IRB TIP SHEET: VULNERABILITY OF SUBJECTS PARTICIPATING IN HUMAN SUBJECTS RESEARCH

IRB members should consider vulnerabilities of potential subjects outside of those addressed in HHS regulations and/or NIH policy when they review protocols. This tip sheet explores types of vulnerability that are not addressed in the regulations or NIH policy.

Neither the Common Rule nor the HHS regulation subparts define vulnerability. Suggested explanations include:

- Council for International Organizations of Medical Sciences (CIOMS): "persons are vulnerable because they are relatively (or absolutely) incapable of protecting their own interests" or "because some feature of the circumstances (temporary or permanent) in which they live makes it less likely that others will be vigilant about, or sensitive to, their interests".
- National Bioethics Advisory Committee: "vulnerability is sensitive to context, and individuals may be vulnerable in one situation and not in another" . . . "vulnerability in the context of research, should be understood to be a condition, either intrinsic or situational, of some individuals that puts them at greater risk of being used in ethically inappropriate ways in research"

Deferential Vulnerability

- Persons who are under the informal/formal authority of others.
- May be based on sex, race, class inequalities, or inequalities of power/knowledge (doctor-patient relationship).
- Such individuals may not be able to make truly free and independent decisions about research participation.

Protections(s): These usually focus on the process of consent. Alternative approach could be conducting the consent process in the absence of the party to whom the subject defers and/or consent monitoring.

Communication Vulnerability

When a subject has challenges in understanding information about participation. This could result from a language barrier, physical challenges (e.g., blindness) or illiteracy.

Protection(s): Use plain language consent forms, supplementary educational measures, interpreters and translated materials, assistive technologies (e.g., screen readers)

Medical Vulnerability (e.g., those with serious health conditions, critically ill, at end-of life):

- Those with serious health conditions for which no satisfactory standard treatment options are available.
- Decision making may be affected by stress, fear, family pressure or medical interventions.
- For these individuals, weighing the research related risks and potential benefits may be difficult, especially if their understanding is clouded by therapeutic misconception (the misunderstanding that primary intent of the research study is for their individual benefit, and which may occur when a subject with a serious medical condition grasps at participation or inclusion as the sole alternative.)

Protections(s):

- Focus on the process of consent and efforts to minimize therapeutic misconception.
- For protocols that are GTMR but without prospect of DB, consider requiring an independent consent monitor.
- Ensure the protocol has a specific plan to assess the capacity of potential subjects.

Economic Vulnerability:

- Arises from disadvantage in the distribution of social goods and services such as income, housing, or healthcare.
- For those with limited access to health care, enrolling in a research study may offer hope of effective treatment or even a cure for illness.
- Possible therapeutic misconception (if one approaches study participation as a way to seek treatment or a cure).

Protection(s):

- Ensure compensation is prorated. Weigh whether payment is so excessive as to represent undue

influence (occurs with an offer of excessive reward or other overture to obtain compliance. These inducements, that would ordinarily be acceptable, may become undue influences if the subject is especially vulnerable.)

- To help limit therapeutic misconception, NIH consent templates require that the section on benefits state either that subjects "will not benefit from being in the study" or that they "might not benefit from being in this study." As appropriate, consent forms should explain that study participation will not necessarily result in a cure, even if subjects experience some improvements.

Social Vulnerability

- Vulnerability is a function of the social perception of certain groups, which includes stereotyping and can lead to discrimination. Perceptions may devalue members of such groups, their interests, their welfare, or their contributions to society.
- Shared experiences or identities that could enhance risk due to research participation include immigration status, homelessness, indigenous community identities, LGBTQ+ identities, or potentially stigmatized communities such as substance users (including those in recovery), people living with HIV, or individuals with mental health diagnoses.

Protection(s):

- IRBs should assess if targeting a specific group is justified.
- Involve the community/members in various stages of the research process such as study planning and decision making. (e.g., Will the research potentially have negative impact on the group's identity/culture or lead to stigmatization?) Understand when such review is required (e.g., approval by Tribal community).
- In addition to obtaining informed consent from subjects, continue to obtain support and have ongoing dialogue with leaders of the respective community and community leaders (i.e., local religious leaders, advocacy groups and community advisory committee leaders).
- Hold community education sessions with community leaders about the disease.

Vulnerability during a disaster (natural or manmade) or public health emergency

- Hazard might result in casualties, displacement from residence, loss of support systems, social/business/health care interruption, and property damage. Disasters may reduce ability to cope with stressors.

Protection(s):

- Review and monitor biomedical and behavioral research plans and survey instruments to ensure the privacy, physical and mental welfare, and other rights of research subjects and communities are protected.

Responsibilities of the IRB

- Decide if inclusion of vulnerable subjects is necessary. The Board should question whether there are less vulnerable subjects whose participation in research could answer the same scientific question.
- Recruitment targeting specific, social, ethnic or minority groups as well as from other cohorts mentioned above should trigger special IRB consideration and assessment of potential vulnerability of the group under study (Is targeting the specific groups justified? Are these groups at increased risk in this study due to their vulnerability?)
- Are there additional issues that are important within the ethnic or minority group being studied? For example, a study to collect and store samples for DNA testing and use in future research studies in an American Indian or African American population may need to address issues of trust in research and researchers as well as plans sharing of research results.
- The IRB should ensure that relevant additional safeguards to protect the rights and welfare of vulnerable subjects are in place.