ii. Individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and

iii. Individuals detained pending arraignment, trial, or sentencing.

Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted or if they are being monitored by the penal system (i.e., probation, house arrest, halfway house, etc.). Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment or trial. The regulatory definition of prisoner likewise includes people who are under house arrest but are mobile (i.e. are monitored with an ankle bracelet or other similar device).

12.4 PROTECTIONS FOR CHILDREN

Subpart D of 45 CFR 46 (DHHS regulations) and Subpart D of 21 CFR 50 (FDA regulations) outline special protections for children (including viable neonates). According to federal regulations, a "child" is a person who has not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

A. Risk Level Determinations

From a federal regulatory perspective, research is classified as involving *no risk, minimal risk, or greater than minimal risk*. According to the regulations [45 CFR 46.102(i)] "*Minimal risk* means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." It is the IRB's responsibility to determine whether or not research can be considered minimal risk. The investigator may request that the IRB consider designating the study as minimal risk, but the investigator may not make this determination on his or her own.

The risk categories set forth in the federal regulations below are used by the IRB when reviewing a study that involves children as subjects.

i. Research not involving greater than minimal risk. (45 CFR 46.404 and 21 CFR 50.51)

Taking into consideration the level of risk and prospect of direct benefit, the IRB can approve research that presents no greater than minimal risk to children.

ii. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. (45 CFR 46.405 and 21 CFR 50.52)

Taking into consideration the level of risk and prospect of direct benefit, the IRB can approve research that carries the potential for *greater than minimal risk* to children. Most importantly, the IRB must determine if the research holds out a prospect of direct benefit for the subjects. An IRB can itself approve research on children involving more than minimal risk if the proposed study presents such a prospect of benefit and "(a) The risk is justified by the anticipated benefits to the subjects; (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches."

iii. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. (45 CFR 46.406 and 21 CFR 50.53)

Taking into consideration the level of risk and prospect of direct benefit, the IRB can approve research that involves greater than minimal risk and provides no potential direct benefit to individual subjects only if the study will "likely yield generalizable knowledge about the subject's disorder or condition." The study must also meet the following conditions:

a. "The risk represents a minor increase over minimal risk;

b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational experiences;

c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and

d. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408." (45 CFR 46.406)

The requirement that the subject have a "disorder or condition" suggests great caution in conducting greater than minimal risk research with normal control subjects.

iv. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. (45 CFR 46.407)

This category of research requires the approval of the DHHS Secretary after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment. An IRB cannot approve such research on its own.

B. Guidelines for Research on Healthy Children

It is the responsibility of the research investigator to demonstrate the need for data collection in normal subjects and children in particular. Investigators should define the level of risk and defend the appropriateness of the age groups selected with regard to the need for the study and the level of risk. The use of normal children in research may invoke the use of 45 CFR 46.407 (Research not otherwise approval under 46.404, 46.405, or 46.406 which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children). In these cases, the research and the IRB's findings that the research may fall under 46.407 must be submitted to OHRP for consultation with a panel of experts and public review and comment. Typically this will be the investigator's responsibility. Only after OHRP's determination is made will the research be reconsidered by the IRB. The informed consent process should be appropriate to the level of risk and should also consider the developmental state of the child.

C. Wards of State

Any participation of Wards of the State in research studies regardless of the risk determination must have the prior approval of the Department of Children and Family Services (DCFS). Any

research conducted under 45 CFR 46.406 or 46.407 must also utilize a Research Subject Advocate, RSA, for each ward to be enrolled. **Please contact the IRB for guidance prior to enrolling Wards of the State on any research study regardless of the assigned risk determination. The IRB Chair is the designated Research Subject Advocate for the Institution.** If the IRB Chair is the PI for the study, the IRB Vice-Chair may be the RSA or may appoint an alternate as appropriate.

Also note that per the federal regulations, children who are wards of the state or any other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 46.407 only if such research is:

i. Related to their status as wards; or

ii. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

12.5 NON-ENGLISH SPEAKING SUBJECTS

A sizable percentage of patients who receive their medical care at the Institution identify a language other than English as their primary language, and these non-English speakers may be eligible for participation in IRB approved research. Noting that non-English speaking people, because of their language barrier, may be more vulnerable to coercion or undue influence when approached for participation in research, the IRB acknowledges that additional provision for the protection of these potential subjects must be taken to ensure that they understand the nature of their participation in research.

Federal regulations dictate, "the information that is given to the subject or the subject's representative shall be in language understandable to the subject or the representative." (45 CFR 46.116 and 21 CFR 50.20) To fulfill this requirement, OHRP strongly encourages providing potential subjects with a full consent document written in a language understandable to them. However, for studies that are not designed to target non-English speaking individuals, this may be an unreasonable requirement. As such, the IRB may allow for the use of a "short form" written consent document in research studies that anticipate that all of or the majority of their subjects will be fluent in English, but that non-English speakers may be encountered occasionally. The "short form" consent process permits oral presentation of informed consent information in conjunction with a short form written consent document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally. A witness to the oral presentation is required, and the subject must be given copies of the short form document and the summary. The "short form" must state, in the subject's language, that all of the required elements of informed consent have been presented orally to the subject or his/her legal representative in a language that he/she understands.

Regardless of the method used to document non-English speakers' consent to participate in the research, the IRB's preference is that a certified interpreter be used in the verbal consent process. The IRB prefers that a certified interpreter, rather than a friend or family member of the subject be used. In the event that the subject requests to have a friend or family member serve as interpreter, care should be taken to ensure that the interpreter's relationship with the subject does not adversely impact the subject's ability to make an independent decision regarding participation. Under no circumstances should a minor be allowed to serve as interpreter.