VCU
Office of the Vice President
for Research and Innovation

Research Community Toolkit Training

Informed Consent

Learning Objectives

- This session will describe the requirements surrounding informed consent procedures for human subjects participating in research
- Discuss considerations for inclusion of vulnerable populations, including Virginia state law requirements
- Differentiate between FDA and HHS requirements for consent disclosure and documentation
- Outline eligibility for waivers or alterations of the consent process and waiver of consent documentation

Agenda

- Informed Consent Overview
- Vulnerable Population Considerations
- Consent Process
- Documentation Requirements
- Consent Waivers / Alterations

Informed Consent

Informed consent is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. It is both an initial and ongoing process, not just a form or document, which enables prospective and current research participants to voluntarily decide whether to participate as a research subject, or to continue participation. (VCU HRPP Policy Statement: Informed Consent Process, Elements, Waiver of Element(s) and Alteration)

- After having been informed of all aspects of a study that are relevant to the subject's decision to participate, the subject voluntarily confirms his or her willingness to participate in a particular research study
- Informed consent is documented by means of a written, signed and dated consent form

Informed Consent

The revised Common Rule (2018) contained several major changes to the general requirements of informed consent to promote subject autonomy:

- Informed consent must give prospective subjects the information that a reasonable person would want to have to make an informed decision about participation
- The information must be presented in sufficient detail and organization to facilitate understanding of complicated information (not just a list of isolated facts)
- Key information about the study must be provided in a concise and focused manner at the beginning: purpose, risks/benefits, alternatives, and any explanations that would enhance decision-making

Informed Consent – General Requirements

- No investigator may involve a human subject in research unless informed consent of the subject (or LAR) has been obtained
- Subjects should have sufficient opportunity to consider whether to participate in research or not
- Coercion and undue influence should be minimized
- The information given to the subject should be in a language understandable to the subject
- No informed consent may include exculpatory language in which a subject is made to waive or appear to waive any of his/her legal rights, or releases, or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence

OHRP Examples

Examples of Exculpatory Language:

By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances.

I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.

I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.

By consenting to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.

OHRP Examples

Examples of Acceptable Language:

- Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
- By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.
- This hospital is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.
- This hospital makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.

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Legally Authorized Representatives

Who may provide consent for cognitively impaired adults or minors?

- HRP-013 - LARs, Children, and Guardians

Legally Authorized Representatives

Limitations on LAR Consent in Virginia, § 32.1-162.18. Informed consent

- Non-therapeutic research unless it is determined by the IRB that such non-therapeutic research will present **no more than a minor increase over minimal risk** to the human subject.

- Participation in human research on behalf of a prospective subject if the legally authorized representative knows, or upon reasonable inquiry ought to know, that **any aspect of the human research protocol is contrary to the religious beliefs or basic values of the prospective subject**, whether expressed orally or in writing.

- Participation in human research involving **non-therapeutic sterilization, abortion, psychosurgery or admission for research purposes** to a facility or hospital.

Legally Authorized Representatives

Additional LAR Considerations per Virginia State Law

- If two or more LARs **disagree** (with each other) as to participation of the prospective subject in human research, the subject shall not be enrolled in the human research that is the subject of the consent.
- No person shall be **forced** to participate; dissent or objection on the part of the participant ought to be respected.
- In the case of persons suffering from organic brain diseases causing progressive deterioration of cognition for which there is no known cure or medically accepted treatment, the implementation of experimental courses of therapeutic treatment to which a legally authorized representative has given informed consent shall not constitute the use of force, unless prior knowledge of participant refusal is known.

Children

Assent from Minors

- Virginia age of majority = 18.

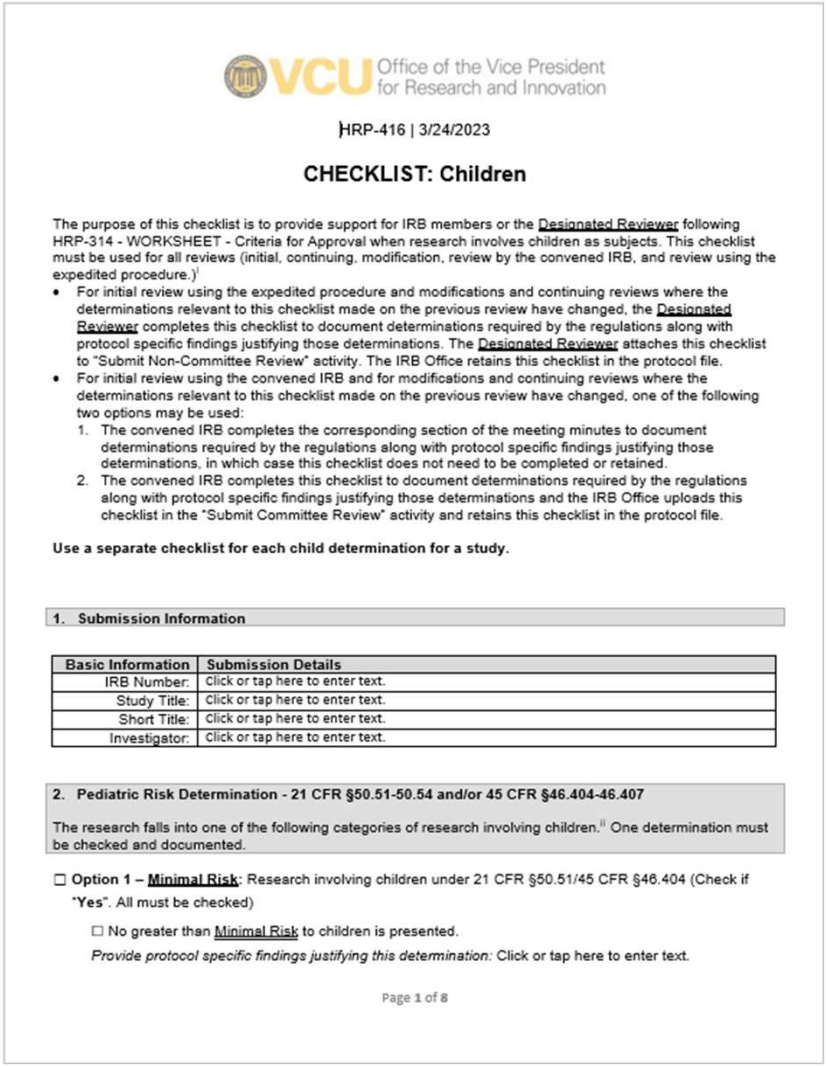
- Research involving **only** treatments or procedures for which minors can give consent for clinical purposes (e.g., research on STDs or pregnancy), the participant would no longer meet the definition of “children” as defined at 45 CFR 46.402(a). They may provide their own informed consent and parental permission (or waiver) is not required.

- Every effort should be made to obtain assent from participants to the extent compatible with the child’s understanding (at the time of enrollment AND during active participation or long-term follow-up). A child’s objection to participation should be honored whenever possible.

Children and Guardians

Consent requirements for children enrolled in research are outlined in HRP-416 - Children

- Section 4 = Assent (all, none, or some; waivers)
- Section 5 = Parental permission
- Section 6 = Waiver of parental permission



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HRP-416 | 3/24/2023

CHECKLIST: Children

The purpose of this checklist is to provide support for IRB members or the Designated Reviewer following HRP-314 - WORKSHEET - Criteria for Approval when research involves children as subjects. This checklist must be used for all reviews (initial, continuing, modification, review by the convened IRB, and review using the expedited procedure.)[I]

- For initial review using the expedited procedure and modifications and continuing reviews where the determinations relevant to this checklist made on the previous review have changed, the Designated Reviewer completes this checklist to document determinations required by the regulations along with protocol specific findings justifying those determinations. The Designated Reviewer attaches this checklist to "Submit Non-Committee Review" activity. The IRB Office retains this checklist in the protocol file.
- For initial review using the convened IRB and for modifications and continuing reviews where the determinations relevant to this checklist made on the previous review have changed, one of the following two options may be used:
  1. The convened IRB completes the corresponding section of the meeting minutes to document determinations required by the regulations along with protocol specific findings justifying those determinations, in which case this checklist does not need to be completed or retained.
  2. The convened IRB completes this checklist to document determinations required by the regulations along with protocol specific findings justifying those determinations and the IRB Office uploads this checklist in the "Submit Committee Review" activity and retains this checklist in the protocol file.

Use a separate checklist for each child determination for a study.

1. Submission Information

Basic Information	Submission Details
IRB Number:	Click or tap here to enter text.
Study Title:	Click or tap here to enter text.
Short Title:	Click or tap here to enter text.
Investigator:	Click or tap here to enter text.

2. Pediatric Risk Determination - 21 CFR §50.51-50.54 and/or 45 CFR §46.404-46.407

The research falls into one of the following categories of research involving children.[II] One determination must be checked and documented.

☐ **Option 1 – Minimal Risk:** Research involving children under 21 CFR §50.51/45 CFR §46.404 (Check if "**Yes**". All must be checked)

☐ No greater than Minimal Risk to children is presented.

Provide protocol specific findings justifying this determination: Click or tap here to enter text.

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Informed Consent Process

- Review HRP-090 - Informed Consent Process for Research

Informed Consent Process

The informed consent process may consist of subject recruitment materials, verbal instructions, and question/answer sessions, as well as reading and signing the informed consent document

The consent document is the basis for a meaningful exchange between the investigator and the subject

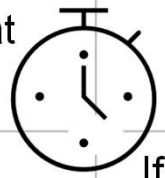
The Principal Investigator (PI) will ensure that informed consent is obtained from each research subject before the subject participates in the research study

The PI will be held responsible even when another research staff member obtains informed consent

Informed Consent Process

The IRB should know who will be conducting the consent interview

The IRB should also be informed of such matters as timing of obtaining consent and any waiting period (between informing subject and obtaining consent) that will be observed



A copy of the consent document must be given to the subject and the original signed consent document should be retained in the study records

The date the subject signs the consent form will be used to verify that the consent was obtained before the subject began participating in the study

If consent is obtained the same day subject starts study procedures, then subject's medical records/case report forms should document that consent was obtained before participating in the first procedure at the visit

Informed Consent Process

- The consent process begins when a potential research subject is initially contacted
- Although an investigator may not recruit subjects to participate in a research study before the IRB reviews and approves the study, an investigator may query potential subjects to determine if an adequate number of potentially eligible subjects is available

Non-English-Speaking Subjects

- When the study subject population includes non-English speaking people or the PI or the IRB anticipates that the consent interviews will be conducted in a language other than English, the IRB should assure that a translated consent form is prepared and assure that the translation is accurate
- A routine ad hoc translation of the consent document should not be substituted for a written translation
- A translator can be helpful for the non-English speaking subject to understand the conversation
- A “short form” consent may be used – if so, the requirements for signature of a witness must be followed

Illiterate English-Speaking Subjects

A subject who speaks and understands English, but does not read and write, can be enrolled in a study by having the consent read to them and by "making their mark" on the consent document, when consistent with applicable state law. -FDA Information Sheets, p. 39

If a participant, or their LAR, is illiterate:

Information in the consent materials will be presented orally by the individual carrying out the informed consent process

Sufficient time should be allowed for questions to be asked and answered, both by the participant, and by the person obtaining consent to ensure the participant comprehends the consent information.

A witness, individual not associated with the protocol, must be present during the entire informed consent discussions, and must sign and date the informed consent document

The person obtaining consent will document in the research record and medical record (if applicable), the method used for communication with the prospective participant and the specific means by which the prospective subject communicated agreement to participant (i.e. "made a mark" on the informed consent document)

Illiterate English-Speaking Subjects

ICH GCPs suggest if a subject is unable to read, or if the LAR is unable to read, an impartial witness should be present during the entire consent discussion and the witness will sign and date the consent form

- ICH E6 4.8.9

The purpose of the witness is to be present during the entire consent interview and to attest to the accuracy of the presentation and the apparent understanding of the subject (or LAR)

-FDA Information Sheets, p. 39

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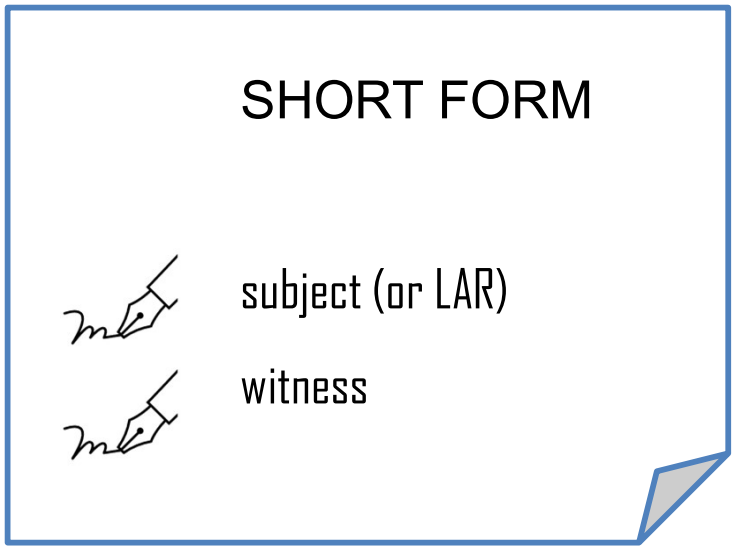
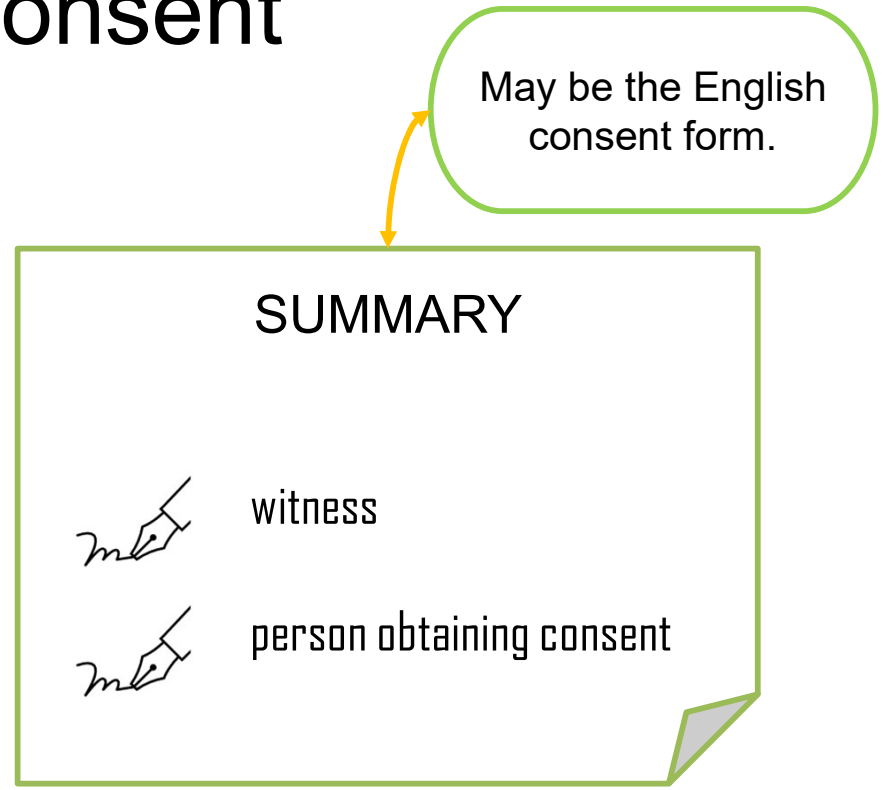
Documenting Informed Consent

- Informed consent shall be documented by use of a written consent form approved by the IRB and signed and dated by the subject (or LAR) at the time of consent
- A copy shall be given to the person signing the form
- The consent form may be either:
  - A written consent form that embodies the elements of informed consent - this form may be read to the subject (or LAR)
  - A short form written consent form stating that the elements of informed consent have been presented to the subject (or LAR) orally
    - When this method is used, must have a witness to the oral presentation who signs the short form and summary
    - The IRB shall approve a written summary of what will be said to the subject

Documenting Informed Consent

- If a short form is used:





Provide a copy of both signed and dated documents to the subject/representative.

Basic Elements of Informed Consent - 21 CFR and 45 CFR

(1) Statement that study involves research, purpose of research, expected duration of subject's participation, description of study procedures, identify any procedures that are experimental	(2) Description of any reasonably foreseeable risks or discomforts to the subject	(3) Description of any benefits to the subject or others which may reasonably be expected	(4) Disclosure of alternative treatments and/or procedures that might be advantageous to the subject, if any
(5) Statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained, **and that notes that FDA may inspect the records**	(6) For research greater than minimal risk, explanation as to whether any compensation and medical treatments are available if injury occurs	(7) Explanation of whom to contact about questions relating to the research and the research subjects' rights, and who to contact for questions related to research-related injuries	(8) Statement that participation is voluntary, refusal to participate will not result in any penalty/loss of benefits, and subject may discontinue at any time also without any penalty/loss of benefits
(9)* One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens: (i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or (ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.			

Additional Elements of Informed Consent

Statement that a particular treatment/procedure may involve risks to subjects (or to an embryo or fetus if the subject is or becomes pregnant) which are currently unforeseeable	Anticipated circumstances under which the subject's participation may be terminated without regard to the subject's consent	Any additional costs to the subject that may result from participation in the research
Consequences of a subject's decision to withdraw from the research and any procedures for orderly termination	Statement that significant new findings that may develop during the course of the research which may relate to the subject's willingness to continue participation will be provided	Approximate number of subjects involved in the study
For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen). (N/A if research is subject to Pre-2018 Requirements)	A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit (N/A if research is subject to Pre-2018 Requirements)	A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions (N/A if research is subject to Pre-2018 Requirements)
Amount and schedule of all payments	Any additional information which should be given to subjects when in the IRB's judgement the information would meaningfully add to the protection of the rights and welfare of subjects	When the study involves genetic testing, a statement that outlines the protections afforded to the subject under the Genetic Information Nondiscrimination Act (GINA)

Additional Required Elements for FDA-Regulated Research

The possibility that the Food and Drug Administration may inspect the records	The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed	The investigator should ask a subject who is withdrawing whether the subject wishes to provide further data collection from routine medical care
For controlled drug/device trials (except Phase I drug trials) and pediatric device surveillance trials: “A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”		

Required for Clinical Trials that Follow ICH-GCP

The approval of the IRB	The probability of random assignment to each treatment	The subject's responsibilities
When applicable, the reasonably foreseeable risks or inconveniences to an embryo, fetus, or nursing infant	The important potential benefits and risks of the alternative procedures or courses of treatment that may be available to the subject	When there is no intended clinical benefit to the subject, a statement to this effect
If the results of the trial are published, the subject's identity will remain confidential	The monitors, auditors, IRB, and regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the subject, to the extent permitted by applicable laws and regulations and that, by signing the consent document, the subject or LAR is authorizing such access	

Additional Considerations for Electronic Consent

- Electronic consent document includes all required elements
- The date of the electronic signature will be captured (N/A if waiver of documentation of consent is requested and justified)
- Questions or methods to gauge subject comprehension of key study elements are clearly defined in the informed consent procedures
- Electronic consent process includes age-appropriate materials to facilitate comprehension
- Electronic consent process is suitable to the study population or procedures are outlined to accommodate subject's needs
- Electronic consent document/process allows subjects to proceed forward or backward or pause for review later

Additional Considerations for Electronic Consent

- Measures are present to ensure that subjects have access to all of the consent related materials, including hyperlinks or other external documents
- Plans are adequate to maintain external hyperlinks or documents and subject access to these documents throughout the lifespan of the study until completion are detailed in the informed consent procedures
- The informed consent process outlines in detail how any included documents will be utilized
- Measures are present to ensure that the identity of the signer and the integrity of the data can be verified when consent is not witnessed by the study team
- For FDA-Regulated Clinical Trials including children as research subjects, if the parent or guardian initially documents the child's assent, procedures are in place to verify the child's identity and assent when the child initially presents to the investigator.

Additional Disclosures

- HIPAA authorization
- Certificate of confidentiality
- Genomic data sharing
- Genetic Information Nondiscrimination Act (GINA)
- Federally funded COVID-19 research
- Additional templated disclosures are included in the new consent template HRP-502

HIPAA

Waiver of HIPAA

- Review HRP-441 - HIPAA Waiver of Authorization
- Describe request and justify waiver of HIPAA in the protocol; confirm data access, confidentiality, and security standards are consistent with VCU IT and VCUHS Privacy Office requirements

Documenting Informed Consent

Toolkit resources related to obtaining and documenting informed consent:

- HRP-013 - LARs, Children, and Guardians
- HRP-090 - Informed Consent Process for Research
- HRP-091 - Written Documentation of Consent
- HRP-314 - Criteria for Approval
- HRP-317 - Short Form of Consent Documentation
- HRP-502 - TEMPLATE CONSENT DOCUMENT
- HRP-506 - TEMPLATE CONSENT DOCUMENT - Emerg or Comp Device Use
- HRP-507 - TEMPLATE CONSENT DOCUMENT - Short Form

* These do not need to be completed or submitted by the study team; rather, they are available for your reference to demonstrate the approval criteria utilized by the VCU IRB

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DHHS Waiver/Alteration of Informed Consent

An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waives the requirement to obtain informed consent if the IRB finds and documents that:

- The research is not FDA-regulated and does not involve non-viable neonates
- The research involves no more than minimal risk to subjects
- Research could not be practicably carried out without the requested waiver/alteration,
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- The waiver/alteration will not adversely affect the rights or welfare of subjects
- When appropriate, subjects or legally authorized representatives will be provided with additional pertinent information after participation

DHHS Waiver/Alteration of Informed Consent

EXCEPTION – 2018 Requirements:

If an individual was asked to provide *broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

**NOTE: Broad consent is not permissible at VCU*

DHHS Waiver/Alteration of Informed Consent

This waiver or alteration may also apply to a research or demonstration project conducted by or subject to the approval of state or local government officials when designed to study, evaluate or otherwise examine:

- Public benefit or service programs
- Procedures for obtaining benefits or services under those programs
- Possible changes in or alternatives to those programs or procedures
- Possible changes in methods or levels of payment for benefits or services under those programs

Full waiver/alteration criteria may be referenced in HRP-410 - CHECKLIST - Waiver or Alteration of Consent Process

Prior DHHS Waiver of Informed Consent

Screening, Recruiting, or Determining Eligibility – Revised 2018 Common Rule Requirements

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

- The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
- The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

The IRB no longer has to grant a consent waiver for these activities.

DHHS Exception to Requirement for Documentation of Informed Consent

An IRB may waive the requirement to obtain a signed consent form if it finds:

- The research is not FDA-regulated
- A written script of information provided orally contains all required elements of consent
- The only record linking the subject and the research would be the consent document and the principal risk would be potential harm from a breach of confidentiality
- Each subject or LAR will be asked whether the subject wants documentation linking the subject with the research and their wishes will govern

If the IRB waives documentation per these regulations, the IRB may require the investigator to provide subjects with a written statement regarding the research

DHHS Exception to Requirement for Documentation of Informed Consent

-OR- an IRB may waive the requirement to obtain a signed consent form if it finds:

- The research is not FDA-regulated and is minimal risk
- A written script of information provided orally contains all required elements of consent
- The subjects or LAR are members of a distinct cultural group or community in which signing forms is not the norm
- There is an appropriate alternate mechanism for documenting that informed consent was obtained

If the IRB waives documentation per these regulations, the IRB may require the investigator to provide subjects with a written statement regarding the research

FDA Exception to Requirement for Informed Consent

21 CFR 56.109(c)(1)
Exception for Documentation of Informed Consent

- The IRB may waive the requirement that subjects sign a written consent form if it finds that the research presents no more than minimal risk and involves no procedures for which written consent is normally required outside of the research context.
- If the IRB documentation per these regulations, the IRB may require the investigator to provide subjects with a written statement regarding the research

2017 Guidance:
IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk

- The FDA does not intend to object to an IRB approving a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 CFR 50.25, or waiving the requirements to obtain informed consent when the IRB finds and documents that:
- The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The clinical investigation could not practicably be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation

FDA Exception to Requirement for Informed Consent

Criteria to waive the consent process for FDA-regulated research involving anonymous tissue specimens

- Outlined in HRP-410 - CHECKLIST - Waiver or Alteration of Consent Process, section 4
- Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable – April 25, 2006

FDA Informed Consent Exception: Emergency Use of a Test Article

Obtaining informed consent shall be deemed feasible unless, both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

1. The human subject is confronted by a life-threatening situation necessitating the use of the test article.

2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.

3. Time is not sufficient to obtain consent from the subject's legal representative.

4. There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

If immediate use of the test article is, required to preserve the life of the subject and time is not sufficient to obtain the independent determination in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The documentation required shall be submitted to the IRB within 5 working days after the use of the test article.

FDA Informed Consent Exception: Planned Emergency Research

- Extensive requirements may be referenced in HRP-419 - Waiver of Consent Process for Emergency Research (Planned Emergency Research)
  - Life-threatening situation with unproven or unsatisfactory treatments available where the collection of scientifically-valid evidence is necessary to determine the safety and effectiveness of particular interventions
  - Consent to be obtained wherever possible (requirements around LARs/family members/post-use notification)
  - For subjects not able to give their informed consent - the intervention is required before consent may be obtained from the LAR; unreasonable to prospectively identify individuals likely to become eligible for participation; may not practicably be carried out without the waiver; family notification to occur
  - Prospect of direct benefit
  - Community consultation and public disclosure

FDA Informed Consent Exception: Planned Emergency Research

- If the research is FDA-regulated, the protocol is being performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies this protocol as including subjects who are unable to consent (even if an IND for the same drug product or an IDE for the same device already exists)
- If the research is FDA-regulated, a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the research has concurred with the above findings

Consent Waivers / Alterations

Toolkit resources related to the waiver or alteration of informed consent or waiver of the documentation of informed consent:

- HRP-410 - Waiver or Alteration of Consent Process
- HRP-411 - Waiver of Written Documentation of Consent
- HRP-322 - Emergency Use
- HRP-419 - Waiver of Consent Process for Emergency Research

* These do not need to be completed or submitted by the study team; rather, they are available for your reference to demonstrate the approval criteria utilized by the VCU IRB

Questions