This exploitation of the vulnerable and "voiceless" led the National Commission for the Protection of Human Subjects to recommend that, even in research on mental disabilities, subjects be from among the non-institutionalized whenever possible. The OSDH supports this position.

Surrogate Consent for Research Subjects

The IRB allows surrogate consent in such cases where the potential subject is not capable of consenting on their own behalf. Surrogate authority is in the following order:

1. spouse,
2. adult child,

[22] 45 CFR § 46.305-306

3. parent,
4. adult sibling, and
5. relative by blood or marriage.

Surrogates cannot override the subject's previously expressed permission/ prohibition.

There are some specific restrictions within this law and certain guidelines, which the IRB must follow to allow for such consent.

The IRB may approve a surrogate consent upon request from the PI. The IRB looks at a variety of issues when determining whether surrogate consent is appropriate. Analysis of the issues includes questions, such as:

- Will participating in the study directly benefit the potential subject?
- Are there alternate standard/approved treatments available for this subject?
- Could this study be done without allowing surrogate consent?

Based upon the answers to these questions, the IRB makes a determination of the appropriateness of surrogate consent. The IRB provides the PI with notification as to the approval or denial of this process and the IRB's rationale. The PI may appeal the decision in writing and provide documentation to the IRB.

Genetic Research

Genetic testing in research studies presents a variety of factors. The convened IRB considers the use of genetic testing in research and evaluates each use on a case-by-case basis.

A convened IRB reviews research involving genetic testing. If the primary IRB at another site reviewed the research by a convened IRB, the research may be eligible for approval under the exempt or expedited process.

For research using prospectively collected or banked materials for future use in genetic research, the subject(s) must:

- be told specifically that their blood or tissue specimen will or may be used for genetic testing,
- be given all information available at the present time concerning the type of genetic research that will take place on their sample,
- be told whether information regarding the results of these studies will be made available or why not, and
- give active consent.

The IRB position is that in most cases the results of the genetic testing should only be available to subjects when:

- a positive result can be achieved by the release of information, such as treatment or behavior modification recommendations are appropriate for their medical care and

- an approved genetic counseling program is available to help the patient deal with this information.

In all cases involving genetic testing, the potential risks, including theoretical risks are included in the consent.

Non-English-Speaking Subjects

Informed consent information is presented orally and in writing in a language understandable to the subject.

The IRB requests the PI submit a consent form written in the appropriate language when it is likely that most subjects do not understand English. The IRB requires a notarized statement by the person who translates the consent that states that the translated consent form represents the same information in the approved English consent form. The PI may contact the office of the IRB administrator for guidance or assistance in obtaining someone to translate this document

For a subject who does not speak English well enough to read, understand, and participate in the written/oral consent process, the IRB requires the PI make provisions for their participation in the study. The IRB requires a short form that explains the basics of the research process and the subject has consented. Someone outside of the study staff must witness the entire process and attest that the study was explained and the subject understood the details of the study in the full version consent.

Fetal Research

Research using fetal tissue from abortion is illegal under Oklahoma law.[23]

VIII. PI Responsibilities

It is the PI's responsibility to comply with agency policy and procedures, state laws, and federal regulations. PIs must collaborate with appropriate OSDH services related to their research. The PI submits the IRB application and all necessary documents at least one week prior to the monthly IRB meetings. The PI certifies that all investigators will comply with all OHRP, FDA, and IRB rules and regulations in conducting the research. The PI will provide the IRB with

[23] 63 O.S. § 1-735

certificates of human research protection training for his or herself as well as any co-PIs and key study personnel.

Additional guidance on PI responsibilities and the information that should be provided to the IRB is available on the OSDH website.

XI. Additional Guidelines

Items not specifically addressed in these policies and procedures are incorporated by reference to the federal regulations that cover the protection of human subjects[24] and state administrative rules that govern the OSDH and human subjects protection.[25]

XII. Scheduled Review

The IRB Administrator is responsible for the review of this policy and procedure at least every 36 months or if there is a change in state law, administrative rule, or other regulation.

XIII. Associated Forms

ODH No.	Title
ODH No.1001	Request for Modification of Approved Research
ODH No.1003	Adverse Event Report
ODH No.1004	Annual Update of Exempt Study
ODH No.1005	Final Closure Report
ODH No.1006	Periodic Progress Report Form
ODH No.1007	Human Subjects Research Application Form
ODH No. 1365	Annual Activity Statement for Expedited Study
ODH No. 1392	Request for OSDH IRB Deferral or Excusal

XIV. Policy and Procedure Review History

The table below identifies the procedure review history regarding the origination date, review date(s) and revision date(s).

[24] 45 CFR Part 46
[25] OAC 310:2-31

Origination Date:	Review Date(s):	Revision Date(s):
November 2011		June 2016 March 2022

694