Research-Related Subject Injury: Findings and Lessons Learned from Implementation of a New Policy

HCCA Research Compliance Conference - Baltimore, MD
Breakout Session 302
June 6, 2016 2:30-4:00 PM

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Agenda

- Background
- Policy Development
- Policy Implementation
- Management and Tracking
- Early Experience & Evaluation
- Challenges & Next Steps

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BACKGROUND

CMS Clinical Trial Policy

Routine costs of a clinical trial include:

- "Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service- - in particular, for the diagnosis or treatment of complications."

Items not covered in a clinical trial include:

- "Items and services customarily provided by the research sponsors free of charge for any enrollee in the trial."
- Medicare Secondary Payer rules

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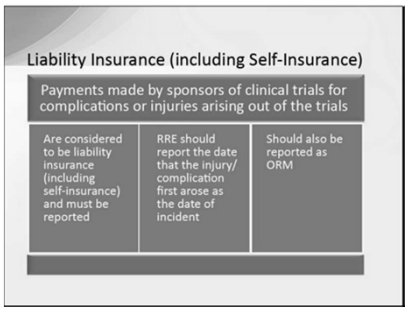
Slide from CMS Reportable Claims Course*



** https://www.cms.gov/Medicare/Coordination-of-Benefits-and-Recovery/Mandatory-Insurer-Reporting-For-Non-Group-Health-Plans/NGHP-Training-Material/Downloads/Reportable-Claims.pdf*

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IRB Responsibility and Research Billing

Regulation/Policy	Guidance
OHRP IRB Guidebook (1993)	Risks to research subjects posed by participation in research should be justified by the anticipated benefits to the subjects or society. This requirement is clearly stated in all codes of research ethics, and is central to the federal regulations. Risk is defined as "The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study."
45 CFR 46.116(b)(3) & 21 CFR 50.25(b)(3)	When appropriate, ICF must include "Any additional costs to the subject that may result from participation in the research"
45 CFR 46.116(a)(6) & 21 CFR 50.25(a)(6)	For research involving more than minimal risk, ICF must include "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"
FDA Guide to Informed Consent – Information Sheet (2011)	If the subjects may incur an additional expense because they are participating in the research, the costs should be explained. IRBs should consider that some insurance and/or other reimbursement mechanisms may not fund care that is delivered in a research context.

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POLICY DEVELOPMENT

Policy Development Lifecycle

http://www.cdc.gov/policy/analysis/process/

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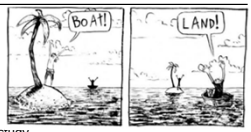
Research-Related Subject Injury Stakeholders and Perspectives



- Research participants
  - Take care of me if I'm injured
  - Inform me of any financial risk
- Investigators
  - Help me to recruit participants
  - Help me take best care of participants in my study
  - Don't eat away at my research grant
- IRB
  - Take care of participants if they're injured
  - Inform participants of any financial risk
- Contract Officers
  - Facilitate optimal contract negotiations with research sponsors
- Institutional leadership
  - Support research endeavors
  - Minimize institutional liability
  - Ensure compliance with regulations and CMS rules

Goals of the Research-Related Subject Injury Policy

- Protect human subjects who participate in research activities
- Ensure that research subjects receive treatment medically necessary to address research-related subject injuries
- Ensure that research subjects are properly informed of any financial liability they may have for the costs of treating research-related subject injuries
- Maintain compliance with CMS research billing regulations and requirements
- Limit institutional financial liability
- Provide support and guidance to clinical researchers for identifying and managing subject injury

Benchmarking Survey

- Survey was intended to gather information about:
  - How institutions define research-related subject injury
  - Institutional policies for coverage of research-related subject injury
  - How research-related injury is covered for investigator-initiated trials
  - Systems for identifying and managing research-related subject injury
  - Common challenges and solutions
- Methods:
  - 16-item survey distributed in June 2014
  - Survey distributed via email to AMCs participating in monthly call organized by the University of California to discuss clinical research billing issues
  - Survey also distributed via networks of cancer centers
  - Survey results discussed during the monthly call organized by the University of California to discuss clinical research billing issues

Benchmarking Survey Responses - Summary

- 21 responses received
- General Lessons learned:
  - Most respondents define subject injury as including both known and unexpected risks.
  - A couple institutions specifically qualified their definition with statements excluding risks that would occur in standard of care treatment.
  - Most respondents did not commit to covering subject injury for investigator initiated studies.
  - No clear responses describing a well defined process for identification, management and tracking of subject injury.
  - No clear responses on role of the subject vs. institution in identifying subject injury.

Policy Development Process

- Discussed as regular agenda item at monthly Clinical Research Management (CRM) meeting with representatives from:
  - Hospital leadership
  - Research leadership
  - Corporate Compliance
  - Research Compliance
  - IRB
  - Patient Financial Services
  - Sponsored Research/Industry Contract Office
  - Research departments – cancer, heart, neurosciences, medicine, surgery
- Drafts written by representatives from Research Compliance & Industry Contract Office with review/direction from Research VP and Corporate Compliance VP
- Benchmarking survey results presented and discussed at CRM meeting
- Past experience with handling research-related injuries analyzed and presented at CRM meeting
- Draft policy presented to small group of department chairs, division chiefs, and institute directors

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Overview of Policy – Defining Research-Related Injury

- Defining Research-Related Subject Injury – what it is:
  - medical condition (1) which is caused by and/or directly related to the research study (that is, the condition would not have existed "but for" the subject's participation in the study), and (2) which is in need of diagnosis and treatment as a matter of medical necessity and standard of care.
- Defining Research-Related Subject Injury – what it is NOT:
  - injuries or illnesses (a) attributable to the subject's underlying medical condition, (b) caused by an investigator's or other physician's negligence or willful misconduct, or (c) caused by non-research-related activities.
- Defining Research-Related Subject Injury – what it is *usually* NOT:
  - The IRB will consider on a case by case basis events that are known risks of standard treatment using currently approved therapies for the subject's condition

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Overview of Policy – Coverage for Research-Related Injury

- Industry-Sponsored Studies:
  - Industry sponsor must agree to cover diagnosis/treatment of research-related injury.
- Investigator-Initiated Studies with Therapeutic Intervention:
  - Subject's insurance is billed for care to diagnose/treat research-related injury. Subject is responsible for denials, co-pays, and deductibles.
- Investigator-Initiated Studies with No Therapeutic Intervention:
  - Institution agrees to cover diagnosis/treatment of research-related injury.
- All Studies:
  - Subjects must be informed in the consent form whether or not diagnosis/treatment of research-related injury will be covered.

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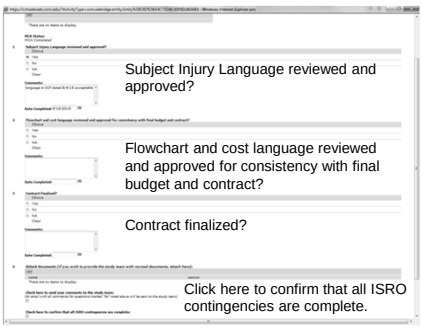
Consistency Check by Industry-Sponsored Research Office



Policy Implementation

Implementation Plan

- Changes to the Informed Consent Form Template
  - Input from Research Compliance, IRB Leadership, Industry-Sponsored Research Office, Research Billing, Risk Management
  - Revised Policy and Draft ICF Template presented to all IRBs at convened meetings.
  - IRB Leadership approved final revised ICF Template
- Meeting held with representatives from Research Compliance, Sponsored Research, Research Billing, and Risk Management, to develop process for handling claims of research-related subject injury that are to be covered by either sponsor or institution.
- IRB adverse event report form revised to capture research-related injury decisions/determinations made by IRB
- Revised ICF Template, process for handling claims, and revised AE report form presented at CRM meeting
- Training provided to IRB staff and ISRO staff
- Notification to the Research Community – investigators and research staff

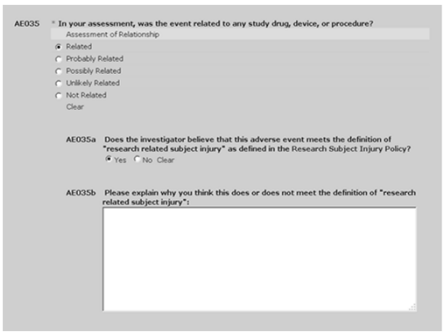
Changes to the Informed Consent Form

- Changes made to ICF RRSI coverage language to be more specific for all scenarios if study involves risk of illness or injury:
  - Industry-sponsored studies, and non-industry sponsored studies with no therapeutic intervention/no possibility of direct benefit to subjects
    - Sponsor or Institution will cover costs associated with the RRSI
  - Non-industry sponsored studies with therapeutic intervention/possibility of direct benefit to subjects
    - Research subject and/or insurance will be responsible for costs associated with RRSI (This section was highlighted in the revised ICF template as a result of feedback received at IRB meetings)
- Revised ICF template was to be used only for new studies submitted to IRB after policy implementation date

Mechanism for reporting, management and tracking of RRSIs

- The Study Team submits an Internal AE report in Webridge
- If the study team assesses the AE/SAE as "related" or "probably-related" to the research, they are required to complete the RRSI question and provide a relevant explanation
- Research Compliance Staff notifies Research Billing/Patient Financial Services to flag this account for a potential RRSI
- Research Compliance Staff works with the study team to gather additional information
- The IRB determines whether the event meets the criteria for a RRSI
- A determination of who will cover the RRSI is made based on coverage information in the approved ICF
- A group email is generated notifying Research Billing/Financial Services, Legal, Risk Management, Sponsored Research Contracts Office
- The PI, study team, and study sponsor are notified of this determination

Reporting RRSIs in the Electronic IRB AE Report Form



RRSI FAQ, Newsletter to CSMC Research Community

CedarsScience

News for the Cedars-Sinai Research Community

Print this page

Policy Changes: Research-Related Subject Injury

Effective Oct. 19, Cedars-Sinai will implement a revised policy on research-related subject injury (RRSI). This policy refers to medical conditions that are considered to be caused by or related to a research study and that would not have otherwise existed. Examples include pneumothorax that results from a lung biopsy performed solely for research or an allergic reaction to a contrast agent used in a research imaging procedure.

This policy update was prompted by Centers for Medicare and Medicaid Services research billing requirements and national trends among academic medical centers. Internally, there was also a need to better define what constitutes a research-related subject injury. Cedars-Sinai is dedicated to protecting all human research subjects and ensuring that they are informed of risks, including the risk of financial liability.

The policy revisions mainly impact non-industry-sponsored clinical trials with therapeutic interventions. The key changes include the following:

- A clearer definition of research-related subject injury

Research-Related Subject Injury

What is a research-related subject injury (RRSI)?

The Cedars-Sinai policy on this topic defines research-related subject injury as a medical condition (1) which is caused by and/or directly related to the research study (that is, the condition would not have existed "but for" the subject's participation in the study), and (2) requires diagnosis and treatment as a matter of medical necessity and standard of care.

How do I report an RRSI?

When a possible RRSI is identified, the study team submits an internal adverse event (AE) report to the Institutional Review Board (IRB) using Huron Eclips. This needs to be done even if the event is not otherwise reportable to the IRB. In order for the IRB to determine whether the event should be considered as an RRSI, Effective October 19, 2015, the form for internal AEs assessed as "probably related" or "related" to the research will require study teams to assess and explain whether they believe the medical event meets

Questions included in the FAQ:

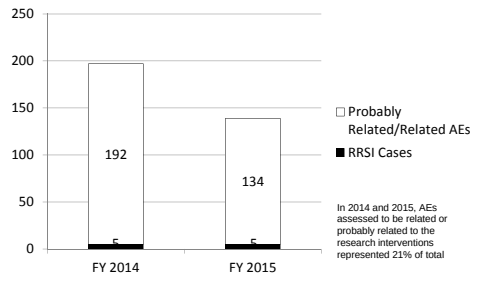
1. What is a research-related subject injury (RRSI)?
2. How do I report an RRSI?
3. What are the recent changes to the RRSI policy?
4. Why were these policy changes made?
5. How does the revised policy impact the informed consent form (ICF)?

Early Experience and Evaluation

Experience and Outcomes Since October 2015

- Proactive reporting by study teams
- Thoughtful assessment by investigators and research staff
- Easy to use and no complaints from research community
- Consistent assessment by IRB medical reviewers
- Prompt determination of RRSI and notification to relevant groups
- Done through electronic IRB system so convenience in tracking RRSIs over time

RRSI Cases Before Revised Policy Implementation



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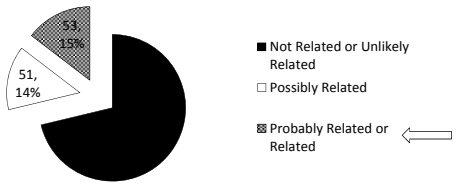
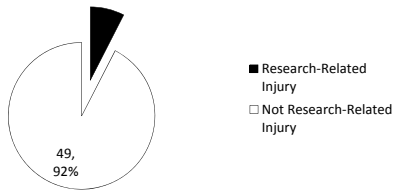
Adverse Events Reported to IRB October 1, 2015 – April 30, 2016

Adverse Events Reported by Assessment of Relationship to Research



Adverse Events Considered for Research-Related Injury
October 1, 2015 – April 30, 2016

Adverse Events Assessed as Probably Related or Related to the Research



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Early Feedback and Changes

- ICF template language posed some issues during contract negotiation, leading to revisions to ICF template to:
  - Distinguish between:
    - –Industry-sponsored studies where the industry sponsor has agreed to cover RRSI
    - –Non-industry sponsored studies with no therapeutic intervention/no possibility of direct benefit to subjects where the institution commits to covering RRSI
  - State the IRB is responsible for determining whether an event represents a RRSI

Challenges and Next Steps

Challenges

- Adequately engaging all stakeholders and gaining buy-in
- Making policy decisions that will satisfy the needs and interests of all stakeholders
- Communicating policy changes effectively
- Developing implementation plan and deciding whether to make changes only moving forward or apply to existing studies
- Ensuring correct ICF template language is used

- After implementation:
  - Ensuring correct ICF template language is used

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Next Steps…

- Internal review currently being conducted to ensure correct usage of RRSI language in the ICF template by study teams and IRB staff
  - Internal review findings will aid forthcoming changes (if required) in 2016-2017
- Analyzing 1st year experience at the end of 2016 fiscal year

Questions?

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