Human Specimen Repositories Requirements of 21 CFR Parts 50 & 56

PRIM & R

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Sally A. Hojvat, Ph.D.
Director of Microbiology Devices
Office of In Vitro Diagnostic
CDRH, FDA
E-mail: SYH@CDRH.FDA.GOV

What I will be Covering

- FDA Human Research Protections
- Comparison of FDA and HHS title 45 CFR Part 46 regulations
- Banked biological raw materials for:
  - Research
  - Product manufacture
  - Validation of *in-vitro* diagnostic products subject to FDA approval by CDRH & CBER

FDA Human Research Protection Regulations

- 21 CFR Part 50: Informed consent and limited emergency exceptions
- 21 CFR Part 56: IRB Review

What I will Not be Covering

- "Comprehensive FDA System"
  - Registration- final (21 CFR Part 1271)
  - Good Tissue Practices- proposed
  - Donor Suitability Regulations- proposed
- "Human Cells, Tissues, and Cellular and Tissue-based Products"
  - Regulated under section 361 of the PHS Act
  - Regulated under section 351 of the F,D&C Act
  - Human subject protection regulated under 21 CFR Parts 50 & 56

Comparing the FDA and HHS Protection of Human Subjects Regulations

- Overall Objective:
  - **FDA:** title 21 CFR Parts 50&56
    - Protects the rights, safety and welfare of subjects involved in clinical investigations involving products regulated by FDA
  - **HHS**: title 45 CFR Part 46 Subpart A
    - Protects the rights and welfare of human subjects involved in research conducted or supported by HHS

Comparing the FDA and HHS Protection of Human Subjects Regulations

- Topics
  - Definitions
  - IRB Review
  - Informed Consent
  - Identifiable Information

Definition Clinical Investigation/Research

- **FDA**
  - Any experiment involving a test article and one or more human subjects that:
    - Must meet requirements for prior submission to FDA or
    - Results of experiments intended to be submitted to FDA as part of application for research or marketing permission
- **HHS**
  - Systematic investigation, including research development, testing and evaluation, designed to develop or contribute to general knowledge

Definition Human Subject

- **FDA**
  - Human who participates in research either as a recipient of the test article or as a control. A healthy human or a patient
  - Subject is an individual on whom or on whose specimen an investigational device is used
- **HHS**
  - A living individual that an investigator conducting research obtains data from through intervention or interaction; or obtains identifiable/ private information

Definition Minimal Risk

- FDA & HHS
  - Risks of harm anticipated in research no greater than encountered in daily life or routine physical or psychological examinations or tests

IRB Review

- **FDA** requires IRB review and approval for any clinical investigation that must meet the requirements of prior submission to FDA. FDA might be permitted to waive one or more of the specific requirements of Part 56 so long as meaningful IRB review and approval remained
- **HHS** request IRB review for all research involving human subjects conducted, supported or otherwise subject to regulation by any Federal Dept. or Agency. It contains several waiver exemptions

Expedited IRB Review

- **FDA & HHS**
  - Yes, if risks to subject is no more than minimal
- **HHS**
  - Minor changes to approved research

Informed Consent

- **FDA / HHS**
  - Requirement to obtain informed consent of subject or legally authorized representative
  - Exemptions to requirement differ

Exemptions to Requirements for Informed Consent

- **FDA**
  - Limited to emergency, life threatening situations, military operations
  - Needs independent physician opinion
  - Emergency research

Exemptions/Waivers to Requirements for Informed Consent

- **HHS**
  - Several exemptions, including collection or study of pathological/diagnostic specimens if sources are publicly available or if subject cannot be identified
  - No more than minimal risk to subject
  - Will not adversely affect rights and welfare of subject
  - Study not practicable without waiver
  - Emergency medical care required

Identifiable Information

- **FDA**
  - Individually Identifiable information not defined or taken into consideration
- **HHS**
  - Exempts some types of research if subject cannot be identified

In-Vitro Diagnostic Device Human Subject Protection Issues

- Specimen use for research, product manufacture and validation of product in clinical trials is subject of debate within industry and FDA
- Complex issues concerning use of “residual” specimens, archival repositories and “rare” specimen panels
- Confusion by IRB' s on applicability of which regulations cover “low-risk” device studies

FDA Short Term/Long Term Initiatives

- **Short Term:**
  - Ongoing discussions within CDRH
  - Working group to write a concept paper
  - Involvement with PRIM & R working group
- **Long Term:** Harmonization with HHS regulation?
- Guidance Document?

FDA Information – Websites

http://www.fda.gov/oc/gcp/default-htm
Regulations and FDA information sheets

http://www.fda.gov/cber/tissue/docs
Human cells, tissues and cellular and tissue-based product

What is an *In-Vitro* Diagnostic Device?

- 21 CFR 809.3
- Reagents, instruments used to diagnose disease, determine health status in order to cure, treat, mitigate or prevent sequelae
- Used to test specimens taken from human body
  - Blood, urine, csf, saliva, nail clippings, etc.
- Testing could be long after specimen collected