Managing Risk

Perspectives on Research-Related Injury
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Background

Why does Research-Related Injury Matter?
What is Required?
Background

Terminology:

- Study-Related Injury
- Research-Related Injury
- Subject Injury

Basic Rule:

Sponsors of Research Have no Statutory Obligation to Pay...But Most US Institutions Require It
History

Litigation / Tort Law (Selected Cases):

- **Halushka v. University of Saskatchewan**¹
  - Failure of researcher to disclose may vitiate any consent given by the subject
  - Clinical research requires full disclosure of all risk factors

- **Mink v. University of Chicago**²
  - Drug administration without proper consent = “offensive contact” →
  - Battery if lack of true consent was intentional

- **Kernke v. The Menninger Clinic**³
  - Manufacturer relieved of duty to warn since PI was advised of risks in investigator brochure
  - No claim against sponsor; duty was PI’s to advise subject

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1. Halushka v. Univ. of Saskatchewan, 1965 CanLII 439 (SK CA)
"Smith, Trilby & Katzenbach, Attorneys. How much justice can you afford?"
Lessons / Developments

- We need a simpler process for dealing with immediate problems and complications
- Research Participants should not have to pay for RRI costs
- Tort law/litigation are still available to Research Participants
- NOTE: RRI in the CTA/Consent is a distinct issue from “indemnification,” which we are not discussing today!
Lessons / Developments

- Informed Consent is a Process!
- Tort system is not ideal for resolving issues of RRI
- Current US Law doesn’t require that:
  - Sponsors carry liability insurance
  - Sponsors pay for RRI expenses
  - Universities pay for RRI expenses
- GCP, the Common Rule, and FDA Drug Testing Regulations require disclosure of available compensation if pre-existing plans have been created (in studies with greater than minimal risk)
- ICH E6: Investigator/site should ensure adequate medical care for RRI
Lessons / Developments

- Presidential Commission for the Study of Bioethical Issues (Dec 2011): “Those who sponsor human subject research have an ethical obligation to protect those who volunteer as research subjects.”

- Medicare Secondary Payer (MSP) Rules: Medicare can only be the secondary payer, not the primary payer on a health care claim if certain other types of coverage are available.

- American Medical Association Ethical Opinion E-8.0315: Physicians should ensure that protocols include provisions for the funding of subjects’ medical care in the event of complications associated with the research.

- Many institutions/AMCs have policies on RRI.
Managing RRI at NU

- Who is involved?
  - OSR:
    - Negotiates the CTA with the Sponsor
    - Verifies Concordance between CTA and Consent
  - IRB:
    - Provides Consent Template Language
    - Responsible for Review
  - Department (coordinator/PI):
    - Negotiates Changes to Consent with Sponsor
    - Alerts OSR of Changes in RRI Language Beyond Template
    - Works with IRB on Submission and Review
Managing RRI at NU

- **OSR:**
  - **RRI in the CTA:**
    - Allocates responsibility for payment of costs associated with RRI
    - Contractual commitment from sponsor to NU that sponsor will pay for those costs
  - **Components:**
    - Injuries, complications or illness arising out of...
    - Participant’s participation in the Study and/or
    - Use of the Study Drug or Study Device
  - **Limitations:**
    - Not applicable to post-approval studies (usually)
    - No coverage for injuries to the extent they result from:
      - Failure to follow PI instructions
      - Negligence of Study team
      - Normal progression of the illness/condition
Managing RRI at NU

OSR, Questions to Consider:

- Who determines relationship?
- What costs are included?
  - Treatment – yes.
  - Diagnosis – yes.
  - Lost wages – no.
  - Pain/suffering – no.
- Insurance?
- Types of care?
  - Emergency v. acute
  - Long-term or chronic care
  - Rehabilitative care
- Where is care provided?
Managing RRI at NU

Sample Contract Language (ACTA):

If a Study subject suffers an adverse reaction, illness, or injury which, in the reasonable judgment of Institution, was directly caused by a Study Drug or Study Device or any properly performed procedures required by the Protocol, Sponsor shall reimburse for the reasonable and necessary costs of diagnosis and treatment of any Study subject injury, including hospitalization, but only to the extent such expenses are not attributable to (i) Institution's negligence or willful misconduct or (ii) the natural progression of an underlying or pre-existing condition or events, unless exacerbated by participating in the Study.
Managing RRI at NU

- OSR Harmonizes CTA RRI language with Consent Language
- Text should not be identical
- Substance should be the same
IRB Perspective on RRI
Regulatory Requirements

§46.116 General requirements for informed consent.
(a) Basic elements of informed consent. Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:

(6) For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
Note that the Federal regulations do not *mandate* that compensation is provided for research–related injury, only that subjects are informed about whether any compensation is available.
For industry sponsored research, the expectation is that the costs for the treatment for any injury resulting from participating in the research will be covered by the industry sponsor.

A research related injury may also result in non-treatment related costs/harms such as lost wages, pain and suffering, missed opportunities for employment, etc. and the payment for such costs may also be taken into consideration by the sponsor or IRB. However, these are usually not delineated in the consent form.
Federal regulations also prohibit consent forms from including exculpatory language that suggests that subjects are waiving their legal rights. (21 CFR 50.20).

FDA considers exculpatory language to be language that has the general effect of freeing or appearing to free an individual or an entity from malpractice, negligence, blame, fault, or guilt.
Examples of Exculpatory Language

I understand the information presented in this consent form and the risks involved in participating in this study.

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.

By consent 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.

I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.
What else do I need to know?

[Include for greater-than-minimal research. Otherwise delete. The language should not be changed except as indicated.]

[Include if study is unfunded, PI-initiated, or federally funded]

If you become ill or get injured as a result of this study (medications, devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.
[Include if study is industry sponsored]
If you have an injury or illness from the study device, taking the study drug, or the procedures required for this study, the reasonable medical expenses required to treat such injury or illness may be paid for by the study sponsor.

The coverage for such injury or illness is only available if the Northwestern University principal investigator and study sponsor, if applicable, have decided that the injury/illness is directly related to the study drug, device, or procedures and is not the result of a pre-existing condition or the normal progression of your disease, or because you have not followed the directions of the study doctor. If your insurance is billed, you may be required to pay deductibles and co-payments that apply. You should check with your insurance company about any such payments.
IRB Recommendations

- If an Industry sponsor proposes consent language that deviates from the NU template provided, please check with OSR prior to submitting the new project submission.

- If OSR agrees the RRI language doesn’t contradict the contract, then provide documentation of this along with the new submission. This will likely make the review process more efficient.
The Department’s Perspective
From the Department’s Perspective

- How can the process be streamlined?
- What is the funding source?
- What language is in the consent template?
- How does this compare to standard NU language?
- Incorporate NU approved language into the template and obtain sponsor consent approval prior to IRB submission
- If push back occurs, follow-up with OSR
From the Department’s Perspective

- How does this language compare to the CTA?
- Have we recently participated in a similar study with the same sponsor?
- If so, can the agreed upon language be incorporated?
- Have we recently participated in similar trials?
- Are there similarities with the language?
- Can the recent experience assist in this agreement?
From the Department’s Perspective

- Do we feel the subject is protected?
- As a department representative is the consent language appropriate?
- What risk exists for the subject?
- How much risk is acceptable for the subject?
- What are the PI’s thoughts?
- Are there reimbursement challenges that are payor specific?
- How will this impact the consent process?
- Ensure the authorized individuals consenting subjects are well versed in this area and have resources
Thank you!

• Questions?