Regulatory and Ethical Framework of Human Subject Research

The Belmont Report

"The U.S. has regulations to protect research subjects that are based on a core set of ethical principles. Three principles—respect for persons, beneficence, and justice were identified and explained in the 1979 Belmont Report. These Belmont Principles became the ethical foundation of the first comprehensive set of Federal regulations to protect human subjects in research, enacted shortly after the Belmont Report was published.

While the regulations have been updated since that time, their ethical foundation remains the same." (HHRP eLearning Program – Lesson 1)

- **Respect for Persons:** Acknowledges that individuals make decisions about how they want to live their lives, including if they want to volunteer for research studies (informed consent).
- **Beneficence:** Acknowledges that research could bring about important contributions to public good (minimizing risks).
- **Justice:** Concerned with the fair distribution of burdens and benefits (equitable selection of subjects).

Federal Regulations

The primary Federal Regulations governing human subject research and the protection of human subjects are found in the US Code of Federal Regulations at 21 CFR 56 (FDA) and 45 CFR 46 (HHS). There are also federal regulations governing HIPAA.

Health and Human Services (HHS) Regulations – 45 CFR 46

The "Common Rule" (45 CFR 46) provides a broad set of protections for research subjects. These protections include review and approval of research protocols by IRBs and requirements for informed consent and privacy and confidentiality protection, among others. Regulations at 45 CFR Part 46, and its Subparts provide basic protections for people who participate in research that comes under HHS's purview.

The subparts establish additional protections for "vulnerable" subjects.

- **Sub Part A** – Basic HHS Policy for Protection of Human Research Subjects
- **Sub Part B** - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

- **Sub Part C** - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- **Sub Part D** - Additional Protections for Children Involved as Subjects in Research

HHS-funded research must comply with both the Common Rule and the other subparts of the regulations. Children's Wisconsin applies the Common Rule to all human subject research conducted at CW, regardless of funding.

The Common Rule (subpart A of the HHS regulations) was recently revised. These revisions became effective in 2018, but its compliance date was delayed until January 21, 2019. Nevertheless, the revised rule is officially called the "2018 Requirements," although many continue to refer to it as the "revised Common Rule," or simply the "new Rule."

For additional details about The Common Rule and its subparts see OHRP eLearning Program – Lesson 1.

FDA Regulations – 21 CFR *50*

The FDA has its own regulations that apply to the clinical investigations it oversees. These regulations align with the Common Rule, but also differ in some important ways. While there is an ongoing effort to harmonize them, it is important for investigators and IRBs to know which regulations are applicable for a particular research project.

When research studies involving products regulated by FDA, the FDA regulations govern that research. If the involves FDA regulated products and is also funded/supported by HHS, the research institution must comply with both the HHS and FDA regulations. For additional details about FDA regulations for human subject protections see OHRP eLearning Program – Lesson 1.

Comparison of FDA and HHS Human Subject Protection Regulations

While HHS and the FDA are trying to harmonize these sets of regulations, there are differences that investigators need to be aware of when research is subject to both the Common Rule and FDA regulations. The FDA has a table comparing these 2 sets of regulations.

State Statutes

In addition to the federal regulations, there may be state specific statues that effect the conduct of research. Investigators should be familiar with any applicable state statutes.

Institutional Policy

Institutions implement their own institutional policies and procedures, which may be more protective than the regulatory requirements. Institutions may have a mechanism to enforce their own requirements, even though the Federal government may not have regulatory authority over research when it is not supported by a Common Rule agency.

Regardless of which IRB is serving as the IRB of record, investigators are expected to follow Children's Wisconsin HRPP SOPs when conducting research that engages Children's Wisconsin (eg. Research being done in CW space, use of CW resources to support the research, enrolls CW patients or involves access to CW medical records).