1. PURPOSE
   1. Adults who lack capacity to provide legally effective informed consent may be unable to understand the nature and consequence of proposed health research interventions, including the subject’s diagnosis and prognosis, the burdens, benefits, and risks of any such research and the alternatives to research, and to reach an informed decision. This guidance outlines when adults who lack capacity to provide legally effective informed consent may be enrolled in research and who may consent to participation in research on their behalf.
2. GUIDANCE
   1. Adults who are determined to lack capacity to provide legally effective informed consent may be enrolled in a research studywhen ALL of the conditions in EITHER 2.1.1 or 2.1.2 are met:
      1. The research offers a reasonable prospect of a direct health-related benefit to the individual (ALL MUST BE MET):
         1. The research must pose no more than minimal risk, as determined by the IRB, **OR** the relation of the anticipated benefit to the risk is at least as favorable as that presented by available alternative approaches;
         2. The knowledge likely to be gained will improve the understanding of the condition, disease, or behavior affecting the subject population **OR** there is a compelling argument for including individuals who lack decision-making capacity.
      2. The research offers *no* reasonable prospect of a direct health-related benefit to the individual (ALL MUST BE MET):
         1. The research involves only a minor increase over minimal risk **OR** the research is likely to yield generalizable knowledge about the subjects disorder or condition which is of vital importance to the understanding or amelioration of the subjects disorder or condition;
         2. Subjects have a disease or condition relevant to the research;
         3. The IRB determines that the research cannot be performed solely with persons who possess decision-making capacity;
         4. The negative impact on the subjects’ well-being is low.
   2. Informed consent from the potential participant:
      1. Capacity to consent is presumed to exist unless there is evidence to the contrary;
      2. If a potential participant has the capacity to consent to the research, informed consent must be obtained from him or her unless the IRB has waived informed consent;
      3. Adults who lack capacity to provide legally effective informed consent must provide assent to participation, if capable, or must not dissent;
      4. Participants with variable capacity may consent to research participation during a period of capacity;
      5. If the participant regains decision-making capacity during the course of their participation in the study, the informed consent process must be repeated with the participant.
   3. Studies which seek to enroll adults who may lack capacity to provide legally effective informed consent must clearly describe in the IRB application how capacity to provide informed consent will be assessed and a time schedule for reassessment of capacity for consent.
   4. Studies which seek to enroll adults who lack capacity to provide legally effective informed consent must have a plan in place to closely monitor research subjects during the research study and withdraw them from the research if they appear to be unduly distressed.
   5. An assessment of a potential research participant’s capacity to consent must be made and documented in the research record before deciding whether there is a need for a surrogate decision-maker.
      1. The assessment of capacity must include the basis for determination that the individual lacks capacity to provide legally effective informed consent;
         1. If the research is minimal risk, an appropriate member of the research team may assess capacity.
         2. If the research is greater than minimal risk, two certifying professionals must assess capacity and document in the research record:
            1. The certifying professionals must include:

one individual licensed to practice medicine in the state where the research will be taking place;

one licensed medical professional who is unaffiliated with the research.

* + - * 1. One of the certifying professionals must examine the individual and document their determination no more than one day prior to starting research procedures.
  1. Adults who lack capacity to provide legally effective informed consent may have research consent provided by someone who, under state or federal law, has the legal authority to make such decisions for the individual. If there is no Legally Authorized Representative (LAR), a Substitute Health Care Decision Maker (as determined by HRP-021) may provide surrogate consent regarding the research participation.
     1. The identity of the Legally Authorized Representative or Substitute Health Care Decision Maker and the rationale for the selection of the individual shall be documented on the Legally Authorized Representative Identification Documentation Form (HRP-582).
  2. The LAR/ Substitute Health Care Decision Maker consent and assent process for the adult who lacks capacity to provide legally effective informed consent must be witnessed and documented in the research record by an individual unaffiliated with the research.
  3. The research record must also document:
     1. The process by which the individual was enrolled or declined to be enrolled in the clinical research;
     2. A specific time schedule for reassessment of capacity for consent