Evidence-Based Clinical Research
Risk Management Program

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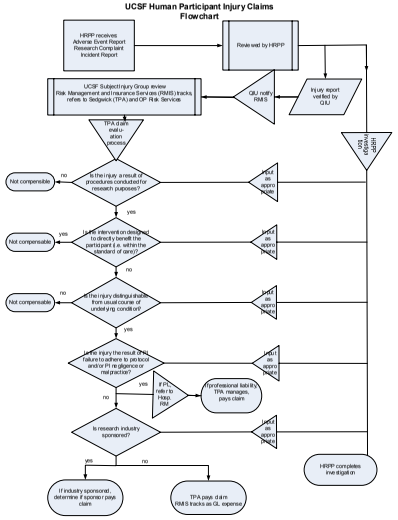
Objectives

To develop, in partnership with the UCSF Human Research Protection Program (HRPP), Office of Research, Office of Legal Affairs, Office of Sponsored Research and the major research institutes, schools, and divisions, proactive systems for oversight of cross-study, research-related subject injury using root-cause analysis (RCA) and fundamental Risk Management (RM) methodologies to help foster an institutional-wide commitment to preventing or reducing human subject risks at UCSF.

Background

Since its initial development in December, 2005, the Clinical Research Risk Management (CRRM) program has focused on: 1) Incident-based response processes to insure maximum timeliness in the reporting, evaluation, and payment of claims for subject injury; 2) Clear descriptions of the roles and responsibilities of key individuals across the institution involved in responding subject injury claims and 3) Refinement of the University's Subject Injury Policy related to coverage for claims of injury at UCSF.



Program Development (Phase I)

While major research institutions, under the requirements of Federal regulations, state laws, institutional policies and accreditation requirements, constitute Institutional Review Boards (IRBs) that are clearly charged with responsibility for weighing the risks (and benefits) to subjects participating in a particular research project, there is often an absence of a similar centralized management processes to address the risks for other individuals involved in clinical research (investigators, their staff, IRB Chairs and members, various administrators). At the same time, the institutional research enterprise can benefit from centralized processes that can respond to, track and analyze research risks.

As mentioned in an article in Clinical Research and Regulatory Affairs (1), the definition of a "research participant" can be expanded to include nearly all the key stakeholders involved in clinical research.

Potential Research Risks
o Deficiencies in indemnification from sponsor
o Unrevealed conflict of interest problems
o Incomplete review and assessment of a project in terms of risk to the patient
o Excessive or inappropriate treatment focused on project goals rather than patient indicators
o Selection of inappropriate candidates for research
o Failure to adequately inform the patient of significant risks
o Failure to remove a subject when continued participation was contraindicated
o Unclear or unauthorized promises of remedial treatment for adverse effects of research participation

Table 1. 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.

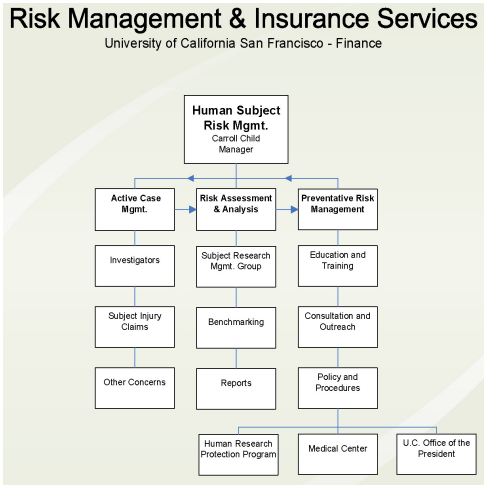
In addition to the risks in Table 1., a wide variety of subject injuries may arise from the drugs (1), devices or biologics being tested; research-related procedures; investigator noncompliance with the approved protocol or failure to perform a study-related procedure correctly (2).

A review of literature describing the standard principles and methodologies of RM and RCA describe problem-solving methods that appear especially well suited for adaptation into institutionally-based clinical research risk management programs.

- **Risk Management**: typically involves identifying trend or pattern of events among a group that may pose negative or positive results within an overall system of activities and assesses the likelihood of that event occurring (risk), the magnitude of the events impact and monitors the effectiveness of strategies developed to protect both individual stakeholders and the enterprise as a whole.
- **Root Cause Analysis**: is a problem solving tool used in Risk Management to identify, reduce or eliminate the root or source cause(s) of a problem (vs. addressing only the immediate and obvious aspects of a problem) to significantly minimize the likelihood of the problem reoccurring.

Used extensively across a wide range of business enterprises, Root Cause Analysis (RCA) and Risk Management (RM) principles and processes provide an established set of methodologies to manage the significant risks associated with human research (3).

Program Development (Phase II)



The next phase of CRRM program development will encompass: 1) analysis of trends and "root causes" of subject injuries and 2) new campus-wide initiatives to proactively facilitate investigator and key university personnel awareness of research safety risks. Moving forward, the CRRM program is applying risk analysis methodology to: 1) Identify the areas of clinical research that pose potential harm to participants' safety and welfare; 2) Employ incident (case)-based root cause analysis to direct outreach and safety-related educational efforts; 3) Conduct focused outreach briefings to share analysis data with key campus stakeholders; 4) With the HRPP, develop and disseminate best research practice training and information and 5) Provide ad hoc, on-site evaluation and consultation for clinical researchers and their support personnel.

Example Risk Event Variables (for Access D-base)
o Cost per risk event case (i.e., subject injury claim/complaint or other research participant case)
o Case duration
o Reporting lag time (days from occurrence to date reported)
o Case associated with litigation
o Case associated with responses to external entity(ies); e.g., OHRP, FDA, etc.
o CRRM assessment of the root causes of case

Table 2. 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 testing of RM methodologies and their impact on our continuing efforts to further the safety and welfare of research subjects and others involved in clinical research activities. In addition, these steps may also strengthen our institution's ability to proactively assess and respond to an ever widening array of clinical research risks for the benefit of all participants engaged in clinical research.

Conclusions

Having constructed a functional and institutionally integrated framework for management clinical research risks, the opportunity now exists to significantly strengthen our risk management program by expanding the management of subject injury risks and claims to the larger context of our clinical research enterprise at UCSF by embracing the fundamental processes of RM and RCA.

Literature

(1) Dodero, F. C., et al. 2007. Legal and risk management issues associated with clinical research. University HeathSystem Consortium. Oak Brook, Illinois 1-21

(2) Steinbrook, R. 2006. Compensation for research subjects. New England Journal of Medicine 354:1871-1973

(3) Mainelli, M. 1999. Taking the Measure of Risk: Benchmarking Risk Management. Handbook of Risk Management Croner Publishing 35:5-8 1999.

Acknowledgments

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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**