IRB Consideration of Possible Third-Party Research Risks

IRBs are tasked with focusing on protection of human research subjects. However, during the conduct of a given study, there may also be risks to individuals who do not meet the definition of human subjects. Examples include family members, sexual partners, bystanders, social or cultural groups of which the subject is a part, research team members and site personnel. These individuals have been referred to as third parties, bystanders, or non-subjects. The IRB can play a significant role in assessing and evaluating strategies that minimize risks to such third-parties.

Definitions:

- Non-subjects: "living individuals who are, or who are likely to be, exposed to research risk and who do not meet the regulatory definition of human subject (SACHRP) [1]
- Bystander risk: "The prospect of harm to identifiable individuals or groups of individuals, other than research subjects themselves, that is a direct consequence of the research activities (as opposed to the knowledge such research activities generate and their application)"[2]

Regulation and Guidance

- **The Common Rule**
  - Refers to required reporting of "any unanticipated problems involving risks to subjects or others," but it does not state that IRBs have a responsibility to minimize risks to others. Also, Subpart B requires IRB consideration of risks to fetuses or neonates (when they are not the target subjects) in research involving pregnant persons.
  - Other than these references, the Common Rule does not address risk to third parties or how IRBs should address protection of such individuals from risk.
- **Belmont Report** notes "Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society)."

Risks to third parties can be:

- Physical- e.g., PHS Tuskegee Syphilis study, radiopharmaceuticals, gene therapy, or live vaccines
- Social, legal, and psychological- e.g., loss of privacy, stigma, or observed unlawful behavior
- Cultural -e.g., publication of data results in community feeling stigmatized and distrustful (Havasupai Tribe)

IRB's role: Despite the fact that addressing risk to third parties is extra-regulatory, IRB's generally believe they have some responsibility to consider protection of third-parties who may be unknowingly exposed to research risk.

IRB Considerations Regarding Risks to Third parties

- Assess if there are any likely risks to third-parties.
- Be especially cautious about third- party risk when it adds new/uncommon risks.
- IRBs do not need to routinely consider risks that are not greater than minimal risk.
- Review the mechanisms proposed in the protocol to manage these risks.
- If other institutional entities are better suited to assess and manage risk, the IRB should delineate responsibilities to avoid duplicate review. (e.g., IBC review for gene transfer study)
- IRBs should consider the following regarding possible risk to third parties:
  - Probability of occurrence: Common vs. unusual risks
  - Magnitude
  - Causal proximity
  - Properties of the risk-will it engender public mistrust or negatively affect public confidence?
  - Identifiability of individuals
  - Individual vs. group harms
  - Any particular vulnerabilities

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[1] SACHRP. *The Protection of Non-Subjects from Research Harm* (2022)

[2] Kimmelman J.OHRP Exploratory Workshop. *Review of the Third-Party Research Risk: Is there a role for IRBS?* (2021)