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# Welcome!

- The session will begin shortly; please take a moment to make sure your microphone is muted.
- There will be a Q&A after the presentation.
  - Please hold questions until then so we can discuss them live, OR
  - Type them into the chat for one of my colleagues from the Operations Team to address

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# Informed Consent in Research

## Regulatory Requirements and Ethical Considerations

Kaori Kubo Germano, Ph.D.
Human Research Compliance

HRC METS
Thursday, August 17th, 2022

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# Overview

**Elements of Informed Consent**

**Writing the Informed Consent Form**

**How do we obtain consent?**

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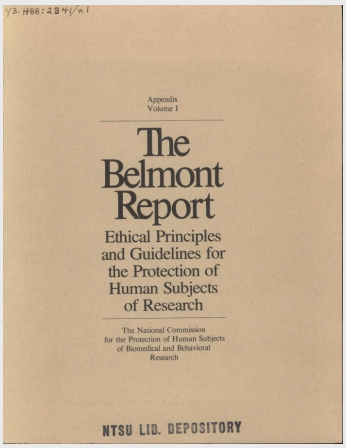
# Why Informed Consent?




- **Regulatory requirement borne out of Nuremberg Trials, among other events**
- **The Belmont Report's basic principles:**
  - **Justice**
  - **Beneficence**
  - **Respect for Persons**

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# Respect for People's Rights and Dignity

**We must:**

- **Ensure comprehension**
- **Avoid undue influence**
  - Explicit or implied threats = **coercion**
  - Excessive compensation = **undue inducement**
- **Obtain informed consent**

**Vulnerable populations must be protected:**

- Children/Neonates
- Prisoners
- Persons with limited decision-making ability
- Pregnant Persons/Fetuses
- Students or Direct Reports of a PI

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# Informed Consent Documentation

*45 CFR 46.117(a): Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject's legally authorized representative. A written copy shall be given to the person signing the informed consent form.*

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# Fundamental Aspects of Informed Consent

**01**

**Disclosure**
Researchers must disclose all aspects of the study

**02**

**Comprehension**
Individuals must have the mental capacity to understand the information presented to them

**03**

**Voluntariness**
Consent must be freely given or truly voluntary

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# Elements of Informed Consent

45 CFR §46.116

**Informed**
- Having full knowledge and understanding of what participation entails

**Consent**
- Autonomous decision to voluntarily participate in the research

**Process**
- A continuous dialogue to ensure ongoing consent to participate

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# 9 Basic Elements of Informed Consent


**9. WHAT HAPPENS AFTER?**
A statement about what will be done with collected information

**8. IS IT MANDATORY?**
A statement that participation is voluntary

**7. WHO IS THE CONTACT?**
Contact information for questions or more information

**6. IS THERE COMPENSATION?**
For greater-than-minimal risk studies, compensation and/or medical treatment

**1. WHAT IS IT ABOUT?**
A statement about, and description of, the study

**2. WHAT ARE THE RISKS?**
A description of risks or discomforts to the subject

**3. WHAT ARE THE BENEFITS?**
A description of any benefits to the subjects

**4. ARE THERE ALTERNATIVES?**
A disclosure of appropriate alternative procedures or courses of treatment

**5. WHO WILL KNOW?**
A statement describing how confidentiality will be maintained

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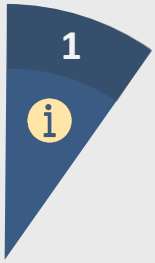


**1. WHAT IS IT ABOUT?**
A statement about, and description of, the study

- **Why is this study being done?**
- **What will you ask your participant to do?**
- **How long will the study last?**
- **How many people will be enrolled?**

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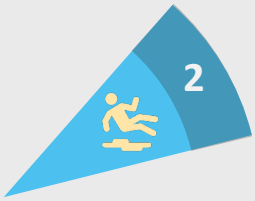


**2. WHAT ARE THE RISKS?**

A description of risks or discomforts to the subject

- **Detail any known risk of harm that the participant may experience**
  - **Physical, psychological, social, economic, legal, or unknown risks**
- **Any/all risks in protocol must be addressed**
- **Include:**
  - **Likelihood**
  - **Magnitude**
  - **Permanence**
  - **Side effects**

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**3. WHAT ARE THE BENEFITS?**

A description of any benefits to the subjects

- **Detail any known direct benefits to the participants here**
- **If the COI committee requires it, provide a description here of how this might benefit the researchers or WCM/NYP**

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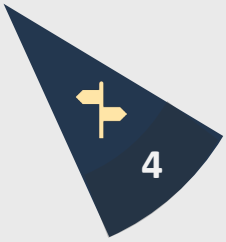


**4. ARE THERE ALTERNATIVES?**

A disclosure of appropriate alternative procedures or courses of treatment

- If there are alternatives to participation, state so here:
  - Commonly used therapies
  - Disclose standard diagnostic procedures or treatment being withheld
  - Other research studies
  - Are study drugs/intervention/devices available off-label or through standard of care?

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**5. WHO WILL KNOW?**

A statement describing how confidentiality will be maintained

- How will information be used and protected?
- Where will data be stored?
- Who will have access to the data?
- How will data be transferred? To whom? Where?
  - When will data be de-identified?
- How secure is storage?
- When/how will data be destroyed?

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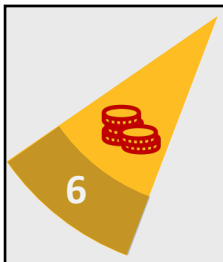


**6.** IS THERE COMPENSATION?

For greater-than-minimal risk studies, compensation and/or medical treatment

- A statement that the participant will be paid/they will NOT be paid
- What if injury occurs?

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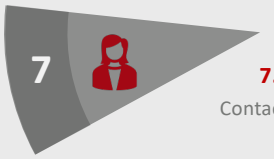


**7.** WHO IS THE CONTACT?

Contact information for questions or more information

- Provide information for:
  - PI/Researcher name
    Department
    Address
    Phone, Email
  - Institutional Review Board
    irb@med.cornell.edu or (646) 962-8200
  - Anonymous Hotline (866) 293-3077

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**8. IS IT MANDATORY?**

A statement that participation is voluntary

- **A statement that it is the participant's decision whether or not to join the study.**
- **Restate their rights to withdraw at any time**
- **If applicable:**
  - **Discuss the process for withdrawing once the project has begun**
  - **How participants can request their data to be withdrawn**
  - **How recordings will be destroyed**
  - **How they may continue treatment or follow-up**

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**9. WHAT HAPPENS AFTER?**

A statement about what will be done with collected information

- **One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:**
  - 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**

  - 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.

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# Additional Elements of Informed Consent

(1) Unforeseeable risk(s)
(2) Possibility of termination of enrollment by investigator
(3) Any additional costs to the subject
(4) Consequences of a subject's decision to withdraw and procedures to withdraw
(5) Provision of significant new findings to the participant
(6) The approximate number of subjects involved in the study.
(7) Use of subject's biospecimens (even if identifiers are removed)
(8) Disclosure of clinically relevant research results, including individual research results
(9) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing

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# Signatures

- **If the participant is a/an:**
  - **Adult:** Their signature
  - **Minor:** Parent/Guardian signature
  - **Member of a vulnerable population:** Legally Authorized Representative (LAR) signature
  - **Adult who cannot read or write:** Witness signature
- **Researcher must also sign the consent**

Vulnerable populations:
- Persons with diminished authority
- Children/neonates
- Prisoners
- Persons with limited decision-making ability
- Pregnant Participants/Fetuses
- Students or Direct Reports of a PI

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# Assessing Capacity to Consent

- Approval of research involving adults unable to provide consent/with impaired decision-making ability contingent on if:
  - The research can reasonably be achieved without this population
  - There are appropriate provisions for:
    - Evaluating capacity
    - Obtaining consent/assent
    - Otherwise protect subjects

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# Waiver of Consent

45 CFR§46.116

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# Waiver of Consent

- Research involves no more than minimal risk
- Research could not practicably be carried out without a waiver
- For research with identifiable data: Research could not practicably be carried out without using such data in an identifiable format
- Waiver or alteration will not adversely affect rights/welfare of subjects
- Information provided after participation

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# Waiver for FDA-Regulated Research


- **Planned research in emergency situations when there is no time to obtain informed consent**
- **Unplanned use of an investigational drug, device, or biologic in an emergency**

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# Is that it? Can I consent?

**No.**

- **Language is important**
  - *IRB101: Writing a Readable Informed Consent Form*
- **The Key Information Section helps**
- **Informed Consent is a *process***
- **Proper training is key**


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# The Key Information Section

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# What is the Key Information Section?

- The first thing your participant sees during the IC process
- Should include the most crucial information needed to decide on participation
- It is NOT an abstract
- It does NOT have all elements of the IC
- It does NOT have to look identical to our template
- It does NOT include exclusions*

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# What is "Key"?

- Voluntary participation is sought for research
- Purpose, duration, procedures, etc. of the research study
- Risk/discomforts to the volunteer
- Direct benefits to the volunteer
- Alternatives to participation (if any)


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# Writing an Informed Consent

How to prepare a readable consent form

Office of Human Research Protection & Compliance
Melissa Epstein, PhD, MBE, CIP *Executive Director*
https://research.weill.cornell.edu/irb

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## What is readable?

- **All informed consent forms (ICFs) must meet the Flesch-Kincaid Grade Level 6-8 readability standards**
  - **Shorter sentences and words**
- **ICFs that do not fall within the Level 6-8 range may be returned for revisions**

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# The Flesch-Kincaid Readability Test

- **Flesch Reading Ease Readability Formula (1948)**

**RE = 206.835 – (1.015 x ASL) – (84.6 x ASW)**


- **Flesch Grade Level Readability Formula (1976)**
  - 90.0 - 100.0: average 5th grader
  - 60.0 - 70.0: 8th and 9th graders
  - 0.0 - 30.0: college graduates

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# For more information…

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## Checking Readability

The Flesch-Kincaid Grade Level Readability Test

Office of Human Research Protection & Compliance
Melissa Epstein, PhD, MBE, CIP *Executive Director*

https://research.weill.cornell.edu/irb

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# Tip #1: Do not use jargon

Use words familiar to the non-medical reader

- "Anticonvulsant" → a drug used to prevent convulsions/seizures
- "Lipid" → fat
- "Mortality" → death

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# Tip #2: Keep it short

- If possible, keep words to 3 syllables or fewer
  - "Anticonvulsant" → a drug used to prevent convulsions/seizures
    too long! 3 syllables vs. 2 syllables
- Write short, simple, and direct sentences
- Keep paragraphs short and limited to one idea

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# Tip #3: Use precise language

- Use active verbs in an active voice
- Use the second person (i.e., ”you”) not the third person (i.e., “the participant”) to increase personal identification
- ~~Don’t~~ Do not use contractions
- Do not use ”e.g.,” “etc.,”
  - e.g. → ”for example”
  - etc. → ”so forth”

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# Tip #4: Format your document well

- Use page numbers on protocol, consent, and any other documents
- Use at least 12-point font and consider a larger font based on your audience
- Highlight important points
  - Use underlines
  - Use **bold**
  - Use boxes

Avoid *italics* or ALL CAPS,
*AS THEY ARE HARDER TO READ ON THE PAGE*

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# Tip #5: Be clear and concise

- Avoid repetition; do not repeat yourself
- Check the text to see if each idea is clear and logically sequential
- Use photos, graphics, or tables if they will help clarify procedures

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# Tip #6: Be consistent

- Be consistent with the use of all terminology, such as drug names and abbreviations
- Spell out acronyms when first used
  - Abbreviations such as DNA, HIV, and AIDS that have come to be accepted as standard need not be spelled out

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# Use of Drug and Device Names

- **Brand names of drugs** (e.g., ~~Paclitaxel~~ PACLITAXEL™) **or devices** (BD ~~Vacutainer~~ VACUTAINER®) **must be capitalized**
- **Generic drug** (e.g., taxol) **or device names** (e.g., blood collection tube) **are lowercase**
- **Use the appropriate abbreviation the first time a drug name is used in the consent**

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# Good rules of thumb

- **Describe study design procedures when the concept(s) is/are first introduced.**
- **Do not describe investigational drugs, devices, or procedures as "new."**
  - Use "investigational" or "experimental" and describe the term
- **When describing randomization for 2 groups use, "like the flip of a coin," for more than 2 groups, use "like drawing numbers from a hat."**
- **If collecting blood or other fluids, give a volume equivalent (for ml. or cc.) in teaspoons/tablespoons**

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# Special items

- **If the FDA may approve the study drug while the research study is in process, include information on whether participants will be responsible for paying for the study drug if it is approved.**
- **For double-blinded studies, include a statement about unblinding.**
- **For optional portions of the study (e.g., asking permission to store samples for future research), insert lines for initials or checkboxes to allow a subject to indicate his/her choice.**

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# Word Usage

- **Do not use the words, "treatment" or "therapy":**
  - To describe an investigational drug, device, or procedure
  - If one of the study arms will be a placebo
- **Do not use "invite"**
  - Use "you are being asked to participate in a research study because…"
- **Do not use symbols such as ">" (greater than)**
- **Use "study doctor" instead of "principal investigator"**
- **Use "research study" instead of "trial"**
- **Use "participant" instead of "patient"**

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# Helpful Resources

**OHRP Guidance**

https://www.hhs.gov/ohrp/regulations-and-policy/guidance/checklists/index.html

**FDA Guidance**

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent

**Email:**
WCM IRB Office: irb@med.cornell.edu
For Training Requests: hrpo@med.cornell.edu

or


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# IRB101: The Informed Consent Process

Lauren Gripp
Director, Clinical Trials

08/18/2022
Jcto.weill.cornell.edu

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Informed Consent is a ***process***, not just a ***document***.

- Numerous regulatory, ethical and legal bodies provide guidance regarding the informed consent process

The Nuremberg Code

THE BELMONT REPORT
*Ethical Principles and Guidelines for the Protection of Human Subjects of Research*

U.S. Department of Health & Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

DECLARATION OF HELSINKI
Medical Research Involving Human Subjects

E6(R2) Good Clinical Practice (GCP)

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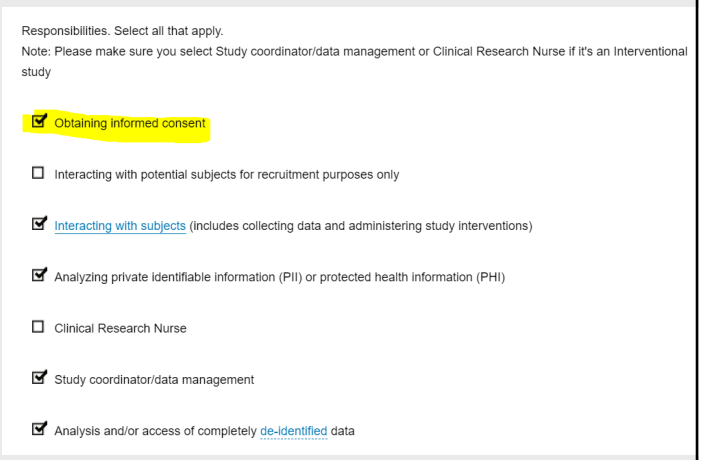
# Who Conducts the Process?

Person(s) delegated to obtain consent must be approved by the IRB before discussing with a potential participant

For FDA regulated studies, personnel must be listed on Form FDA1572

For Oncology studies, only physician-investigators are permitted to sign and date the consent document(s) for interventional studies

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# Consent Environment

Consent discussion location should be:

- Private
- Confidential
- Quiet
- Unrushed setting

| Acceptable Locations | Not Acceptable Locations |
|---|---|
| Physician's Office | Waiting room |
| Exam Room | Pre-Op area |
| | Infusion/clinic space |

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# Types of Consent Documents

- **Written or electronic informed consent**
  - Approved eConsent methods are DocuSign and REDCap
- **Oral consent script and/or information sheet**
  - Waiver of signed documentation of informed consent has been approved by the IRB
- **Parental Permission and Assent forms**
  - Assent form is required for children between 7-17
- **Translated informed consent form**
  - Non-English speaking participants
- **Short form for Unexpected non-English speaking participants**
  - Translated ICF is unavailable

**No study procedures can occur prior to informed consent.**

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# Informed Consent Process

Review Content → Allow Time → Address Questions → Obtain Signatures → Document Process

- Participant must understand participation is **voluntary** and **decline/withdrawal of consent** will not impact their medical care.
- Consenting Investigator must ensure the participant comprehends of the study's purpose, potential risks, possible benefits, and structure of the study.

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# Collecting Signatures


- Participant must:
  - Print, sign, and date in the designated areas
  - Complete optional checkboxes, initial lines, and signature lines, as appropriate.
- Person obtaining consent must individually print their name, and current date, and sign the ICF.
- A copy of the signed document should be provided to the participant for records.
- Original signed or electronic ICF is filed in research chart and uploaded into EMR.

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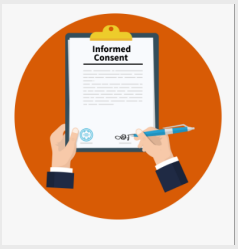
# Documentation of Consent




- Obtaining signatures on ICF is not sufficient documentation.
- Documentation of the consent process should appear in the participant's medical record or in a research chart for non-WCM patient participants regardless of the consent type.
  - Only exception is when the IRB issues a waiver of documentation of informed consent.
- Clarify any consent discrepancies (i.e., participant and researcher signed on different dates) in the consent note.
- Examples of consent notes can be requested by emailing jctooperations@med.cornell.edu

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# Important Reminders


- Ensure the document given is the version most recently approved by the IRB.
- The Consenting Investigator should sign AFTER the participant signs. Document should not be signed in advance of the consent discussion.
- Clear documentation of the chronological order in the medical record showing that the consent was obtained PRIOR TO testing.
- Wet Ink signatures are standard practice, but electronic signatures have become more prevalent during the COVID-19 pandemic.

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# Electronic Consent

Electronic Consent (eConsent) allows the consent form to be completed and signed digitally.

WCM offers two systems for collecting electronic consent:

1. **REDCap** - platform for building and managing online databases and survey tools. System is not 21 CFR Part 11 compliant so only non-FDA regulated studies can use REDCap for eConsent.
2. **DocuSign** - platform specifically designed for electronic completion of documents. Only system offered that is 21 CFR Part 11 compliant.

The use of eConsent must be IRB approved before implemented.

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# eConsent information and training

More info at: **https://jcto.weill.cornell.edu/investigators/study-activation-and-conduct/esignature**

**TWIST presentations located in JCTO TWIST Archive**

REDCAP: Your Guide to Creating eConsent Forms – 2/17/2022

DocuSign: Your Guide to Implementing FDA Compliant e-Signatures – 8/11/2021

Contact **econsent-support@med.cornell.edu** for assistance

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# Other Consent Processes

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## Legally Authorized Representatives (LAR)

- Used when an adult research participant lacks the capacity to provide their own consent
- New York State has guidelines regarding who can be considered a LAR for a participant.
  - Court-appointed LAR
    - Healthcare Proxy
      - Spouse or domestic partner
      - Son or daughter >=18 years old
      - Sibling over >= 18 years old
      - Close friend >= 18 years old

**Document the Consent Process!**

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# Parental Permission and Assent Forms

- **Parental/Legal Guardian Permission**
  - Required for all research conducted on children.
- **Assent for minors**
  - Child between 7-17 must also assent to participate.
  - Discussion must be appropriate for age of participant.

**Document the Consent Process!**

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# Non-English Speaking Participants

- **Expected enrollment of Non-English speaking participants**
  - Full ICF must be translated into language(s) of expected population.
  - Coordinate an interpreter if consenting investigator does not speak participant's native language to facilitate conversation.

**Document the Consent Process!**

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# Non-English Speaking Participants

- **Unexpected enrollment of Non-English speaking participants**
  - Short form can be used in interim until full ICF has been translated.
  - Interpreter orally translates the English version of the approved ICF and facilitates discussion.
  - An unbiased witness who speaks both languages must be present to attest to the adequacy of the Informed Consent process and to observe the research participant's voluntary consent.
  - Translated consent must be supplied to participant when available.

**Document the Consent Process!**

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# Translation Services

**For document translations:**
Inlingua Metro New York
551 Fifth Avenue
New York, NY 10176
www.inlinguaMetroNY.com
translationsNY@inlingua.com

inlingua

**To schedule interpreter services:**
Pacific Interpreters
Call 1-800- 876-3059
Access code 821027

pacificinterpreters℠
A LanguageLine Solutions® Company

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# Reconsent Required

- Original consent document was not properly executed.
- When required by the IRB, check your IRB approval Letter
- A minor participant has reached the age of majority (18 years of age). Note: Age of majority re-consent needs to precede continuation on study.
- Study has been amended (i.e., changes in study procedures).
- Additional information (i.e., drug safety) becomes available, which may affect the participant's willingness to continue participation.
- Information regarding the long-term side effects of the study drug becomes available.

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# Timing of Reconsent

- Reconsent at next scheduled visit.
- Contact participant upon IRB approval when additional risks are identified.
- **Remember to …**

**Document the Consent Process!**

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# Coming Soon…

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## Future METS

- **9/15/22:** Regulating Research: Ethics and the Responsible Conduct of Research
- **10/13/22:** FDA-Regulated Research
- **11/17/22:** Single IRB and Reliance
- **12/15/22:** Tips and Tricks for Successful IRB Submissions and Reviews

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# The New IRB Initial Review Application

- **Facilitates an improved application submission process**: This is done by greatly reducing the length of the application in WRG streamlining the overall process. (10-15 total questions).
- **Improves the efficiency of IRB review**: The application and new supplemental forms collect all pertinent IRB-required information with more targeted and less repetitive questions, making it easier for study teams to complete the application and quicker turnaround times for IRB approval.

**Launching 9/15/2022**

**Training dates:**

- Wednesday, 8/24
- Thursday, 8/25
- Tuesday, 8/30
- Tuesday, 9/6
- Friday, 9/9
- Monday, 9/12

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# Questions?

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