

Creative Flexibility

This packet is for institutions considering implementing a flexibility policy. An overview of the three sections is provided below; establishing policies, opportunities for flexibility, and informed consent efficiencies.

Section A: Flexibility Policy Framework: describes the framework to implement a flexibility policy, using USC as a model

- I. “Unchecked Box”
- II. Flex Policy
- III. Exclusions/inclusions to Flexibility
- IV. Standard Operating Procedures (SOPs)
- V. Audit/Monitor Flexed Studies

Section B: Flexibility Initiatives: describes opportunities for flexibility

- I. Consent Form/Process
- II. HIPAA
- III. IRB Staff
- IV. Approval Criteria
- V. Subparts A-D
- VI. Generic Protocols
- VII. Not Human Subjects Research
- VIII. Electronic Submission
- IX. Review of Research
- X. Innovative IRB Review (Ceded)
- XI. Research Staff
- XII. Engagement in Research

Section C: Available Flexibility in the Informed Consent Process: describes flexibility opportunities in the informed consent form and process

- I. Documentation of Consent (signatures)
- II. Short form/ Alternatives
- III. Unnecessary Elements of Consent
- IV. Waivers
- V. Child Assent
- VI. Administrative Documentation
- VII. Human Tissues, consent for in vitro device studies

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A: FLEXIBILITY POLICY FRAMEWORK

I. "Unchecked Box"

- Uncheck all boxes on Federalwide Assurance (FWA) **or** check box for Subpart A but uncheck Subparts B, C, D (allows for different flexibilities)

II. Flex Policy

- For studies that are no greater than minimal risk
- For studies with no federal funding
- Provide equivalent protections to subjects commensurate with risk level

III. Exclusions to Flex Policy

- Greater than minimal risk studies
- No-cost extension studies
- Projects in which a student is paid or supported from a federal training grant or otherwise paid or supported from the faculty advisors' federal funds
- Federally-sponsored studies, including federal training grants
- Studies with FDA-regulated components
- Studies with contractual obligations or restrictions that preclude eligibility in this policy
- Studies with clinical interventions
- Studies using prisoners as subjects
- Studies seeking or obtaining Certificates of Confidentiality

IV. Standard Operating Procedures (SOPs)

- Flex policy can be integrated in IRB Policies and Procedures (e.g., revise applicable sections) or be a stand-alone policy
- Implement campus-specific policy, if necessary (Socio-Behavioral Research vs. Biomedical)

V. Audit/Monitor Flexed Studies

- Establish mechanisms and written metrics to routinely monitor and annually audit all flexed studies

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B: FLEXIBILITY INITIATIVES

(may be adopted by institutions independent of Flex Policy implementation)

I. Consent Form/Process (see Section C)

- Only require necessary signatures based on type of research (e.g., no translator or witness signature)
- Do not limit use of short forms to translations
- When written consent is normally not required (outside of research), grant waivers of documentation for studies approved using expedited procedure
- Make use of available waiver of elements (e.g., omit elements irrelevant to the research)
- Waiver of consent/assent or its documentation is allowed by the regulations
- Apply flexibility available in regulations for child assent (e.g., waivers)

II. Health Insurance Portability and Accountability Act (HIPAA)

- Have IRB serve function of Privacy Board
- Use boilerplate, fill-in-the-blank HIPAA forms that require de minimus information
- Create short, smartform application for research using limited datasets

III. IRB Staff

- Can verify that minor contingencies are satisfied
- Can perform all non-committee functions
- Can handle all regulatory issues that do not require an IRB
- Appoint as member or alternate
- Designate as Expedited Reviewer
- Designate as Exempt Reviewer

IV. Approval Criteria (45CFR§46.111)

- The following criteria are automatically met if study is flex policy eligible:
 - Risks to subjects are minimized (a)(1)
 - Risks to subjects are reasonable in relation to anticipated benefits (a)(2)
 - Selection of subjects is equitable (a)(3)
 - Research plan makes adequate provision for monitoring (a)(5)
 - When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights of vulnerable subjects (b)
- Waive written documentation of consent for all minimal risk research (unless otherwise required by law) regardless of whether this is requested by the investigator (a)(5)

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Subpart A

- Establish additional exempt categories for no greater than minimal risk activities not covered in regulations.
 - Examples:
 - Research that does not conform to a specific exempt category under 45 CFR 46
 - *online surveys, in-person focus groups, and/or interviews involving minors as long as the information collected does not place the individual at greater than minimal risk*
 - *behavioral games*
 - *studies requiring performance of tasks that incur no risk*
 - Research where activity is limited to study of existing or prospective identifiable data
 - *medical record reviews where data is extracted from records*
 - *data analysis of information already collected from court records*
 - *data/specimens collected during a previous research study*
- For exempt category 4, broaden the interpretation of "existing data" to include data that exist at the time the research is proposed or will exist in the future for non-research purposes
- Expand examples of noninvasive procedures to include: skin biopsy (without sutures); ionizing radiation (<100 mrem/yr (1 Sv)); blood draws via indwelling catheter (regardless of frequency); blood draw 5 mL/kg/day or 9.5 mL/kg/8 weeks; additional collection of blood, cerebrospinal fluid, bone marrow during a clinically indicated procedures; additional endoscopic gastro-intestinal biopsies
- Allow investigators to close a study once enrollment is permanently closed, all subjects have completed mandated interventions and interactions and all protocol mandated collection of identifiable private information about the subjects is complete (investigators subsequently submit short application limited to data analysis procedures)
- Extend approval time for activities limited to data analysis-only
- Create short, smartform application for chart reviews
- Create short, smartform application for use of de-identified datasets
- Allow study to begin after Certificate of Confidentiality application has been submitted (not necessary to wait until it is obtained)

Subpart B

- Exploit flexibility as FDA regulations have no Subpart B
- Obtain permission from the mother only (for neonates/fetuses)
- Consider flexibility for social-behavioral research
- Consider not applying Subpart B to minimal risk research

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Subpart C

- Exploit flexibility as FDA regulations have no Subpart C
- Consider flexibility for social-behavioral research
- Do not require IRB review or prisoner representative for types of research specific to institutional policies when individuals are incarcerated after study enrollment
- Do not apply to subjects who become incarcerated after study enrollment
- Expand definition of who is not a prisoner (house arrest, community service, parole, court-ordered treatment)

Subpart D

- Only require signature of one parent for unfunded studies, regardless of risk
- Change assent requirements/eliminate written assent

V. Generic Protocols

- Allow investigators to write protocols in more general terms so that minor modifications to research are not necessary.
Examples:
 - Changes in sequence of intervention
 - Ranges of compensation instead of specific dollar amount
- Create generic protocols for common research activities where urgency exists

VI. NHSR ("Not Human Subjects Research")

- Establish policy to exclude projects that do not meet the federal definition of Human Subjects or Research
- Create brief online application to verify NHSR projects and provide documentation of NHSR decision to researchers
- Publicize/make investigators aware of NHSR, especially students

VII. Electronic Submission

- Make sure the electronic IRB submission system incorporates flex policies
- Ask funding question early on to identify flex-eligible projects to avoid unnecessary questions applicable to funded projects
- Ask Conflict of Interest questions early on to address the conflict or re-route application based on institutional practice

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VIII. Review of Research

- Review each protocol at the least-restrictive level of review
- Evaluate risks in terms of probability and magnitude

IX. Innovative IRB Models

- Establish a flexible IRB model that consists of smaller number of regular IRB members offset by larger alternate member roster, utilizes consultants for scientific expertise and meets more frequently with few items per agenda
- Establish a Rapid Activation IRB structured to address minimum regulatory requirements in reviewing compassionate use requests, emergency/urgent projects and protocols that have a defined/limited study activation window
- Establish MOU/SOPS to cede entire IRB review to other institutions for studies that are conducted at multiple institutions, involve institutional conflicts of interest or share collaborative research

X. Research Staff

- Describe research staff generically so amendments to the study are not necessary (e.g., a registered pharmacist will dispense study drugs)
- Automate/simplify how education requirements are tracked (e.g., automatic uploading of human subjects research education)
- Automate a "personnel change" button (excluding Principal Investigator, Co-Investigator and Faculty Advisor) in place of amendment submissions

XI. Engagement in Research

- Do not consider "engagement" for exempt studies
- Relax engagement requirements
- Do not require formal inter-institutional IRB agreements

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C: AVAILABLE FLEXIBILITY IN THE INFORMED CONSENT PROCESS

Problem Statement on Informed Consent as Developed by Secretary's Advisory Committee on Human Research Protections (SACHRP) Subpart A Subcommittee (SAS):

The goal of the informed consent process is to ensure an individual's voluntary informed decision to participate in research. Although the regulations that govern informed consent are designed to promote flexibility and the basic and additional elements of consent have remained unchanged, the level of detail provided in consent forms has grown steadily since the regulations were enacted.

Current approaches to consent forms and processes are falling short of the goal of promoting voluntary decision making based on adequate understanding. Anecdotal and empirical evidence indicates that potential participants may fail to understand critical aspects of the research, and that an overemphasis on the inclusion of detail has led to lengthy and complex documents, a lack of attention to process, and problems with comprehension.

Factors that contribute to the problem include:

- IRB review of consent documents that is increasingly focused on editorial review rather than a more meaningful review of the process by which consent will be obtained;
- Form has become the catch-all vehicle for related information that may not be central to the decision to participate (e.g. HIPAA; GINA; protocol registries; sponsor and institutional liability concerns);
- Over-interpretation of regulatory requirements combined with a fear of omitting important information;
- Current education on human subjects protections typically stops short of training investigators and their staff on how to promote and implement an effective informed consent process.

Opportunities for Flexibility

The following areas identified below provide opportunities for flexibility in the informed consent process that are often underused and/or misunderstood by IRBs. They are: **documentation of consent, use of short forms and alternatives, unnecessary elements of consent, waivers, child assent, administrative documentation, and consent for use of human tissues.**

I. Documentation of Consent (i.e. signatures)

- Waiver of documentation of consent is underused and allowed by the regs
- Waiver of written documentation is allowed in expedited research
 - In almost all cases, when written consent is normally not required, when procedures in categories (1)-(7) are performed outside of the research

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context therefore, consent documentation may be waived for almost all research approved using the expedited procedure.

- IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.
- OHRP does allow electronic signaturesⁱⁱ on informed consent documents (as long as they are legally valid within the jurisdiction where the research is to be conducted)
- OHRP only requires a witness signature when the use of a short form is used. Otherwise, a witness/signature is not required on informed consent
- Faxed/mailed signed informed consents are acceptable by OHRP
- PI is not required to sign consent
- PI and subject need not sign on same day
- Consent form does not have to be signed on the day consent process is initiated
- Signatures/initials of subject or witness are not required on every page
- Exact time that the consent is signed is not required on consent form
- Use of legally authorized representative may be flexible in certain jurisdictions and allow LAR to consent

II. Short form/Alternatives

- Use of short forms is an option for any kind of research (very few know about this or that it is an option) regs do not limit use of short form to translations only
- Exempt research does not require informed consent (info/fact sheet can be recommended and is often more relevant to exempt research)
- Significant new information or findings (SNIFs) as required in the regs for transmittal to currently enrolled subjects should be provided in a separate, focused document as soon as possible and provided to enrolled subjects. Only new study subjects should get a full revised informed consent (approved by the IRB).
- Extraneous information and detailed study procedures may be placed in educational materials or study handouts, all do not have to be in the consent
- Screening Consent is an option prior to inclusion/study informed consent
- University of Rochester RSRB investigator guidance:
 - “Unless permission is obtained, identifiable data on individuals who do not pass the screening or who do not give consent to the study cannot be kept in study records”
 - “In studies where a screening/selection process is needed, it may be necessary to obtain consent for the screening in addition to or combined with the study consent”
- Situations allowing info/fact sheet (rather than consent) are under utilized
- OPRR Guidance (1995) “Obtaining and Documenting Informed Consent of Subjects who do not speak English”
 - “When a person obtaining consent is assisted by a translator, the translator may serve as the witness.”

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III. Unnecessary Elements of Consent (those that are irrelevant to some types of research are allowed to be omitted)ⁱⁱⁱ

- Any experimental procedures.
- Any reasonably foreseeable risks or discomforts.
- Any reasonably expected benefits to participants or others.
- A disclosure of appropriate alternatives, if any.
- The extent, if any, to which confidentiality will be maintained.
- For research involving more than minimal risk, ...
- No requirement to disclose what is not part of the research, not a consequence of the research, or not related to the research.
- If disclosure element includes “any” and there is nothing that falls into the disclosure category, may consider this element not to apply.

IV. Waivers

The following waivers are all available as requested by PI and justified by IRB:

- Waiver of signed/documented informed consent/parental permission/assent
- Waiver of informed consent/parental permission/assent entirely
- Waiver/alteration of certain elements of informed consent
- Emergency Research Consent Waiver must meet strictly limited but differing conditions when subject to FDA regulations or when not subject to FDA regulations (OPRR Reports 1996 Informed Consent Requirements in Emergency Research)
- Waiving the requirement for the investigator to obtain a signed consent form for some or all participants if the IRB finds:
 - That the research presents no more than minimal risk of harm to participants; and
 - Involves no procedures for which written consent is normally required outside of the research context. [45 CFR 46.117(c)(2), 21 CFR 56.109]

V. Child Assent

- Minors who initially were enrolled under parental consent and reach the legal age of consent while enrolled in a study need to be consented as an adult (unless the IRB waives the consent requirements)
- Waiver of assent for minors is allowed if the conditions for waiver of consent with adults is met (46.116.(c),(d))
- Documenting of child of assent is not required by regs.

VI. Administrative Documentation

- Informed consent stamping is not required
- Recruitment documents need not be stamped

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- Studies may begin after Certificate of Confidentiality has been applied for (not obtained). Data are protected retroactively^{iv}

VII. Human Tissues, consent for use in In Vitro Device Studies Regulated by FDA

- Read recommendations provided in “Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable Guidance for Sponsors, Institutional Review Boards, Clinical Investigators and FDA Staff - Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable”
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm127022.htm>

End Notes

ⁱ Documentation is completed via an IRB approved consent form or description of the consent procedure within the IRB approved study plan. If there is no signature line on the IRB approved consent form, the IRB has waived the requirement to obtain a signature. If there is no consent form approved, the default is that there is no consent form required. Minutes may reflect these decisions but this further documentation is not required

ⁱⁱ An electronic signature is any electronic means that indicates that a person adopts the contents of an electronic message. The U.S. Code defines an electronic signature for the purpose of US law as “an electronic sound, symbol, or process, attached to or logically associated with a contract or other record and executed or adopted by a person with the intent to sign the record.”^[1] It may be an electronic transmission of the document which contains the signature, as in the case of [facsimile](#) transmissions, or it may be encoded message, such as [telegraphy](#) using [morse code](#). Increasingly, encrypted [digital signatures](#) are used in [e-commerce](#) and in regulatory filings as digital signatures are more secure than a simple generic electronic signature.^{[2][3][4]} (http://en.wikipedia.org/wiki/Electronic_signature)

ⁱⁱⁱ For elements of consent that do not fit the research the IRB may approve the omission or these can just be left out of the consent

- The way the regs are worded (46.116(a)(4,5,7)): “if any” provides the out. Although the information regarding a research related injury is the exception as there is no “if any.”
- (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;
- (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;
- (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject

^{iv} NIH Frequently Asked Questions: Certificates of Confidentiality <http://grants.nih.gov/grants/policy/coc/faqs.htm#354>