

## INSTITUTIONAL REVIEW BOARD POLICY

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## **INSTITUTIONAL REVIEW BOARD POLICY**

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### **I. STATEMENT OF PURPOSE**

The purpose of this policy is to specify the manner in which research proposals will be reviewed, overseen and acted upon; in order to protect the rights and welfare of human research subjects participating in Department of Mental Health and Addiction Services (DMHAS) sponsored or approved research; and in order to comply with federal regulations regarding the protection of human subjects.

Compliance with Department of Health and Human Services (DHHS) regulations (Federal Policy for the Protection of Human Subjects, known as the Common Rule) is required whenever DMHAS becomes engaged in human subjects research conducted or supported by any federal department or agency that has adopted the Common Rule, unless the research is otherwise exempt from the requirements of the Common Rule or a department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance. Compliance with Food and Drug Administration (FDA) regulations is required when research involves products regulated by the FDA.

DHHS regulations relating to the protection of human subjects are codified at [Title 45 CFR Part 46](#) and are enforced by the Office of Human Research Protection (OHRP). The FDA regulations are codified at [Title 21 CFR Part 50 & 56](#) and are enforced by the FDA. In large part, the FDA regulations mirror 45 CFR 46 with some differences. Research conducted by or at DMHAS facilities most often falls under the jurisdiction of DHHS, but in the event of dual jurisdiction, both regulations apply.

### **II. JURISDICTION OF DMHAS OOC IRB**

The Office of the Commissioner (OOC) Institutional Review Board (IRB) has jurisdiction over review and approval of activities categorized as research involving human subjects.

Research is defined by the regulations [\(45 CFR 46.102 \(d\)\)](#) as a "systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

Human subjects are defined by the regulations [\(45 CFR 46.102 \(f\) \(1\), \(2\)\)](#) as "living individual(s) about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information".

The OOC IRB will review, prospectively and on a continuing basis, research involving human subjects where the research is either sponsored or conducted by DMHAS or where the research is conducted by a non-DMHAS institution at a state operated facility. The OOC IRB is responsible and has authority to approve research, require modifications, disapprove research and suspend or terminate approval. (Because CMHC is jointly operated by both DMHAS and Yale University, proposals for research to be conducted at CMHC are reviewed and approved by the Yale Human Investigations Committee unless the research will also be conducted at another DMHAS facility.)

When conducted by a non-DMHAS institution, not under contract by DMHAS, research must also be reviewed through a multi-stage process. This process is most usually initiated when the state-operated facility where the study recruitment or interventions will occur forwards a letter of endorsement to the DMHAS Research Director and the investigator forwards an IRB Application to the DMHAS IRB. Following receipt of both the letter of endorsement and the IRB Application, the DMHAS Research Director will initiate the Commissioner's review, which involves review of scientific merit, review of administrative impact upon DMHAS and review of human subject protections by the IRB in accordance with federal regulations. Final approval by the Commissioner will be based upon IRB approval, a favorable assessment related to scientific merit and a favorable assessment related to administrative impact (see also *Review of Research Where DMHAS is Not Engaged in the Research* below)..

Research that has been reviewed and approved by the IRB may be subject to further review by the Commissioner or designee. However, another DMHAS body may not approve a research proposal that has been disapproved by the IRB.

### **III. APPLICABILITY OF FEDERALWIDE ASSURANCE**

The terms of DMHAS' Federalwide Assurance (FWA) apply whenever DMHAS becomes engaged in human subjects research conducted or supported by any federal department or agency that has adopted the Common Rule unless the research is otherwise exempt from the requirements of the Common Rule or a department or agency conducting or supporting the research determines that the research shall be conducted under a separate assurance. As such, DMHAS and the IRB designated under its assurance will comply with the Federal Policy for the Protection of Human Subjects (45 CFR 46 and subparts B,C, and D) when engaged in federally conducted or funded research.

The terms of DMHAS' FWA have not been extended to non-federally conducted or supported research with humans; and DMHAS has not elected to assure application of 45 CFR 46 and subparts B,C and D to non-federally conducted or funded research with humans.

However when reviewing non-federally funded research the DMHAS IRB will generally apply the regulations and DMHAS IRB standards in the same manner as with federally funded research. But review and subsequent IRB actions in such cases is subject to flexibility as deemed appropriate by the IRB.

#### **IV. REVIEW OF RESEARCH WHERE DMHAS IS NOT ENGAGED IN THE RESEARCH**

Where an institution is not engaged in non-exempt human subject research, the regulations at 45 CFR 46 do not apply and IRB review is not required. However, there are circumstances where DMHAS is not engaged in research, but still elects to conduct prospective and ongoing IRB review of such research. This most generally occurs when a non-DMHAS institution or individual investigator requests permission to 1) conduct recruitment activities at a state-operated DMHAS facility; and/or 2) conduct research activities at a state-operated DMHAS facility.

When DMHAS reviews research as described above, the review and findings of the IRB are not subject to the regulations at 45 CFR 46. However in such cases the DMHAS IRB will generally apply the regulations and DMHAS IRB standards in the same manner as with all other research. But review and subsequent IRB actions in such cases is subject to flexibility as deemed appropriate by the IRB.

Please also see *Expedited Review* below for a detailed explanation of the criteria for expedited continuing review of research where DMHAS is not engaged.

#### **V. MEMBERSHIP AND RESPONSIBILITIES**

The IRB will consist of at least five members. Members should be sufficiently diverse to enable adequate review of the range of research that is commonly reviewed by the Department. Membership will be constituted according to the following guidelines.

At least one member will fall into each of the following categories:

- primary concern is in the scientific area
- primary concern is in the non-scientific area
- is not affiliated with DMHAS and is not part of the immediate family of a person who is affiliated with DMHAS.

When research under review is to include prisoner participants the convened IRB will include at least one member representing prisoner participants.

The individual designated as the Signatory Official for the DMHAS' FWA will appoint the IRB chair and IRB members. Appointment will be for a two-year term. There is no limit on the number of terms the chair or a member may serve. New members may review and vote on IRB applications and other matters only after completion of new member orientation and education.

As deemed necessary, a specific individual may be designated as an alternate for a specific committee member. The alternate should, in general, have the same professional background, experience and expertise as the standing member. The Signatory Official also appoints alternate members and the alternate's term is consistent with the standing member's term. It is the standing members' responsibility to ensure that the alternate has adequate information and preparation related to specific issues and studies to enable the alternate to make an informed vote. Alternate members will receive all of the same IRB and study materials that standing members receive. Alternate members may attend any IRB meeting but may vote only in the absence of the standing member.

If any member anticipates an extended leave of absence (more than two meetings), due to unavoidable factors, the member may request to be categorized as "on temporary leave" from the committee. During the leave the member will not be considered when determining whether or not there is a quorum. Should the leave extend beyond six months the member will be withdrawn from the committee with the option of rejoining at a later date.

#### **A. Responsibilities Of IRB Chair**

The IRB Chair will either complete or ensure completion of the following tasks:

- Compliance with regulations governing IRB activities
- Scheduling of meetings
- Preparation of agendas
- Production of IRB minutes and distribution to IRB members
- Maintenance of IRB records as outlined in this policy
- Maintenance of a current list of all projects under the review of the IRB including actions taken and corresponding dates
- Notification to investigators, and others as appropriate, of IRB action
- Schedule timely continuation reviews
- Conduct expedited reviews when applicable
- Orientation of new members
- Ongoing education
- Represent the DMHAS IRB in communications with investigators, DMHAS staff, and others as required.

#### **B. Responsibilities Of IRB Members**

IRB members will be responsible for the following:

- Regular attendance at IRB meetings
- Review research proposals prior to the meetings in sufficient detail to enable informed voting
- Vote on research proposals and other actions before the IRB committee.
- Bring issues to the attention of the full committee as appropriate
- Complete required educational activities

## **VI. CONDUCT OF MEETINGS**

The IRB will meet monthly or at intervals sufficient to review new proposals, monitor ongoing studies and conduct the ongoing business of the committee.

Materials related to the studies scheduled for review will be distributed sufficiently in advance of the meeting to allow adequate time for review prior to the meeting.

Attendance sheets will be signed to document attendance.

Attendance of non-members at IRB meetings is by invitation only.

A quorum is achieved when a majority of members (50% of members, plus one) is in attendance. Once a quorum has been achieved issues can be decided based upon majority vote. Non-expedited research proposals may only be voted upon at a convened meeting where there is a quorum and where attendance includes one member whose primary interest is in non-scientific areas. If a quorum is lost during the meeting no further action (voting) may be taken in relation to the studies under review. Minutes of the meeting should reflect loss of the quorum and the reason for the loss, e.g. early departure, etc.

As necessary, members who have received and have access to materials related to the study(ies) under review may participate in deliberations and may vote via teleconference. Members participating via teleconference are included as part of the quorum. Minutes of the meeting should reflect participation via teleconference.

Members who will be absent from a meeting may submit their comments related to studies under review. These comments will be shared with the full committee; however the absent member may not vote.

When deemed necessary, the IRB may invite individuals with expertise and knowledge in specialized areas for the purpose of providing consultation and opinion regarding a proposal. However, these individuals may not vote.

The principal investigator or their designee will be invited to attend the IRB review, in person or via teleconference, in order to respond to questions raised by IRB members. The principal investigator or their designee cannot be present during the IRB's final discussion and vote.

Members who are not directly involved in a research project may still experience a conflict of interest regarding their IRB role based upon a variety of factors, e.g. past or present work or personal relationship with PI or member of the research team. Members will attest to a lack of conflict of interest for each proposal that they review and vote on by signing a Conflict of Interest Declaration. An IRB member who has a conflict of interest related to a study under review may not participate in the review other than to provide information about the proposal. A member with a conflict of interest is not required to absent the room during final discussion and vote; but may absent the room depending on the degree of conflict as reported by the member with the conflict, the comfort of the IRB member with the conflict and the opinion of the IRB committee. Members with a conflict of interest will recuse themselves from the vote.

## **VII. IRB RECORDS**

The IRB Chair will ensure that records are maintained in a manner sufficient to adequately document IRB activities. IRB records, including specific study files, will be maintained at the Office of the Commissioner

Documentation will be maintained as outlined below.

### **A. Research Files**

Research files will contain the following:

- IRB Application/proposal
- Grant proposal, if applicable
- Conflict of Interest Declaration
- Approved protocol, consent form and other material related to approved study with approval and approval expiration dates affixed by the IRB Chair
- Application for continued approval
- Notification of IRB action(s)
- Correspondence related to study
- Statements of significant new findings provided to subjects
- Reports of adverse events
- Minutes of meetings where the study was discussed
- Other documents as deemed relevant

### **B. Minutes**

Minutes will be maintained for all IRB meetings and will reflect the following information:

- Meeting date and location
- Attendance and whether a quorum was achieved; loss of quorum
- Research proposals reviewed
- Type of review
- Summary of discussions of controverted issues and their resolution
- Where HHS regulations require specific findings on the part of the IRB, documentation of the findings and, where necessary, protocol-specific information related to each finding.
- IRB action including total number in attendance and members voting for, against and abstaining.
- Time frame for approval, i.e., one year, 6 months, etc
- Basis for requiring changes and for disapproval.
- Other activity of the committee.

Minutes may be forwarded to members prior to regularly scheduled meetings in order to enable review and feedback by all members. Minutes will be formally approved at convened meetings. Minutes are confidential and are available only to IRB members, the signatory official related to the DMHAS Federalwide

Assurance, and the person to whom the IRB Chair directly reports, unless the latter two are involved in the research under question, in which case minutes would not be available to these parties.

### **C. IRB Membership**

A list of IRB members will be maintained containing the following information:

- Name
- Earned degree
- Representative capacity
- Indication of experience sufficient to describe chief anticipated contribution
- Employment status with or relationship to DMHAS.

Records related to the conduct and documentation of IRB activities will be maintained for three years. Specific research files will be maintained for at least three years after completion of the research.

## **VIII. TYPES OF IRB REVIEW**

### **A. Exempt from IRB Review**

The IRB may find some research to be exempt from further IRB review. An investigator who believes that their research is exempt from IRB review must still submit an IRB Application, but should cite the qualifying section of the regulation at the time of submission. The chair or designee determines if proposed research is exempt in accordance with regulations included in [45 CFR 46.101\(b\)](#). The chair or designee may use their discretion as to whether the research will be reviewed by full committee. The chair, designee or the full committee may request minor changes or clarifications before a finding of exemption is granted.

If the IRB finds that a research proposal is exempt, the IRB Chair will provide written notification to the investigator and others as necessary. Notification will cite the qualifying category of research activity.

When reviewed outside of a convened meeting, the chair will notify the IRB membership of any study reviewed and found to be exempt at the next regularly scheduled IRB meeting.

### **B. Expedited Review**

Expedited review is a review conducted by the chair or another designated member outside of a convened meeting. The chair or designee will determine if the proposed research is appropriate for expedited review in accordance with regulations included in [45 CFR 46.110](#) and [21 CFR 56.110](#) (see also below *Review of Research Where DMHAS is Not Engaged in the Research*) The reviewer may exercise all of the authorities of the IRB except that the reviewer may not disapprove a proposal - a research activity may be disapproved only after full committee IRB review. Applications for initial IRB approval are generally

reviewed by a full committee regardless of whether or not the study meets the criteria for expedited review. However, following determination that research is eligible for expedited review, the chair or designee may use their discretion as to whether the research will be reviewed by an expedited process or by full committee.

In the event of approval via expedited review, the chair will provide written notification to the principal investigator, and others as necessary. Notification will specify that the review was conducted via an expedited review process and will cite the qualifying category of research activity.

The chair will notify the IRB membership of any expedited review and approval at the next regularly scheduled IRB meeting.

It is possible that research activities that previously qualified for expedited review have changed or will change such that the research activities are no longer eligible for expedited review.

### **1. Expedited Continuing Review for Research Where DMHAS is Not Engaged**

At the time of continuing review of research, where DMHAS is not engaged in the research, there are occasions where the status of DMHAS clients is very different from the status of other research participants who were enrolled from different sites. In such cases the DMHAS IRB may conduct an expedited review where the criteria for expedited continuing review applies to DMHAS participants, but not necessarily to other participants. Specifically, the DMHAS IRB may conduct an expedited review of research previously approved by the convened IRB as follows:

a) where (i) the research is permanently closed to the enrollment of DMHAS participants;(ii) all DMHAS clients have completed all research related interventions; (iii) and the only remaining activity with respect to DMHAS clients would be long term follow up. These criteria would apply even if other participants from unaffiliated institutions are still active participants; and even if the institution engaged in the research conducts their own ongoing review.

b) where no DMHAS clients have been recruited or enrolled in the study and where no additional risks have been identified (no adverse events, no complaints, no additional information/literature has suggested a change in risk since initial approval). These criteria would apply even if participants from other unaffiliated institutions have been recruited or enrolled; and even if the institution engaged in the research conducts their own ongoing review.

c) where the remaining research activity related to DMHAS participants is limited to data analysis. These criteria would apply even if other participants recruited from other institutions are still actively involved in research activities; and even if the institution engaged in the research conducts their own ongoing review.

### **C. Full Committee Review**

A full review consists of a convened meeting with a majority of members present including a member whose primary interest is in the non-scientific area.

## **IX. CRITERIA FOR IRB APPROVAL**

### **A. Basic Criteria**

In order to approve research the IRB must determine that the following requirements are satisfied in compliance with [45 CFR 46.111\(a\)](#) :

- Risks to subjects are minimized
- 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 (except where a waiver is granted under [46.116 \(c\) or \(d\)](#)).
- Informed consent will be appropriately documented (except where a waiver is granted under [46.117\(c\)](#)).
- 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, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

### **B. Requirements related to informed consent**

Requirements related to informed consent are found at [45 CFR 46.116](#). Unless the IRB has granted a waiver under [45 CFR 46.116\(c\)](#) the researcher must make provisions to obtain the informed consent from each subject who will participate in the research (or that of the subject's legally authorized representative). Except where waived under [45 CFR 46.117\(c\)](#) the informed consent process will be documented either by a written consent form that includes all of the required elements outlined below; or where non-English speaking participants are involved, by a short form written consent as outlined under [45 CFR 46.117 \(b\) \(2\)](#):

- A statement that the study involves research, an explanation of the purpose of the study, the expected duration of participation, a description of the activities that the subject will be involved in and identification of any experimental procedures;
- A description of any reasonably foreseeable risks or discomforts to subjects
- A description of any benefits to the subject or to others which may reasonably be expected from the research;

- Where indicated, disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- 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;
- 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; and
- 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.

When appropriate, one or more of the following elements of information shall also be provided to each subject:

- A statement that the particular treatment or procedure may involve risks which are currently unforeseeable;
- Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
- Any additional costs to the subject that may result from participation in the research;
- The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and
- The approximate number of subjects involved in the study.

The IRB will also evaluate the informed consent to ensure that:

- The information is presented in a manner that is clear, understandable and appropriate to the subject's cognitive and language skills;
- The conditions under which the participant is engaged and informed consent is obtained are free from coercion and undue influence;
- Where applicable, adequate provisions have been made to obtain the informed consent of conservators.

If the investigator wishes to request a waiver of any informed consent requirement they should submit an Application for Waiver of Informed Consent Requirements. The IRB chair and/or full committee will evaluate the waiver application within the limits of the applicable regulations.

### **C. Requirements related to the HIPAA Privacy Rule**

The Dept of Health and Human Services, as part of the Health Insurance Portability and Accountability Act (HIPAA), issued the *Standards for Privacy of Individually Identifiable Health Information* (“Privacy Rule”). The Privacy Rule establishes conditions under which certain groups and organizations covered by the rule can use or disclose individually identifiable information (aka protected health information). The Privacy Rule requires that individuals generally be given an opportunity to agree to the use and disclosure of their protected health information by signing an Authorization form. This Authorization requirement applies to research participants unless an IRB or privacy board has approved a waiver of the Authorization requirement. Although the Privacy Rule does not require an IRB or privacy board to review the HIPAA Authorization covering the use of protected health information, the OOC IRB will generally review such Authorizations as part of the overall review and approval process. The Privacy Rule does require that an IRB or privacy board review and approve requests for waiver of the HIPAA Authorization requirement. The OOC IRB is the DMHAS body responsible for reviewing, approving and documenting waiver of the HIPAA authorization requirement when use or disclosure of protected health information is for research purposes. The Privacy Rule is codified at [45 CFR Parts 160 and 164](#)).

If the investigator wishes to request a waiver of the HIPAA authorization requirement they should submit an Application for Waiver of HIPAA Authorization Requirements. The IRB chair and/or full committee will evaluate the waiver application within the limits of the applicable regulations.

#### **D. Additional requirements related to specific vulnerable populations.**

Inclusion of certain vulnerable populations in research requires specific additional protections. These additional protections relate to 1) research, development and related activities involving fetuses, pregnant women and human in Vitro fertilization; 2) biomedical and behavioral research involving prisoners; and 3) children. The specific protections are found within 45 CFR 46 under Subparts [B,C](#) and [D](#) respectively. Where these populations are involved in research, the IRB will review the research within the context of the applicable Subpart and apply the review criteria and required findings.

#### **E. Requirements related to confidentiality certificates**

[Certificates of Confidentiality](#) are issued to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. Examples are information related to use of alcohol or other substance use, illegal behavior, sexual behavior, or other information that, if revealed, could potentially be damaging to the participant. When such identifiable information is collected and recorded during the course of a study, the IRB suggests that the investigator consider applying for a Certificate of Confidentiality.

The Certificate of Confidentiality is not intended to protect researchers from reporting information regarding child abuse, elder abuse or the threat of harm to self or others if revealed by a study participant.

Where application for a Certificate of Confidentiality will be made, study participants must be informed at the time of the informed consent process, of the accurate status of the application, e.g., it has either been applied for or has been obtained.

The investigator is responsible for promptly documenting to the IRB receipt of the Certificate of Confidentiality.

#### **F. Requirements related to education of key research personnel in protection of human subjects.**

Federal guidelines require that investigators complete appropriate training before conducting research involving human subjects; and further require that the IRB obtain documentation of such training from research investigators as a condition for conducting research involving human subjects. The IRB chair will document receipt and acceptance of such training before IRB approval is granted. At any point during the course of a study, if deemed necessary, the IRB may require that the investigator and/or other research staff obtain additional training. See Guidelines for Investigators also located at this website.

### **X. AUTHORIZATION AGREEMENTS WITH NON-DMHAS INSTITUTIONS**

In certain circumstances the DMHAS OOC IRB may agree to be designated as the IRB of record for another institution (referred to hereafter as Institution B). When this occurs the DMHAS IRB assumes responsibility for the review and continuing oversight of research on behalf of Institution B. This type of agreement is documented by way of an executed Authorization Agreement signed by the signatory officials designated in DMHAS' and Institution B's Federalwide Assurance. The agreement may be limited to a specific research project(s) or may be broader in scope. The Authorization Agreement will specify the scope of the agreement. The DMHAS IRB will report its findings and actions to Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request. Institution B remains responsible for ensuring compliance with the DMHAS IRB's determinations and with the Terms of its OHRP-approved FWA. The Authorization agreement should be kept on file by both parties and will be provided to OHRP upon request.

Conversely, in certain circumstances, the DMHAS OOC IRB may agree to accept the findings of another institution's IRB. In this case DMHAS will be designated as Institution B; the other institution's IRB (referred to hereafter as Institution A) becomes the IRB of record and assumes responsibility for the review and continuing oversight of the research on behalf of DMHAS. The same responsibilities and reporting requirements as outlined above will hold. Also as above, this agreement will be documented by way of an

Authorization Agreement; Institution A will report its findings to DMHAS and DMHAS will ensure compliance with Institution A's findings.

## **XI. EXTENDING DMHAS' FEDERALWIDE ASSURANCE TO A NON-ASSURED INSTITUTION**

Department of Health & Human Services (HHS) regulations require that each institution engaged in HHS-conducted or -supported human subjects research provide written assurance, satisfactory to HHS, that it will comply with the requirements of the HHS regulations for the protection of human subjects, unless the research is exempt under 45 CFR 46.101(b). HHS regulations at 45 CFR 46.103(b) require that each institution engaged in HHS-conducted or -supported human subjects research certify to the HHS funding agency that the research has been approved by an IRB designated in the assurance.

In certain circumstances DMHAS may agree to extend the terms of its Federalwide Assurance to another non-assured institution involved in collaborative research with DMHAS. Generally DMHAS will agree to extend its Federalwide Assurance to another institution if the institution does not have its own Federalwide Assurance owing to the fact that the institution does not routinely conduct human subjects research. DMHAS may also extend its Federalwide Assurance to independent investigators collaborating with DMHAS if the independent investigator is not affiliated with an assured institution. Both institutional and independent investigators must meet the conditions for extending a Federalwide Assurance as outlined by [OHRP in its 1-31-05 Guidance](#).

The extension of DMHAS's Federalwide Assurance is documented by way of an executed Individual Investigator Agreement signed by the non-assured institution designee or independent investigator and the signatory official designated in DMHAS' Federalwide Assurance. The agreement may be limited to specific research projects or may be broader in scope. The Individual Investigator Agreement will specify the scope of the agreement. When DMHAS extends its Federalwide Assurance to another institution or individual the DMHAS OOC IRB becomes the designated IRB of record for the non-assured institution or independent investigator with respect to the research project(s) covered by the Individual Investigator Agreement.

## **XII. IRB REVIEW PROCESS**

Prior to the initiation of any research, proposals must undergo review and receive IRB approval. Following initial approval, the IRB will conduct continuing reviews at least annually and more frequently where deemed necessary. When changes in the protocol or consent form are proposed the investigator must obtain IRB approval prior to implementation.

The following describes the process related to initial review, continuing review and review of proposed changes to approved protocols.

IRB Applications, and where possible all other study materials, should be submitted electronically; followed by a signed hard copy.

## A. Initial Review

The investigator should submit sufficient information about the proposed research in enough detail to enable the IRB to adequately understand and evaluate the proposal in terms of human subject involvement and protection.

The following information should be submitted prior to the initial review:

- DMHAS IRB Application
- Documentation of education in the protection of human subjects for all key personnel

Where applicable the following documents should be included:

- Grant application
- Copies of IRB approvals from other institutions
- Copy of proposed informed consent
- Any form/material that participant will see or be asked to sign such as release of information form, future contact form, consent to audio tape, etc.
- Recruitment materials – any material that prospective participants will see or hear such as, newspaper ads, posters, flyers, television announcements, radio announcements, scripts utilized to guide verbal recruitment, etc.
- Any materials or documents given or administered to participants such as information sheets, diagnostic tools, questionnaires, surveys, etc.
- Other documents as applicable

The chair or designee will review the application and related materials to determine if the proposed research is appropriate for full committee review, expedited review or if the research is exempt from further review.

All IRB members will receive the application and related material outlined above with the exception of the grant application. Where applicable, the Chair or designee will review the grant application to ensure consistency with the IRB application. Where interview or other instruments consist of many pages the chair may choose to omit them from the materials distributed to IRB members. In such cases the chair will review the materials; provide a general description of the materials to the committee; and will also make them available to committee members and at the meeting during which the study will be reviewed.

The IRB may take the following actions at the time of initial review:

- Approve with no modifications being requested
- Approve contingent upon specific modifications being made\*\*
- Defer action pending modifications and/or clarification.
- Disapprove.

\*\*When the IRB stipulates specific and unambiguous changes that require simple concurrence by the investigator and are unlikely to require further review, the members may vote to allow the chair or another designated member to review

the modifications outside of a convened meeting. If the modifications respond to the IRB committee's request and raise no further questions, the approval will be considered effective on the date that the revisions were reviewed. Review and acceptance of the modifications will be reported at the next convened IRB meeting. Where the modifications do not respond to the Committee's request or where further questions arise, the study will be scheduled for further discussion at the next convened IRB meeting.

At the time of initial approval, the IRB must specify the schedule for continuing review (see below for additional information regarding continued review).

The IRB Chair will provide written notification to the investigator, and others as necessary, of approval, the need for revisions or clarification or of disapproval (See below for additional information regarding notification).

In situations where the IRB is requesting revisions, if such revisions are not submitted to the IRB within three months, a reminder letter will be forwarded to the investigator. Following this reminder, if revisions are not received within two months, the IRB study file will be closed and the investigator will be notified. The investigator may re-submit a new study application in the future if they so choose.

## **B. Continuing Review**

Continuing reviews are held in order to ensure that provisions to safeguard research participants continue to be adequate and that any change in risk to participants over the course of the study is identified and adequately responded to and addressed.

Continuing review of research must be conducted at least once annually, but may occur more frequently at the discretion of the IRB. At the time of initial approval, the primary factor to be considered when determining the continuing review schedule is the degree of risk involved. Related factors to be considered may include type of intervention to be utilized; issues related to the target population; or other issues as deemed relevant by the IRB.

The regulations do not allow continuation of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. When research is scheduled for annual review and the IRB conducts continuing review within 30 days before the IRB approval is to expire, the IRB may retain the anniversary date as the date by which the next continuing review must occur. In this way the IRB approval period may remain constant from year to year.

At any point while still an active study under the jurisdiction of the IRB, the committee may modify the schedule for continuing review to become more or less frequent (but never less frequently than annually). A change in review schedule may be based upon changes in the procedures, changes in the level of risk, the occurrence of complaints or injuries related to the research, other adverse incidents, report or discovery of protocol deviations, report or discovery

of unapproved changes in protocol, concern regarding adherence to the approved protocol, or other factors as deemed relevant by the IRB.

The IRB may also request verification from a source other than the investigators that no material changes have occurred in the procedures since the previous IRB approval. A request for such verification may be based upon the occurrence of complaints or injuries related to the research, other adverse incidents, report or discovery of protocol deviations, report or discovery of unapproved changes in protocol, concern regarding adherence to the approved protocol, or other factors as deemed relevant by the IRB.

In relation to the continuing review, the investigator must submit the following information at least one month prior to the expiration of the current IRB approval:

- Application for Continued Approval
- Copy of currently approved OOC IRB protocol that includes any changes that have been approved since the last IRB review

Where applicable:

- Documentation of education in the protection of human subjects for any newly installed key personnel involved in the conduct of the study
- Copy of currently approved consent form
- Any currently approved form/material that participant will see or will be asked to sign (as outlined above under Initial Approval).
- Currently approved recruitment material (as outlined above under Initial Approval)
- Where changes to procedures and/or any study documents is being proposed, copy of proposed revised protocol and/or consent form or other material as appropriate. Proposed changes should be highlighted, underlined or otherwise clearly identified and the revision date should be noted on the materials.
- Clean copies (no highlighting or old approval stamp) to be stamped following approval.
- Other documents as applicable

An expedited review process may be utilized for continuing review of research as outlined in [45 CFR 46.110](#).

Where an expedited review process is not utilized, all IRB members will receive copies of the Application for Continuing Approval, consent forms, recruitment materials, any documents related to proposed changes and any other material relevant to the review process. Where changes are being proposed that would be reflected in the approved protocol the IRB members will receive a copy of the protocol. If there are no changes to the currently approved protocol, the IRB chair will review the protocol and will distribute to IRB members only when in the opinion of the chair it would be helpful for members to re-review the entire protocol.

The investigator will be notified of the approval expiration date and the timeframe for submitting a Continuation Application at the time of initial approval and at least six weeks prior to the approval expiration date. However, it is ultimately the responsibility of the investigator to submit the application in a timely manner. IRB approval cannot be extended without review and approval of the application. In the event that continued approval is not granted by the expiration date, all research related activity must cease until continued approval is granted. The only exception would be when termination of research activity would potentially be harmful to the participants. In such a case the IRB would consider the specific situation and together with the investigator arrive at an appropriate plan of action.

The IRB may take the following actions at the time of the continuation review:

- Approve with no modifications being requested
- Approve contingent upon modifications being made\*\*
- Suspend approval pending receipt of additional information or upon receipt of modifications (see below)
- Terminate approval (see below under Suspension or Termination of IRB Approval).

\*\*When the IRB stipulates specific and unambiguous changes that require simple concurrence by the investigator and are unlikely to require further review, the chair or another designated member may review changes outside of a convened meeting as outlined above under Initial Review.

The IRB Chair will provide written notification to the investigator, and others as necessary, of the IRB action taken (see below for additional information regarding notification).

### **C. Review of Application for Approval of Revision**

IRB approval must be obtained prior to the implementation of any change in the research procedures involving human participants or in the consent form or other study documents. In order to obtain approval for a change in previously approved procedures or study documents the principal investigator must submit an Application for Approval of Revision outlining the proposed change as well as the rationale for the change. Copies of revised procedures, consent form, and/or other revised documents should be included along with the currently approved document in question. Changes should be underlined, highlighted or otherwise clearly identified. Clean copies (no highlighting or old approval stamp) of relevant documents should also be submitted to be stamped following approval.

Requests for changes may be reviewed via an expedited review process as outlined above when the proposed changes are minor and do not represent a material change in the research. The OOC IRB defines minor as: 1) changes that do not adversely alter the overall risk-benefit ratio; 2) changes that would not potentially affect the willingness of current participants to remain in the study, or the willingness of potential participants to enroll in the study; and 3) changes that do not alter the scientific validity of the study.

The IRB Chair will provide written notification to the investigator, and others as necessary, of the IRB action taken (see below for additional information regarding notification). Where applicable, the investigator will be asked to incorporate approved changes into the written protocol.

### **XIII. NOTIFICATION OF IRB ACTION**

The investigator, and others as necessary, will be informed in writing of all actions taken by the IRB.

IRB actions will generally be conveyed via the use of the following notification letters:

#### **A. Notification of Investigators**

##### **1. Notification of IRB Approval and Notification of Continued IRB Approval**

Notification will convey the following information:

- Date of IRB approval
- Date of IRB approval expiration
- Type of review (expedited or full committee)
- When expedited, the qualifying category
- Instructions regarding submission of Application for Continued Approval
- Notification that re-approval must be granted in order for any research activity to continue beyond the approval expiration date
- Notification that no changes to the approved protocol, informed consent or other aspect of the research can be made without prior IRB approval.
- Instruction related to reporting of adverse events.
- Instruction related to reporting of protocol deviations.

##### **2. Notification of IRB Approval Expiration**

This notification will convey the following information:

- Date of IRB approval
- Date of IRB approval expiration
- Date of Continuing Review
- Notification that re-approval must be granted in order for any research activity to continue beyond the approval expiration date
- Date for submission of Application for Continuing Approval.

##### **3. Notification of IRB Approval of Revision to Previously Approved Procedures and/or Study Documents**

This notification will convey the following information:

- Date of approval

- Date of IRB approval expiration
- Type of review (expedited or full committee)
- Description of approved change

#### **4. Notification of IRB Disapproval**

This notification will convey the following information:

- Date of IRB review
- The type of review or request
- The basis for disapproval.

#### **5. Notification of Suspension or Termination of IRB Approval**

This notification will convey the following information:

- Date of the action
- The basis for suspension of approval and, where applicable, changes necessary to reinstate approval; or
- The basis for termination of approval
- Other parties to be notified.

#### **6. Notification of IRB Feedback**

When applicable, this notification will be forwarded to the investigator following IRB review and will be in written form. The information will outline feedback from the IRB review including requested changes to the research protocol and/or related study documents that must be made in order for approval to be considered or granted. When changes are minor and/or few in number the chair or designee may convey the requested changes to the investigator verbally. Regardless of how the requested changes are communicated to the investigator, they will also be documented in the IRB minutes.

### **B. Notification of State-operated Facilities**

Where recruitment or study interventions occur at a state-operated facility the following information will be forwarded to the respective facility:

- Notification of Initial IRB approval.
- A copy of the approved IRB Application, informed consent document, and any recruitment material that will be utilized at the facility.
- Notification of Continuing Approval. No additional materials will be forwarded unless changes have been approved in the procedures that are relevant to the state operated facility.
- Notification of study closure or notification that recruitment and/or all research activity has ended at the facility.
- Notification of expiration of approval.
- Notification of suspension or termination of IRB approval.

### **C. Notification of Institutions Engaged in an Authorization Agreement with DMHAS**

Where DMHAS has an Authorization Agreement with another institution, whereby DMHAS conducts review and oversight of the other institution's research, DMHAS will forward the following information to such institution:

- Notification of Initial IRB approval
- Notification of Continuing Approval
- Notification of study closure
- Notification of expiration of approval
- Notification of suspension or termination of IRB approval.

### **D. Notification of Institutional or Independent Investigators Covered by DMHAS' Federalwide Assurance**

Where DMHAS has extended its Federalwide Assurance to an Institutional or Independent Investigator, DMHAS will forward the following information to the institution or individual:

- Notification of Initial IRB approval
- Notification of Continuing Approval
- Notification of study closure
- Notification of expiration of approval
- Notification of suspension or termination of IRB approval.

## **XIV. REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO RESEARCH PARTICIPANTS AND OTHERS**

Federal Regulations require that unanticipated problems involving risks to research participants or others be promptly reported to the IRB (CFR 46.103 (b)(5)) Unanticipated problems involving risk may involve any aspect of a research study and may involve either research participants, research staff or others not directly related to conduct of the research.

There is a range of events that could potentially be classified as unanticipated problems involving risk to participants or others. Depending on their nature, the following events might be assessed as an unanticipated problem:

- Adverse event related to the conduct of the research
- Protocol deviation
- Complaint regarding conduct of the study
- Interim results
- Negative consequence to research staff or others

Other events not noted above could also represent unanticipated risk. The point to keep in mind is that regardless of how information comes to light, any unintended or

unanticipated event related to the conduct of the research should be evaluated by the principal investigator to determine if the event represents unanticipated risk to participants or others. If the answer is yes, the event should be reported to the IRB.

## **XV. REPORTING ADVERSE EVENTS**

The IRB Committee requires that the investigator report any adverse event, occurring after the most recent approval, related to the conduct of the research with human participants.

An anticipated adverse event is defined as an experience or reaction related to the conduct of the research that is identified or outlined in the research procedure and the informed consent form. Anticipated adverse events will be reported at the time of the continuing review.

An unanticipated adverse event is defined as an experience or reaction related to the conduct of the research that is not identified or outlined in the research procedure and the informed consent form, including a change in the nature, severity or frequency of the experience or reaction from what was outlined in the research procedure; and/or any unanticipated problem associated with the conduct of the research related to the level of risk to the participants. The investigator will report unanticipated adverse events in writing to the IRB within 7 business days of occurrence.

Serious adverse events include, but are not limited to those that result in death; are life threatening or potentially life-threatening; result in disability; result in hospitalization or other significant and unanticipated treatment; or other events deemed to be serious by the investigator. The investigator will report serious adverse events within 3 days. If reported by phone a written report must follow within 5 business days.

The written report will be made using the Report of Adverse Event form.

The Chair or designee will review all reports of unanticipated and serious adverse events and notify the full IRB as deemed appropriate. Depending upon the nature of the adverse event, the Chair may report and schedule discussion of the adverse event at the next regularly scheduled IRB meeting or may convene a more immediate meeting to review the event in terms of the risks to participants.

Depending upon the severity or nature of the adverse event, the IRB may decide to reconsider approval of the research project; require modifications to the procedures and/or the informed consent form; and/or revise the schedule of continuing review.

## **XVI. REPORTING OF PROTOCOL DEVIATIONS**

A protocol deviation is defined as a change in the protocol that has not been reviewed and approved by the IRB.

As noted above, IRB approval must be obtained prior to the implementation of any proposed change in the research procedures involving human participants or in the consent form. However, there may be instances where deviations from the protocol are

made either intentionally to meet the immediate needs of an individual participant or situation or unintentionally in error. In either case, the protocol deviation should be reported to the IRB if the deviation is deemed as having the potential to increase the risk to the participant. If the deviation represents minimal potential for increased risk it should be reported at the time of the continued review. If the deviation represents more than minimal potential for increased risk it should be reported to the IRB within 10 business days.

The written report will be made using the Report of Protocol Deviation form.

## **XVII. REPORTING OF STUDY RELATED COMPLAINTS**

The IRB Committee requires that the Principal Investigator report complaints made by participants or others regarding conduct of the study.

A complaint is defined as a formal expression of dissatisfaction or an allegation of wrongdoing, related to the conduct of research, made by a research participant or other(s). A complaint may be expressed verbally or in writing and may be directed to the principal investigator, research staff, or other contact people noted on the consent form or other study materials. Complaints may also be directed to the IRB.

When the principal investigator reports a complaint it should be made using the Report of Study Related Complaint. When someone other than the principal investigator reports a complaint to the IRB, there is no specific format required.

If a complaint is prompted by an event that is assessed as a reportable adverse event or a reportable protocol deviation, the following reporting procedures should be followed:

- Guidelines related to reporting either an adverse event or a protocol deviation should be followed
- The applicable reporting form should be utilized
- The report should note that a complaint has been made in relation to the event
- At the time of the continuing review the event should be reported as both a complaint and an adverse event or protocol deviation as applicable.

If a complaint is not associated with an adverse event or a protocol deviation, but suggests actual or possible unanticipated risk, it should be reported to the IRB within 10 business days.

## **XVIII. OTHER REPORTABLE UNANTICIPATED PROBLEMS**

Unanticipated problems involving risks to participants or others not covered above may also occur and should also be reported to the IRB with 10 business days.

**General note regarding required reporting:** As noted, categories of reportable events may overlap. What is important is not so much which category of report is used, but rather, that events or circumstances suggesting unanticipated risk or problems are

identified, responded to appropriately and reported to the IRB. The IRB chair may be contacted for consultation.

### **XIX. REPORTING UNANTICIPATED PROBLEMS TO INSTITUTIONAL OFFICIALS AND OTHERS**

In evaluating unanticipated problems, the IRB may find the need to notify institutional officials as well as the funding agency, OHRP and/or the FDA as appropriate. In the event that the IRB determines the need to report an unanticipated problem to any of the above parties, the time frame for reporting will be specified by the IRB.

### **XX.FINAL REPORT UPON COMPLETION OF RESEARCH**

The investigator will forward a final report to the IRB upon completion of the research project. The research is considered completed when the following occurs:

- No additional participants are being enrolled and,
- All intervention with human participants has ended and,
- Data analysis is complete and/or all identifiable data has been de-identified and,
- All other research related activity has ended.

The investigator will use the Application for Continued Approval/Final Report form.

### **XXI. INVESTIGATOR NON-COMPLIANCE**

The IRB requires that all research be conducted in compliance with DHHS regulations for the protection of human subjects, with FDA regulations when applicable, and with IRB requirements or determinations.

Non-compliance with federal regulations and/or IRB determinations may come to the attention of the IRB in a variety of ways including, but not limited to, the principal investigator, research staff, study participants, others, or through IRB audit or ongoing review. It is up to the IRB to determine whether the information reported or obtained constitutes a protocol deviation or an instance of non-compliance and in the latter case whether the non-compliance should be categorized as serious or continuing.

In circumstances where the IRB chair becomes aware of possible non-compliance they will evaluate the information at hand and make a preliminary determination as to how the information or event should be categorized. Depending upon the nature of the event the chair may either report the event to the full committee at the next regularly scheduled meeting or convene a more immediate meeting to review the event in terms of potential risk to participants and potential needed action. The final designation of an event as either serious or continuing non-compliance, as well as the action required, will be determined at a convened IRB meeting.

### **XXII. SUSPENSION OR TERMINATION OF IRB APPROVAL**

Suspension or termination of approval may occur in connection with a Continuing Review, but may occur at any time that the IRB deems such action is appropriate and necessary. Suspension or termination of approval will generally be based upon the concern or conclusion that the research is not being conducted in accordance with the IRB's requirements, and/or that the risk/benefit ratio is no longer acceptable. Related factors that may contribute to suspension or termination are the occurrence of complaints or injuries related to the research, other adverse incidents, or other factors as deemed relevant by the IRB.

If a suspension or termination of approval occurs while there are still active participants, the IRB will require that the investigator develop a plan to inform participants, to discontinue intervention and where appropriate, to refer to alternate services.

In the event of suspension or termination of approval the IRB Chair will provide written notification to the investigator including the basis for the action. The chair will also notify the DMHAS Commissioner, Signatory Official, Research Director and the site(s) where the research is being conducted. The chair will also notify the appropriate agency when the research is federally funded, as well as OHRP and the FDA as appropriate.

Questions related to these guidelines may be directed to the OOC IRB Chair at any time.