Revisions of Existing Terms and Definitions/Terms Not Added to Definitions

Even though only three new terms were added, revisions were made to existing terms and definitions.

Minor Clarifications to Wording

"Intervention," "interaction," "private information," and "identifiable private information" were elevated to get their own subsection numbers and have been changed only to clarify wording.

Significant Revisions to Existing Definitions

Three Definitions have been changed in significant ways.

Legally Authorized Representative	**The definition now adds specific authorization to use institutional policy when there is no applicable laws that addresses the issue. This change is intended to bring consistency to the consent process and it allows institutional policies in either the clinical context or other non-research contexts to authorize who may serve as a legally authorized representative in that institution.**
Research	**The definition has been expanded to list activities that are specifically deemed not to be research. The Final Rule specifies that the collection of information is permitted under public health surveillance, but subsequent research using information collected from public health surveillance activities would fall under the definition of research as**
Human Subject	**The definition now references "information and biospecimens" (replacing "data") and adds obtaining, storing, using, studying, analyzing or generating identifiable private information or identifiable biospecimens as trigger events. 46.102(e)(1)(i) clarifies that investigators may "obtain" information and biospecimens without triggering the human subject definition until they use, study or analyze the information or biospecimens.**

Terms Not Added to Definitions

It is important to take note of terms used in the Final Rule that are not defined, as word selection and usage are extremely important in regulations. It can be challenging trying to determine how the federal regulation is using a term and what the significance or meaning is, and how it is applicable to research practice. There may be clues in the context of the regulation – when the term is used, how it is used, and sometimes and explanation is provided. Also federal guidance can help provide direction on how to understand and comply with undefined terms in research practice.

- **Vulnerable** (to coercion or undue influence)

  The definition of "vulnerable" is not included in the definitions section, but it has been updated to both IRB membership requirements (45.107) and criteria for approval of research (46.111). The Final Rule no longer includes pregnant women or handicapped and physically disabled individuals as examples of populations that are potentially vulnerable to coercion or undue

influence. The Final Rule uses the term "individuals with impaired decision-making ability" to replace the term "mentally disabled persons." The Final Rule's preamble states that the possibility of coercion or undue influence could affect the ability to make an informed decision about participating in research. Therefore, the vulnerability of the subjects in research studies should be considered as a function of the possibility of coercion or undue influence. The preamble states that this type of vulnerability alone should be the IRB focus of concern in determinations about vulnerable populations. The preamble also notes that the assessment of the equitable selection of subjects should include factors like societal marginalization or discrimination. The preamble discusses that the criterion includes risks that some might term "vulnerabilities," which are not covered by the regulatory term.

- **Deception**

The definition of "deception," like "vulnerable," is not included in the definitions section, but it is specified in 46.104(d)(3)(iii) and the Final Rule preamble, which states, "authorized deception would be prospective agreement by the subject to participate in research where the subject is informed that he or she will be unaware of or mislead regarding the nature of purposes of the research."

- **Generalizable Knowledge**

The term "generalizable knowledge" remains undefined and unaddressed in the Final Rule. Each institution should define, in its standard operating procedures what standard is used. SRU defines this term as, "the thought that the results are intended/expected to be applied to a larger population beyond the site of data collection or the population studied."

- **Single IRB (sIRB) Review and Cooperative Research**

"Single IRB review" is also not specifically defined in the Final Rule. However, 46.114 adds a requirement for institutions located in the U.S., that are engaged in federal cooperative research, to rely upon approval by a sIRB for the portion of research that is being conducted in the U.S. "Cooperative research" is explained within the regulation as research "involving more than one institution." Single IRB is synonymous with "reviewing IRB" and "IRB of record." All other IRBs are "relying IRBs." Further guidance is expected from OHRP.