Pre-Questions

Mastering Clinical Research
July 29, 2015
1. To be compliant with SOP 2.1 “Obtaining Informed Consent for greater than minimal risk interventional clinical trial”, which Licensed Professional may obtain informed consent if delegated this task on the DOA log:

A. Nurse Practitioner
B. Licensed Social Worker
C. Clinical Research Nurse
D. All of the above
2. To be compliant with SOP 3.10 “Clinical Trials Subject Transfer from an Unaffiliated Site”, what needs to be done PRIOR to accepting a transfer subject?

A. CRC/CRN verify that all CRFs have been submitted
B. CRC/CRN verify that all queries resolved
C. PI must approve subject transfer
D. All of the above
3. An approved drug used in a research study:

A. Will always be IND exempt
B. Is IND exempt if used routinely in clinical care
C. Never considered IND exempt
D. None of the above
4. The following studies may qualify for IND exemption:

A. Approved HIV drug used for lung cancer treatment

B. Dietary supplement used to prevent cancer

C. Different dose levels of an unapproved drug

D. All of the above
5. When do you need to submit Justification for IND Exemption Form?

A. Wait to see if IRB requests
B. When PI determines use of approved drug is IND exempt
C. It is a new form so check with the regulatory specialist to see if required
D. When study uses a dietary supplement
Audit Updates and Important Reminders

Tatiana Kurilo, MPH, CCRC
Quality Management and Education
Pregnancy Test Internal QM audit

• Results from Feb 2015 audit:
  ➢ 48 female FCBP active study subjects from all Working Groups were selected
  ➢ Baseline/screening pregnancy test missed on 4 subjects. Required per protocol subsequent test were missed 6 subjects.

• Results from July 2015 audit after implementation of CTO CAPA:
  ➢ 33 female FCBP active study subjects from all Working Groups were selected
  ➢ 0 cases of missed baseline/screening pregnancy test required per protocol subsequent test were missed 1 subject

QM team will perform 3rd Pregnancy Test audit in Oct 2015
Reconsent Internal QM audit

• Results of the audit:
  ➢ Among 45 subjects, 24 (53%) were not reconsented under the most current version
  ➢ In 8 cases, subjects were reconsented under the most current version, however, were not reconsented under some versions in between initial and most current consents

• Per SOP 8.1, all Amendments must be reviewed at the weekly Working Group meetings
• Oncore database CRA Console – superscripts $^RR$ above each subject that needs to be reconsented
Important Reminders

• Per QMP, PI is required to address all the **urgent significant** findings within **24** hours of the email notification
• New Winship Investigator Orientation Binder is available
• “SOP Made Simple” - SOP monthly training sessions
• Oncology Educational Sessions for Clinical Trials staff
• **Educational Clinical Trials EXPO** for Winship clinic staff and faculty “Clinical Trials Festival”

Goal: Improve communication and promote Clinical Trials
The materials from EXPO are now a part of New Infusion Nurse Orientation Binder and New Winship Investigator Orientation Binder

*Another EXPO will be held in Fall 2015 (TBA)*
Questions..
SOP Updates

Carolina Lecours, BA
Quality Management and Education
Outline

- **SOP 2.1** Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

- **SOP 2.2** Obtaining Informed Consent for Minimal Risk Interventional and Non-Interventional Clinical Trials

- **SOP 3.5** Reporting Unanticipated Problems/Adverse Events

- **SOP 5.2** Opening a Clinical Trial to Accrual

- **NEW SOP 3.10** Clinical Trials Subject Transfer From an Unaffiliated Site

- **SOP 8.4** Completing Form FDA 1572
2.1 Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

General requirements:

• Must be IRB approved, on the DOA, trained, etc.
• Should obtain the current IRB-approved consent from OnCore® (if studies managed in a facility that uses the OnCore® database)
• Study procedures cannot be done prior to obtaining consent
• Documentation of the consent process is required
2.1 Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

- The investigator or sub-investigator on DOA and when required on the 1572 will have the initial discussion about the study, answer questions, and document this discussion in the record.
- The investigator may obtain consent or may delegate obtaining informed consent to another designated licensed professional who is delegated this task on DOA log.
- The physician-investigator or consenting licensed professional shall complete and sign the Informed Consent Documentation Form.
2.1 Obtaining Informed Consent for Greater than Minimal Risk Interventional Clinical Trials

- The investigator may delegate obtaining informed consent to another designated licensed professional who is delegated this task on DOA log:
  - Medical Doctor (MD)
  - Pharmacy Doctor (PharmD)
  - Nurse Practitioner (NP)
  - Physician’s Assistant (PA)
  - Clinical Research Nurse (CRN)
  - Registered Nurse (RN)
  - Licensed Clinical Social Worker (LCSW)
2.2 Obtaining Informed Consent for Minimal Risk Interventional and Non-Interventional Clinical Trials

General requirements:

- Must be IRB approved, on the DOA, trained, etc.
- Should obtain the current IRB-approved consent from OnCore® (if studies managed in a facility that uses the OnCore® database)
- Study procedures cannot be done prior to obtaining consent
- Documentation of the consent process is required
2.2 Obtaining Informed Consent for Minimal Risk Interventional and Non-Interventional Clinical Trials

• Minimal Risk Interventional Clinical Trials
  – The investigator or sub-investigator on DOA and when required on the 1572 will have the initial discussion about the study, answer questions, and document this discussion in the record
  – The investigator may obtain consent or may delegate obtaining the consent to another designated member of the research team who is delegated this task on the DOA log. It could be a CRC
  – The consenting professional shall complete and sign the Informed Consent Documentation Form
3.5 Reporting Unanticipated Problems/Adverse Events

- PI is ultimately responsible for overseeing all AEs, but **may delegate AE assessment** (grading and attribution) to **licensed** study staff (NP, PA, CRN, RN, PharmD) who is delegated this task on the DOA log
  - It cannot be a CRC
- A competency test on AE assessment is available per PI’s request
3.5 Reporting Unanticipated Problems/Adverse Events

For Serious and Unexpected AEs!

- The Investigator, with assistance of CRC/CRN will complete the Emory, VA, or CHOA Reportable Events Assessment Form

- The Investigator, CRC, or CRN will email notification to the study PI, regulatory specialist, and all study staff

- For Investigator Initiated Clinical Trials enter all SAE(s) and UP(s) into OnCore®
Purpose: To provide guidance to research faculty and staff in accepting a clinical trials subject transferring from a non-Emory site

CRC/CRN will verify the following requirements prior to decision to accept:

• All CRFs have been submitted, queries resolved
• Active Emory IRB approval status for specific trial
• Receiving PI is approved
• Sponsor has approved transfer
• Program manager for cooperative group trial study subject has been notified
• PI has approved subject transfer
3.10 Clinical Trials Subject Transfer From an Unaffiliated Site

When subject is ready to begin participation at the receiving site, the CRC/CRN will:

- Contact the subject to arrange for a first visit, if not already done during the transfer process
- Ensure the informed consent and HIPAA authorization are obtained at the first visit prior to any study-related procedures
- Register subject in ERMS
- Ensure the subject is entered into OnCore® as a transfer patient
- Ensure that research records and study calendar are created for subject
The following must be completed and documented:

• IRB approval with release of consent document
• eNOA received
• Study orders approved by the PI and available
• Study drugs available in the investigational pharmacy
• All lab supplies available
• Site initiation completed
• Case report forms available
• Documentation of study specific training provided to **ALL** individuals with delegated responsibilities including infusion staff
• DOA log completed and signed by principal investigator
• Regulatory documents completed
8.4 Completing Form FDA 1572

The SOP was revised to be consistent with FDA guidance

Important changes you need to know about:

• Only complete 1572 Form for IND-held Sponsor-Investigator Studies
• No longer requiring signature on CVs (unless required by the sponsor)
• No need to update CVs every 2 years (unless required by the sponsor)
• Make sure to enter addresses for all research facility where the research is being conducted: Winship Cancer Institute (Clifton campus), Emory University Hospital Midtown, Emory St. Joseph Hospital, Emory Johns Creek, Children’s Healthcare of Atlanta, Grady Memorial Hospital, Atlanta Veterans Affairs Medical Center
8.4 Completing Form FDA 1572

The designated Winship Clinical Trials Office staff will access the online Form FDA 1572 found at http://ctep.cancer.gov/investigatorresources/docs/fda_form_1572_final.pdf and complete the form as follows:

- Name and address of the Investigator
- Education, training and experience
- Name and address of the institution, hospital or other research facility where the research is being conducted
- Name and address of the Institutional Review Board
- Names of all Sub-investigators
- Sponsor protocol number, study title and sponsor name
- Clinical protocol information
- Commitments
- Signature of Investigator
- Date
Important Reminders

• All SOPs are available:
  – In the CTO
  – At each Winship site
  – On the Winship intranet under Clinical Trials
    https://apps.winship.emory.edu/intranet/clinicaltrials/index.php

• The Monthly Protocol Card is now available on the Winship intranet under Clinical Trials
Questions?
IND Exemptions

Kim Nguyen, BS
Assistant Director, Regulatory Affairs
• When is an IND needed for research?
• When is an IND not needed for research using marketed drugs?
• How is IND exemption determined?
• When does FDA make an IND exemption determination?
• What is the IRB review process for studies requesting IND Exemption?
Definitions:

• **Drug**: Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and articles (other than food) intended to affect the structure or any function of the body.

• **IND** (Investigational New Drug): a new drug or biologic that is used in a clinical investigation

• **IND Exempt**: meets all exemption criteria listed in § 21 CFR 312.2(b)

• **IND waiver**: FDA may grant a waiver of IND requirements based on request with justification from sponsor § 21 CFR 312.10

• **Sponsor**: the person who takes responsibility for and initiates a clinical investigation. When the investigator holds an IND, the investigator is the Sponsor, even when a company or drug manufacturer provides drug used in the study. Emory University is not the sponsor.

• **Sponsor-Investigator (S-I)**: an individual who both initiates and conducts the clinical investigation and under whose immediate direction the investigational drug is being administered used or dispensed.
When is an IND needed for research?

- The research involves a drug
- The research is a clinical investigation
- The investigation is not exempt

In general, an Investigational New Drug (IND) application is required when any clinical research study proposes the use of:

- An article that is not approved (for marketing) in the US as a drug.
- An approved drug that is not used according to the approved label (or used in a new combination of approved drugs).
- Approval to market as a drug in the US is for a specific manner as defined by the drug labeling. In research, “off-label use” of a lawfully marketed drug would be considered use of an unapproved drug. Studies involving the on-label use of a drug do not require an IND as long as data will not be used in a marketing application.
- A dietary supplement is not an approved drug and may require an IND if the clinical investigation is intended to evaluate the dietary supplement’s ability to diagnose, cure, mitigate, treat, or prevent a disease.
When is an IND not needed for research using marketed drugs?

Studies using commercially available drugs may or may not require an IND.

Step 1: Confirm that the drug to be used in the study is lawfully marketed.
Step 2: Determine if the use in the study is according to the approved labeling.

If not, all of the following must apply to be considered exempt from IND regulations:

– The investigation is not intended to be reported to the FDA as a well-controlled study in support of a new indication, significant change in labeling of the product, or significant change in the advertising of the product.

– The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.

– The investigation is conducted in compliance with the requirements concerning the promotion and sale of drugs.

– The investigation is conducted in compliance with the requirements for IRB review and informed consent.

– The investigation does not intend to invoke §21 CFR 50.24; a waiver of informed consent in an emergency room setting.
How is IND exemption determined?

The FDA allows the potential sponsor or sponsor-investigator (S-I) of a planned clinical investigation using a marketed drug to determine whether the investigation meets the criteria for an exemption. If the IRB does not agree with the investigator determination, then FDA must make the determination. Typically the greatest challenge to investigators in determining exemption from IND regulations is deciding whether the investigation significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the investigational drug. Investigators must evaluate risks associated with changes in patient population, route of administration, dose, drug combinations, or drug modifications.

Investigators should refer to the Guidance for Clinical Investigators, Sponsors, and IRBs: Investigational New Drug Applications (INDs)—Determining Whether Human Research Studies Can Be Conducted Without an IND (PDF - 210KB) to determine whether their clinical investigations may be conducted without submitting an IND application. Additionally FDA provides Guidance for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer to assist in determining whether research use of marketed drugs or biologics for the treatment of cancer meets the regulatory requirements for exemption from the IND regulations.
When does FDA make an IND exemption determination?

Sponsors or S-Is may be uncertain if their proposed investigation meets the criteria for IND exemption or the company providing the drug or funding may require FDA input. The FDA Review Division responsible for the relevant therapeutic area of the proposed trial can be contacted. In some cases FDA staff may provide this advice informally by e-mail. Generally it’s best to submit a summary of the proposed investigation in writing for FDA review. FDA staff will either advise the sponsor to submit a full IND application for the proposed investigation for FDA review or provide documentation that the IND application meets the criteria for exemption.
What is the Emory IRB review process for studies requesting IND Exemption?

For research studies using investigational drugs, the Emory IRB requires:

a) The FDA-assigned IND number or
b) Documentation showing that the drug is exempt from IND requirements.

If the FDA-regulated drug proposed for use in a research protocol does not already have an IND number for that proposed use, and the PI believes that the use is exempt from IND requirements, the PI is required to provide justification to the IRB. The Investigator must complete the Investigator Justification for IND Exemption Form with information necessary to determine IND exemption eligibility or submit to FDA for determination. This form is to be uploaded in eIRB in the drug section of the Smartform under Question 6 for each applicable drug.

For more information, see the Emory Policies and Procedures section 69.
Investigator Justification for IND Exemption

For research studies using investigational drugs, the Emory IRB requires a) the FDA-assigned IND number or b) documentation showing that the drug is exempt from IND requirements. If the FDA-regulated drug proposed for use in a research protocol does not already have an IND number for that proposed use, and the PI believes that the use is exempt from IND requirements, the PI will provide the justification to the IRB. For more information, please see the Emory Policies and Procedures section 69. Note, this form should not be used for Vitamins or Supplements; please use the Dietary Supplements and/or Medical Foods Used in Research Form instead.

Investigator: Please complete this form if using a drug that is not FDA-approved for the Indication described in the protocol and the Investigator determines that it meets the criteria for IND exemption. Upload this form in the drug section of the Smartform under Question 6 for each applicable drug.

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<thead>
<tr>
<th>IRB number:</th>
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<tbody>
<tr>
<td>PI Name:</td>
</tr>
<tr>
<td>Study Title:</td>
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<tr>
<td>Investigator completing this form:</td>
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Q1. Indicate if the following criteria apply:

☐ The research is a clinical investigation involving blood grouping serum, reagent red blood cells, or anti-human globulin, that a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure and, b) it is shipped in compliance with 21 CFR 312.160.

☐ The drug is intended solely for tests in vitro or in laboratory research animals that is shipped in accordance with 21 CFR 312.160.

☐ For substance used as placebo: The research is a clinical investigation involving use of a placebo that does not otherwise require submission of an IND.

*If Q1 criteria do not apply, move on to following questions.

Q2-A. Is the investigational agent an FDA approved drug (for any indication)?

No ☐ Yes ☐ (If no, an Investigational New Drug [IND] submission is required under part 312).

Q2-B. Does the investigational use involve a route of administration or dosage level, or use in a subject population, or other factor that significantly increase the risks (or decreases the acceptability of the risks) associated with the use of the drug product?

No ☐ Yes ☐ (If yes, an Investigational New Drug [IND] submission is required under part 312).

If No, provide justification, (e.g. literature, clinical experience):

Q2-C. Indicate that the following criteria also apply:

☐ The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug.

☐ If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product.

☐ The investigation is conducted in compliance with the requirements concerning the promotion and sale of drugs.

☐ The investigation is conducted in compliance with the requirements for IRB review and informed consent.

☐ The investigation does not intend to invoke 21 CFR 50.24; a waiver of informed consent in an emergency room setting.

IRB Version 05/06/2015
IND Questions?

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Questions?