Beyond Subject Injury: A Comprehensive Clinical Research Risk Management Program

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Objectives

To develop, in partnership with the University of California, San Francisco's (UCSF) Human Research Protection Program (HRPP), Risk Management, Office of Legal Affairs, Office of Sponsored Research and the major research institutes, schools, and divisions, a broad-based Clinical Research Risk Management program that utilizes risk management trending and root cause analysis methodologies to identify, prevent and/or reduce a range of research-related risks encompassing but not limited to subject injury, affecting the entire clinical research enterprise at UCSF.

Problem/Issue Statement

While major research institutions, under federal regulations, state laws, and accreditation requirements, constitute Institutional Review Boards (IRBs) that are charged with responsibility for analysis and mitigation of research risks to subjects, there is an absence of a corresponding set of external regulations to drive risk assessment and mitigation for other, non-subject-injury related risks which may affect the individuals involved in clinical research (investigators, their staff, IRB chairs and members, and administrators) as well as the sponsoring institution as a whole.

Risk Management:

Standard principles and methodologies of Risk Management (RM) include:

- **Risk Assessment**: typically identifies trends or patterns of events that may pose risks in (research) activities; assesses the likelihood and the magnitude of the risk; monitors the effectiveness of strategies to protect both individual stakeholders and the overall enterprise (risk mitigation).

- **Root Cause Analysis** (RCA): identifies, reduces or eliminates the root or source cause(s) of a problem (vs. addressing only the immediate and obvious aspects of a problem) to minimize the likelihood of the problem reoccurring.

Used extensively across a wide range of business enterprises, Risk Management principles and processes provide an established set of methodologies to manage the significant risks associated with human research (1).

Program Development **Phase I: Development of a Subject Injury (SI) Program**

Since its initial development in December, 2005, the Clinical Research Risk Management (CRRM) program at UCSF has focused on the clarification and refinement of:
1) Incident-based response processes to insure maximum timeliness in the reporting, evaluation, and payment of claims for subject injury;
2) Campus-wide procedures and individuals roles and responsibilities and
3) Implementation of the University of California's systemwide Subject Injury Policy.

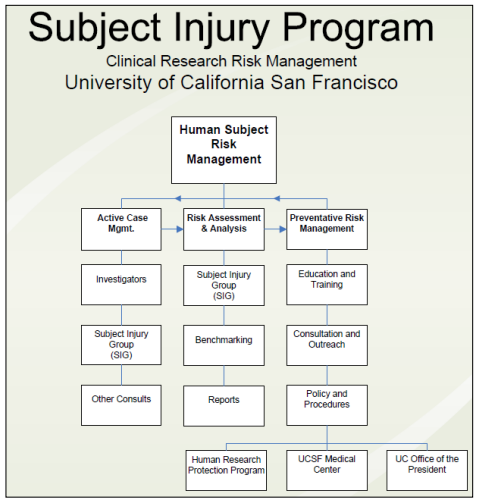

Diagram 1. The next level of Phase I development will encompass:
1) Analysis of trends and "root causes" of subject injuries and
2) New initiatives to proactively facilitate investigator and key personnel awareness of subject injury safety risks.

Examples of Research Injury Case Variables for Analysis
Type of event
Severity of event
Cost of treatment
Cost of settlement
Connection to litigation
Timeliness of reporting (days from occurrence to date reported)
Case duration
Associated with responses to external entity(ies); e.g., OHRP, FDA, etc.
Root cause analysis of the injury event

Table 1. Describes an initial list of data to be prospectively collected and entered into an Access d-base. The systematic collection and analysis of these data will allow application of RM methodologies to further the safety and welfare of subjects or others filing claims of research injury. This analysis process may also serve as a platform from which the institution could proactively assess and respond to an ever widening array of clinical research risks for the benefit of other participants engaged in clinical research.

Program Development **Phase II: Expansion to a Comprehensive Clinical Research Risk Management (CRRM) Program**

Are subject injury cases the only research risks to track and manage – or are they just the tip of the iceberg?

In collaboration with the HRPP, the CRRM will move forward to expand its use of risk management for subject injury to encompass assessment of a broader array of clinical research-related activities, procedures, and structures at UCSF in order to identify those aspects of clinical research that pose potential risks to non-subject participants, and interests of the institution.

As mentioned in Clinical Research and Regulatory Affairs (2), the definition of a "research participant" can be expanded to include nearly all the key stakeholders involved in clinical research.

Potential Research Risks
Deficiencies in indemnification from sponsor
Incomplete review and assessment of risk to the participants
Excessive or inappropriate treatment focused on project goals rather than subjects
Undisclosed conflicts of interest
Failure to adequately inform subjects of significant risks
Failure to remove a subject when continued participation was contraindicated
Unclear or unauthorized promises of remedial treatment for adverse effects of research participation
Improper Medicare or private insurance billing practices

Table 2. Illustrates that, in addition to the risks of subject injury or harm, investigators, the IRB, study sponsors and/or the institution engaged in research may also face significant research risks.

In addition to the risks in Table 2, a wide variety of subject injuries may arise from the drugs, devices or biologics being tested; research-related procedures; investigator noncompliance with the approved protocol or failure to perform a study-related procedure correctly(3).

Diagram 2. Illustrates numerous areas of risk, in addition to subject injury, that may directly or indirectly impact key personnel involved in the clinical research enterprise at UCSF and to the overall financial, operational, and reputational interests of the institution.

Discussion:

Can an institution's research enterprise benefit from an analysis-based program that not only assesses and manages subject injury events, but that also tracks and responds to a broad array of other clinical research risks by:

- Expanding the scope of risk management activities to encompass all key individual engaged in the clinical research enterprise (both subject and non-subject);

- Developing and implementing targeted education/training on risk prevention and mitigation strategies; and

- Constructing a functional evaluation component of the program to facilitate assessment of both the utility and cost effectiveness of the Phase II expansion, and its applicability to other HRPP and research risk management programs?

References

(1) Mainelli, M. Taking the Measure of Risk: Benchmarking Risk Management. *Handbook of Risk Management* Croner Publishing 1999; 35:5-8.
(2) Brown, D. Liability issues and the IRB. *Clinical Research and Regulatory Affairs*. 1995; 12(2): 111-118
(3) Dodero, F. C., et al. 2007. Legal and risk management issues associated with clinical research. *University HeathSystem Consortium.* Oak Brook, Illinois 1-21

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For further information

Please contact: **carroll.child@ucsf.edu**. More information on this and related programs can be found at: **https://www.rmis.ucsf.edu**