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Face the Future with Confidence

COMPLIANCE WITHIN YOUR HUMAN RESEARCH PROTECTION PROGRAM

June 2019

Internal Audit, Risk, Business & Technology Consulting

1

Nathalia Henry

Nathalia, MS, CHRC, CIP has over 16 years of regulatory, clinical operations and research compliance experience across various environments (Industry, Academia and Hospitals) and she currently serves Northwestern University's Office for Research as the Executive Director of the IRB Office. In her current role, Nathalia is responsible for the administration of Northwestern University's Human Research Protection Program for both biomedical and social/behavioral research, serves as the Human Protections Administrator, and oversees the strategic direction and daily operations of the IRB Office.

Nathalia came to Northwestern from the Shirley Ryan Ability Lab, formerly the Rehabilitation Institute of Chicago, where she served as the Research Associate Compliance Officer and Human Protections Administrator.

Prior to the Shirley Ryan Ability Lab, Nathalia held several roles at Northwestern Memorial Hospital, Northwestern University and Pharmacia-Pfizer. Prior to her current role, Nathalia also served for 8 years as an IRB panel member. Nathalia is a certified IRB Professional (CIP) and certified in Healthcare Research Compliance (CHRC).

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2

Leyla Erkan

Leyla is a Protiviti's Global Healthcare Compliance Practice Lead as well as the Midwest Healthcare Leader. Leyla has 20 years of healthcare experience in acute and post-acute care settings with extensive experience in regulatory compliance, clinical research, HIPAA/HITECH, conflicts of interest, risk management, investigations, and governmental audit.

Prior to joining Protiviti, Leyla served as the Chief Compliance and Privacy Officer for the Shirley Ryan AbilityLab, formally the Rehabilitation Institute of Chicago, the number one rehabilitation hospital in the nation, where she oversaw all compliance related matters for the hospital, research, physician practice and over 30 sites of care, including 5 strategic hospital alliances.

Prior to the Shirley Ryan Ability Lab, Leyla was the Compliance Director and Privacy Officer for Ann & Robert H. Lurie Children's Hospital of Chicago. Leyla taught courses on compliance and enforcement at Northwestern University and sits on the Northwestern University Institutional Review Board. Leyla is certified in Healthcare Compliance (CHC), Healthcare Privacy Compliance (CHPC) and Healthcare Research Compliance (CHRC).

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OBJECTIVES

- **Define a HRPP and what you have to comply with**
- **Identify key HRPP components and structures**
- **Explore mechanisms for monitoring compliance programs**

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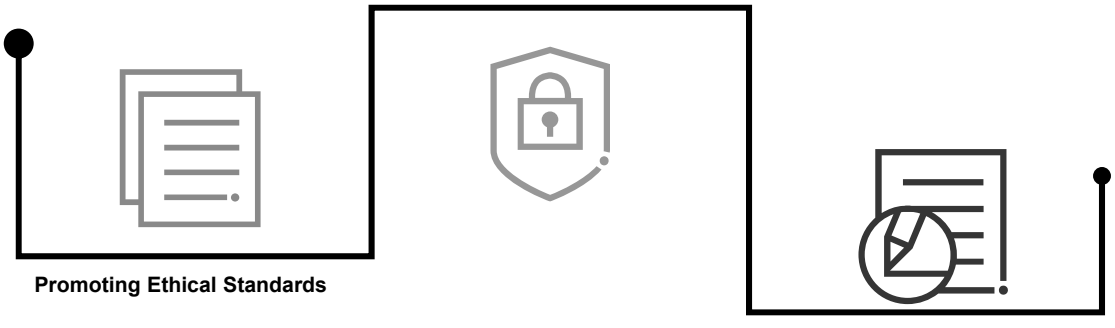
HUMAN RESEARCH PROTECTION PROGRAM

5

WHAT IS A HUMAN RESEARCH PROTECTION PROGRAM?

A human research protection program (HRPP) comprises policies, procedures and processes developed to protect the rights and welfare of human research participants by

Facilitating Compliance with Laws and Regulations



Promoting Ethical Standards

Reporting Allegations of Noncompliance

An effective HRPP protects not only human participants, but anyone that directly impacts, or is directly impacted by research.

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6

HUMAN SUBJECT RESEARCH (HHS)

Human Subject (45 CFR 46.102 (e))

- A living individual about who an investigator conducting research:
  - Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
  - Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Research (45 CFR 46.102 (l))

- A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

HUMAN SUBJECT RESEARCH (FDA)

Human Subject (21 CFR 50.3 (g))

- An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or patient.
- A human subject includes an individual on whose specimen a medical device is used.

Research (21 CFR 50.3 (c))

- Any experiment that involves a test article and one or more human participants and that meets and one of the following:
  - Requirements for prior submission to the USFDA under section 505(i)- Any use of a drug other than an approved drug in the course of medical practice;
  - Requirements for prior submission to the USFDA under section 520(g)- any activity that evaluates the safety, or effectiveness of a device; OR
  - Any activity the results of which are intended to be later submitted to, or held for inspection by the USFDA as a part of an application for a research or marketing permit

COMPONENTS OF HUMAN PARTICIPANT RESEARCH

Research Participants/Community

- Research study is conducted according to a research plan known as the protocol which is designed to answer specific research questions and safeguard the health of participants.
- Research studies have eligibility standards (criteria) documented in the protocol outlining who can participate.
- Factors that allow someone to participate in a research study are called inclusion criteria, and the factors that disqualify someone from participating are called exclusion criteria. They are based on characteristics such as age, gender, the type and stage of a disease, treatment history, and other medical conditions.

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Investigators and Research Teams

- Research is typically led by a principal investigator
- Human subjects research also typically includes a research team that may include doctors, nurses, social workers, research assistants, and other health care professionals.

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Sponsors

Research studies can be sponsored, or funded, by pharmaceutical companies, academic medical centers, voluntary groups, and other organizations, in addition to Federal agencies such as the NIH, U.S. Department of Veterans Affairs.

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Types of Research

- Biomedical
- Social Behavioral

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TO PROMOTE ETHICAL STANDARDS

Nuremberg Doctors' Trial

The Nuremberg Doctors' Trial, in 1946, was an international military tribunal that tried and convicted Nazi doctors who conducted horrific, unethical experiments on concentration camp prisoners during the Holocaust. It resulted in the Nuremburg Code, a set of international ethical guidelines for conducting human research.

Declaration of Helsinki

In 1964 the World Medical Association (WMA) developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving humans. The code of ethics has been widely adopted by medical associations in various countries. It is regularly revised and amended by the WMA.

The Tuskegee Study

In 1932, the Public Health Service collaborated with the Tuskegee Institute to begin the "Tuskegee Study of Untreated Syphilis in the Negro Male" which recorded the natural history of syphilis with the goal of justifying treatment programs for blacks. The study resulted in severe ethics violations, including (but not limited to):

- No evidence that researchers had informed the men of the study or its real purpose.
- Men had been misled and had not been given all the facts required to provide informed consent.
- Men were never given adequate treatment for their disease even when penicillin became the drug of choice for syphilis in 1947, researchers did not offer it to the subjects.
- Men were never given the choice of quitting the study, even when this new, highly effective treatment became widely used.

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10

TO PROMOTE ETHICAL STANDARDS

The Belmont Report
The Belmont Report was written in 1976 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Informed by monthly discussions, the Commission published the Belmont Report, which identifies three basic ethical principles that address ethical issues arising from human subjects research.

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TO COMPLY WITH LAWS AND REGULATIONS

In 1974, the Department of Health, Education, and Welfare first published regulations for the protection of human participant research.

In 1981, HHS and FDA developed and implemented human research regulations under their respective statutory authorities based on the three ethical principles of the Belmont Report.

In 1991, the Federal Policy for the Protection of Human Subjects or the "Common Rule" was published and codified in separate regulations by 15 Federal departments and agencies. 45 CFR 46 codified the Common Rule and included the following subparts:

A. Basic HHS Policy for Protection of Human Research Subjects
B. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
C. Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
D. Additional Protections for Children Involved as Subjects in Research
E. Registration of Institutional Review Boards

Revised Common Rule, became effective in July 2018, with general compliance effective January 21, 2019

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COMMON RULE (45 CFR 46)

Subpart A provides the framework for the human research protection including the basic provisions for Institutional Review Boards, Informed Consent, and Assurance of Compliance.

Subpart's B, C, and D provide added protections for human participants, due to diminished physical or mental capacity, may require additional protections against the risks of involvement in a human research.

These protected human subjects include:

- Pregnant Women, Human Fetuses and Neonates
- Prisoners
- Children

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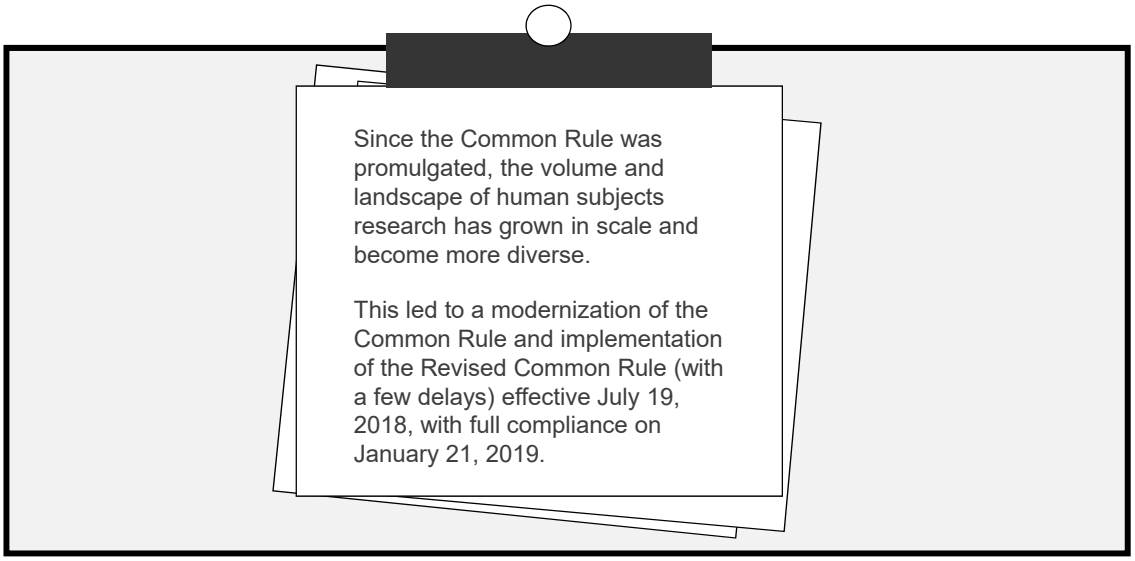
REVISED COMMON RULE (1/2)



Since the Common Rule was promulgated, the volume and landscape of human subjects research has grown in scale and become more diverse.

This led to a modernization of the Common Rule and implementation of the Revised Common Rule (with a few delays) effective July 19, 2018, with full compliance on January 21, 2019.

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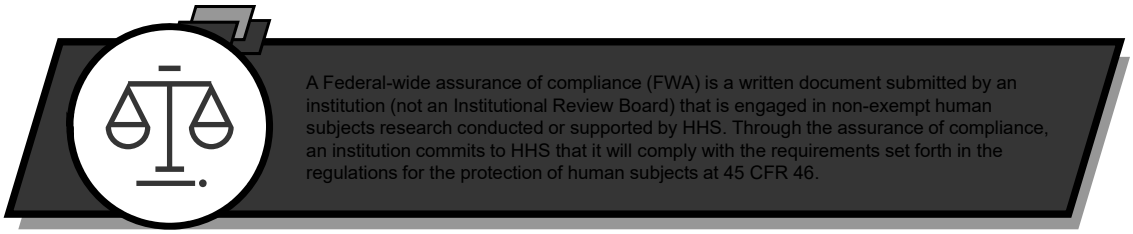
14

REVISED COMMON RULE (2/2)

In summary, the Revised Common Rule strengthened protections for study participants and lightened the administrative workloads for researchers.

S.No.	Key Revised Common Rule Modifications
1	Requires that multi-institutional studies (cooperative research) use a single IRB for review. (January 20, 2020)
2	Focuses informed consent form more towards the research subject to enhance subject comprehension of the study, risks, costs, etc.
3	Requires consent form posting on a federal website (ClinicalTrials.gov; Regulations.gov) so they are publicly available.
4	Confirms that expedited studies may no longer require continuing reviews.
5	Creates additional exempt categories of research requiring limited IRB review.
6	Allows broad consent pertaining to storage, maintenance, and secondary research with identifiable private information or identifiable biospecimens.
7	Updates what is NOT defined as human subjects research, including but not limited to: • Scholarly and journalistic activities • Public health surveillance activities • Authorized operational activities in support of national security missions by a government agency

ASSURANCE OF COMPLIANCE



A Federal-wide assurance of compliance (FWA) is a written document submitted by an institution (not an Institutional Review Board) that is engaged in non-exempt human subjects research conducted or supported by HHS. Through the assurance of compliance, an institution commits to HHS that it will comply with the requirements set forth in the regulations for the protection of human subjects at 45 CFR 46.

To ensure that ethical and legal regulations related to the protection of human subjects are met, institutions must rely on an institutional review board for oversight and monitoring of its human subject research studies.

INSTITUTIONAL REVIEW BOARD (1/3)

Overview

- Each federally supported or conducted human subject research study, including clinical investigations regulated by the FDA must be reviewed, approved, and monitored by an institutional review board (IRB).
- An IRB is comprised of scientists, non-scientists and members of the community.
- Role is to make sure that the study is ethical and that the risks and welfare of participants are protected.
- Ensures research risks are minimized and are reasonable in relation to any potential benefits, among other responsibilities.
- Reviews the research study documents (such as protocol, informed consent…etc)
- Institutions may have their own developed and registered IRB or may rely on another institution's IRB for monitoring and oversight purposes.

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INSTITUTIONAL REVIEW BOARD (2/3)

IRB Registration

Both the OHRP and FDA require IRB Registration for IRBs that are respectively under a Federalwide Assurance (FWA) and/or that review FDA regulated studies.

Institutions that have established their own IRB are responsible for submitting an IRB Registration Form.

The IRB Registration Form is to be used for the following purposes:

- To register an IRB if an institution or organization has not previously registered an IRB
- To update or renew the registration of an IRB previously registered by an institution or organization
- To add another IRB to those previously registered by an institution or organization

Institutions that do not have their own IRB but rely on the IRB of another institution should not submit an IRB Registration.

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INSTITUTIONAL REVIEW BOARD (3/3)

Reliance Agreements

Reliance agreements are arrangements between institutions allowing the IRB of one institution to rely (cede) on the IRB of another institution (IRB of Record) for review of human subjects research. Reliance agreements can be in many different forms, including but not limited to the following:

- IRB Authorization Agreement
- Individual Investigator Agreement
- Memorandum of Understanding
- Master Reliance Agreement

19

NIH SINGLE IRB POLICY

1. The NIH has implemented a requirement that NIH-funded (non-exempt) multi-site clinical studies (same protocol) use a single IRB (sIRB) to provide the ethical review required for human subjects protection over the entire study.
2. The use of a single IRB of record for multi-site studies that are conducting the same protocol helps streamline and enhance the IRB review process by eliminating the unnecessary administrative repetition of those reviews across sites without compromising ethical principles and protections for human research participants.
3. The NIH requirement applies to domestic sites of NIH-funded multisite studies.
4. The NIH requirement applies to applications with due dates on or after January 25, 2018, and contract solicitations published on or after January 25, 2018.
5. Applicants are expected to include a plan for the use of a sIRB in the grant applications and contract proposals they submit to the NIH.

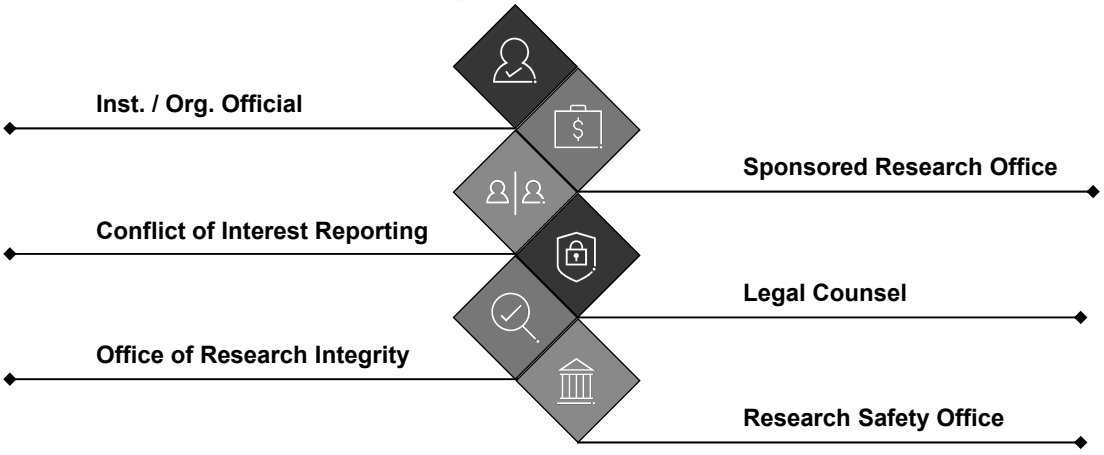
20

HRPP COMPONENTS AND STRUCTURES

21

HRPP COMPONENTS AND STRUCTURES

In addition to the IRB, HRPP is comprised of a network of individuals and groups that work together to uphold the protection of human research participants. This includes, but is not limited to groups such as:



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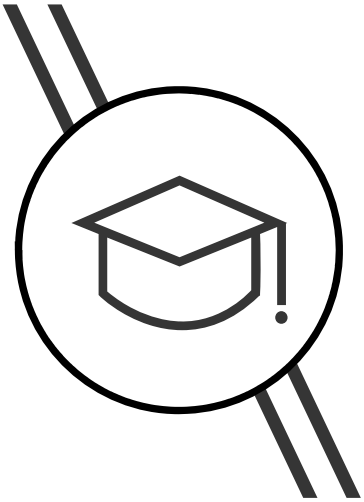
22

HRPP ACCREDITATION



- The Association for the Accreditation of Human Research Protection Programs, Incs. (AAHRPP) promotes high-quality research through an accreditation process that helps organizations worldwide strengthen their HRPPs.
- AAHRPP accredits high-quality human research protection programs in order to promote excellent, ethically sound research. Through partnerships with research organizations, researchers, sponsors, and the public, AAHRPP encourages effective, efficient, and innovative systems of protection for human research participants.

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23

MECHANISMS TO MONITOR HRPP

24

7 ELEMENTS OF AN EFFECTIVE COMPLIANCE PROGRAM

> The Seven Elements of a compliance program are important individually, but are most effective on an interdependent basis.
>
> - CMS

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THE 7 ELEMENTS OF A HRPP AND OIG RISK AREAS

In 1998, the OIG issued guidance regarding hospital compliance program. Supplemental guidance was provided in 2005.

7 Elements

1. Oversight
2. Policies and Procedures / Code of Conduct
3. Education and Training
4. Auditing and Monitoring
5. Open Lines of Communication / Reporting
6. Response and Prevention
7. Enforcement and Discipline
8. *Risk Assessments*

An 8th element was later added to stress the importance of tailoring a compliance program to fit the needs of the organization

In 2005, the OIG issued guidance for recipients of PHS Research Awards.

7 Elements

1. Compliance Officer and Compliance Committee
2. Written Policies and Procedures
3. Training and Education
4. Monitoring and Auditing
5. Effective Lines of Communication
6. Problem Response and Corrective Action
7. Enforcing Standards
8. **Defining Roles and Responsibilities**

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1. OVERSIGHT

Overview

The OIG recommends designating a Compliance Officer and other appropriate oversight bodies, such as a Compliance Committee and Board of Directors to monitor the Compliance Program.

Mission and Vision

- A mission statement identifies HOW the program will achieve its overall vision.
- It defines the purpose and primary objectives related to program needs and team goals.
- It answers the questions, “What do we do? What makes us different?”
- Mission directs the company to its vision (dream)

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27

1. OVERSIGHT

Compliance Program Oversight Structure

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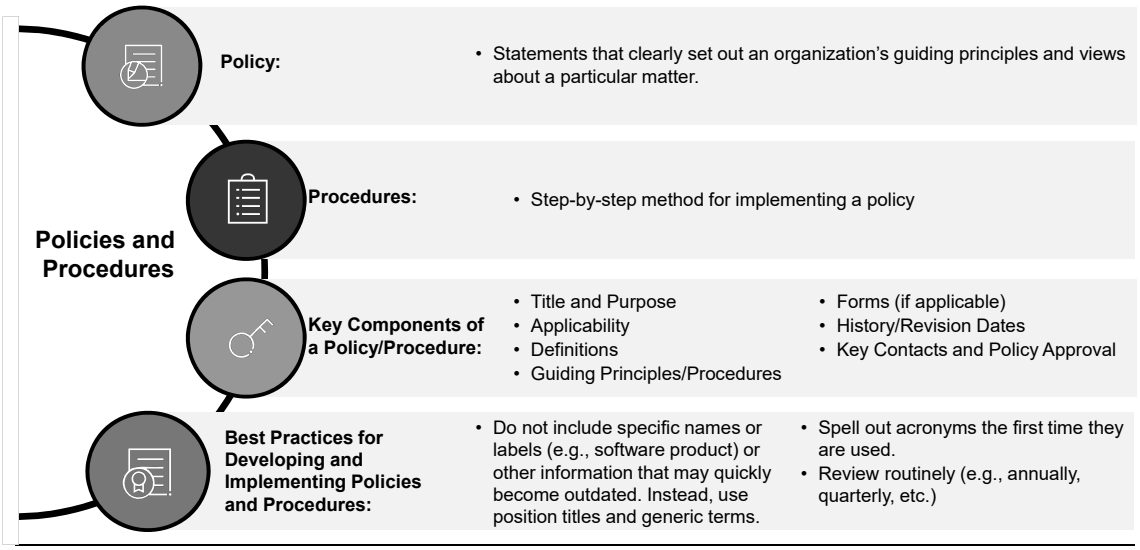
28

2. POLICIES AND PROCEDURES



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2. CODE OF CONDUCT

Defines the rules, values, ethical principles and vision of the organization.

1 Purpose

- Spirit, tone, culture and ethical attitude
- Requirements and expectations
- Helps define:
  - Acceptable conduct
  - Process for proper decision-making
  - What to do if employee has a question
  - Who to tell if the employee suspects misconduct
  - Empowers employees

2 Characteristics

- Readability
- Tone

3 Best Practices

- Tone at the Top - begin with an introductory letter or statement from the CEO and/or Board Chair
- Mission and Vision / Values
- Directions for Asking Questions and Reporting Concerns
- Whom do they contact?
- Can they go to someone other than their supervisor?
- Can they report anonymously?
- Is their a Hotline - what is the number?
- What will happen when they report a concern – what is the process?

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3. EDUCATION AND TRAINING

Ensures that each member of the institution involved in research is fully capable of executing his or her role in compliance with rules, regulations, and other research standards. Helps researcher understand how to do something.

Who should receive training?

- Board
- Researchers and PIs
- Employees
- Contractors / Vendors
- Volunteers
- Medical Staff
- Students

How to Conduct Training

- Consider audience and content
- Use training experts if you have them
- Employ various methods (online, video, webinar, etc.)

Focus training on key risk areas

- OIG Work Plan
- Internal/external factors
- Conflicts of interest
- Human research protection
- Quality of care
- HIPAA
- Time and Effort (OIG)
- Allocating charges (OIG)
- Reporting of financial support from other sources (OIG)

Best Practices

- Specific to roles and responsibilities – train based on role, including the Board
- Senior leadership endorsed/approved
- Required (new hires, annually, and as needed)
- Test understanding
- Obtain attestation

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4. AUDITING AND MONITORING

Auditing

Auditing is a formal, systematic and disciplined approach designed to evaluate and improve the effectiveness of processes and related controls.

- Conducted by individuals independent of the process being audited
- Formal, systematic and structured approach - involves planning, sampling, testing, and validating
- Formal communication with recommendations and corrective action measures
- Documented follow-up of corrective actions
- Audit accountability is typically to the Chief Audit Executive and the Audit Committee

Monitoring

Monitoring is an on-going process usually directed by management to ensure processes are working as intended. Monitoring is an effective detective control within a process.

- Often less structured than auditing, though audit techniques may be employed
- Usually completed by operations
- Involves on-going checking and measuring
- Periodic spot checks, daily/weekly/monthly tests
- May involve internal audit or compliance

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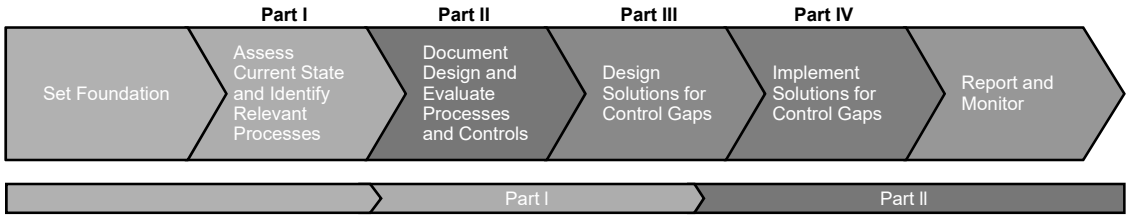
4. AUDITING AND MONITORING

Audit and Monitoring Framework



Organize Project
- Kickoff Meeting
- Project sponsor, team members
- Define Roles & Responsibilities and communication protocols

Agree on Approach/Plan
- Define objectives
- Establish timelines

Develop Project Scope
- Identify current processes and controls
- Understanding existing documentation

Develop Part II Action Plan
- Develop time and resource estimates
- Plan and schedule

Initiate Training Plan
- Develop training materials
- Finalize communication protocols

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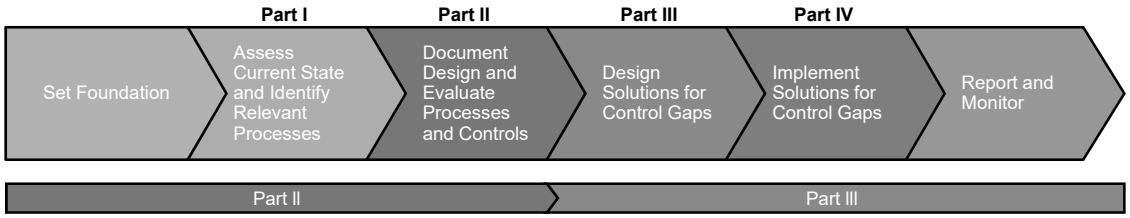
4. AUDITING AND MONITORING

Audit and Monitoring Framework



Assess Controls
- Gather controls documentation
- Risk Assessment survey
- Evaluate results
- Additional testing

Assess Controls Design and Validate Operation
- Assess control design effectiveness
- Assess controls operation
- Test

Develop Part III Action Plan
- Identify gaps requiring CAP
- Identify responsible individual

Evaluate Identified Control Gaps
- Evaluate nature of gaps

Design Solutions for Control Gaps
- Decide and document design improvements

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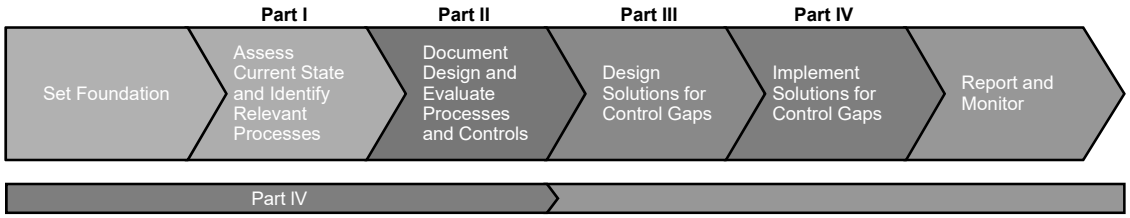
4. AUDITING AND MONITORING

Audit and Monitoring Framework



Implement Solutions for Control Gaps

- Build and test design improvements
- Implement improvements
- Update Policies & Procedures
- Provide training
- Measure performance

Report and Monitor

- Formally document issues, risks and CAPs
- Report findings
- Continuous monitoring
- Continue to report ongoing risks and non-compliance

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4. AUDITING AND MONITORING

Research Compliance Auditing and Monitoring

- Conduct reviews of human research studies (e.g. FDA, HIPAA, clinical trial billing compliance, informed consent)
- Conduct site visits to investigator labs, offices, and facilities where human research is conducted:
  - Review compliance with approved human research protocols
  - Interview researchers involved with human research
  - Assess regulatory binders
  - Review training records
  - Review billing claims in accordance with the Medicare Coverage Analysis
  - Generate written reports with results of site review and identify strengths and deficiencies or deviations from federal regulations, policy, or GCP
- Assist researchers in developing corrective measures
- Serve as a resource for researchers regarding requirements and policies and procedures for conducting human research
- Advise management and the IRB, as appropriate, of unresolved discrepancies/non-compliance related to protocols
- Assist in preparing for and responding to external audits (e.g. FDA audits)
- Conduct not-for-cause and for-cause reviews of human subjects research
- Review UPIRSO, Adverse Events, and study deviations

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5. OPEN LINES OF COMMUNICATION / REPORTING

It is important to encourage internal reporting and have a communication method for researchers to anonymously report their concerns.

Best Practices

- Open door policy (organizational-stance, Compliance Officer)
- Confidentiality and anonymity
- Mechanism to report anonymously (Hotline)
  - Internal or External Hotline
  - Publicized (newsletter, Internet/Intranet, etc.)
  - Phone Number / Website
  - Generally Human Resources/Employment related
- Track investigations and results
  - Identify patterns and trends
  - Document, document, document!
- Share issues and results with Board and other relevant departments, as necessary
- Non-retaliation policy
- Encourage internal reporting first before external reporting
- Report to the IRB and agencies/sponsors, as needed

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6. RESPONSE AND PREVENTION

After a report of non-compliance is made, conduct an investigation, document the steps taken, and implement a corrective action plan to prevent the act from happening again.

1 How can an investigation start?

- Audit result
- Hotline call
- Complaint internally or externally
- Self-disclosure
- Whistleblower
- Subpoena

2 Investigate report

- Enough facts to investigate?
- How serious is it?
- Get internal/external counsel involved? Attorney/client privilege needed?
- Consult other appropriate areas (e.g., Human Resources, Internal Audit, ORI)
- Investigations are confidential

3 Investigation response/prevention

- Stop the non-compliant behavior immediately!
- Document report, investigation, results and action taken
- Retention/Destruction Policy
- Report results to applicable leadership (remember anonymity)
- Implement new/revised internal controls (e.g., policies, staff), where needed
- Educate, where needed
- Determine if it's enough risk to conduct future audit on

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7. ENFORCEMENT AND DISCIPLINE

Disciplinary policies should explain the consequences of violating the organization's standards of conduct, policies, and procedures.

Best Practices

- Disciplinary standards well-publicized and available
- Sanctions for non-compliant behaviors
- Sanctions for failure to report non-compliance
- Fair, equitable and consistent - progressive discipline vs. automatic termination
- Collaboration with Human Resources and Legal
- Retention/Destruction Policy
- External reporting obligations

8. RISK ASSESSMENT

A compliance risk assessment is a systematic process of evaluating the potential risks associated with lack of or non-compliance with requirements.

Helps identify, mitigate and prioritize risks / focus areas

Best Practices

- Risk assessments should be ongoing and conducted on a regular – typically annual – basis.
- Quantitative and qualitative methodologies
- Ensure proper documentation of the risk assessment
- Utilize results to determine audit plan
- Obtain risk assessment approval by the Board, Research/Compliance Committee and Compliance Officer

8. ROLES AND RESPONSIBILITIES

- Defining roles and responsibilities promotes accountability and is essential to the overall internal control structure of an institution.
- Institutions should clearly delineate the responsibilities of all persons involved with the conduct of federally supported research, including both administration or department personnel with oversight responsibility as well as PIs and other personnel who are engaged in research.
- Roles and responsibilities for each position should be clearly communicated and accessible.

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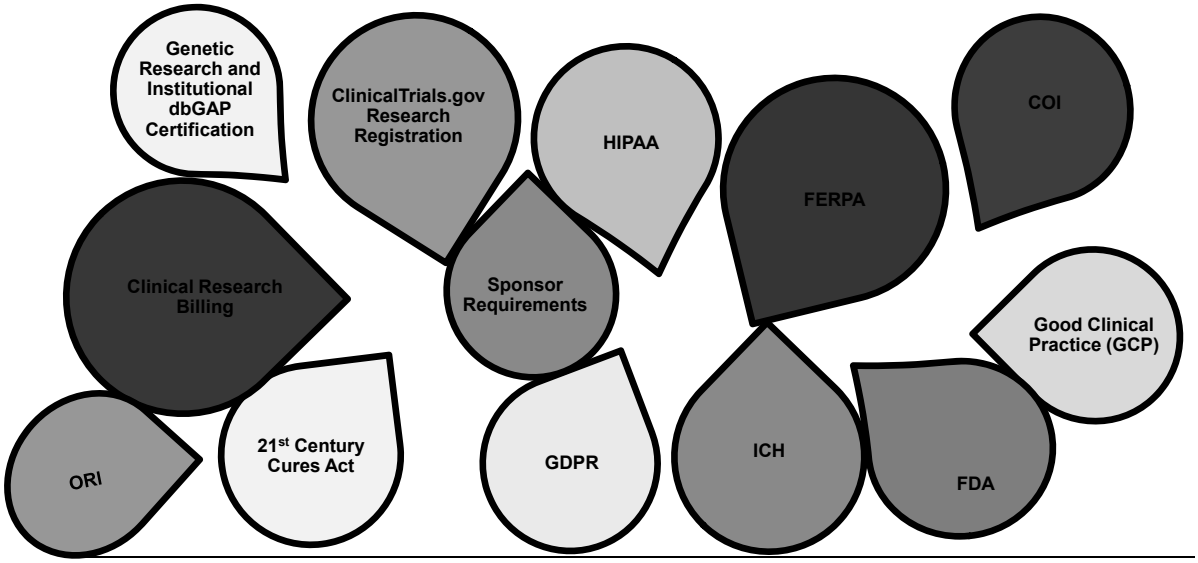
41

ADDITIONAL REGULATIONS AND GUIDANCE

Including, but not limited to….

42

ADDITIONAL REGULATIONS AND GUIDANCE



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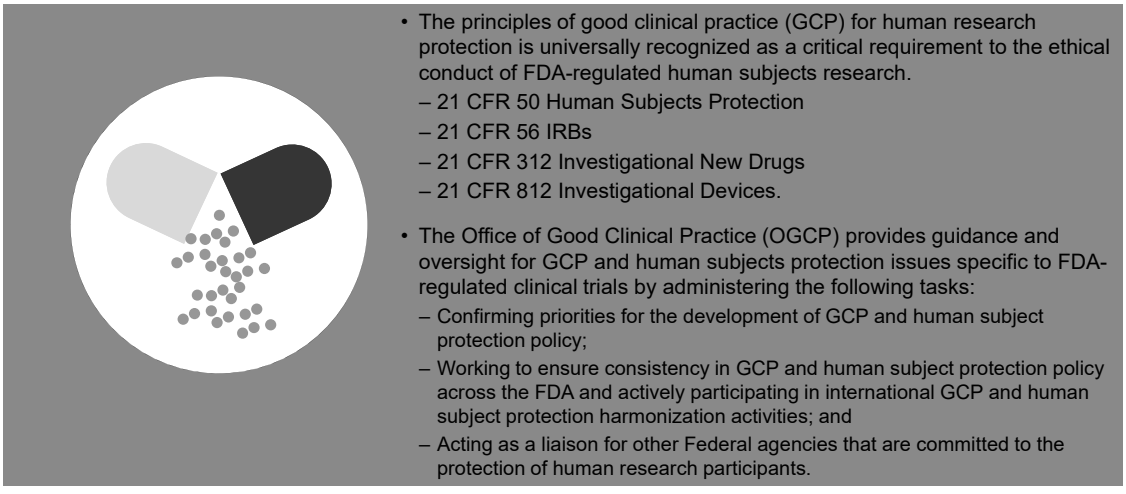
FDA AND GOOD CLINICAL PRACTICE



- The principles of good clinical practice (GCP) for human research protection is universally recognized as a critical requirement to the ethical conduct of FDA-regulated human subjects research.
  - 21 CFR 50 Human Subjects Protection
  - 21 CFR 56 IRBs
  - 21 CFR 312 Investigational New Drugs
  - 21 CFR 812 Investigational Devices.
- The Office of Good Clinical Practice (OGCP) provides guidance and oversight for GCP and human subjects protection issues specific to FDA-regulated clinical trials by administering the following tasks:
  - Confirming priorities for the development of GCP and human subject protection policy;
  - Working to ensure consistency in GCP and human subject protection policy across the FDA and actively participating in international GCP and human subject protection harmonization activities; and
  - Acting as a liaison for other Federal agencies that are committed to the protection of human research participants.

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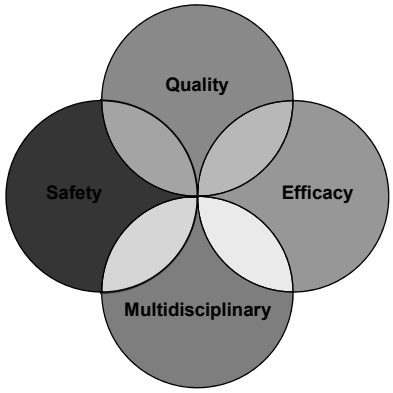
ICH

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) was developed in 1990 and with the objective of bringing together FDA regulatory authorities and the pharmaceutical industry to discuss scientific and technical aspects of drug registration and drug development. ICH's mission is to achieve greater harmonization worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.



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45

CONFLICT OF INTEREST

1. Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought (42 C.F.R. Part 50, Subpart F)

- Promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct, and reporting of research funded by a PHS agency (or any other sponsor) will be free from bias resulting from Financial Conflicts of Interest.
- Requires that prior to the expenditure of funds, any conflicts of interest be satisfactorily managed, reduced or eliminated in accordance with the Institution's COI policy.

2. Physician Payments Sunshine Act ("Sunshine Act"), part of Affordable Care Act

- Requires manufacturers of drugs, medical devices, and biologicals that participate in U.S. federal health care programs to track and then report certain payments and items of value given to U.S. physicians and U.S. teaching hospitals ("Covered Recipients")
- Payments made public on the CMS website.
- Among the data that must be reported includes "Total amount of the research payment, including all research-related costs for activities outlined in a written agreement, research protocol, or both."

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46

HIPAA

Health Insurance Portability and Accountability Act of 1996 (HIPAA) is a federal law that applies to covered entity and gives patients and research subjects authority over their information. For example, HIPAA grants research subjects the following privileges:

1. **Access to Medical Records**
   Research subjects have the right to request and obtain a copy of their medical records.
2. **Review of Medical Records**
   Research subjects can ask that any incorrect or incomplete sections of their medical records be amended
3. **Knowledge of Medical Record Access and View**
   Research subjects can ask who has accessed or seen their medical records (outside of TPO)

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47

GDPR

General Data Protection Regulation (GDPR) became effective on May 25, 2018 and is designed to harmonize data privacy laws across Europe, to protect and empower all EU citizens data privacy, and to reshape the way organizations across the region approach data privacy.

1. Applies to the processing of personal data by a controller or processor when the processing is related to (a) offering goods or services to data subjects in the EEA or (b) the monitoring of behavior of data subjects who are in the EEA.
   - Personal data is defined as information relating to an identified or identifiable natural person (data subject); an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, online identifier, or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural, or social identity of that person.

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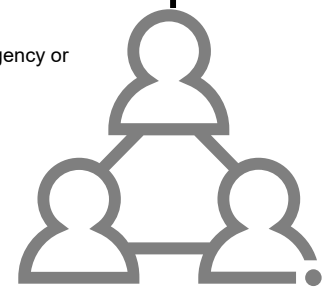
48

FERPA

1. The Family Educational Rights and Privacy Act (FERPA) is a Federal law that protects the privacy of student education records.
   - The term education records is broadly defined to mean those records that are:
     1. Directly related to a student; and
     2. Maintained by an educational agency or institution or by a party acting for the agency or institution.
2. FERPA applies to educational agencies and institutions that receive funds under any program administered by the U.S. Department of Education.
3. This includes virtually all public schools and school districts and most private and public postsecondary institutions, including medical and other professional schools.
4. If an educational agency or institution receives funds under one or more of these programs, FERPA applies to the recipient as a whole, including each of its components, such as a department within a university



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CLINICALTRIALS.GOV RESEARCH REGISTRATION

On September 16, 2016, the Department of Health and Human Services (HHS) issued its final rule on clinical trials registration and results submission (effective January 18, 2017), specifying new requirements and expanding the scope and application of the regulation for the submission of research data ClinicalTrials.gov.

Key Updates

- Must be one (and only one) responsible party for submitting information about an applicable clinical trial.
- Clinical trials with one or more arms and with one or more pre-specified outcome measures to be controlled clinical trials.
- Register applicable clinical trials no later than 21 calendar days after enrolling the first human subject.
- Submission of summary results information for applicable clinical trials of drug products (including biological products) and device products that are approved, licensed, or cleared by FDA.
- Submission of results information not later than 1 year after the completion date of the clinical trial.
- Results information submission may be delayed for up to 2 additional years from the date of submission of a certification under certain circumstances.
- Request extensions to the results information submission deadlines for "good cause."
- Outlines the potential civil or criminal actions for failure to comply with the rule's requirements.
- A federal public website that satisfies the Revised Common Rule requirement for consent form posting

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21ST CENTURY CURES ACT

- Signed by President Obama, December 13, 2016 to promote and fund the acceleration of research and medical product development and bring new innovations and advances to patients who need them faster and more efficiently.
- Enhances the ability to modernize clinical trial designs and clinical outcome assessments, which will speed the development and review of novel medical products.
- Provides new authority to help FDA improve our ability to recruit and retain scientific, technical, and professional experts and it establishes new expedited product development programs.

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GENETIC RESEARCH AND INSTITUTIONAL DBGAP CERTIFICATION

- Institutions are responsible for assuring, through an Institutional Certification, that plans for the submission of large-scale human genomic data to the NIH meet the expectations of the Genomic Data Sharing Policy.
- An Institutional Certification must accompany the submission of all large-scale human data to the NIH Database of Genotypes and Phenotypes (dbGAP).
- The Institutional Certification (for sharing human data), should be provided to the funding NIH Institute or Center prior to award, along with any other Just in Time information (for extramural researchers) or at the time of scientific review (for intramural researchers).
  - The Institutional Certification should designate whether the data is “sensitive” and should be maintained in controlled-access database or should be maintained in an unrestricted database.
  - Institutions that submitted Institutional Certifications prior to November 1, 2018, have six months (by May 1, 2019) to indicate if Genomic Summary Results (GSR) from any of their studies should be designated as “sensitive” and therefore maintained in controlled-access due to concerns about the sensitivity of study information.

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CLINICAL RESEARCH BILLING COMPLIANCE

- On July 10, 2006, CMS confirmed its current Clinical Trial Policy through the National Coverage Determination (NCD) process (effective July 9, 2007) that defines routine costs of a clinical trial as well as the qualification process/criteria for Medicare reimbursement of the routine patient care costs and medical complications related to human participation in research.
- Clinical research billing typically adheres to the Center for Medicare and Medicaid Services (CMS) billing, coding and documentation rules/regulations.
- Clinical trial expenses are typically paid by the sponsor, institution, Medicare/Medicaid, third-party payor or the patient.
- The research sponsor first defines the payment and billing structure of the medical procedures/services provided, to ensure that research institutions appropriately bill/invoice the correct payor, and that the research documentation accurately reflects billing regulations and the billing structure.
- Research institutions conduct coverage analyses to identify clinical items or services associated with a clinical trial and the financially accountable party.

RECAP AND CONCLUSION

In order to ensure the highest ethical, legal and quality standards during human research, it is necessary that research institutions implement a robust HRPP.

Development and implementation of a HRPP helps uphold human participant protection as well as protection to all individuals associated with research.

Proper monitoring of the HRPP through the 7 elements assists in monitoring human participant protection.

REFERENCE AND RESOURCES (1/2)

Human Subject Research	https://www.ecfr.gov/cgi-bin/text-idx?SID=9764880e441ec8f61224ac82b5e86ad2&mc=true&node=se45.1.46_1102&rgn=div8
Common Components of Human Participant Research	https://clinicaltrials.gov/ct2/about-studies/learn
To Promote Ethical Standards	https://www.ushmm.org/information/exhibitions/online-exhibitions/special-focus/doctors-trial https://history.nih.gov/research/downloads/nuremberg.pdf https://www.cdc.gov/tuskegee/timeline.htm https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/
To Promote Ethical Standards – The Belmont Report	https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html
To Comply with Laws and Regulations	https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html https://www.govinfo.gov/content/pkg/CFR-2016-title45-vol1/pdf/CFR-2016-title45-vol1-part46.pdf
Common Law	https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html https://www.govinfo.gov/content/pkg/CFR-2016-title45-vol1/pdf/CFR-2016-title45-vol1-part46.pdf
Institutional Review Board - Overview	https://clinicaltrials.gov/ct2/about-studies/learn https://grants.nih.gov/policy/humansubjects/single-irb-policy-multi-site-research.htm
Institutional Review Board – IRB Registration	https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/forms/irb-registration-instructions/index.html
Institutional Review Board - Reliance Agreements	https://irb.northwestern.edu/reliance-agreements
Institutional Review Board (IRB) – NIH Single IRB	https://grants.nih.gov/policy/humansubjects/single-irb-policy-multi-site-research.htm
Assurance of Compliance	https://www.hhs.gov/ohrp/register-irbs-and-obtain-fwas/fwas/fwa-protection-of-human-subjecct/index.html
Revised Common Law	https://www.govinfo.gov/content/pkg/FR-2017-01-19/pdf/2017-01058.pdf https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html#broad-consent-in-the-revised-common-rule
HRPP Components	https://irb.northwestern.edu/sites/irb/files/documents/HRP-101%20 %20Human%20Research%20Protection%20Program%20Plan_03152019.pdf
	https://irb.northwestern.edu/sites/irb/files/documents/HRP-101%20-%20Human%20Research%20Protection%20Program%20Plan_03152019.pdf
	https://ori.hhs.gov/education/products/columbia_wbt/rcr_conflicts/foundation/

REFERENCE AND RESOURCES (2/2)

HRPP Components (cont'd)	https://irb.northwestern.edu/sites/irb/files/documents/HRP-101%20-%20Human%20Research%20Protection%20Program%20Plan_03152019.pdf
	https://ori.hhs.gov/about-ori
	https://irb.northwestern.edu/sites/irb/files/documents/HRP-101%20-%20Human%20Research%20Protection%20Program%20Plan_03152019.pdf
HRPP Structures	https://clinicaltrials.gov/ct2/about-studies/learn
HRPP Accreditation	http://www.aahrpp.org/learn/about-aahrpp/our-mission
The 7 Elements of a HRPP and OIG Risk Areas	https://oig.hhs.gov/authorities/docs/cpghosp.pdf https://oig.hhs.gov/fraud/docs/complianceguidance/phs%20research%20awards%20draft%20cpg.pdf
Good Clinical Practice	https://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/default.htm
ICH	https://www.ich.org/home.html https://www.ich.org/products/guidelines.html
HIPAA	https://www.hhs.gov/sites/default/files/ocr/privacy/hipaa/understanding/consumers/consumer_rights.pdf
GDPR	https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-b-implementation-of-the-european-unions-general-data-protection-regulation-and-its-impact-on-human-subjects-research/index.html
FERPA	https://www2.ed.gov/policy/gen/guid/fpco/ferpa/index.html
CinicalTrials.gov Research Registration	https://www.aamc.org/initiatives/research/472020/clinicaltrials.html https://clinicaltrials.gov/ct2/manage-recs/fdaaa#WhoIsResponsibleForRegistering
21st Century Cures Act	https://www.fda.gov/regulatoryinformation/lawsenforcedbyfda/significantamendmentstothefdcact/21stcenturycuresact/default.htm
Genetic Research and Institutional dbGAP certification	https://osp.od.nih.gov/scientific-sharing/institutional-certifications/ https://grants.nih.gov/grants/guide/notice-files/NOT-OD-19-023.html
Clinical Research Billing	https://www.cms.gov/regulations-and-guidance/guidance/transmittals/downloads/r74ncd.pdf
Auditing and Monitoring	https://ahia.org/assets/Uploads/pdfUpload/WhitePapers/DefiningAuditingAndMonitoring.pdf


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57