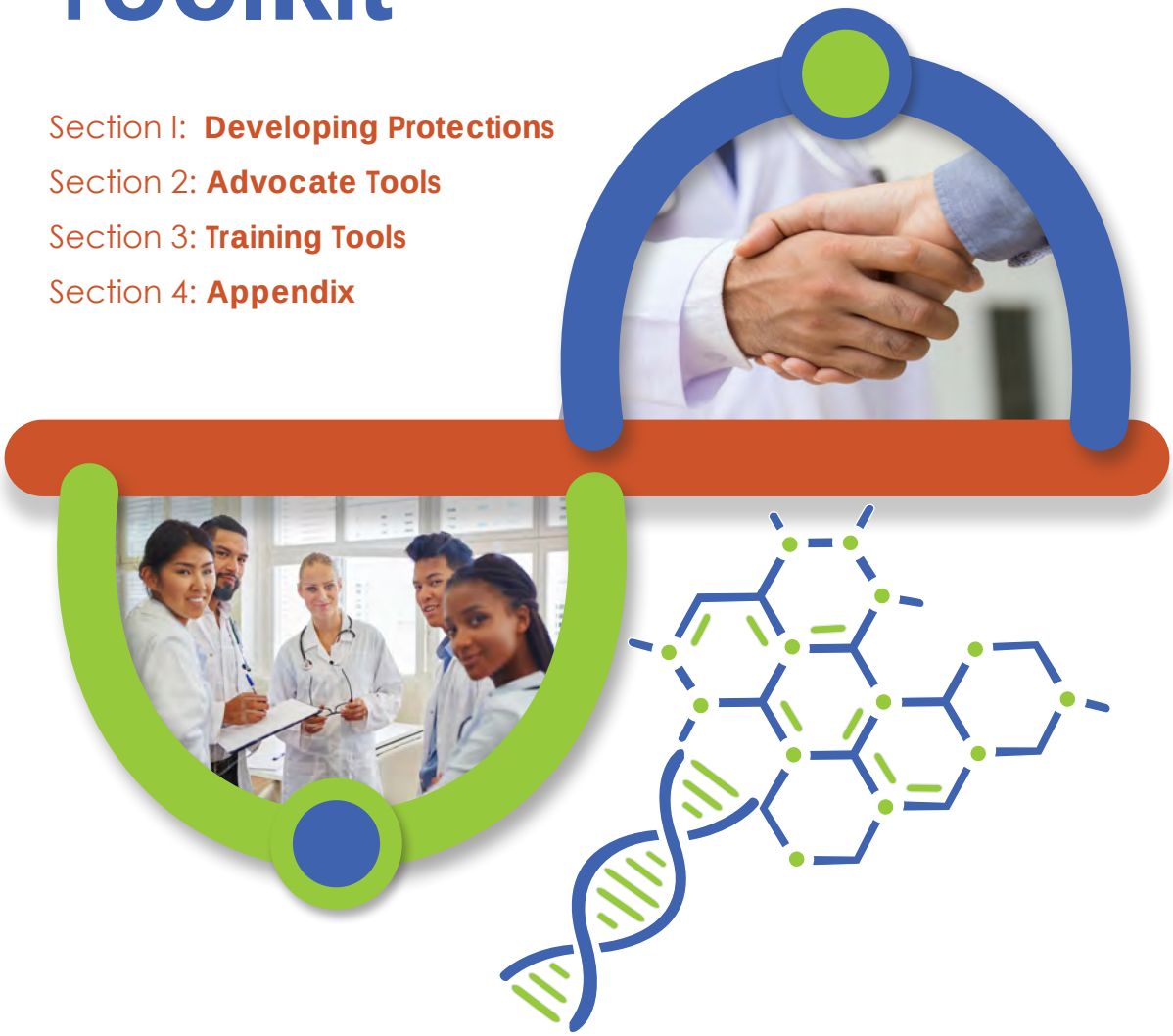
National Institute of Mental Health

Human Subjects Research Protections Toolkit



National Institute of Mental Health

Office of the Clinical Director **Human Subjects Protection Unit,** May 25, 2022

A human research protection program (HRPP), in part, aims to protect human research subjects. The National Institute of Mental Health (NIMH) protects potentially vulnerable **SUBJECTS** with **ADVOCATES** who support the individual subject as well as educate and advise **RESEARCHERS**.

The *NIMH Toolkit for Human Subjects Research Protections* is based on the NIMH's experience conducting research with potentially vulnerable subjects. Our aim is to help research organizations assess, implement, and refine appropriate levels of human subjects protections during all phases of research (submission of the initial protocol to the Institutional Review Board [IRB] through subject transition out of the protocol). Research organizations need to tailor these practices to suit their own standards and legal and policy requirements.

Disclaimer: *This NIMH Toolkit does not incorporate state or local law or organizational policies, nor does it address possible applicable federal law or speak to regulatory interpretation of 45 C.F.R. § 46. It does not address specifics for a particular type of protocol or IRB requirements. This Toolkit is the opinion of the NIMH intramural program and is subject to change.*

National Institute of Mental Health

5.25.2022

Office of the Clinical Director **Human Subjects Protection Unit**
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Developing SECTION 1 Protections

Section 1 introduces the NIMH Human Subjects Protection Unit (HSPU) program. It describes the elements of a protections program and how to assess which elements a research organization might incorporate.

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Background: **Toolkit History and Frame of Reference**

History

The National Institute of Mental Health (NIMH), under the auspices of the U.S. Department of Health and Human Services and the National Institutes of Health (NIH), consists of an extramural and an intramural program. The extramural program provides grants and educational services to research programs and community agencies around the country and worldwide. The intramural program conducts basic and human subjects research relating to a broad spectrum of mental health disorders at the NIH Clinical Center (CC) in Bethesda, MD.

Human subjects protections sometimes develop in response to past abuses (e.g., Nazi experiments, Tuskegee syphilis study). In 1998, the National Bioethics Advisory Commission (NBAC) published *Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity*. NBAC recommendations included that Institutional Review Boards (IRBs) should require independent, qualified professionals to assess a potential subject's capacity to consent for some greater than minimal risk studies.*

> *When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.***

NIMH took the lead and proactively created a program to enhance human subjects protections for potential subjects and subjects participating in NIMH protocols.

- In July 1999, the NIMH Office of the Clinical Director established an independent monitoring group to operate at the NIH CC. Initially named the Centralized Office for Recruitment and Evaluation (CORE), the impetus for the creation of the CORE was the belief that "respect for persons incorporates at least two ethical convictions; first, individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection."*** The CORE aspired to improve protections for research subjects during all phases of research.

*National Bioethics Advisory Commission (NBAC). *Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity*: *Report and Recommendations of the National Bioethics Advisory Commission*. Rockville, MD: NBAC, 1998, Vol. 1.
**Criteria for IRB Approval of Research, 45 C.F.R. § 46.111 (b), 2018.
***National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, Bethesda, MD: U.S. Govt. Print. Off., 1978, Part B: Basic Ethical Principles, Section 1. Respect for Persons.

- In 2007, the CORE was re-named the Human Subjects Protection Unit (HSPU) and its clinicians titled Clinical Research Advocates (CRAs). The dual focus of recruitment and subjects protection was redirected to implement more comprehensive oversight of human subjects protections.
- The HSPU program continues to evolve, as does the definition of potentially vulnerable populations and recommendations for their protection.

The NIMH Toolkit is based on the HSPU's experience and best practices. It is available at no cost to the public and to research organizations aspiring to define their own human subjects protections programs.

Frame of reference

When designing a human subjects protections program, it is important to take into consideration the following NIMH Toolkit frame of reference:

- The NIMH Toolkit uses the term subject to refer to those people enrolling or enrolled in research. The term was chosen to match federal regulation language. The term patient is not used to avoid therapeutic misconception. In practice, the preferred term is participant or volunteer.
- A subject population identified as potentially vulnerable (e.g., subjects diagnosed with a mental disorder) does not, in and of itself, identify all individuals within that population as vulnerable. Similarly, not being identified as part of a potentially vulnerable population does not provide immunity to becoming vulnerable. Situational context (e.g., subjects who are employees, relatives of the researcher, or who have a medical condition) may impact vulnerability.
- The NIH CC is a research-based hospital and every person seen in the clinics or inpatient units is enrolled in a protocol.
- The HSPU is a program within the NIMH that implements enhanced human subjects protections for potentially vulnerable subjects as part of a larger NIMH intramural human research protection program (HRPP). A complete HRPP may also include safety and compliance oversight (e.g., data safety monitoring board or independent safety monitor).
- Subject monitoring at the HSPU level is with an individual subject in real-time, as opposed to subject monitoring as part of a protocol safety plan that reviews groups of subject data at specific points in time over the course of the research.

- The NIMH allocates resources to maintain the HSPU. Outside organizations may take portions of this NIMH Toolkit and implement them in a manner suitable to their structure and resources (e.g., through a bioethics department or other independent group).

- At the NIH CC, documentation takes place in the medical record. Outside research organizations should follow their own documentation policies and procedures.

- This NIMH Toolkit does not interpret federal policy. References to 45 C.F.R. § 46 are footnoted for the reader's convenience.

Background: **The NIMH HSPU Program**

The HSPU program

The HSPU functions under the auspices of the NIMH Office of the Clinical Director whose authority and support are crucial for the implementation of the program. The HSPU protects potentially vulnerable subjects participating in NIMH intramural research. The HSPU advises researchers in assessing, developing, and implementing appropriate levels of human subjects protections during all phases of research, from protocol development through a subject's completion of a protocol.

The HSPU consists of NIMH CRAs who report directly to the Clinical Director, are not engaged in clinical research recruitment, and are not researchers. This approach eliminates any undue pressure and assures independence from the researchers. If the researcher and the advocate are in conflict, the NIMH Clinical Director serves as arbiter.

Additionally, the HSPU joined with the NIH CC Bioethics Department to form the Ability to Consent Assessment Team (ACAT) to provide assessments and consultation throughout the NIH CC.

The HSPU functions

The following HSPU functions are essential both for the protection of potential subjects and subjects and to the integrity of the protocols in which they are enrolled.

- **Human subjects protections**
  The HSPU assures protection of and support to potentially vulnerable subjects participating in research. Assessment and monitoring activities are
  - Capacity assessment
  - Ability to assign a surrogate decision-maker assessment
  - Surrogate decision-maker assessment
  - Consent monitoring
  - Subject monitoring

- **Consultation**
  As a non-voting consultant, the HSPU reviews protocols and makes recommendations for improving human subjects protections to the IRB. Additionally, the HSPU interprets and assists in the application of federal, NIH, and NIMH human subjects research regulations and policies.

- **Researcher education and training**
  The HSPU provides human subjects protections education and training throughout the NIH, to outside organizations, and at national meetings. All NIMH researchers and NIH trainees authorized to obtain informed consent are required to complete the HSPU's Elements of a Successful Informed Consent training. This training includes how to obtain consent, the elements of the informed consent process, and relevant federal and organizational policies.

  Additionally, the HSPU administers an *Objective Structured Clinical Examination (OSCE) for the Evaluation of the Informed Consent Process* (see Toolkit Section 2) to evaluate the ability of researchers to obtain informed consent.

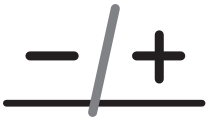
Designing a Program: **Developing a Program**

If any one of the following situations exists, developing a program with specific tools to enhance human subjects protections may be helpful.

- Researchers will enroll potentially **VULNERABLE POPULATIONS** as subjects

- Anticipated protocol is **MORE THAN MINIMAL RISK** and there is **NO PROSPECT OF DIRECT BENEFIT**

- Anticipated research is **CONTROVERSIAL**



Enhanced protections plans may be initiated by

- **RESEARCHER** request

- Organizational **POLICY** decision

- **IRB** requirement

Designing a Program: **Costs and Considerations**

A human subjects protection program should have advocates and logistical and administrative support.

Advocates

Advocates are a primary component of a human subjects protections program. The number of advocates required for a program depends on the number of protocols and level of advocate involvement. Most of the advocate's time is spent monitoring, assessing, and supporting subjects; attending interdisciplinary rounds; consulting with interdisciplinary research teams; and documenting, both in-person and virtually. The advocate's remaining time is spent training researchers and consulting with the IRB. The advocate's schedule includes time for both planned and unexpected consults. Coverage plans are made for advocate absences.

Workspace

Ideally, each advocate has an individual desk, computer, and telephone, as well as access to a private space for consultation and discussion.

Legal support

Advocates need access to legal counsel. Laws vary from state to state and may change over time. Legal counsel may review and clarify a potential subject's legal documents. For example

- Custody arrangements (i.e., which parent[s] is authorized to consent for a minor)
- Legal guardianship of an adult (i.e., whether a legal guardian is authorized to give consent for a potential subject to participate in a specific protocol and under what circumstances)

Quality assurance

A human subjects protections program should be reviewed periodically with feedback from organizational leadership, researchers, the IRB, and subjects.

Ongoing training

Advocates should

- Maintain professional licenses
- Stay current on research ethics, federal regulations, and human research subjects protections issues

Designing a Program: **Advocate Qualifications**

A human subjects protections program is based on advocates having both a clinical and an ethics background.

Clinical training

Advocates are masters prepared clinicians (e.g., social workers, psychologists, or nurses). Questions and situations that arise as part of their work can be complicated and nuanced. Advocates require strong clinical understanding, knowledge of systems, critical thinking, flexibility, and the ability to negotiate conflict.

Experience

Experience in both clinical and research settings allows advocates to understand the complex nature of subject enrollment and to provide support and education. The ability to recognize the subtleties of human interactions, as well as knowledge of organizational and other applicable policies is required.

Bioethics training

Knowledge and training in the ethical principles underpinning human subjects protections are essential to the application and monitoring of ethical research practices by advocates.

Independent of the research

Advocates must be independent of the research (i.e., are not researchers on the protocol; do not report to, nor are supervised by, the researcher; and are not obligated in any way to influence recruitment or retention of subjects). The independence of advocates allows for neutrality when assessing and monitoring a subject.

Assessment Descriptions: **Capacity Assessment**

Determines the potential subject's ability to provide consent to research participation

A capacity assessment is an evaluation by a trained advocate of an adult potential subject's ability to provide informed consent for a specific protocol at a specific time. The researcher educates the potential subject about the protocol prior to the advocate administering the capacity assessment. The advocate documents the assessment outcome according to organizational policy.

The terms capacity and competence are often misunderstood and used incorrectly. The terms are not interchangeable.

- Capacity is an assessment, determined by a clinician, of a potential subject's ability to understand and make decisions about participating in a specific protocol at a specific time. It is not related to a potential subject's abilities and rights outside of the research setting.
- Competency is a legal status often determined by a court of law. It is a broader determination than capacity.

Potential subjects determined not to have consent capacity will fall into one of two categories:

- Those who previously had the ability to provide informed consent but at the time of assessment no longer have that ability
- Those who have never had the ability to provide informed consent

Additional points to consider

- Consent capacity may fluctuate during research participation and may be influenced by factors such as medication or worsening symptoms.
- Capacity assessments are designed to assess capacity at time of initial consent but can be adapted for assessment of consent capacity during protocol participation.
- The potential subject can be found to have consent capacity for a minimal risk protocol but not for a more than minimal risk protocol.

Capacity assessments generally assess four domains: understanding, appreciation, reasoning, and choice. It is useful to have two types of capacity assessments:

- A protocol-specific capacity assessment (see Toolkit Section 2) is used when a protocol requires some or all potential subjects be formally assessed prior to consenting. It is created in advance of anticipated potential subjects enrolling. To create the tool, the advocate incorporates specific protocol information including the diagnosis or illness being studied, the protocol procedures, and anticipated risks and benefits.

- A generic capacity assessment (see Toolkit Section 2) is a basic assessment format that can be adapted when an unanticipated need for an assessment arises. To adapt the tool, the advocate incorporates specific protocol information including the diagnosis or illness being studied, the protocol procedures, and anticipated risks and benefits.

The tools should be created prior to administering the assessment.

Assessment Descriptions: **Ability to Assign a Surrogate Decision-Maker Assessment**

Evaluates the ability of an adult potential subject to choose a surrogate to make decisions on behalf of a potential subject

Although the potential subject may not have consent capacity, the potential subject may be able to identify a trusted person to help make decisions about healthcare and research participation. When the protocol allows for surrogate decision-maker consent and there is no surrogate decision-maker identified, the advocate assesses the potential subject's ability to identify a surrogate decision-maker for healthcare decisions in research (see Toolkit Section 2, *Ability to Assign a Surrogate Decision-Maker Assessment*). The advocate documents the assessment outcome according to organizational policy.

If the potential subject is able to and does assign a surrogate decision-maker, this assessment is followed by the *Surrogate Decision-Maker Assessment* (see Toolkit Section 2). A potential subject who has consent capacity is considered able to assign a surrogate decision-maker and does not need a formal assessment to do so.

Background

The surrogate decision-maker (also referred to as substitute decision-maker, surrogate, legally authorized representative [LAR],* or proxy) may be a(n)

- Legal guardian
- Agent named in an advance directive (AD) such as a durable power of attorney (DPA) for health care or a living will
- Next-of-kin (NOK)

State law and organizational consent policies usually dictate when a surrogate decision-maker may be used for research. For example, a policy could state NOK may not be used except in limited circumstances (see Toolkit Section 4, *NIMH Consent Process Flowchart*).

There are two categories of surrogate decision-makers:

- Those whose status is in effect. This status applies to legal guardians who are appointed by a court of law. The legal guardian can provide consent for the potential subject. The potential subject may provide only assent because the potential subject does not have legal competency.
- Those whose status is in effect only in specific circumstances. This status could exist with a surrogate decision-maker assigned through an AD, DPA, living will, or NOK policy. It is invoked only when the potential subject loses consent capacity.

When the potential subject has a pre-existing surrogate decision-maker, the advocate may consult with legal counsel regarding any limitations to research participation (e.g., DPAs may cover only financial decisions or a state may allow surrogate consent only for research that has a prospect of direct benefit).

*Definitions for Purposes of this Policy, 45 C.F.R. § 46.102 (7) (ii) (i), 2018.

Assessment Descriptions: **Surrogate Decision-Maker Assessment**

Evaluates the surrogate decision-maker's ability to provide consent and, ideally, to represent the potential subject's wishes

The *Surrogate Decision-Maker Assessment* (see Toolkit Section 2) evaluates the appropriateness of a person to serve as the potential subject's surrogate decision-maker. If the potential subject is found not to have consent capacity, the surrogate decision-maker may provide consent on behalf of the potential subject. This assessment is not a capacity assessment of the surrogate decision-maker.

Once a surrogate decision-maker is identified and before research moves forward, the appropriateness of the surrogate decision-maker is assessed by the advocate. This assessment may include whether the surrogate decision-maker understands the difference between research and clinical care and the risks and potential benefits of each. The surrogate decision-maker should understand the essential elements of the protocol as explained in the informed consent document. Ideally, the surrogate decision-maker should understand the potential subject's values, preferences, and choices regarding research participation.

Researchers and organizations should consider whether participation will proceed if a surrogate decision-maker is found to be appropriate, but the potential subject does not want to participate in the protocol. Advocates can help determine the concerns involved and indicate when additional consultations (e.g., ethics or legal) should be considered. For a practice exercise, see *Assent Monitoring*, page 3.21.

The advocate documents the assessment outcome according to organizational policy.

Monitoring Descriptions: **Consent Monitoring**

Assures the elements of the protocol consent are discussed by a researcher and a potential subject

Consent monitoring may be required by organizational policy or the IRB* or by researcher request. The advocate is present during the consent discussion between the researcher and the potential subject or the surrogate decision-maker and assures the required elements of the protocol consent are discussed (see Toolkit Section 2, Consent Monitoring Checklist). The advocate monitors the quality of the conversation to assure information is accurate, descriptions are clear, and any questions or concerns raised by the potential subject or the surrogate decision-maker are answered and clarified. The advocate witnesses the consent process and documents according to organizational policy.** This standard may change with the facts of a situation (e.g., the purpose and requirements of a witness if a short form consent is used***). A signed copy of the consent form is given to the person(s) providing consent.†

There can be a need to obtain consent remotely. For example, the protocol requires consent from both parents, but only one can be present at the time of the consent process. The IRB must approve the virtual consent process in advance.

The advocate assures the party participating off-site has a copy of the consent form. The advocate is present with the researcher at the time of the consent conversation to monitor the consent process.

*IRB Review of Research, 45 C.F.R. § 46.109 (c), 2018.
**The advocate may sign as the witness. Check your organizational policy for any specific requirements.
***Documentation of Informed Consent, 45 C.F.R. § 46.117 (b) (2), 2018 requires a witness to the oral presentation.
†Documentation of Informed Consent, 45 C.F.R. § 46.117 (a), 2018.

Monitoring Descriptions: **Assent Monitoring**

Assures the quality of the assent discussion for adults without decision-making capacity and minors by verifying the agreement of the potential subject to participate in research

The assent discussion is a less complex review of a consent and may take place at the same time as consent. Advocates need to know if assent is required for a protocol per IRB determination.* The advocate is present for the assent discussion between the researcher and the minor potential subject or the adult potential subject who lacks consent capacity. While the parent(s) or surrogate decision-maker participates in the full consent discussion, the researcher's assent discussion is with the potential subject and focuses on that person's decision to participate in the protocol.

The assent process includes monitoring for subject dissent. Failure of the potential subject to object to participation in the protocol should not be construed as assent.** There may be situations in which the IRB has determined assent is not required (e.g., in a pediatric protocol with a prospect of direct benefit that is important to the health or well-being of the potential subject and is available only in the context of the research).

Dissent may be expressed behaviorally--for example, through body language, lack of engagement in the assent process, or refusal of procedures after research begins. Depending on the flexibility of the protocol, it may be possible for a potential subject to decline to participate in some procedures while participating in others.

Advocates, researchers, and research organizations need to know applicable state law regarding the age of consent. Researchers should anticipate and plan for continued enrollment if subjects do not have consent capacity when they reach the age of majority.

The advocate documents the assent discussion according to organizational policy.

*Requirements for Permission by Parents or Guardians and for Assent by Children, 45 C.F.R. § 46.408, 2018.
**Definitions, 45 C.F.R. § 46.402 (b), 2018.

Monitoring Descriptions: **Subject Monitoring**

Assures ongoing consent during inpatient or longer-term protocol participation

Subject monitoring is with an individual subject in real-time, as opposed to subject monitoring as part of a protocol safety plan that reviews groups of subject data at specific points in time over the course of the research or that requires prompt reporting of certain medical or other problems.

To verify ongoing informed consent, the advocate regularly visits subjects over the course of their participation to assess current wishes, understanding, questions, and concerns regarding continued participation in the protocol.

The advocate monitors the ongoing informed consent of subjects during face-to-face conversations (see Toolkit Section 2, *Subject Monitoring Guide*). Additionally, the advocate reviews the medical record and participates in interdisciplinary meetings with the research and clinical staff. The advocate encourages the subject to communicate questions and concerns to the researcher. If needed, the advocate acts as the subject's voice to bring concerns to the attention of the researcher. The advocate facilitates the resolution of issues to assure the subject's wishes regarding research participation are respected.

The advocate documents these discussions according to organizational policy.

Advocate SECTION 2 Tools

Section 2 provides tools and samples which can be adapted for specific protocols and for individual organizations implementing a human subjects protections program for potentially vulnerable subjects.

Prepare

Determining Tools Needed
Scheduling Worksheet
Pre-Consent Checklist

Assess

Capacity Assessment: Protocol-Specific
Capacity Assessment: Generic
Ability to Assign a Surrogate Decision-Maker Assessment
Surrogate Decision-Maker Assessment

Monitor

Consent Monitoring Checklist
Subject Monitoring Guide

Evaluate the Researcher

Objective Structured Clinical Examination (OSCE) for the Informed Consent Process

Determining Tools Needed

Advocate Tools

Prepare

A protections program may include the following tools. An affirmative answer to any of the questions below indicates which tools to consider for integration into a protocol.

For example, if a new protocol includes a potentially vulnerable population and is more than minimal risk, the Institutional Review Board (IRB) or researcher may consider requiring a capacity assessment and consent monitoring.

Capacity Assessment

- ❑ Does the protocol include a potentially vulnerable subject population?
- ❑ Is the protocol more than minimal risk, without a prospect of direct benefit?
- ❑ Does the protocol involve complex procedures?
- ❑ Is the subject's capacity expected to change over time?

Ability to Assign a Surrogate Decision-Maker Assessment

- ❑ If the potential subject without consent capacity does not have an identified surrogate, does organizational policy allow the potential subject to assign one?

Surrogate Decision-Maker Assessment

- ❑ Does the protocol allow for surrogate decision-maker consent?

Consent Monitoring

- ❑ Does the protocol include a potentially vulnerable subject population?
- ❑ Is the protocol more than minimal risk, without a prospect of direct benefit?
- ❑ Does the protocol involve complex procedures?

Assent Monitoring

- ❑ Does the protocol include a potentially vulnerable subject population?
- ❑ Is the protocol more than minimal risk, without a prospect of direct benefit?
- ❑ Does the protocol involve complex procedures?
- ❑ Does the protocol include adult subjects without consent capacity?
- ❑ Does the protocol allow for the enrollment of minors?

Subject Monitoring

- ❑ Is this an inpatient or longer-term protocol?
- ❑ Does the protocol include a potentially vulnerable subject population?
- ❑ Is the protocol more than minimal risk?
- ❑ Does the protocol involve complex procedures without a prospect of direct benefit?
- ❑ Is the subject's capacity expected to change over time?
- ❑ Is symptom worsening expected?

Scheduling Worksheet

The researcher requests an assessment by contacting the advocate.

The researcher provides the following information:

- ❑ Date, time, and location of the assessment(s)
- ❑ Potential subject's name
- ❑ Type of assessment(s) requested (e.g., capacity assessment, ability to assign a substitute decision-maker assessment, surrogate decision-maker assessment)
- ❑ Protocol number
- ❑ Interpreter services scheduled if needed
- ❑ Copy of the consent
- ❑ Access to the protocol
- ❑ Risk level of the research
- ❑ Benefit level of the research
- ❑ Confirmation the researcher obtaining consent is approved by the Institutional Review Board (IRB) to do so

For capacity assessments, confirm

- ❑ The researcher educated the potential subject about the protocol.
- ❑ The potential subject was given an explanation of the upcoming assessment(s).

For protocols allowing surrogate consent, confirm

- ❑ The surrogate decision-maker is authorized to consent to the research.
- ❑ The potential subject and the surrogate decision-maker were given an explanation of the upcoming assessment(s).
- ❑ The surrogate decision-maker will be present for the consent process.

Pre-Consent Checklist

Before the consent conversation begins, the researcher, staff, or the advocate assures pre-consent logistics have been addressed to avoid last minute confusion, inadequate preparation, or problems obtaining consent.

Potential subject whose language is not English

- ❑ Confirm the potential subject's preferred language.
- ❑ Confirm the consent has been translated into the potential subject's preferred language and approved by the Institutional Review Board (IRB), or the IRB has approved use of the short form.*
- ❑ Reserve interpreter services for the entire consent process. It is not recommended a family member serve as the interpreter.

Minor potential subject

- ❑ Assure any custody arrangement is reviewed (e.g., by researcher or legal counsel).
- ❑ Determine whether both parents are required to give consent by custody arrangement or by the protocol.
- ❑ Confirm whether assent is required by the IRB.

Adult potential subject

If the potential subject requires a capacity assessment, an ability to assign a surrogate decision-maker assessment, or a surrogate decision-maker assessment, refer to the *Scheduling Worksheet* (see Section 2).

Consent setting

- ❑ Confirm that a private space has been reserved for the consent process.
- ❑ Greet the potential subject, explain the advocate's role, and address questions and concerns.
- ❑ Provide the potential subject with advocate contact information and printed materials describing the advocate role (see Section 4, NIMH HSPU brochure).
- ❑ Limit the number of people present as appropriate (e.g., member of the potential subject's family, the researcher obtaining consent, and the advocate).
- ❑ Request permission from the potential subject for additional staff to observe, noting the potential subject is not required to allow observers. Make this request privately when possible.
- ❑ Ensure the potential subject has a copy of the consent form.

*Documentation of Informed Consent, 45 C.F.R. § 46.117 (b) (2), 2018.

Capacity Assessment: Protocol-Specific

Advocate Tools

Assess

These responses have been created for an NIMH Alzheimer's Disease protocol. You must create expected responses to reflect your protocol.This tool is clinically derived. It is not validated.

Instructions for NIMH Clinical Research Advocates (CRAs)

CRAs must be trained before administering this assessment.

Prepare for the assessment

- Use two trained CRAs to assess the potential subject. Use one CRA if circumstances dictate (e.g., the potential subject is highly anxious).
- Designate one CRA as the interviewer. Both CRAs are raters, and each rater completes a copy of the assessment form.
- Allow observers only when necessary.

Administer the assessment

- Explain the purpose of the assessment. Inform the potential subject you will take notes during the interview.
- The format of the interview is conversational and does not require the questions to be read verbatim.
- The domain descriptions (Understanding, Appreciation, Reasoning, Choice) are for your reference. Do not read them aloud.
- If the potential subject gives the expected information, check the box and proceed to the next question. If not, provide the prompt. You may need to ask clarifying questions.
- If the potential subject clearly does not have capacity, stop this assessment and transition to the next assessment if necessary (e.g., *Ability to Assign a Surrogate Decision-Maker*).

Rate the responses

During the assessment

- Complete **Rater's Comments.** Enter comments, concerns, and recommendations. Note when prompting is required.
- Complete **Rater Scale.** (Question 9 has no scale.) These numbers are not tallied as a score. Indicate the level of understanding by marking the appropriate description:
  - 1 = Understands
  - 2 = Has partial understanding
  - 3 = Does not understand

After the assessment, without the potential subject present

- Complete the **Global Impressions** section. Indicate ability to give informed consent by marking the appropriate description:
  - **A ABLE**
  - **B QUESTIONABLE ABILITY**
  - **C UNABLE**
- Resolve any differences between raters to determine an outcome.
- **Interviewer only:** enter the outcome and plan on the form.
- Document the outcome and plan according to organizational policy.

The CRA or researcher, as appropriate, informs the potential subject of the outcome.

Capacity Assessment: Protocol-Specific

Advocate Tools

Assess

These responses have been created for an NIMH Alzheimer's Disease protocol. You must create expected responses to reflect your protocol.This tool is clinically derived. It is not validated.

Examples of capacity assessment outcomes and plans

A ABLE

- Researcher may obtain consent

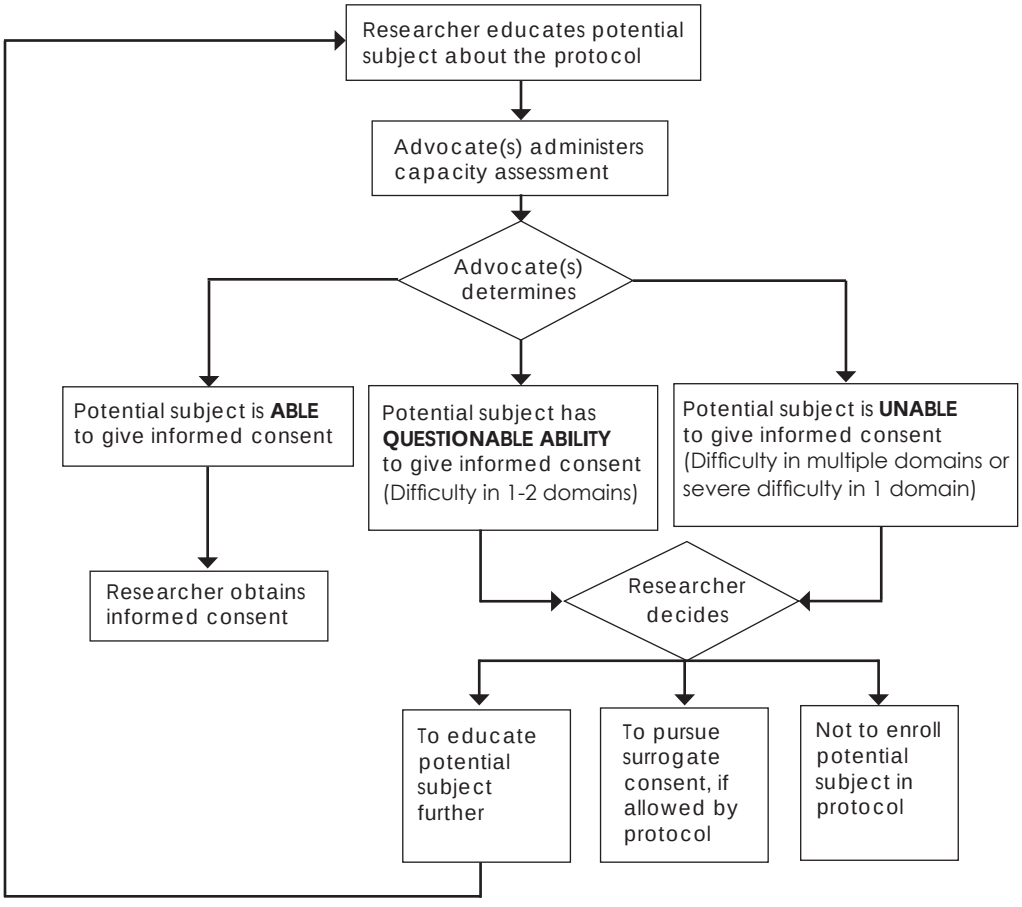
B QUESTIONABLE ABILITY

- Recommend further education in domains where difficulty was noted
- Re-assess

C UNABLE

- Researcher may pursue surrogate consent as allowed in this protocol
- Assess ability to assign a surrogate decision-maker
- Assess appropriateness of the surrogate

Capacity assessment algorithm



Capacity Assessment: Protocol-Specific

Advocate Tools

Assess

2.6

NIMH Human Subjects Research Protections Toolkit

Advocate Tools

These responses have been created for an NIMH Alzheimer's Disease protocol. You must create expected responses to reflect your protocol.This tool is clinically derived. It is not validated.

Protocol number _____ **Date** _____

Potential subject _____ **Age** _____

Interviewer _____ **Rater** _____

UNDERSTANDING *of disclosed information about the nature of the research project and its procedures**

1. What is the purpose of this research and who is being studied?

❑ Expected: To evaluate people with signs and symptoms of Alzheimer's Disease and determine whether they qualify for other studies

Prompt: *The purpose of this study is to evaluate people with signs of memory loss to see if they qualify for other studies.*

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

2. What are some of the things you will be asked to do during this study?

❑ Expected: Tests, such as blood draws, brain scans (MRI and PET), and cognitive testing

Prompt: *During the study the researchers will ask you to do brain scans, blood draws, and paper-and-pencil tasks.*

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

3. What are the most significant risks to you during this study?

❑ Expected: Discomfort from the blood draws, intravenous catheter placement, radiation exposure, and claustrophobia while in the scanner(s)

Prompt: *The possible risks associated with this study include discomfort during blood draws, IV placement, minimal radiation exposure, and claustrophobia while lying in the scanner.*

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

4. What benefits might you receive as a result of participating in this study?

❑ Expected: No direct benefit

Prompt: *This study will not treat your symptoms. By participating you may help others in the future.*

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

Capacity Assessment: Protocol-Specific

Advocate Tools

Assess

These responses have been created for an NIMH Alzheimer's Disease protocol. You must create expected responses to reflect your protocol.This tool is clinically derived. It is not validated.

APPRECIATION *of the effects of research participation (or failure to participate) on subjects' own situations**

5. How is being in this study different from going to your regular doctor?

- ❑ Expected: This research does not provide ongoing clinical care.
- ❑ Expected: Your regular doctor will treat your symptoms.
- ❑ Expected: You would not do research tasks such as the PET scan for clinical care.

Prompt: *There are differences between participating in research versus receiving regular medical care in the community. This research does not treat your memory problems. Your regular doctor provides continuous treatment and medicine.*

Rater's Comments_____

Rater Scale 1 _____ 2 _____ 3 _____

REASONING *in the process of deciding about participation, focusing on subjects' abilities to compare alternatives in light of their consequences**

6. Based on what we discussed, why are you interested in participating in this study?

- ❑ Expected: Raters assess whether the subject is able to use information from questions 1-5 to decide on participation in this protocol (e.g., I know this study won't benefit me, but I want to learn more about Alzheimer's and contribute to future treatment).

Prompt: *The information we have discussed will help you decide whether to participate in this study.*

Rater's Comments_____

Rater Scale 1 _____ 2 _____ 3 _____

7. What would you do for treatment if you decide not to participate in this study?

- ❑ Expected: Continue care in the community

Prompt: *There are alternatives to participating in this study, including continuing care with your regular doctor.*

Rater's Comments_____

Rater Scale 1 _____ 2 _____ 3 _____

CHOICE *expressing a choice about research participation**

8. Whose decision is it to enter this study?

- ❑ Expected: Mine

Prompt: *Research participation is voluntary. It is your choice to participate or not at any time during the study.*

Rater's Comments_____

Rater Scale 1 _____ 2 _____ 3 _____

Capacity Assessment: Protocol-Specific

Advocate Tools

Assess

These responses have been created for an NIMH Alzheimer's Disease protocol. You must create expected responses to reflect your protocol.This tool is clinically derived. It is not validated.

9. Have you decided to enroll in this study? ❑ Yes ❑ No

Please tell us why_____

What would happen if you choose not to participate in this study?

_____

Rater's Comments_____

10. How would you let us know if you wanted to stop participating in this study?

_____

Rater's Comments_____

Rater Scale 1 _____ 2 _____ 3 _____

GLOBAL IMPRESSIONS

- ❑ **A ABLE** to give informed consent at this time
- ❑ **B QUESTIONABLE ABILITY** to give informed consent at this time
- ❑ **C UNABLE** to give informed consent at this time

Identify any specific concerns for each domain.

Understanding_____

Appreciation_____

Reasoning_____

Choice_____

Signature of Rater_____

INTERVIEWER ONLY: Raters' final determination

- ❑ **A ABLE** to give informed consent at this time
- ❑ **B QUESTIONABLE ABILITY** to give informed consent at this time
- ❑ **C UNABLE** to give informed consent at this time

PLAN_____

_____

_____

_____

*Paul S. Appelbaum and Thomas Grisso, *MacArthur Competence Assessment Tool for Clinical Research* (*MacCAT-CR*) (Sarasota, FL: Professional Resource Press, 2001), 1. Domain names and definitions used with permission.

Capacity Assessment: Generic

Advocate Tools

Assess

This tool is the NIMH Generic Capacity Assessment. It is a basic format to use when an unanticipated assessment need arises. You must create expected responses to reflect the protocol.This tool is clinically derived. It is not validated.

Instructions for NIMH Clinical Research Advocates (CRAs)

CRAs must be trained before administering this assessment.

Prepare for the assessment

- Use two trained CRAs to assess the potential subject. Use one CRA if circumstances dictate (e.g., the potential subject is highly anxious).
- Prior to the assessment, determine the expected responses for each question.
- Designate one CRA as the interviewer. Both CRAs are raters, and each rater completes a copy of the assessment form.
- Allow observers only when necessary.

Administer the assessment

- Explain the purpose of the assessment. Inform the potential subject you will take notes during the interview.
- The format of the interview is conversational and does not require the questions to be read verbatim. You may need to ask clarifying questions.
- The domain descriptions (Understanding, Appreciation, Reasoning, Choice) are for your reference. Do not read them aloud.
- If the potential subject gives the expected information, proceed to the next question. If not, provide a prompt and re-ask the question.
- If the potential subject clearly does not have capacity, stop this assessment and transition to the next assessment if necessary (e.g., *Ability to Assign a Surrogate Decision-Maker*).

Rate the responses

During the assessment

- Complete **Rater's Comments.** Enter comments, concerns, and recommendations. Note when prompting is required.
- Complete **Rater Scale.** (Questions 12-14 have no scale.) These numbers are not tallied as a score. Indicate the level of understanding by marking the appropriate description:
  - 1 = Understands
  - 2 = Has partial understanding
  - 3 = Does not understand

After the assessment, without the potential subject present

- Complete the **Global Impressions** section. Indicate ability to give informed consent by marking the appropriate description:
  - **A ABLE**
  - **B QUESTIONABLE ABILITY**
  - **C UNABLE**
- Resolve any differences between raters to determine an outcome.
- **Interviewer only:** enter the outcome and plan on the form.
- Document the outcome and plan according to organizational policy.

The CRA or researcher, as appropriate, informs the potential subject of the outcome.

Capacity Assessment: Generic

Advocate Tools

Assess

2.10

This tool is the NIMH Generic Capacity Assessment. It is a basic format to use when an unanticipated assessment need arises. You must create expected responses to reflect the protocol.This tool is clinically derived. It is not validated.

NIMH Human Subjects Research Protections Toolkit

Advocate Tools

Examples of capacity assessment outcomes and plans

A ABLE

- Researcher may obtain consent

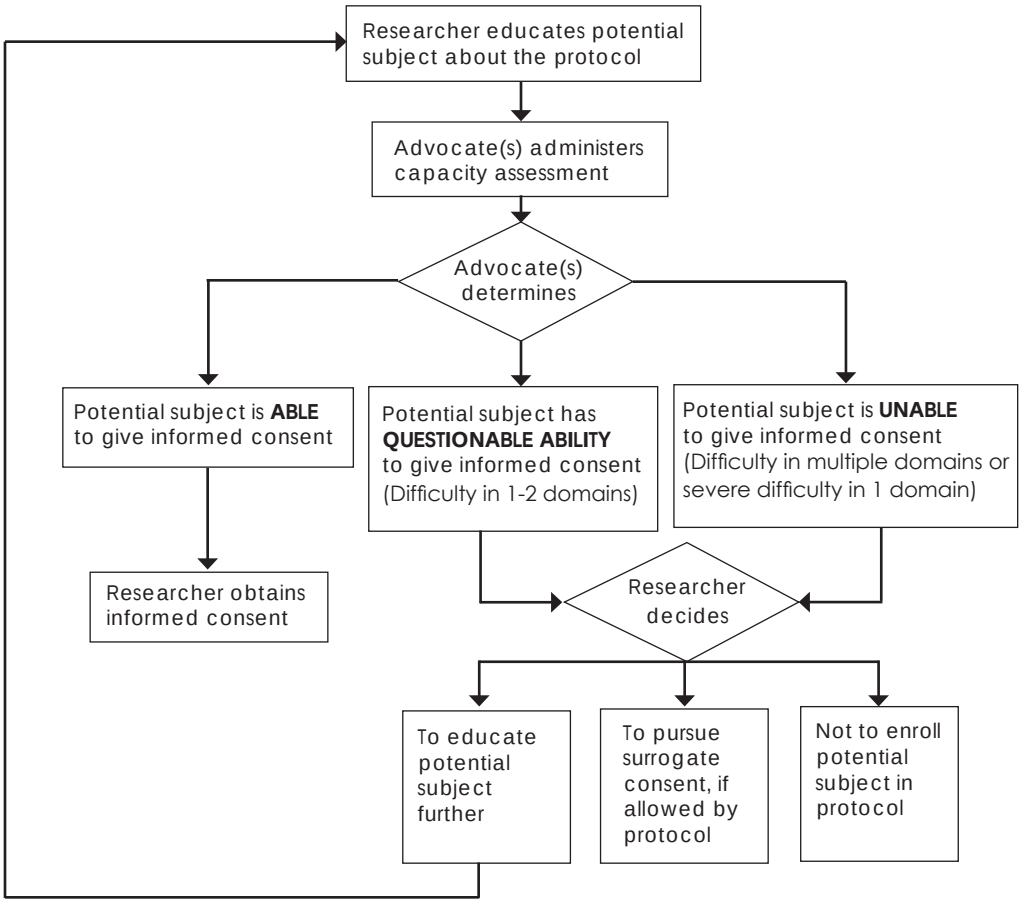
B QUESTIONABLE ABILITY

- Recommend further education in domains where difficulty was noted
- Re-assess

C UNABLE

- Researcher may pursue surrogate consent as allowed in this protocol
- Assess ability to assign a surrogate decision-maker
- Assess appropriateness of the surrogate

Capacity assessment algorithm



Capacity Assessment: Generic

Advocate Tools

Assess

This tool is the NIMH Generic Capacity Assessment. It is a basic format to use when an unanticipated assessment need arises. You must create expected responses to reflect the protocol.This tool is clinically derived. It is not validated.

Protocol number _____ **Date** _____

Potential subject _____ **Age** _____

Interviewer _____ **Rater** _____

UNDERSTANDING *of disclosed information about the nature of the research project and its procedures**

1. What made you decide to come here?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

2. What are the researchers attempting to learn with this study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

3. What are some of the things you will be asked to do during this study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

4. What are the most significant risks to you during the study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

5. What benefits might you receive as a result of participating in this study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

APPRECIATION *of the effects of research participation (or failure to participate) on subjects' own situations**

6. How is being in this study different from going to your regular doctor?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

7. How will being in this study affect your routine?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

Capacity Assessment: Generic

Advocate Tools

Assess

This tool is the NIMH Generic Capacity Assessment. It is a basic format to use when an unanticipated assessment need arises. You must create expected responses to reflect the protocol.This tool is clinically derived. It is not validated.

REASONING *in the process of deciding about participation, focusing on subjects' abilities to compare alternatives in light of their consequences**

8. What are the alternatives to participating in this study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

9. Based on what we discussed, why are you interested in participating in this study?

Raters assess whether the subject is able to use information from questions 1-8 to decide on participation in this protocol (e.g., I know this study won't benefit me, but I want to learn more about my illness and contribute to future treatment).

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

CHOICE *expressing a choice about research participation**

10. Whose decision is it to enter this study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

11. How would you let us know if you wanted to stop participating in this study?

Rater's Comments_____
Rater Scale 1 _____ 2 _____ 3 _____

12. Have you decided to enroll in this study? ❑ Yes ❑ No

13. Please tell us why _____

Rater's Comments_____

14. What would happen if you choose not to participate in this study?

Rater's Comments_____

*Paul S. Appelbaum and Thomas Grisso, *MacArthur Competence Assessment Tool for Clinical Research* (*MacCAT-CR*) (Sarasota, FL: Professional Resource Press, 2001),1. Domain names and definitions used with permission.

Capacity Assessment: Generic

This tool is the NIMH Generic Capacity Assessment. It is a basic format to use when an unanticipated assessment need arises. You must create expected responses to reflect the protocol.This tool is clinically derived. It is not validated.

GLOBAL IMPRESSIONS

- ❑ **A ABLE** to give informed consent at this time
- ❑ **B QUESTIONABLE ABILITY** to give informed consent at this time
- ❑ **C UNABLE** to give informed consent at this time

Identify any specific concerns for each domain.

Understanding_____

_____

Appreciation_____

_____

Reasoning_____

_____

Choice_____

_____

Signature of Rater_____

INTERVIEWER ONLY: Raters' final determination

- ❑ **A ABLE** to give informed consent at this time
- ❑ **B QUESTIONABLE ABILITY** to give informed consent at this time
- ❑ **C UNABLE** to give informed consent at this time

PLAN_____

_____

_____

_____

_____

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_____

_____

_____

_____

Ability to Assign a Surrogate Decision-Maker Assessment

Advocate Tools

Assess

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

This assessment is a guide to help determine a potential subject's ability to assign a surrogate decision-maker and includes items to be considered that may go beyond the legal requirement. For background information on this assessment tool, see Toolkit Section 1, *Assessment Descriptions.*

Raters must be trained before administering the assessment.

Guidelines

- Use this assessment if the potential subject is willing to assent to research but does not have consent capacity.
- This assessment tool is intended as a guide, not a script. Which questions to ask will depend on the case. How deeply to probe specific issues will depend on previous answers and the circumstances.
- If the chosen surrogate is unexpected (e.g., seemingly illogical choice, lower on the next-of-kin [NOK] hierarchy, or unavailable) probe for an explanation of the choice.

Instructions

- Use one or two independent, trained raters to administer the assessment.
- One rater is designated the interviewer and completes the form.
- Ideally, raters are familiar with the specific protocol, the study population, and any information available about the potential subject.
- The assessment is conducted in a private space, with the fewest observers present, and without the potential surrogate as appropriate.
- Provide verbal feedback to team, potential subject, and surrogate as appropriate.
- If the potential subject is found able to assign a surrogate, administer the *Surrogate Decision-Maker Assessment* (see Section 2, *Assessment Tools*) to evaluate the appropriateness of this person to serve as the potential subject's research surrogate.
- Document the assessment outcome according to organizational policy.

Ability to Assign a Surrogate Decision-Maker Assessment

Advocate Tools

Assess

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

Potential Subject _____ **Date** _____

Interviewer _____ **Rater** _____

Introduction

Begin the assessment with a brief introduction. For example,

Everyone who comes here is being considered for participation (or continued participation) in a research study. In order for you to participate, we need to get permission from someone else who knows you and whom you trust to help make decisions for you. I am here to talk with you about choosing the person you want to help you make decisions.

Domain 1: Understanding and Appreciation

While you participate (or continue to participate) in research, someone else will help you make decisions and give permission. You are allowed to choose the person who will help you.

- *Does that make sense to you?*
- *Would you like to choose who that person will be?*
- *What will happen if you do not choose a surrogate?* (Requires discussion about possible options such as not participating in research or enrollment by NOK if policy and protocol allow)

Potential subject's **understanding** of what it means to choose a surrogate and **appreciation** of how their choice affects them personally.

❑ Sufficient ❑ Insufficient

Ability to Assign a Surrogate Decision-Maker Assessment

Advocate Tools

Assess

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

Domain 2: Reasoning and Choice

If the potential subject wants to assign a surrogate, continue the assessment. If not, conclude the discussion.

- *Who would you like to help you make decisions or make them for you when you can't make decisions for yourself?*

  Name _____

  Relationship _____

- *Why did you pick this person?*
- *Can you talk to this person about what you would and would not want to do?*
- *Have you talked with this person about what you might be willing or not willing to do here?*
- *How would this person know if you did not want to do something?*

If the potential subject wants to choose someone but is having difficulty, then ask:

- *Is there someone who normally helps you make decision? For example, when you visit a doctor.*
- *Does that person make good decisions for you?*
- *What happens if you disagree with this person?*

Potential subject's **reasoning** in selecting a surrogate and **choice** of a surrogate are

❑ Sufficient ❑ Insufficient

FINAL OUTCOME

Potential subject's ability to assign a surrogate decision-maker is

❑ Sufficient ❑ Insufficient

Surrogate Decision-Maker Assessment

Advocate Tools

Assess

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

This assessment is a guide to help determine the surrogate decision-maker's ability to provide consent and, ideally, to represent the subject's wishes. It includes items to be considered that may go beyond the legal requirement.

For background information about this assessment, see Toolkit Section 1, *Assessment Descriptions*. More information about types and hierarchy of surrogates can be found in Toolkit Section 1, *Ability to Assign a Surrogate Decision-Maker Assessment* description.

Raters must be trained before administering the assessment.

Background

- Administer after a surrogate decision-maker has been identified by legal and/or organizational procedure.
- This tool is intended as a guide, not a script. Which questions to ask will depend on the case. How deeply to probe specific issues will depend on previous answers and the circumstances.
- Ideally, raters are familiar with the specific protocol, the study population, and information available about the subject.

Instructions

- Assessment of whether the surrogate understands the research should occur after it has been explained.
- Use one or two independent, trained raters.
- One rater is designated the interviewer and completes the form.
- The assessment is conducted in a private space, with the fewest observers present, and without the subject as appropriate.
- The interviewer should omit questions or probe more deeply depending on the discussion and circumstances specific to each assessment.
- A rater documents the assessment outcome according to organizational policy.

In this assessment, surrogate = the surrogate decision-maker; X = the potential subject.

Surrogate Decision-Maker Assessment

Advocate Tools

Assess

2.18

NIMH Human Subjects Research Protections Toolkit

Advocate Tools

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

Surrogate name _____ **Date** _____

Relationship to potential subject _____ **Protocol #** _____

Type of surrogate _____

Interviewer _____ **Rater** _____

Introduction

Begin with a brief introduction. For example

Our job is to make sure the people who come here understand what is being proposed and have their questions answered. I want to make sure the study has been explained to you, and you are willing to help make decisions for X.

- *What is your relationship to X?*
- *How do you know X?*
- *How long have you known X?*

Domain 1: Capacity to consent

Does the potential surrogate sufficiently understand the essential elements of consent?

Personal situation

- Tell me why you and X are here.
- What illness/medical concerns does X have?
- How do they affect X?

❑ Sufficient ❑ Insufficient

Proposed study

- *What is the goal of the study?*
- *What are the researchers trying to learn?*
- *How long will the study last?*

❑ Sufficient ❑ Insufficient

Procedures

- *What procedures are involved in the study?*
- *What will X have to do if X joins the study?*
- *What impact will participating in the study have on X?*

❑ Sufficient ❑ Insufficient

Surrogate Decision-Maker Assessment

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

Domain 1 (cont.)

The study involves research

- *Are there procedures the study team plans to do that are not for X's benefit?*
- *Why are they doing those procedures?*
- *How will being in the study differ from receiving clinical care in the community?*

❑ Sufficient ❑ Insufficient

Risks

- *Is there any chance X could be hurt or bad things might happen to X as a result of being in the study?*
- *What bad things might happen?*
- *What are the chances these things might happen or X might be hurt in these ways?*

❑ Sufficient ❑ Insufficient

Potential benefits

- *Is the study expected to help X?*
- *In what ways might being in the study help X?*
- *What are the chances X might benefit in these ways?*

❑ Sufficient ❑ Insufficient

Alternatives

- *What could X do for this condition instead of being in the study?*

❑ Sufficient ❑ Insufficient

Reasoning

- *How do the risks and potential benefits of joining the study compare to the other options available?*
- *Which option do you think makes most sense for X? Why?*

❑ Sufficient ❑ Insufficient

Voluntariness

- *Whose decision is it whether X enrolls in the study?*
- *Do you feel comfortable saying "no" if you or X decide not to join the study?*
- *Do you think anything bad would happen if X does not join the study?*

❑ Sufficient ❑ Insufficient

Surrogate Decision-Maker Assessment

Advocate Tools

Assess

2.20

This tool is based on the assessment developed by the Ability to Consent Assessment Team at the NIH Clinical Center. Adapt the tool according to your protocol requirements and organizational policy. This tool is clinically derived. It is not validated.

NIMH Human Subjects Research Protections Toolkit

Advocate Tools

Domain 2: Ability to represent the wishes or best interests of the subject

Does the surrogate have sufficient reason to believe their decisions regarding the research are consistent with the subject's preferences?

Consistency with subject preferences

- *If X could decide, what do you think X would do?*
- *Would X want to enroll in this study? Why or why not?*
- *How do you think X feels about being in a study designed to learn things that might help others?*

❑ Sufficient ❑ Insufficient

Ability to serve as surrogate

- How are decisions usually made about X's life?
- Have you made medical decisions for X previously?
- How do you feel about making decisions for X about being in the study?
- Are you willing to make decisions for X?
- What impact will it have on you?
- Will you involve anyone else in making decisions on X's behalf?

❑ Sufficient ❑ Insufficient

Ability to advocate

- Would it be difficult to tell the researchers that X doesn't want to do certain things?
- Do you feel comfortable standing up for X?
- How will X let you know if there is something X does not want to do?
- How do you plan to include X in making decisions about this research?

❑ Sufficient ❑ Insufficient

Closing questions

- Is there anything else that you would like to know?
- Do you have any additional questions for me?
- Is there anything else you would like me to know?

FINAL DETERMINATION

The surrogate decision-maker's ability to provide consent and, ideally, to represent the subject's wishes is determined to be

❑ Sufficient ❑ Insufficient

Consent Monitoring Checklist

Advocate Tools

Monitor

2.21

NIMH Human Subjects Research Protections Toolkit

Advocate Tools

This checklist is a tool to use with the potential subject or surrogate decision-maker to assure all parts of the consent process are completed.

Before the consent

- ❑ Assure the consent and/or assent discussion takes place in a quiet, private space.
- ❑ Assure the correct version of consent and/or assent is used.

During the consent

- ❑ Pay attention to non-verbal communication.
- ❑ Observe the potential subject's understanding of the information presented. If the potential subject does not understand, know the next steps to take (e.g., consider stopping and moving to a capacity assessment).
- ❑ Assure all required consent elements* are reviewed and discussed by the researcher and the potential subject. Additional situational elements may be required.**
  - ❑ Purpose of the research
  - ❑ Participation is voluntary
  - ❑ Expected duration of participation
  - ❑ Protocol procedures
  - ❑ Potential risks and discomforts
  - ❑ Potential benefits
  - ❑ Identification of experimental procedures
  - ❑ Alternative treatments
  - ❑ Confidentiality including exceptions (e.g., mandated reporting)
  - ❑ Research related injury
  - ❑ Compensation
  - ❑ Researcher contact information
  - ❑ A statement on the collection of identifiable private information or identifiable biospecimens
- ❑ Ask whether the potential subject has any questions or concerns.
- ❑ Ask whether the potential subject wants to participate in the research.
- ❑ Confirm the researcher, the potential subject, and the witness sign the correct version of consent and/or assent document(s).

*General Requirements for Informed Consent, 45 C.F.R. § 46.116 (b), 2018. Your IRB may require additional elements.

**General Requirements for Informed Consent, 45 C.F.R. § 46.116 (c), 2018.

Consent Monitoring Checklist

After the consent

- ❑ Encourage the subject to ask questions of the researchers throughout the protocol, not just during the consent process.
- ❑ Remind the subject that a decision to participate may be changed any time, even after signing consent.
- ❑ Document the consent process according to organizational policy.
- ❑ Give the subject a copy of the signed consent.

Subject Monitoring Guide

The questions below are suggestions to guide a conversation with the subject about the ongoing research experience. The advocate documents according to organizational policy.

Does the subject know what and how many procedures remain to be done?

_____

_____

_____

_____

How has the experience been so far?

_____

_____

_____

_____

Does the subject have any questions or concerns?

_____

_____

_____

_____

If so, have the questions or concerns been communicated to the team or appropriate persons?

_____

_____

_____

_____

Does the subject want to continue in the research?

_____

_____

_____

_____

Objective Structured Clinical Examination (OSCE)

for the Evaluation of the Informed Consent Process

Advocate Tools

Evaluate the Researcher

Instructions

This OSCE is used to evaluate a researcher's ability to obtain informed consent from a potential subject who is eligible to participate in a specific protocol. The evaluator observes (in person or virtually) the consent process between the researcher and a real or mock potential subject. The researcher is evaluated in three areas:

- Professionalism
- Interpersonal and communication skills
- Required consent elements

The researcher begins the consent discussion with a self-introduction and explanation of the evaluator's presence. For example,

> *My name is _____. I am going to review the informed consent form with you. The person accompanying me is evaluating me and will take notes as we go along. However, my focus is on making sure you have all the information you need to make a decision about participating in this study.*

The researcher reviews the consent form. For each section, the evaluator circles one of the following choices:

1. Meets expectations
2. Meets expectations with recommendations
3. Needs improvement and recommend doing another OSCE

The evaluator prompts the researcher if needed (e.g., if an element of consent is missed) and notes feedback and observations in the comment section.

The OSCE results and feedback are shared with the researcher. Verbal or written feedback should specifically address any recommendations or areas that need improvement and provide ways in which to improve. Additional OSCEs are scheduled as needed to demonstrate the researcher's improvement.

Objective Structured Clinical Examination (OSCE)

for the Evaluation of the Informed Consent Process

Advocate Tools

Evaluate the Researcher

2.25

NIMH Human Subjects Research Protections Toolkit

Advocate Tools

Researcher's name_____ **Institute**_____

Professionalism

1. **Introduces** self and role
2. Assures **privacy** during interview
3. Promotes subject **comfort** during interview
4. Utilizes **non-coercive** style of questioning
5. **Limits** number of observers present as appropriate
6. **Allows** involvement of significant other as appropriate

Circle one:

1. **Meets expectations.** *Demonstrated all of the above elements.*
2. **Meets expectations with recommendations.** *Missed an element or needs to make adjustments in future consents (e.g., a prompt is required for an element, did not have a copy of the consent form for the subject).*
3. **Needs improvement.** *Missed multiple elements or required multiple prompts (e.g., did not explain researcher role, allowed interruptions such as people in and out of the room or phone calls, did not ask subject preferences as to others in the room, did not have correct consents, discussed unrelated protocols, gave too much self-disclosure). Recommend doing another OSCE.*

Comments

Interpersonal and Communication Skills

1. **Presentation style**
   a. Presents in an **organized** way with sufficient detail*
   b. Utilizes a **conversational** manner
   c. Avoids **reading** content verbatim
   d. Is attentive and **empathic**
   e. Elicits **questions** effectively
   f. Allows sufficient time for **discussion** including reasons why one might want to participate or not participate*

Circle one:

1. **Meets expectations.** *Demonstrated all elements in a way that facilitated comprehension including having consent forms prepared.*
2. **Meets expectations with recommendations.** *Demonstrated elements with minor exceptions (e.g., required a prompt, read too much of the consent, missed non-verbal cue, rushed).*
3. **Needs improvement.** *Required prompts for multiple elements (e.g., researcher read the entire consent, was not familiar with the consent form, did not ask clarifying questions, did not allow time for discussion, unorganized or difficult to follow along). Recommend doing another OSCE.*

Comments

Objective Structured Clinical Examination (OSCE)

for the Evaluation of the Informed Consent Process

Advocate Tools

Evaluate the Researcher

Interpersonal and Communication Skills (cont.)

2. **Body and verbal language**
   a. Maintains appropriate **eye contact**
   b. Uses language **understandable** to the subject**
   c. Uses language that is **clear** and appropriate to the subject's education level

Circle one:

1. **Meets expectations.** *Demonstrated all elements.*
2. **Meets expectations with recommendations.** *Demonstrated elements with minor exceptions (e.g., required a prompt, used some jargon, spoke too fast).*
3. **Needs improvement.** *Required multiple prompts (e.g., missed non-verbal cues, didn't use an interpreter, used excessive jargon). Recommend doing another OSCE.*

Comments

General Requirements for Informed Consent

Basic consent elements**

1. A statement that the study involves **research**	❑ Yes	❑ Prompt
2. A statement that participation is **voluntary**	❑ Yes	❑ Prompt
3. An explanation of the **purposes** of the research	❑ Yes	❑ Prompt
4. The **expected duration** of the subject's participation	❑ Yes	❑ Prompt
5. A description of the **procedures** to be followed	❑ Yes	❑ Prompt
6. Identification of procedures that are **experimental**	❑ Yes	❑ Prompt
7. A description of **risks/discomforts**	❑ Yes	❑ Prompt
8. A description of any **benefits** to the subject or to others	❑ Yes	❑ Prompt
9. A disclosure of appropriate **alternative** procedures or courses of treatment that might be advantageous	❑ Yes	❑ Prompt
10. A statement that the **confidentiality** of records will be maintained	❑ Yes	❑ Prompt
11. An explanation about **compensation**	❑ Yes	❑ Prompt
12. An explanation about available medical treatments for **a research-related injury**	❑ Yes	❑ Prompt

Objective Structured Clinical Examination (OSCE)

for the Evaluation of the Informed Consent Process

Advocate Tools

Evaluate the Researcher

Basic consent elements

13. Identification of **contact** person for questions about the research, research subject's rights, or research-related injury ❑ Yes ❑ Prompt
14. A statement on the **collection** of identifiable private information or identifiable biospecimens ❑ Yes ❑ Prompt

Additional consent elements***

15. Any additional elements (e.g., conflict of interest) in the consent form were reviewed ❑ Yes ❑ Prompt ❑ n/a

Circle one:

1. **Meets expectations.** *"Yes" marked for all elements (or n/a for element 15).*
2. **Meets expectations with recommendations.** *Required a prompt or needs to make adjustments in future consents.*
3. **Needs improvement.** *Required multiple prompts. Recommend re-doing the OSCE.*

Comments

Researcher signature_____ **Date**_____

Evaluator signature_____ **Date**_____

*General Requirements for Informed Consent, 45 C.F.R. § 46.116 (a), Basic Elements of Informed Consent, 2018.

**General Requirements for Informed Consent, 45 C.F.R. § 46.116 (b), Basic Elements of Informed Consent, 2018.

***General Requirements for Informed Consent, 45 C.F.R. § 46.116 (c), Additional Elements of Informed Consent, 2018.

Training SECTION 3 Tools

Section 3 provides examples and practice exercises to develop advocate skills in specific consent processes.

Assessment and monitoring outcomes are nuanced and complex. Outcomes presented in this section are possible conclusions based on a particular interpretation of the facts presented. It is possible to come to a different conclusion based on a different interpretation of the facts and application of organizational policy.

Examples

Capacity Assessment
Ability to Assign a Surrogate Decision-Maker Assessment
Surrogate Decision-Maker Assessment
Consent Monitoring
Assent Monitoring
Subject Monitoring

Practice Exercises

Capacity Assessment
Ability to Assign a Surrogate Decision-Maker Assessment
Surrogate Decision-Maker Assessment
Consent Monitoring
Assent Monitoring
Subject Monitoring

Capacity Assessment

B, a 21-year-old diagnosed with recent onset schizophrenia, plans to enroll in an inpatient double-blind, placebo-controlled protocol. The Institutional Review Board (IRB) determined that the protocol

- Is more than minimal risk
- Has no prospect of direct benefit
- Requires an advocate to administer a capacity assessment to all potential subjects before participation

B has not received any treatment in the community and, by participating in this protocol, will not receive standard treatment until participation in the protocol is complete.

During the capacity assessment held prior to the consent process, B clearly is not aware of alternative treatments available in the community. The advocate discusses the difference between research and clinical care with B, but B continues to have difficulty appreciating the difference between the two.

Points to consider

- The potential subject does not understand that alternative standard treatments are available in the community.
- The potential subject does not understand the difference between research and clinical care.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

B is determined not to have consent capacity for this protocol at this time. The advocate discusses the result with B and the researcher. The researcher recommends pursuing treatment in the community. The advocate documents the outcome according to organizational policy.

Ability to Assign a Surrogate Decision-Maker Assessment

Training Tools

Examples

C, a 39-year-old with frontal lobe epilepsy, is invited to participate in a protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has a prospect of direct benefit
- Allows surrogate decision-maker consent

The advocate determined the potential subject does not have consent capacity at this time.

C is accompanied by his mother who is not his legal guardian. C does not have an advance directive (AD). The advocate recommends and administers an assessment of C's ability to assign a surrogate decision-maker for research.

Points to consider

- A potential subject without consent capacity may be able to assign a surrogate decision-maker.
- The protocol allows designation of a surrogate decision-maker.
- There is a difference between a legal guardian and an agent named in an AD.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

C is determined able to assign a surrogate decision-maker. C selects his mother. The advocate helps C complete an AD form for research. The advocate assesses the appropriateness of the surrogate decision-maker. The advocate documents the outcome according to organizational policy.

Surrogate Decision-Maker Assessment

D, a 79-year-old with symptoms of dementia, plans to enroll in a 2-year protocol requiring multiple visits. The IRB determined the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Allows for surrogate decision-maker consent with subject assent
- Requires an advocate to administer a capacity assessment at each visit

Using a protocol-specific capacity assessment, the advocate determines D does not have consent capacity at this visit. D has a pre-existing durable power of attorney (DPA) for healthcare identifying her husband as her surrogate decision-maker. Legal counsel reviews the document and determines the surrogate decision-maker can authorize consent for research participation.

Before obtaining consent, the advocate assesses the appropriateness of the surrogate decision-maker. D's husband states, "This study is important. I want D to get better." The advocate clarifies that participating in this protocol will not cure or treat D's dementia. Her husband confirms his understanding and says, "I know these scans will not help D directly, but I think it will help science. D has told me before that she wants to help others in the future, even if there is no cure for her."

Points to consider

- The protocol allows surrogate decision-maker consent with subject assent.
- The surrogate decision-maker may not understand "no prospect of direct benefit."
- The surrogate decision-maker is able to express the potential subject's wishes as opposed to his own.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

The advocate determines that D's husband has sufficient understanding to provide surrogate consent and can appropriately represent D's wishes concerning research participation. The advocate documents the outcome according to organizational policy.

Consent Monitoring

E, a 41-year-old with depression, plans to enroll in an inpatient mood disorder protocol. The IRB determined the protocol

- Is more than minimal risk
- Has a prospect of direct benefit
- Requires consent monitoring by an advocate

The researcher obtaining consent asks E, with the trainees present, if they may observe the consent process. E agrees, but the advocate notices that E's tone of voice, demeanor, and body language indicate discomfort. The advocate pauses the consent process and speaks individually with E to confirm whether these observations are accurate. The advocate emphasizes that, if E is not comfortable with additional people attending the consent process, the observers do not have to be present. E states, "I would prefer fewer people in the room." The advocate conveys E's preference to the researcher.

Points to consider

- Determine the number of people necessary for the consent process.
- Be sensitive, reasonable, and flexible about additional observers.
- Obtain the potential subject's permission and honor refusal.
- Avoid asking the potential subject's permission with observers present. It may place undue pressure on the potential subject's decision.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

Per E's request, the researcher communicates to the trainees that they will not observe this consent process.

Assent Monitoring

Training Tools

Examples

Pediatric Assent

F, a 12-year-old, plans to enroll in an inpatient pediatric mental health protocol. The IRB determined the protocol

- Is a minor increment over minimal risk
- Has no prospect of direct benefit
- Requires consent and assent monitoring by an advocate

The researcher conducts the consent and assent process with F and her parents with the advocate present. The researcher discusses each element of the consent with F and answers her questions. F verbally demonstrates throughout the process that she is thoroughly informed regarding her condition, the protocol procedures, and possible risks. F is enthusiastic that she may help others by participating in the protocol. She is aware she can change her mind about her participation.

Points to consider

- Engage the potential subject in conversation rather than read the consent form.
- Clarify protocol terms and concepts as needed.
- Address the potential subject's questions and concerns.
- Understand the potential subject's motivation for participation.
- This scenario does not incorporate applicable organizational policies.

Possible outcome

F gives her assent and her parents provide consent. The advocate documents the outcome according to organizational policies.

Assent Monitoring

Training Tools

Examples

Pediatric Dissent

G, an 11-year-old, comes with his parents to enroll in an outpatient protocol. The IRB determined that the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Requires subject assent
- Requires consent and assent monitoring by an advocate

During the consent and assent process, the researcher describes the voluntary nature of research and explains that all procedures are for research purposes and not for clinical care. The parents are eager for G to participate in this protocol. However, G begins shaking his head when reviewing the protocol procedures. G states, "I've told my parents over and over that I'm not interested in written tests, and I'm afraid of small spaces and do not want to do the MRI."

The advocate pauses the process. The researcher discusses G's concerns with him to determine whether they can be mitigated. The advocate speaks with the parents about assent and respecting dissent.

Points to consider

- The potential subject's assent is required for enrollment in protocol.
- Dissent is respected.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

G is consistent in stating he does not want to participate. This protocol will not benefit him and provides no clinical care. He does not enroll at this time but has the option to enroll at a later date should he change his mind. The advocate documents the outcome according to organizational policy.

Assent Monitoring

Training Tools

Examples

Adult Assent

H, a 50-year-old with a traumatic brain injury, is eligible to enroll in an outpatient brain imaging protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has a prospect of direct benefit
- Requires a capacity assessment
- Allows surrogate decision-maker consent with subject assent as appropriate
- Requires consent and assent monitoring by an advocate

H is assessed and determined to have consent capacity at the first visit. The researcher conducts the consent process, and H provides her own consent.

One month later, H returns to participate in another protocol with the same IRB requirements. She is assessed and is determined not to have consent capacity but able to assign a surrogate decision-maker. H chooses her spouse, who is assessed to be an appropriate surrogate decision-maker. The surrogate decision-maker provides consent, and H assent. The advocate monitoring the assent process observes that H is engaged in the conversation, asks questions, and states her intention to participate in the protocol.

Points to consider

- The protocol requires potential subject assent as appropriate.
- The subject's choice to participate does not change even if her consent capacity fluctuates.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

Over a one-month period, H's decision-making capacity to give consent fluctuates, but the advocate observes that her expressed choice to participate in research generally and the protocol specifically, does not. The advocate documents the outcome according to organizational policy.

Assent Monitoring

Training Tools

Examples

Adult Dissent

J, a 21-year-old with Fragile X syndrome, is eligible to enroll in an outpatient brain imaging protocol. The IRB determined that the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Requires an advocate to administer a capacity assessment to all potential subjects
- Allows surrogate decision-maker consent with subject assent

J's mother is his legal guardian. Legal counsel confirms the guardianship order allows his mother to provide consent for this research. A capacity assessment by the advocate is not required since the court has already determined J cannot provide his own consent. J's mother understands the parameters of the protocol and provides consent. J indicates his willingness to participate in the protocol and gives assent.

Technical difficulties occur during a procedure, and the procedure is stopped before gathering usable data. The IRB approves the repetition of the procedure but requires re-consent and assent.

During the re-consent process, the advocate notes a change in J's non-verbal behavior (e.g., lack of eye contact, grimacing, folding his arms over his body). The advocate consults with J's mother who states J's behavior indicates he does not wish to undergo a second attempt at the procedure.

Points to consider

- Guardianship papers should be reviewed (e.g., by legal counsel).
- Use the surrogate decision-maker's familiarity with the potential subject's behavior as a resource.
- Both verbal and behavioral dissent are respected.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

J's dissent is respected, and the repeat procedure does not occur. The advocate documents the outcome according to organizational policy.

Subject Monitoring

Training Tools

Examples

K, a 32-year-old, enrolls in an inpatient schizophrenia protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has no prospect of direct benefit
- Requires subject monitoring by an advocate

During their weekly meeting, K shares with the advocate her increasing doubts about continuing in the protocol. Specifically, being off medications is harder than she expected, but she feels guilty about disappointing the researcher.

Points to consider

- Informed consent is an ongoing process, not a one-time signing of a document.
- The subject's circumstances, symptoms, and willingness to continue participation in the protocol may fluctuate over time.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

With the advocate's support, K conveys her concerns to the researcher and withdraws from the protocol. The researcher meets with K and designs an appropriate discharge plan. The advocate documents the outcome according to organizational policy.

Subject Monitoring

Training Tools

Examples

L, a 14-year-old diagnosed with childhood onset schizophrenia, enrolls in an inpatient pediatric protocol. The IRB determined that the protocol

- Is greater than minimal risk
- Has a prospect of direct benefit
- Requires subject assent

L begins to refuse protocol-related tasks. The researcher, unit staff, and the advocate meet with L over several days to discuss his willingness to remain in the protocol. L continues to state he wants to participate. However, despite this statement, L routinely declines protocol tasks.

After several discussions with his advocate, L admits he no longer wants to be in the protocol and is concerned his parents will be upset with him. L communicates clearly and consistently his wish to withdraw from the protocol. L and his advocate meet with the researcher who assures him his reasons for wanting to stop are valid and will be discussed with his parents.

Points to consider

- Subject dissent is consistent.
- Both verbal and behavioral dissent are considered.
- Tasks refused by the subject are protocol-related, not clinical.
- Alternative treatments are available in the community.
- This scenario does not incorporate applicable organizational policy.

Possible outcome

The researcher meets with the parents to discuss L's withdrawal of assent, and L ends his research participation. The advocate documents the outcome according to organizational policy.

Capacity Assessment

Training Tools

Practice Exercises

M, a 26-year-old with a diagnosis of schizophrenia, is invited to participate in a protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has no prospect of direct benefit
- Requires an advocate to administer a capacity assessment to all potential subjects

The advocate administers a protocol-specific capacity assessment and determines M has a clear understanding of the purpose and procedures involved in the protocol. M states that her most significant risk is a worsening of symptoms associated with the tapering of her anti-psychotic medications.

Toward the end of the assessment, the advocate asks M about her choice to participate in the protocol. M states, "I don't really want to be in the study, but my husband says I have to. He is getting ready to travel for work and will be gone a long time. He doesn't want me to be home alone."

What is your determination of the potential subject's capacity to provide informed consent?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Capacity Assessment

PROMPTS

- How can the advocate help the potential subject identify her choices and preferences regarding protocol participation?
- What are the alternatives to protocol participation?
- In what ways can the advocate help the potential subject identify and discuss her right to autonomy versus her husband's suggestion about protocol participation?
- Should the advocate speak with the spouse?
- What organizational policies may apply?

POSSIBLE OUTCOME

M has capacity to provide informed consent. She understands the purpose, procedures, and risks of the protocol. M chooses not to participate in the protocol at this time but is open to participation in future protocols. After a discussion with the advocate and the researchers, M's husband arranges for her clinical care in the community. The advocate documents the outcome according to organizational policy.

Ability to Assign a Surrogate Decision-Maker Assessment

Training Tools

Practice Exercises

N, a 21-year-old with Down syndrome, plans to enroll in a protocol. The IRB determined that the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Allows surrogate decision-maker consent with subject assent

The researcher determines N has cognitive limitations and is unable to provide her own consent for research at this time. The researcher contacts the advocate to assess N's ability to assign a surrogate decision-maker.

The advocate explains the purpose of the assessment to N. N shares that her father usually takes her to her medical appointments in the community. She states, "Sometimes I get shy about speaking up, and sometimes I am confused by what the doctor is saying. My father understands and knows what I like and don't like to do." N further states she trusts him to speak for her and help her make decisions. N says she does volunteer work in the community and likes helping others.

Does the potential subject have the ability to assign a surrogate decision-maker?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Ability to Assign a Surrogate Decision-Maker Assessment

PROMPTS

- Whom does the potential subject trust to speak on her behalf about medical care and preferences?
- Has the potential subject discussed medical care issues with this person?
- How would the potential subject inform researchers if she does not agree to procedures or tests?
- What organizational policies may apply?

POSSIBLE OUTCOME

The advocate determines N has the ability to assign a surrogate decision-maker. N's father already serves as her surrogate decision-maker for medical care in the community, and N relies on him to communicate for her. While N may not fully understand the protocol, she values helping others. The advocate documents the outcome according to organizational policy.

Surrogate Decision-Maker Assessment

Training Tools

Practice Exercises

P, a 70-year-old with Alzheimer's disease, enrolls in an outpatient protocol. The IRB determined that the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Allows surrogate decision-maker consent with subject assent
- Requires a surrogate decision-maker assessment by an advocate

P was determined not to have consent capacity at this time. P previously named her husband as the agent of her AD.

P's husband accompanies her to the visit and is authorized to provide consent. The advocate assesses the appropriateness of the surrogate. During the assessment, P's husband confirms he and P have discussed research participation prior to her dementia worsening. "My wife's motivation for participating is the knowledge that Alzheimer's disease runs in her family. She is concerned for our children and grandchildren and wants to contribute to finding a future treatment or cure."

P's husband understands the protocol procedures and potential risks and confirms he knows the protocol will not directly benefit his wife. He states that, although he gives consent, he feels comfortable stopping P's participation if she no longer wants to continue. He explains P will communicate her dissent by scowling, shaking her head, or leaving the room if she does not want to do something.

Is the husband an appropriate surrogate decision-maker?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Surrogate Decision-Maker Assessment

PROMPTS

- Does the protocol allow for surrogate decision-maker consent?
- Has an appropriate surrogate decision-maker been identified?
- Is the potential surrogate decision-maker willing to serve in this capacity?
- What conversations have the potential surrogate decision-maker and the potential subject had about research participation? Did they discuss non-beneficial research?
- During the protocol, how will the surrogate decision-maker know if the subject withdraws assent?
- What organizational policies may apply?

POSSIBLE OUTCOME

The advocate determines P's husband is an appropriate surrogate decision-maker. The researcher may now invoke the AD and obtain consent from him and assent from P. The advocate documents the outcome according to organizational policy.

Consent Monitoring

R, a 35-year-old, plans to enroll in an inpatient bone marrow transplant protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has a prospect of direct benefit
- Requires identification of a surrogate decision-maker in case the subject's capacity fluctuates
- Requires consent monitoring by an advocate

Prior to the consent process, R identified his wife as his surrogate decision-maker. His wife requests that the researcher conduct the discussion with her alone. She is aware of the procedures and risks and feels anxious about the treatment protocol. In addition, she wants R to remain optimistic and fears the possibility of needing a surrogate decision-maker will have a negative impact. She insists, "Please don't talk to R about these complications. This will get into his head, and he will feel worse. I can sign the informed consent for him. I want him to have the right mind set and be optimistic about the treatment."

What do you tell the potential subject's wife?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Consent Monitoring

Training Tools

Practice Exercises

PROMPTS

- Is it allowable for the potential subject's wife to provide research consent? Why or why not?
- What is the role of self-determination and autonomy in research participation?
- How can the advocate help educate the wife about the consent process?
- What organizational policies may apply?

POSSIBLE OUTCOME

Potential subjects provide their own consent unless unable to do so.* The advocate provides education about the voluntary nature of research and reassures R's wife the discussion will be more helpful than harmful to R. R's wife understands and is willing to include R in the consent process. The researcher discusses all the consent elements with both R and his wife. The advocate documents the outcome according to organizational policy.

*National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research,* Bethesda, MD: U.S. Govt. Print. Off., 1978, Part B: Basic Ethical Principles, Section 1, Respect for Persons.

Assent Monitoring

Training Tools

Practice Exercises

S, a 32-year-old with an intellectual disability whose parents are his legal guardians, is eligible to participate in a protocol. The IRB determined that the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Allows surrogate decision-maker consent with subject assent
- Requires consent and assent monitoring by an advocate

Legal counsel determined the guardianship order authorizes the parents to consent for this research, and the advocate found the parents to be appropriate surrogate decision-makers.

As part of the consent and assent process, the researcher describes protocol procedures which include an IV, an MRI, and computer tasks. S states, "I'm afraid the MRI will hurt. No, I don't want to do this." The researcher talks with S about S's concerns. He further clarifies that this procedure is for research and not for clinical care. The parents would like S to participate. However, S continues to say, "No."

Can the potential subject dissent independently?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Assent Monitoring

Training Tools

Practice Exercises

PROMPTS

- Is assent by the potential subject required when the legal guardians are providing consent?
- Is the MRI for research or clinical care?
- Is the MRI required for protocol participation?
- What organizational policies may apply?

POSSIBLE OUTCOME

If the MRI is not required, S could assent to the other procedures. If the MRI is required, even though his legal guardians could provide consent, S's dissent is respected and research does not proceed. The advocate documents the outcome according to organizational policy.

Assent Monitoring

Training Tools

Practice Exercises

T, a 75-year-old diagnosed with moderate dementia, is eligible to enroll in a protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has a prospect of direct benefit
- Requires an advocate to administer a protocol-specific capacity assessment
- Allows surrogate decision-maker consent with subject assent

T previously executed an AD which included research and designated her husband as her surrogate decision-maker. Over the years, T and her husband have discussed her desire to contribute to science for the benefit of others who may suffer with a similar diagnosis.

The advocate determined that T is unable to provide her own consent at this time and that T's husband is an appropriate surrogate decision-maker.

During the assent discussion, T tells the advocate and the researcher that she does not want to participate in the brain scan for fear it would make her symptoms worse, but if her husband thinks it's a good idea, then T will do the scan.

Is the potential subject providing assent?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Assent Monitoring

PROMPTS

- What is the impact of the couple's earlier conversation about research participation?
- Is it possible to address the potential subject's concern?
- Should the surrogate decision-maker's wishes override the potential subject's concern?
- What organizational policies may apply?

POSSIBLE OUTCOME

The researcher explains to T that the brain scan will not make her symptoms worse. T could respond in two ways:

- T states she now understands the scan will not hurt her. Earlier conversations with T's husband confirm T's willingness to participate in this protocol. T is providing assent at this time.
- T is agitated, insisting the scan will hurt her. Due to the nature of her illness, T becomes frustrated and confused when feeling frightened. T is not providing assent at this time.

The advocate documents the outcome according to organizational policy.

Assent Monitoring

V, an 8-year-old, comes with his parents for enrollment in an inpatient protocol. The IRB determined that the protocol

- Is greater than minimal risk
- Has a prospect of direct benefit
- Requires consent and assent monitoring by an advocate

During the consent process, V states he is worried about the blood draw. The researcher explains that the nurse will numb the skin first so that it will feel more like a pinch. V states, "OK." He asks questions about what it will be like on the inpatient unit. He then excitedly states, "My parents said I'll be helping kids like me by being here."

Is the potential subject giving assent?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Assent Monitoring

PROMPTS

- Is the potential subject engaged in the conversation?
- Does he have concerns? If so, were they addressed?
- Have he and his parents discussed what it means to be in research?
- What organizational policies may apply?

POSSIBLE OUTCOME

V is giving assent. V's concern about the blood draw is addressed, and he expresses a desire to help others with a similar condition. The advocate documents the outcome according to organizational policy.

Assent Monitoring

Training Tools

Practice Exercises

W, a 16-year-old with depression, is referred by her therapist to enroll in an outpatient protocol. The IRB determined that the protocol

- Is minimal risk
- Has no prospect of direct benefit
- Requires consent and assent monitoring by an advocate

During the consent conversation with W's mother present, W crosses her arms, says nothing, looks down, and turns her back to the rest of the people in the room. After the researcher reviews all the consent elements, the advocate asks W if she wants to participate in the protocol. W replies, "No! But my parents won't let me go to a concert this weekend unless I do this."

Is the potential subject giving assent?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Assent Monitoring

PROMPTS

- What is the potential subject conveying verbally and non-verbally?
- Is there alternative treatment available in the community?
- Can the parents insist the potential subject participate?
- What organizational policies may apply?

POSSIBLE OUTCOME

W's dissent should be respected. Despite the parents' good intentions, making concert attendance contingent on research participation is coercive. The protocol does not provide a prospect of direct benefit, and W can continue treatment in the community. The advocate documents the outcome according to organizational policy.

Subject Monitoring

Training Tools

Practice Exercises

Y, a 42-year-old, is enrolled in an inpatient double-blind, placebo-controlled schizophrenia protocol. The IRB determined that the protocol

- Is more than minimal risk
- Has no prospect of direct benefit
- Requires subject monitoring by an advocate

Y confides to the advocate that he has had only three hours of sleep for the past three nights. Y appears distracted and extremely tense. Y shares that he is experiencing increased anxiety and is terrified that "something bad is going to happen." Y admits that his auditory hallucinations have increased but is reluctant to divulge their content.

When the advocate asks Y if he wants to continue in the protocol, he responds, "I don't want to let the research team down." He further requests the advocate withhold this information from the researchers.

Has the subject confirmed his consent?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Subject Monitoring

PROMPTS

- What concerns might the advocate have following this interaction?
- Should the advocate honor the subject's request not to share this information with the researcher?
- What organizational policies may apply?

POSSIBLE OUTCOME

Y's increasing symptoms may impact his ability to provide ongoing informed consent. In addition, delaying treatment of symptoms by the possibility of being on placebo may not be in Y's best interest. The advocate addresses the subject's concerns and reminds him that information relevant to his safety cannot be withheld from the researcher. The advocate facilitates a discussion with the researcher about Y's continued participation. The advocate documents the outcome according to organizational policy.

Subject Monitoring

Training Tools

Practice Exercises

Z, a 12-year-old, is enrolled in a two-month inpatient mood dysregulation protocol. The protocol includes a tapering of Z's current medications, a double-blind medication trial, and research tasks such as brain imaging and cognitive testing. The IRB determined that the protocol

- Is a minor increment over minimal risk
- Has a prospect of direct benefit

Z attends an in-hospital school, enthusiastically participates in recreational therapy activities, and completes protocol tasks without complaint. One month into the protocol, Z abruptly announces to one of the nurses that he no longer wants to participate in the protocol. Z states, "I know I can change my mind about being here, and I want to leave!"

The teacher discloses that Z had difficulty with that morning's lessons and became very upset about not being able to complete them. The advocate is consulted to ascertain whether the subject is withdrawing assent.

Did the subject withdraw his assent?

Write the points you will consider:

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Write your outcome:

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Prompts and possible outcome on next page

Subject Monitoring

PROMPTS

- Does this incident occur during the medication taper when mood symptoms may increase?
- Has the subject given previous indication of dissatisfaction with being in the protocol?
- Has the subject been participating in all aspects of therapeutic and protocol activities?
- What organizational policies may apply?

POSSIBLE OUTCOME

A one-time statement made in momentary frustration is not necessarily a withdrawal of assent although the statement should be further discussed with Z and his parents. If Z's behavior continues and he states his desire to leave when calm as well, Z has withdrawn assent. The advocate documents the outcome according to organizational policy.

Appendix SECTION 4

Section 4 provides a glossary, additional examples, and resources from the NIMH Human Subjects Protection Unit (HSPU).

NIMH Abbreviations and Glossary
NIMH Consent Process Flowchart
NIMH HSPU Brochure
Sample Electronic Medical Record
Sample Protocol Language
Sample Consent Language
Sources for More Information

NIMH Abbreviations and Glossary

Abbreviations

AD Advance directive
ACAT Ability to Consent Assessment Team
CC Clinical Center
CORE Centralized Office of Recruitment and Evaluation
CRA Clinical Research Advocate
DPA Durable power of attorney
HRPP Human research protection program
HSPU Human Subjects Protection Unit
IRB Institutional Review Board
LAR Legally authorized representative
NBAC National Bioethics Advisory Commission
NIH National Institutes of Health
NIMH National Institute of Mental Health
NOK Next-of-kin
OSCE *Objective Structured Clinical Examination*

Glossary

***Ability to Assign a Surrogate Decision-Maker Assessment*:** Tool used to determine whether a potential subject has the ability to choose another person to make decisions during research participation.

advance directive: Written instruction, such as a living will or durable power of attorney for health care, recognized under state law (whether statutory or as recognized by the courts of the state), relating to the provision of health care when the individual is incapacitated.

advocate: Primary component of a human subjects protection program. Trained clinician responsible for assessing, developing, and implementing safeguards for potentially vulnerable subjects enrolling in research.

assent: Agreement to participate in a protocol by an adult without decision-making capacity or by a minor. Failure to dissent does not establish assent.

assent monitoring: Process to assure the quality of the assent discussion for adults without decision-making capacity and minors by verifying the agreement of the potential subject to participate in a protocol.

capacity: An adult potential subject's ability to provide informed consent for participation in a specific protocol. Contrast **competency.**

capacity assessment: Assessment of an adult potential subject's ability to provide informed consent for a specific protocol at a specific time.

***Capacity Assessment: Generic*:** Basic assessment format for assessing a potential subject's ability to provide informed consent. Must be adapted when an unanticipated need for an assessment arises.

***Capacity Assessment: Protocol-Specific*:** Tool customized to assess a potential subject's ability to provide informed consent for a specific protocol. Used for protocols requiring some or all potential subjects to be assessed.

NIMH Abbreviations and Glossary

Code of Federal Regulations: United States administrative law published by the executive departments and agencies of the federal government. Title 45 Public Welfare, Part 46 Protection of Human Subjects is the Health and Human Services federal policy for the protection of human subjects. Subpart A is also referred to as the Common Rule.

competency: A person's ability to understand legal rights and responsibilities and the authority to exercise them. Often determined by a court of law. Contrast **capacity**.

consent: Agreement to participate in research given by an adult or a surrogate decision-maker for a minor or an adult without consent capacity.

consent monitoring: Process by which an advocate assures the elements of consent are discussed by a researcher and a potential subject and/or a surrogate decision-maker.

dissent: Refusal to participate in research given verbally or behaviorally by a potential subject or a subject.

durable power of attorney: Legal document designating a person to make decisions on another's behalf if the person becomes incapacitated.

legal guardian: Person who has the legal authority and responsibility to care for another individual who is considered incapable, generally as determined by a state court.

legally authorized representative: Person who is authorized to be a surrogate decision-maker for another individual.

living will: Legal document that allows a person to state in advance the kinds of care the person would or would not want should the person become unable to make decisions.

next-of-kin: Person who serves as a surrogate decision-maker for an individual based on relationship (e.g., spouse, parent, or adult child).

short form: Consent document stating the required elements of informed consent have been presented orally to a potential subject or a potential subject's legally authorized representative.

subject: Person enrolled in a research protocol.

subject monitoring: Periodic visits by an advocate to assess a subject's current wishes, understanding, and concerns regarding continued participation in research.

surrogate decision-maker: Person assigned to act on behalf of another individual.

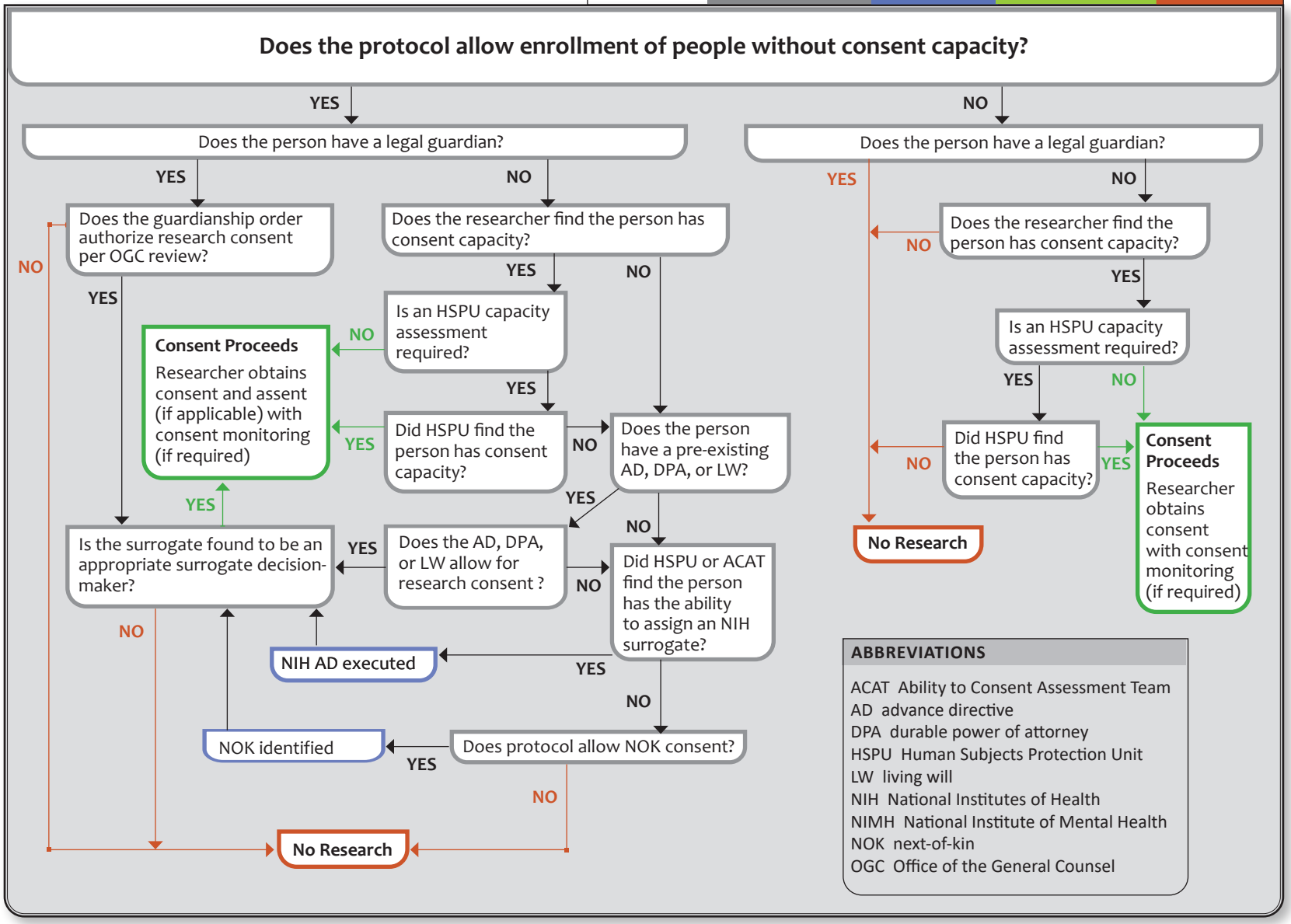
***Surrogate Decision-Maker Assessment*:** Tool used to evaluate a potential surrogate decision-maker's ability to represent a subject's wishes regarding research participation.

therapeutic misconception: Failure of a research subject to appreciate the distinction between the imperatives of clinical research and of ordinary treatment, and therefore inaccurately attributes beneficial intent to research procedures.

vulnerable populations: Individuals who may require additional safeguards (e.g., capacity assessment, subject monitoring) to protect them from coercion or undue influence to participate in research.

NIMH Consent Process Flowchart

COLOR KEY | Researcher Decision | Action Item | Consent Proceeds | No Research



The Clinical Research **Advocates** monitor, assess, and support **Participants** throughout research, and advise **Researchers** on human subject protections.

Participants
Advocates
Researchers

National Institute of Mental Health
Office of the Clinical Director
Human Subjects Protection Unit

8.1.2019

Clinical Research Advocates

National Institute of Mental Health

Office of the Clinical Director, **Human Subjects Protection Unit**

Clinical Research Advocates (CRAs)

are experienced clinicians with the Human Subjects Protection Unit (HSPU) which is part of the Office of the Clinical Director of the National Institute of Mental Health (NIMH). CRAs report directly to the NIMH Clinical Director and have no direct connection to any research programs or researchers.

CRAs provide safeguards to you throughout your study participation. Their independence is important to assure that CRAs are neutral when monitoring, assessing, and providing support.

Your CRA provides the following:

Capacity Assessment
Some studies require that you be assessed by a CRA to determine if you have sufficient understanding to proceed with consenting to the research.

Ability to Assign a Surrogate Decision-Maker Assessment
Should you be unable to make or communicate your own decisions about participating in a study, you may be able to assign someone to help you. A CRA can discuss this process with you.

Surrogate Decision-Maker Assessment
If you have chosen someone to help you with research decisions, your CRA may meet with that individual to discuss their understanding of the study and your participation.

Consent Monitoring
A CRA may be present for the discussion between you and the researcher to assure you understand what you will be asked to do and the risks associated with the study. Your CRA can help address any questions or concerns raised during this conversation.

Assent Monitoring
Assent is the affirmative agreement given by a child or an adult who is unable to give consent. Monitoring an assent discussion and your agreement to participate in research is one role a CRA provides.

Subject Monitoring
Your CRA will visit you regularly to discuss your inpatient research experience and will advocate for you as needed.

Your Clinical Research Advocate is:

Insert business card

Sample Electronic Medical Record

Capacity Assessment

The subject's ability to give informed consent was assessed using a modified MacArthur Competence Assessment Tool for Clinical Research.

The subject is being considered for inclusion in protocol number

The raters administering the tool were

At this time the subject

- ❍ is able to give informed consent
- ❍ has questionable ability to give informed consent
- ❍ is unable to give informed consent

The plan is

- ❍ research consent may proceed
- ❍ further education recommended
- ❍ research consent may not proceed

The following staff were notified of the outcome

Sample Electronic Medical Record

Consent Monitoring

Protocol number

Conducted by

Attended by

Clinical Research Advocate contact information provided	❍Yes	❍No	
Consent elements discussed			
Voluntary nature of research	❍Yes	❍No	
Purpose of research	❍Yes	❍No	
Expected duration	❍Yes	❍No	
Experimental procedures	❍Yes	❍No	
Protocol procedures	❍Yes	❍No	
Risks and discomforts	❍Yes	❍No	
Benefits	❍Yes	❍No	
Alternatives to research	❍Yes	❍No	
Confidentiality	❍Yes	❍No	
Research related injury	❍Yes	❍No	
Compensation	❍Yes	❍No	
Researcher contact information	❍Yes	❍No	
A statement on the collection of identifiable private information or identifiable biospecimens	❍Yes	❍No	
Assent	❍Yes	❍No	❍Not applicable

Additional comments: Include explanation of "No" responses

Sample Protocol Language

This language is a protocol-specific sample for a minimal risk protocol which includes adults without consent capacity. There is no prospect of direct benefit. This language will need modifications in order to apply to your protocol. Some states do not allow for legally authorized representatives to provide consent for non-beneficial research. Consequently, it is important to consult organizational representatives (e.g., legal counsel) and policies.

Sample advocate language for a protocol

Capacity to give informed consent will be assessed by an advocate. If the subject is determined to have capacity, the researcher may obtain consent with consent monitoring by the advocate. A subject may lack capacity to give informed consent, but may retain the ability to understand an advance directive (AD) and identify a substitute decision-maker. In all cases, subject dissent will be respected.

If the subject has a legal guardian, a capacity assessment is not administered. The advocate will meet with the guardian to discuss the role of the guardian and the guardian's understanding of the subject's wishes. The researcher may then obtain consent from the guardian and assent from the subject with consent and assent monitoring by the advocate.

If the subject does not have a legal guardian, lacks capacity to provide informed consent, and does not have a pre-existing AD that allows for research participation, the advocate assesses the subject's ability to assign a surrogate decision-maker. If it is determined the subject has the ability to assign a surrogate decision-maker, an AD form (e.g., durable power of attorney for health care) for research is completed. The researcher follows the AD and obtains consent from the surrogate decision-maker and assent from the subject with consent monitoring by the advocate.

If the subject does not have a legal guardian or pre-existing AD, lacks capacity to provide informed consent, and is unable to assign a surrogate decision-maker, the subject will not participate in the research.

If the subject does not have a legal guardian, does not have capacity to provide informed consent, and has a pre-existing AD that allows for research participation, the advocate will assess the appropriateness of the surrogate decision-maker. The researcher may invoke the AD, seek consent from the surrogate decision-maker and assent from the subject with consent and assent monitoring by the advocate.

Sample Consent Language

This language is a protocol-specific sample for a more than minimal risk inpatient protocol with a prospect of direct benefit for a potentially vulnerable population and will need modifications for your protocol.

Consent monitoring
An advocate, who is not part of the research team, will be assigned to you and will be present during the informed consent process. Informed consent is the discussion held between you and a member of the research team about this study. The advocate will assure that you have received the information you need to make an informed decision about participating in this study.

Capacity assessment
If the researcher has concerns about your ability to give informed consent, you may have a brief interview with your advocate. This interview, called a capacity assessment, will help determine your understanding of what is involved in the study and whether you need to have someone else, whom you have selected, give consent for you to participate.

Subject monitoring
If you are admitted to the hospital for this study, the advocate will visit you on the unit over the course of your stay to discuss your wishes regarding continued research participation.

Advance directive*
An advance directive (AD), allows you to name someone to make medical research and health care decisions for you should you become unable to make decisions yourself. An AD is a document you can use to state your health care choices, record your wishes about research participation, and identify someone to make decisions for you. If you lose your ability to make decisions, your doctor will use your AD and discussions with your identified decision-maker(s) to make medical research decisions on your behalf based on your preferences. The best substitute decision-maker is someone you discuss your medical wishes with and who knows you well. The person you name as your substitute decision-maker must be eighteen years or older and cannot be your physician.

***It is important to know your state regulations regarding research participation and legally authorized representatives. Please seek guidance from your organization's policies and legal counsel.

Sources for More Information

Belmont Report
https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

Code of Federal Regulations, Title 45 Public Welfare, Part 46 Protection of Human Subjects
https://ecfr.federalregister.gov/current/title-45/subtitle-A/subchapter-A/part-46

The Ethical and Regulatory Aspects of Clinical Research Online Training
https://www.bioethics.nih.gov/courses/ethical-regulatory-aspects.shtml

Evaluating the Ability to Consent to Research: A Twenty-Year Track Record
https://onlinelibrary.wiley.com/doi/10.1002/eahr.500119

Human Subjects Protection Unit (HSPU) National Institute of Mental Health (NIMH) Office of the Clinical Director
https://www.nimh.nih.gov/ocd-hspu
Contact: nimhhspu@mail.nih.gov

Informed Consent Checklist
https://www.hhs.gov/ohrp/policy/consentckls.html

MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR)
Appelbaum, Paul S., and Thomas Grisso. Sarasota, FL: Professional Resource Press, 2001.

NIH Clinical Center (CC) Bioethics Department
https://www.bioethics.nih.gov

NIH Clinical Trials
https://www.clinicaltrials.gov/

NIMH Human Subjects Protections Toolkit
https://www.nimh.nih.gov/hspu

Office for Human Research Protections
https://www.hhs.gov/ohrp/

Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity National Bioethics Advisory Commission
https://bioethicsarchive.georgetown.edu/nbac/capacity/TOC.htm