

INSTITUTIONAL REVIEW BOARD GUIDELINES FOR INVESTIGATORS

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OOO IRB GUIDELINES FOR INVESTIGATORS

1) INTRODUCTION

The Office of the Commissioner - Institutional Review Board is constituted in order to protect the rights and welfare of human research subjects participating in DMHAS sponsored or approved research. The OOC IRB operates in compliance with federal regulations regarding the protection of human subjects. 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. While the terms of DMHAS' FWA have not been extended to non-federally conducted or supported research with humans, when reviewing such research, the DMHAS IRB will generally apply the regulations and DMHAS IRB standards in the same manner as with federally funded research.

The OOC IRB reviews research involving human subjects conducted in state operated facilities - including research sponsored by DMHAS and research sponsored by non-DMHAS institutions.

Investigators who are not affiliated with DMHAS or are not under contract by DMHAS to conduct research or who have not otherwise obtained OOC endorsement of their research who wish to recruit participants or conduct study interventions at DMHAS operated facilities must seek approval through a multi-stage process. This process is initiated by submitting a research proposal to the state-operated facility(ies) where the proposed research activity will occur. If following review the proposed research is endorsed at the facility level the facility head will forward a letter of endorsement to the DMHAS Research Director and the investigator will submit an IRB Application to the DMHAS IRB. Upon 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 DMHAS 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. Research conducted by student employees of DMHAS whose research is related to educational requirements is considered to be non-DMHAS sponsored. Please also see "Study Proposals Originating Outside Of DMHAS for Research Involving DMHAS Facilities And/Or Clients"

The guidelines below refer specifically to the IRB process.

2) TYPES OF IRB REVIEW

a) Exempt Review

The IRB may, after initial review, find some research to be exempt from further IRB review. Unless otherwise required by the Department, research that meets the criteria as outlined in [45 CFR 46.101\(b\)](#) will 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 will cite the qualifying section of the regulation as part of the application process. The determination of eligibility for exemption will then be made by either the IRB chair or by the full IRB committee.

Once found to be exempt, no further IRB review will be conducted unless a change in procedures is planned. If changes are proposed following the initial determination the investigator must submit the proposed changes to the IRB prior to implementation of any changes

b) Expedited Review

Expedited review is a review conducted outside of a convened IRB meeting.

Expedited reviews are generally conducted by the chair but may be conducted by one or more experienced designated IRB members.

The criterion for expedited review is outlined in [45 CFR 46.110](#).

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 – unless the study is exempt. However, if a study is eligible for expedited review, the chair may use their discretion in either conducting an expedited review or in scheduling the study for full committee review.

c) Full Committee Review

Full committee review consists of a convened meeting with a majority of members present including a member whose primary interest is in the non-scientific area. Where a study involving prisoner participation is being reviewed a prisoner representative must be present at the convened meeting.

3) 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](#):

- 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 \(a\)](#). Unless the IRB has granted a waiver under [45 CFR 46.116\(c\)](#) the investigator 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 as outlined below; or, where non-English speaking participants are involved, by a short form written consent as outlined under [45 CFR 46.117 \(b\) \(2\)](#) -. See "Obtaining and Documenting Informed Consent of Participants Who Do Not Speak English" below.

- 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.

c) Obtaining and Documenting Informed Consent of Participants Who Do Not Speak English

Regulations require that informed consent information be presented in language understandable to the study participant and, unless waived by the IRB, that informed consent be documented in writing.

Where non-English speaking study participants are involved and where documentation of consent has not been waived, one of the following procedures must be followed:

- i) The English informed consent form is translated in its entirety; and a translator fluent in both English and the study participant's spoken language will be available to assist in or conduct the consent process; or alternatively,
- ii) [A "short form" procedure](#) may be utilized and should include all of the following elements:
 - (1) All of the information contained in the English consent form will be presented orally by a translator fluent in both English and the study participant's language.
 - (2) A short form document will be presented to the study participant. The short form summary will be in a language understandable to the participant. The short form document should be signed by the participant or his/her legally authorized representative; and by a witness. A translator may serve as the witness.
 - (3) A written summary of what was presented orally will also be presented to the participant. The English version consent form may serve as this summary. The summary should be signed by the individual authorized to

- obtain consent; and by a witness. A translator may serve as the witness.
- (4) The study participant will be given a copy of the short document and the summary.

Additional guidance regarding the informed consent process can be found in ["Tips on Informed Consent"](#) from the OHRP website.

d) Waiver or Alteration of Requirements Related to Informed Consent

Regulations allow for waiver of some or all of the requirements related to obtaining informed consent from research participants. Criteria for waiving or altering elements of the requirement to obtain informed consent can be found at [46.116 \(c\) and \(d\)](#) (this refers to a situation where the investigator may not inform the participants of their study involvement). Criteria for waiving the requirement to document informed consent can be found at [46.117 \(c\)](#) (this refers to a situation where the investigator must obtain verbal consent but is not required to have the participants sign a consent form).

If the investigator wishes to request a waiver of any informed consent requirement they should also complete, at the time of the initial application, the [Application for Waiver of Informed Consent Requirements](#). The IRB chair and/or full committee will evaluate the waiver request within the limits of the applicable regulations.

Administration and documentation of informed consent should be considered the norm. Even where a waiver may be technically allowed the IRB may require that an informed consent be conducted unless adequate justification for a waiver is presented.

Please also see "Waiver of HIPAA Authorization" below

e) Requirements Related to the HIPAA Privacy Rule

The Standards for Privacy of Individually Identifiable Health Information ("Privacy Rule") was issued by the Dept of Health and Human Services as part of the Health Insurance Portability and Accountability Act (HIPAA). The Privacy Rule establishes conditions under which certain groups and organizations covered by the rule can use or disclose protected health information. Protected health information is individually identifiable health information, created or received by a health care provider, health plan, employer or health clearinghouse that relates to the past, present or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present or future payment for provision of care to an individual. The Privacy Rule is codified at [45 CFR Parts 160 and 164](#) and lists data elements that are considered individually identifying at [164.514 \(b\)\(2\)\(i\)](#)

f) Requirements Related to HIPAA Authorization

The Privacy Rule requires that individuals provide specific written authorization for others to use or disclose their protected health information. This Authorization requirement applies to research participants unless an IRB or privacy board has approved a waiver of the Authorization requirement. [Section 164.508](#) of the privacy rule outlines the elements that must be contained or addressed in a valid

authorization that is in compliance with the privacy rule.

HIPAA Authorization relates specifically and is limited to the use and disclosure of protected health information. HIPAA Authorization is distinct from an Informed Consent Form. A HIPAA Authorization is used to gain permission to use or disclose protected health information as part of a study; it is not used to gain consent for overall participation in a research study. Conversely, the informed consent form and process is used to obtain consent for overall participation in a study, which depending upon the study design, may or may not include permission to use or disclose private information.

The term “HIPAA Authorization” refers to the elements that must be contained in an authorization that is in compliance with the privacy rule. These elements do not necessarily have to be contained in a specific or separate document. The Privacy Rule allows authorization for the use or disclosure of protected health information for a research study to be combined with any other type of written permission for the same research study, such as an informed consent form. However, in general, where protected health information will be used or disclosed as part of the research, the use of a release of information form, in addition to the consent form, is suggested. Whether the release is referred to as a “Release of Information” or as a “HIPAA Authorization” will be determined by the investigator. The Privacy Rule does not require an IRB or privacy board to review the HIPAA Authorization covering the use of protected health information. However, the OOC IRB will generally review such Authorizations as part of the overall review and approval process to determine if the use or disclosure of protected health information is adequately explained to prospective study participants. The Privacy Rule does require that an IRB or privacy board review and approve requests for waiver of the HIPAA Authorization requirement (see below).

g) Requirements Related to Waiver of HIPAA Authorization

The Privacy Rule allows for waiver of the requirement to obtain authorization for use or disclosure of protected health information for research purposes provided that the research meets the criteria for waiver. The criterion for waiver of authorization is found at [164.512](#).

Generally, when a waiver of the HIPAA authorization is requested, a waiver of the requirements related to obtaining informed consent will also be requested. The IRB will review these requests to determine that the criteria for waiver have been met in accordance with both the HIPAA Privacy Rule and DHHS regulations –“Protection of Human Subjects”.

If an investigator wishes to request a waiver of the HIPAA Authorization requirement, they should also complete, at the time of the initial application, the [Application for Waiver of HIPAA Authorization Requirement](#).

h) 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.

i) Requirements Related to Participation of Prisoners

The provisions of [Subpart C](#) are found at 46.301 through 46.306 and apply to any research where incarcerated individuals are enrolled as participants. This applies even where individuals become incarcerated subsequent to their initial enrollment in a study. If a research participant becomes incarcerated following their initial enrollment no research intervention may occur in the prison setting unless and until the IRB has reviewed and approved the inclusion of prisoners. Approval for inclusion of prisoners can be requested at the time of initial IRB review or subsequent to initial review and approval. Investigators may wish to consider prospective approval of prisoner involvement when the study's target population is at high risk of incarceration and where the study design calls for follow-up interviews.

In addition to reviewing these regulations investigators may wish to review the OOC IRB [Check list for Prisoner Participation](#) elsewhere at the DMHAS IRB website. This checklist is a tool used by IRB members when reviewing research involving prisoners and lists the special findings that must be made in relation to prisoner participation.

The types of studies involving prisoners reviewed by the DMHAS IRB generally, but not always, include participants who have become incarcerated subsequent to their initial enrollment. In considering the enrollment of incarcerated participants the investigator should consider the following issues in addition to the requirements of subpart C:

- The impact of incarceration upon the procedures – will procedures need to be modified for incarcerated participants? For example, some survey items may not be applicable for an incarcerated participant
- Similarly, does incarceration impact the level of risk and is the risk impacted in such a way as to require modifications in procedures. For example, access to a mental health professional or other helping person cannot generally be guaranteed within the prison setting unless clear danger to self is evidenced. Therefore survey questions that have potential for evoking significant emotional distress or upset, such as questions related to trauma history, would likely need to be omitted in a prison setting.
- Will compensation for participation need to be handled differently for an incarcerated participant? Generally, incarcerated participants cannot receive compensation until their release. Therefore participants will need to be informed of this and alternate arrangements will need to be made.
- How will the incarcerated participant contact the investigator or other individual with questions about the study, or with complaints or questions about their rights as a research participant? Often, incarcerated individuals encounter obstacles in gaining access to a phone during the day. Providing incarcerated participants with a self-addressed stamped envelope is one alternative method of ensuring a means to contact the investigator or other designated contact person.
- Where a study involves both incarcerated and non-incarcerated individuals two

- separate consent forms must be utilized.
- The investigator will need to coordinate with the correctional facility(s) in order to gain access to participants and to accommodate procedures to the prison setting.

j) Requirements Related to Participation of Children

The provisions of [Subpart D](#) are found at 46.401 through 46.409 and apply to any research where children are enrolled as participants. In addition to reviewing these regulations it may be helpful to review the OOC IRB [Check list for Child Participation](#) elsewhere at the DMHAS IRB website. This checklist is a tool used by IRB members when reviewing research involving children and lists the special findings that must be made in relation to children's participation.

k) 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 recommends 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.

Additional information regarding confidentiality certificates, including the application process may be found at the NIH Office of Extramural Research.

l) Requirements Related To Education Of Key Research Personnel In Protection Of Human Subjects.

Federal guidelines require that investigators and all other key personnel complete appropriate training before conducting research involving human subjects; and further require that the IRB obtain documentation of such training from investigators as a condition for conducting research involving human subjects. Key personnel include those individuals who have responsibilities and activities in the following areas: design of the research; oversight responsibility for the research; contact with

study participants such as those conducting screening interviews; arranging appointments; administering informed consent, interviewing or intervening with the participant; have access to identifying data; and other activities as deemed applicable. Individuals may be considered key personnel regardless of whether their contact with the study participant is face to face or by telephone.

The intent of this requirement is to ensure that all key personnel involved in the conduct of research are knowledgeable as to the philosophy and key concepts underlying the Federal regulations as well as the specific regulations governing the conduct of research and protection of human subjects. The IRB must receive documentation of completed education before any research activity is initiated.

Although there is not a list of accepted educational programs or activities, information regarding educational resources can be found at the web site of the [Office for Human Research Protections \(OHRP\)](#).

One training resource that has been commonly used, and is acceptable to the DMHAS IRB, is the computer-based training developed by the [National Institutes of Health](#).

Key personnel often join a study following the initial or continuing review. The Principal Investigator should ensure that new personnel receive education in the protection of human subjects before they become involved in any research activity. The addition of new key personnel should be reported at the time of the next scheduled continuing review and documentation of completion of education should be provided at that time as well.

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.

4) STUDY PROPOSALS ORIGINATING OUTSIDE OF DMHAS FOR RESEARCH INVOLVING DMHAS FACILITIES AND/OR CLIENTS

These types of study proposals include university, hospital or other organization-based researchers recruiting study participants at DMHAS facilities for participation in research projects. Also included in this category of study proposals are graduate students or other individuals requesting the cooperation of DMHAS in recruiting study participants for research projects.

The following procedures are to be followed for such applications. (Because CMHC is jointly operated by both DMHAS and Yale University, proposals for research to be conducted at CMHC are exempted from these procedures unless the research will also be conducted at another DMHAS facility.)

- a) A detailed written proposal of the research project must be provided to the head of the DMHAS facility(ies) proposed as a study site(s). The proposal may be submitted using the [DMHAS IRB Application](#), but use of the application is not required at this point in the approval process. Documentation that the proposed research has been approved by the applicant's human subject protection committee should also be submitted with the proposal. If the proposed research protocol includes obtaining access to confidential information, then the

application must clearly indicate who will have access to such information in sufficient detail for a reader to be able to assess whether the request falls within state statutes and complies with HIPAA regulations.

- b) The head of the facility(ies) must consider the burden to DMHAS of participating in the research (e.g. amount of staff hours, days of client care, or other DMHAS resources to be devoted to the proposed project over-and-above what would be used in the absence of the proposed research, as well as any resources to be gained by DMHAS in exchange for participating in the proposed research). Therefore, the Principal Investigator should provide information to the head of the facility(ies) about expectations of the facility(ies). The facility heads will take the findings of this review into account when deciding whether to endorse the research proposal.
- c) If the facility is part of a Local Mental Health Authority, the Director of the LMHA must also indicate his/her endorsement of the proposal
- d) Once a proposal has received the above-mentioned endorsement(s) the facility or LMHA Director should forward a letter of endorsement to the DMHAS Research Director. In addition, the investigator must now submit an IRB Application to the DMHAS IRB.(provide link here). Upon receipt of both the letter of endorsement and the IRB Application, the DMHAS Research Director will initiate the Commissioner's review process. This process involves a review of scientific merit, a review of Administrative requirements upon DMHAS and a review of human subject protections. Final approval by the Commissioner will be based upon a favorable assessment related to scientific merit, administrative impact, benefit of research to DMHAS, and IRB approval.
- e) The Commissioner or his designee will notify the relevant parties as to the Commissioner's decision. Such approval must be received prior to participation by DMHAS in any such research projects.

5) IRB REVIEW PROCESS AND SUBMISSION OF APPLICATIONS

GENERAL NOTE: Applications and, where possible, all other related study materials should be submitted electronically and followed by hard copies. Translated non-English study documents should be submitted at the same time as other study documents.

a) Initial Review and Approval

i) Review Process

As noted previously, the full IRB committee reviews most initial applications.

Unless an expedited review is conducted, the Principal Investigator is invited to attend the IRB meeting, either by phone or in person, and will be contacted to confirm the date and time of the meeting.

When deemed necessary to enable adequate review of a proposal, the IRB may also invite individuals with expertise and knowledge in specialized areas for the purpose of providing consultation and opinion regarding a proposal.

At the time of the initial review the following actions may be taken:

- Approve with no modifications being requested
- Approve contingent upon specific modifications being made (see note at end of section)
- Defer action pending modifications and/or clarification.
- Disapprove.

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.

At the time a research proposal is approved, the IRB will specify a schedule for continuing review. Continuing review must occur at least annually; however, reviews may be scheduled at more frequent intervals at the discretion of the IRB. 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 study intervention to be utilized; specific issues related to the target population; or other issues as deemed relevant by the IRB.

ii) Submission of Application

One (1) copy of the following materials should be submitted to the IRB on the first of the month during which the study is expected to be reviewed.

- Grant Application
- Documentation of education in the protection of human subjects for all key personnel involved in the conduct of the study
- Application for IRB Approval
- Application should be completed electronically on your PC
- Application materials should be submitted electronically but should also be followed by hard copy signed by principal investigator
- All sections of the application must be completed
- Sufficient information about the proposed research should be submitted in enough detail to enable the IRB to adequately understand and evaluate the proposal in terms of human subject protection.
- Where applicable, IRB approval notification letters from other institutions
- Consent Form(s)
- Any other form/material that participant will see or be asked to sign such as release of information forms, future contact form, consent to audio tape, etc.
- Recruitment materials – any material that prospective participants will see or hear such as newspaper, posters, flyers, radio, television 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.
- Version dates should be noted on study documents..

b) Continuing Review and Approval

i) Review Process

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.

Research related activities can not continue beyond the expiration date without continued approval.

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

The Principal Investigator will be notified of the pending approval expiration date, the continuing review date and the due date for the submission of the Application for Continued Approval.

This reminder notice will be forwarded approximately six to eight weeks prior to the scheduled review date.

While notification of the approval expiration date is forwarded by the IRB, it is ultimately the responsibility of the principal investigator to submit the Application for Continued Approval in a timely manner.

At the time of the continuing review the following actions may be taken:

- Approve with no modifications being requested
- Approve contingent upon specific modifications being made (see note at end of section)
- Defer action pending modifications and/or clarification.
- Disapprove.

Continuing reviews will be held until the research project is completed. See below under Final Report.

ii) Submission of Application

The following materials should be submitted to the IRB by the 1st of the month in which the continuing review will occur:

- Documentation of education in the protection of human subjects for any newly installed key personnel involved in the conduct of the study
- Application for Continuing Approval
- Application should be completed electronically on your PC
- Application should be submitted electronically but should also be followed by hard copy signed by principal investigator
- All sections of the application must be completed
- Currently approved OOC IRB protocol that includes any changes that have been approved since the last IRB review
- Currently approved consent form
- Any other 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. Please highlight, underline or otherwise clearly identify proposed changes and note revision date on materials.
- Clean copies (no highlighting or old approval stamp) to be stamped following approval.

c) Review and Approval of Revisions to Previously Approved Procedures and/or Study Documents

i) Review Process

IRB approval must be obtained prior to the implementation of any change in the research procedures or in study documents such as the consent form, release of information form, script to be used by research staff, recruitment material, survey, questionnaire or other instrument utilized in the study, etc.

In order to obtain approval for a change the Principal Investigator must submit a written request outlining the proposed change as well as the rationale for the change.

The chair will screen the request to determine if a full committee review is required or if the request is eligible for an expedited review.

Expedited review is permissible if the changes are minor and do not represent a material change in the research.

Changes are considered to be minor if they meet the following criteria:

- Changes that do not adversely alter the overall risk-benefit ratio;
- 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;
- Changes that do not alter the scientific validity of the study.

ii) Submission of Application

One (1) copy of the following materials should be submitted to the IRB when any changes are being proposed:

- Application for Approval of Revision
- Application should be submitted electronically but should also be followed by hard copy signed by principal investigator
- Where applicable, copy of the initial Application for IRB Approval with the proposed changes clearly highlighted, underlined or otherwise clearly identified.
- Where applicable, copies of the proposed consent form, and/or other relevant documents should be included with the request. The proposed changes should be clearly highlighted, underlined or otherwise clearly identified and a revision date should be noted on the materials.
- Clean copies (no highlighting or old approval stamp) of relevant documents to be stamped following approval.

General Notes Relating to Initial and Continuing Reviews and Review of Changes

If the IRB requests revisions in order for approval to be granted, the chair will provide feedback to the investigator outlining the requested changes. This feedback will generally be in writing but may be verbal where needed revisions are very minor and limited in number.

Where a full committee review has been conducted, and where the IRB stipulates specific and unambiguous changes that require simple concurrence by the investigator and are unlikely to require further review, the IRB members may vote to allow the chair 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 may be granted. The investigator will be notified in writing by the chair of the effective approval date. 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.

6) REVIEW BY MULTIPLE IRBs

Investigators often must seek approval not only from the DMHAS IRB but from other IRBs as well, such as when the investigator is affiliated with a non-DMHAS institution or where there are multiple study sites. At times different IRBs will reach different findings and requirements related to study procedures and documents. When more than one IRB is involved the investigator must ensure that the study protocol and study documents reviewed by DMHAS and other IRBs are consistent with one another before research activity is initiated. Alternatively, it is acceptable to the DMHAS IRB for the investigator to use DMHAS IRB approved consent and other study materials for participants recruited from DMHAS SO facilities and to use slightly modified versions for study participants recruited elsewhere, so long as these modified versions convey substantially the same information and so long as they have been approved by an IRB. Any proposed change to DMHAS IRB approved procedures or study materials, whether proposed by the investigator or requested by another IRB, must be submitted to the DMHAS IRB for review and approval prior to

the implementation of any change.

7) NOTIFICATION OF IRB ACTION

a) Notification to Investigators

The investigator will be notified in writing of any IRB action regarding their study.

Notification will generally be forwarded within five (5) business days of action.

Notification of IRB approval will include the date of approval, approval expiration date, any special provisions related to the approval such as any waiver or alteration of consent requirements, approval for participation of vulnerable populations, special requirements, etc.

If a study is disapproved, the written notification will note the rationale for the action.

b) Notification to State-Operated Facilities

Where recruitment or study interventions are to occur at a state-operated facility the following information will be forwarded by the IRB 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 will also be forwarded with the notice of initial approval.
- 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 or study intervention has ended at the facility.
- Notification of expiration of approval.
- Notification of suspension or termination of IRB approval.

8) REPORTING UNANTICIPATED PROBLEMS INVOLVING RISKS TO PARTICIPANTS

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 (all adverse events are reportable – see #7 below)

- Protocol deviation (see #8 below)
- Complaint regarding conduct of the study (see #9 below)
- Interim results (see #10 below)
- Negative consequence to research staff or others (see #10 below)

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.

Numbers 7 through 10 below provide some guidance related to IRB reporting requirements.

9) REPORTING OF ADVERSE EVENTS

The IRB Committee requires that the Principal Investigator report any adverse event related to the conduct of the research with human participants. Following receipt of the report, and depending upon the nature of the adverse event, the Chair may either report the adverse event to the full committee at the next regularly scheduled IRB meeting; or convene a more immediate meeting to review the event in terms of the entire study, the risks to participants and the need for intervention.

a) Anticipated Adverse Event

i) Definition and Reporting Requirements

An anticipated adverse event (see note below) 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 should be tracked on an ongoing basis and reported at the time of the continuing review in the Application for Continued Review.

ii) Examples

Administration of trauma questionnaire where discomfort or emotional upset is identified as a possible risk: Evidence of mild to moderate upset in reaction to the overall questionnaire with no extended debriefing required

Study utilizing medication where side effects have been identified as a possible risk: The occurrence of side effects at the same rate as that found in the general population.

b) Unanticipated Adverse Event

i) Definition and Reporting Requirements

An unanticipated adverse event (see note below) 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; and/or any unanticipated problem associated with the conduct of the research related to the level of risk to the participants. The Principal Investigator will report unanticipated adverse events to the IRB within 7 business days of occurrence using the Adverse Event Report.

ii) Examples

Administration of trauma questionnaire where discomfort or emotional upset is identified as a possible risk: The occurrence of anxiety/depression following a research interview, where the participant felt the need to stay home from work the next day, but did not experience any lasting emotional or work problems and did not require a change in treatment.

Study utilizing medication where side effects have been identified as a possible risk: The occurrence of medication side effects at a substantially higher rate than predicted; or the occurrence of a medication side effect not previously identified.

c) Serious Adverse Event

i) Definition and Reporting Requirements

Serious adverse events (see note below) 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 Principal Investigator will report serious adverse events in writing or by phone to the IRB within 3 calendar days of the investigator learning of event. If reported by phone, a written report, using the Adverse Event Report, must follow within 5 business days.

ii) Examples

Administration of trauma questionnaire where discomfort or emotional upset is identified as a possible risk: A reaction of distress sufficient to warrant a change in treatment plan such as increased visits or hospitalization.

Study utilizing medication where side effects have been identified as a possible risk: medication reaction requiring hospitalization; or a hospitalization that might be attributed to the medication.

iii) Other Examples

A breach of confidentiality would be reportable as an unanticipated or a serious adverse event depending on the impact upon the participant(s).

An unintended deviation from the protocol might be reported as an unanticipated or serious adverse event depending on the specific circumstances and the impact upon the participants (see below for more information regarding protocol deviations).

Note regarding adverse events: At times, the differentiation between an anticipated and unanticipated adverse event will be based primarily upon the intensity or frequency of the participants' reaction. The examples provided are intended to provide guidance in determining reporting categories and how reporting should be approached. The principal investigator will need to use their best judgement, keeping in mind their need to identify any factors that alter the risk/benefit ratio, that point to the need to revise the informed consent, or to alter the study design and/or the need to provide additional information to participants. If questions arise related to the reporting of a specific event, the IRB Chair may be contacted for consultation.

10) REPORTING OF PROTOCOL DEVIATIONS

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 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.

a. Definition and Reporting Requirements

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

If the deviation does not represent any potential for increased risk a report is not required. 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 report should be made using the Report of Protocol Deviation.

b. Examples

The following examples are intended to provide guidance in reporting protocol deviations. As with reporting of adverse events, the examples provided are intended to illustrate how reporting should be approached. In some cases a deviation may be reportable as an adverse event depending upon the impact upon the participant. The principal investigator will need to use their best judgement, again keeping in mind their need to identify any factors that alter the risk/benefit ratio, that point to the need to revise the informed consent, or to alter the study design. As noted above, the IRB Chair may be contacted for consultation.

(i) Deviation with no increase in risk to participant- report is not required.

In a behavioral health program evaluation study the protocol specifies that participants will be interviewed six weeks after completion of the program.

Deviation: some of the participants are not interviewed until 9 weeks following completion of the program.

(ii) Deviation with minimal potential to increase risk to participant - report is required at time of continuing review.

In a behavioral health program evaluation study the inclusion criteria includes consent by the participant's conservator.

Deviation: a participant is enrolled in the study without the conservator's consent. The error is detected within days and permission of the conservator is then obtained.

(iii) Deviation with more than minimal potential to increase the risk to participant - report is required within 10 days of occurrence.

In a behavioral health program evaluation study the consent form notes that certain individuals associated with the participant will be interviewed.

Deviation: individuals other than those noted on the consent are interviewed in error.

In a behavioral health program evaluation study activities related to the study are conducted after the consent period has lapsed.

In a study utilizing medication the protocol calls for weekly blood tests to detect the occurrence of side effects.

Deviation: a participant's blood test is skipped for one or more weeks.

11) REPORTING STUDY RELATED COMPLAINTS

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

a. Definition and Reporting Requirements

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.

b. Examples

The following examples are intended to provide guidance in reporting complaints. The examples provided are intended to illustrate how reporting should be approached. In some cases a complaint may be reportable as an adverse event or a protocol deviation depending upon the nature of the event that prompts the complaint. The principal investigator will need to use their best judgment, keeping in mind their need to identify any factors that alter the risk/benefit ratio, that point to the need to revise the informed consent, or to alter the study design, or to alter other aspects of the research project such as study procedures or training. The IRB Chair may be contacted for consultation.

i. Complaint is prompted by an event that is assessed as a reportable adverse event or a reportable protocol deviation – reporting guidelines for adverse event or protocol deviation should be followed

Study participant complains that when attempting to contact the participant by phone, a research staff revealed to a family member that the participant was in a program evaluation of a substance abuse program. Note: this would be reported as either an adverse event or a protocol deviation depending upon the judgment of the principal investigator.

ii. Complaint is not prompted by an adverse event or obvious protocol deviation, but suggests actual or possible unanticipated risk – report is required within 10 business days

Study participant contacts principal investigator following a research interview stating that they were unprepared for and angry about the personal nature of the interview questions. Study participant does not report any ill effects as a result of the interview. Note: More than one such complaint might suggest protocol deviation.

12) OTHER EXAMPLES OF REPORTABLE UNANTICIPATED PROBLEMS INVOLVING RISKS

- i. **Interim study results:** Where interim results reveal unanticipated risk they should be reported to the IRB within 10 days.
- ii. **Unanticipated risk to staff or other non-participants:** if

personnel involved in the conduct of research or others not involved in conduct of the research experience events or circumstances that reveal a previously unanticipated risk this should be reported to the IRB within 10 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.

13) 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.

14) 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.

Each instance of potential or actual non-compliance will be evaluated based upon the facts as known to or gathered by the IRB. The following describes a range of examples of non-compliance and the range of actions available to the IRB. This list is not all inclusive of all potential instances of non-compliance or of all possible IRB actions, but is provided as a general guideline.

Examples of non-compliance

- Late submission of adverse events, protocol deviations or other reportable events

- Late submission of changes in protocol or study documents requiring either expedited or full IRB committee approval
- Late submission of continuing approval application
- Alteration of the informed consent document or other study materials (that require IRB approval) without IRB approval
- Use of recruitment material not approved by the IRB
- Use of an informed consent document not approved by the IRB
- Inappropriate recruitment of study participants
- Failure to report adverse events, protocol deviations or other reportable events
- Failure to disclose conflict of interest on the part of the principal investigator or other key personnel
- Repeated non-compliance with federal regulations or IRB requirements
- Failure to respond to an IRB request for information
- Failure to provide full data as requested by the IRB
- Egregious action or inaction that results in endangerment to study participants
- Retaliation against anyone who has reported non-compliance

Examples of actions available to the IRB

- Communication to the principal investigator from the IRB identifying the instance of non-compliance and outlining the applicable requirement
- Letter of warning identifying the instance of non-compliance and outlining the applicable requirement
- Formulation of a plan for remediation and prevention of recurrence, outlining specific time frames and requirements to be fulfilled by the principal investigator
- Requirement for refresher or additional training for all or some research staff
- Audit by the IRB
- Monitoring of study activities by the IRB
- Temporary suspension of study pending investigator response and, where appropriate, proposed corrective action
- Termination of study approval
- Temporary or permanent investigator suspension from all current studies
- Report to the DMHAS Signatory Official, funding agency or sponsor, OHRP or FDA as appropriate. In the event that the IRB determines the need to report serious or continuing non-compliance to DMHAS institutional officials, funding agency or sponsor, OHRP or the FDA, the time frame for reporting will be specified by the IRB committee.

As noted above, the lists are not exhaustive or inclusive of all possible instances of non-compliance or resulting IRB actions. The IRB retains the discretion to take action as it deems appropriate to the situation, taking into account the seriousness of the incident, past history, the possibility of honest error or misinterpretation of IRB requirements, or other factors deemed relevant by the IRB.

15) 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, Medical Director, 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.

16) FINAL REPORT

The Principal Investigator will forward a final report to the IRB upon completion of a research project. The research project 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;
- All other research related activity has ended.

The final report should be submitted using the Application for Continuing Review/Final Report.

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