



Standard Operating Procedure

Clinical Research Subject Injury

Effective Date: August 1, 2022

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Applicable to: All UC Irvine Health Workforce

Regulation: Centers for Medicare and Medicaid Services (CMS) Medicare National Coverage Determination (NCD) for Clinical Trials 310.1, 42 CFR 411.50, and 42 CFR 422.108; HHS - 45 CFR 46.116(a)(2)&(6) and FDA - 21 CFR 50.25(a)(6); Section 111 of the Medicare, Medicaid, and SCHIP Extension Act of 2007

Purpose:

The purpose of this document is to promote adherence to the applicable Federal, State, and University of California guidelines, as well as sponsor and Medicare and Medicaid Services (CMS) research billing requirements, governing the provision and reimbursement of medical costs to human research participants for injuries and illnesses resulting from participation in research.

Policy:

University policy requires that, subject to certain conditions, in the event a human research participant is injured as a direct result of his or her participation in an authorized University research activity, the University must provide all reasonably necessary medical treatment to the subject. Moreover, where the injuries are a direct result of a subject's participation in a study testing an intervention (such as a drug, device, biologic, gene therapy, or new therapeutic system) pursuant to a private sponsor's protocol, the sponsor must assume responsibility for reimbursing the University for the reasonable cost of such treatment.

See *Appendix A* for University of California guidance on the meaning of terms used in the University's policies regarding human subject injury in research.

Non-Industry-Sponsored Research

The University of California will provide to any injured subject any and all medical treatment reasonably necessary for any injury or illness which a human subject suffers as a direct result of participation in an authorized University activity covered by University policy on the protection of human subjects in research or reimburse the subject for the costs of such treatment, except when the injury or illness is a consequence of a medical research procedure which is designed to benefit the subject directly. This obligation of the University shall be subject to the following conditions:

- It must be demonstrated that the injury resulted directly from participation in the specified activity;
- Written notification of any such injury is to be given to the University by the human subject within a reasonable time after discovery; and
- Any claim for reimbursement is to be supported by appropriate documentation.

Except for claims arising from demonstrated negligence on the part of the University, the University's policy does not provide for compensation of injured subjects through payments for lost wages, cost of pain and suffering, or additional expenses beyond those of medical care.

It is the preference of the University that the medical treatment available under this policy be provided at a University of California medical facility. Where such treatment is not available or feasible, the Human Subject Research Injury Program ("HSR Program"), a no-fault based reimbursement program funding through the General Liability Program and managed by the Professional Medical Hospital Liability Program, provides reimbursement to the subject(s) for reasonably necessary medical care and treatment in instances in which the subject does not have private insurance and does not qualify for coverage from a government health program.

In addition to the limitations outlined above, the HSR Program will not provide reimbursement for:

- Sponsor-initiated clinical trials;
- Care provided at a University facility;
- Medical treatment or care required as a result of third-party liability or for those injuries that are alleged to be the result of negligence by the University, its employees or providers. If a subject alleges medical negligence, such claims will be opened, investigated and managed as professional liability claims by the Professional Medical Hospital Liability Program; or
- Medical treatment that would normally be required as a result of clinical treatment for an underlying disease or condition for which the research subject is suffering.

Any compensation claims received for reimbursement of costs and expenses beyond the provision of medical care and not covered under the University's Professional and Medical Liability Self-Insurance program (malpractice) must be handled on a case-by-case basis in consultation with the Office of General Counsel of The Regents and the Office of the Senior Vice President--Academic Affairs.

Industry-Sponsored Research

Private sponsors must reimburse the University for the treatment and diagnosis of injuries directly resulting from a subject's participation in research, even if the purpose of the intervention causing the injury was intended to benefit the subject directly.

The University may seek sponsor payment directly to a non-UC facility for treatment provided by the non-UC facility. Similarly, the University may also require the sponsor to directly reimburse the subject for any costs of treatment the subject has directly incurred.

Procedure:

Informed Consent Documents

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to assure that research participants have knowledge of compensation and treatment availability for injury that may occur as a result of participation in research activities.

For studies that involve greater than minimal risk, unless waived by the IRB, all participants must be provided with an explanation in the consent form as to whether any medical treatments are available if injury occurs and, if so, what they consist of and where further information may be obtained. The wording of the UCI treatment and compensation statement was formulated with the advice of UC legal counsel with the intent of adhering to the requirements of federal regulations and UC's subject injury policy.

Agreements with Private Industry Sponsors

Contractual agreements are negotiated through Sponsored Projects Administration in the Office of Research. For studies tested under a private sponsor's protocol, compensation or payment of reasonable and necessary medical care to treat injury related to participation in research activities shall be provided according to the contractual

agreement between the sponsor and UC Irvine, which must make explicit that the sponsor assumes responsibility for reimbursing the University for the reasonable cost of medical treatment for injuries directly resulting from participation in the study. Contract language must ensure that the University will not experience a financial loss. It is not acceptable for such agreements to require billing of third party insurance companies in lieu of recovery of such costs from the sponsor, nor is it appropriate to accept provisions restricting participation of human subjects on the basis of medical insurance coverage status or on the subject's ability to pay.

In order for the institution to fulfill its responsibilities in protecting the rights of human subjects in research the IRB maintains the final authority to approve research contingent upon the provisions contained in contractual agreements as outlined above.

Identification and Management of Subject Injury

The Research Revenue Integrity (RRI) team identifies potential subject injury (i) by monitoring for unscheduled visits (e.g. clinic visits, emergency department visits, etc.) of research participants through the RBR charge review process, and (ii) through notification from research study teams.

Upon identification of an unscheduled visit for a research participant, RRI reviews documentation to determine whether the event requires further evaluation for subject injury by assessing the documentation in combination with the informed consent, master protocol, and investigator's brochure. When the event warrants additional subject injury review, RRI requests the Adverse Event (AE) Log and additional information, as applicable, from the research study team, which includes an assessment of causality by the principal investigator (PI), in order to determine whether the event constitutes subject injury and warrants an invoice to the sponsor for payment.

Ad Hoc Consultative Review

RRI may initiate an ad hoc consultative review for further evaluation of the event details when review of the AE Log and relevant information is insufficient to make a determination regarding subject injury. The consultative team may include stakeholders such as the study PI, RRI, Compliance and Privacy Office, Risk Management, Legal Counsel, IRB administrative staff, Sponsored Projects Administration, amongst others.

The team will review the event in detail to determine whether the event is directly resulting from the participation in the research. Specifically, the team will determine whether the event resulting from procedures performed in accordance with the protocol and would not have been performed were it not for the study participants participation in the study, including injuries resulting from failures of the study participant to follow protocol procedures.

Payment for Subject Injury

When an event is determined to be subject injury, RRI will invoice the sponsor for payment and perform the necessary follow up to ensure payment according to the terms of the clinical trial agreement (CTA) between UCI and the sponsor.

References

- ✓ [21 CFR 50.25 \(b\)\(3\): FDA Regulation on Human Subjects, Informed Consent](#)
- ✓ [45 CFR 46.116\(b\) \(3\): Department of Health and Human Services \(DHHS\) Regulations on the Protection of Human Research Subjects](#)
- ✓ [Centers for Medicare and Medicaid Services \(CMS\) Medicare National Coverage Determination for Clinical Trials 310.1](#)
- ✓ <http://www.ucop.edu/raohome/cgmemos/95-05.html>
- ✓ Research Policy Analysis & Coordination Operating Guidance Memo 13-01 - Guidance on Issues Relating to Subject Injury in University of California Research
- ✓ [UCI Human Research Protections Policy # 26: Compensation for Injury that Occurs During Participation in Research](#)

- ✓ [UC Operating Requirement No. 95-5](#)
- ✓ [UC Operating Requirement No. 13-01](#)
- ✓ University of California Presidential Memorandum of January 19, 1979
- ✓ University of California Office of Risk Services [Professional Medical and Hospital Liability Program](#)
- ✓ *University of California Professional Medical and Hospital Liability Program and General Liability Self-Insurance Program for Human Subject Research Injury Claims ("HSR Program")* dated 06Feb2018
- ✓ [18-310 through 18-340 of the Contracts and Grants Manual](#)

Appendix A

GUIDANCE FOR INSTITUTIONAL REVIEW BOARDS, INDUSTRY AND CONTRACTS AND GRANTS OFFICERS ON ISSUES RELATING TO SUBJECT INJURY IN UNIVERSITY RESEARCH

Executive Summary

Purpose of this Guidance Document

This guidance document is intended to clarify University policy governing the provision and reimbursement of medical costs to human research participants for injuries and illnesses as a result of their participation in University research. This document also clarifies University policy regarding sponsor reimbursement of such medical treatment where the University research is conducted pursuant to a private sponsor's protocol. Specifically, after providing a history and text of each of the University's subject injury policies, this guidance offers clarity on the meaning of the following phrases in the Presidential Memorandum of January 19, 1979 (as restated in Contracts & Grants Manual 18-310 through 18-340 ("Presidential Memorandum"), and UC Operating Requirement No. 95-5:

- **Presidential Memorandum:**
 - "medical treatment";
 - "reasonably necessary";
 - "direct result";
 - "authorized University activity"; and
 - "designed to benefit the subject directly"

- **UC Operating Requirement No. 95-5:**
 - "private sponsor's protocol";
 - "reimbursing the University";
 - "reasonable cost";
 - "medical treatment"; and
 - "directly resulting"

University policies require that, subject to certain conditions, in the event a human research participant is injured as a direct result of his or her participation in an authorized University research activity, the University must provide all reasonably necessary medical treatment to the subject. Moreover, where the injuries are a direct result of a subject's participation in a study testing an intervention (such as a drug, device, biologic, gene therapy, or new therapeutic system) pursuant to a private sponsor's protocol, the sponsor must assume responsibility for reimbursing the University for the reasonable cost of such treatment.

These policies have been subject to varying interpretation across the University, and this guidance seeks to clarify the meaning of terms used in the University's policies regarding human subject injury in research, the [Presidential Memorandum](#) and [UC Operating Requirement No. 95-5](#). The Office of Research and Graduate Studies has developed guidance on the University's human subject injury policy in order to ensure that the University of California system implements a standardized and consistent approach towards: (1) providing medical treatment to injured or ill subjects as a result of their participation in University research; (2) sponsor reimbursement of subject injury; (3) compliance with federal and other billing requirements; and (4) managing and protecting University resources.

Background

Presidential Memorandum

On January 19, 1979, pursuant to a [Presidential Memorandum](#), the University announced its policy for the provision of medical treatment of human subjects for injuries resulting from participating in research (also restated in parts [18-310 through 18-340 of the Contracts and Grants Manual](#)). Pursuant to this Presidential Memorandum, the University declared:

The University of California will provide to any injured subject any and all medical treatment reasonably necessary for any injury or illness which a human subject suffers as a direct result of participation in an authorized University activity covered by University policy on the protection of human subjects in research or reimburse the subject for the costs of such treatment, except when the injury or illness is a consequence of a medical research procedure which is designed to benefit the subject directly.¹

In order for the University to provide or reimburse for subject injury, the Presidential Memorandum declared that the following conditions must be met: (1) it must be demonstrated that the injury resulted directly from participation in the specified activity; (2) written notification of such an injury must be given to the University by the human subject within a reasonable time after discovery of the injury; and (3) any claim for reimbursement by the University must be supported by appropriate documentation.² The Presidential Memorandum also declared that the University's policy governing subject injury does not provide compensation for lost wages, pain and suffering, or additional expenses beyond those of medical care.³

Operating Requirement No. 95-5

On February 15, 1995, the University, through [Operating Requirement No. 95-5](#), provided requirements regarding the provision or reimbursement of medical treatment to subjects participating in the testing of drugs or devices pursuant to a private sponsor's protocol. This memorandum requires that:

In cases where a proprietary drug or device is to be tested under the private sponsor's protocol, an agreement between the sponsor and The Regents must be signed by a University official who has been delegated authority for contracts and grants. Such an agreement should be in process prior to the protocol being submitted to the IRB for review. In any case, IRB final approval will be contingent upon completion of an appropriate signed agreement between the University and sponsor. The agreements are subject to applicable policies and procedures, including those promulgated by in the University of California Contract and Grants Manual, and must be reported in the Corporate Contracts and Grants System.

The agreement must make explicit that the sponsor assumes responsibility for reimbursing the University for the reasonable cost of medical treatment for injuries directly resulting from participation in the study. It is not acceptable for such agreements to require billing of third party insurance companies in lieu of recovery of such costs from the sponsor, nor is it appropriate to accept provisions restricting participation of human subjects on the basis of medical insurance coverage status or on the subject's ability to pay.⁴

¹ University of California. Contracts & Grants Manual 18-310. Available at: <http://www.ucop.edu/research-policy-analysis-coordination/resources-tools/contracts-and-grants-manual/chap18.html#18-310>.

² Ibid. at 18-320. Available at: <http://www.ucop.edu/research-policy-analysis-coordination/resources-tools/contracts-and-grants-manual/chap18.html#18-320>.

³ Ibid. at 18-360. Available at: <http://www.ucop.edu/research-policy-analysis-coordination/resources-tools/contracts-and-grants-manual/chap18.html#18-360>.

⁴ University of California Research Administration Office. UC Operating Requirement 95-5: Requirements for Administration of Agreements with Private Sponsors for Drug and Device Testing Using Human Subjects. February 15, 1995. Available at: <http://www.ucop.edu/raohome/cgmemos/95-05.html>.

The terms of both Presidential Memorandum, restated in [Contract & Grant Manual 18-310](#), and [UC Operating Requirement No. 95-5](#) have been subject to varying interpretation across the University. This Memorandum offers clarification on the meaning of terms in the University’s human subject injury policies.

Neither policy requires payment for complications or other injuries that do not directly result from participation in University research, such as injuries or illnesses due to normal or expected disease progression or those resulting from care that would have been provided regardless of the subject’s participation in the research. Further, pursuant to the Presidential Memorandum, the University generally has no obligation to pay for treatment of diagnosis costs when the medical intervention is intended to benefit the subject directly. In contrast, pursuant to UC Operating Requirement No. 95-5, private sponsors must reimburse the University for the treatment and diagnosis of injuries directly resulting from a subject’s participation in research, even if the purpose of the intervention causing the injury was intended to benefit the subject directly.

Presidential Memorandum and Contracts & Grants Manual 18-310

This Memorandum provides guidance on the meaning of the highlighted terms as stated in the Presidential Memorandum and restated in the [Contract & Grant Manual 18-310](#):

The University of California will provide to any injured subject any and all **medical treatment reasonably necessary** for any injury or illness which a human subject suffers as a **direct result** of participation in an **authorized University activity** covered by University policy on the protection of human subjects in research or reimburse the subject for the costs of such treatment, except when the injury or illness is a **consequence of a medical research procedure which is designed to benefit the subject directly**.

Unlike Operating Requirement No. 95-5, the Presidential Memorandum/Contracts & Grants Manual 18-310 does not preclude the University from billing the costs for reasonably necessary medical treatment of injuries or illnesses that are a direct result of authorized University activities to insurance or federal or state health programs, such as Medicare. The University will be responsible for the cost of any **reasonably necessary medical treatment** to the extent the subject does not have private insurance or does not qualify for coverage from a government health program.

1. Medical Treatment

Definition:

Diagnosis or treatment of human injury, illness, or disease by a health care facility or by a licensed medical professional acting within the scope of his or her license.

Examples:

Meets definition	Does not meet definition
<ul style="list-style-type: none"> • Physical examinations • X-rays and other diagnostic tests • Hospitalization • Prescription drugs • Psychiatric treatment 	<ul style="list-style-type: none"> • Items and services provided by individuals who are not licensed medical professionals acting within the scope of their license • Custodial or domiciliary care (e.g., services or supplies provided primarily to assist with activities of daily living, regardless of who performs them or where) • Personal or comfort items • Educational and employment services • Transportation • Lost wages

- Pain and suffering

2. Reasonably Necessary

Definition:

Medical treatment is **reasonably necessary** if it:

- (1) Consists of clinically appropriate (in terms of type, frequency, extent, site and duration) health care items or services that a prudent physician would provide to a patient to diagnose or treat injury, illness, disease or their symptoms;
- (2) Is considered consistent with generally accepted standards of medical practice and effective for the participant’s injury, illness or disease; and
- (3) Is not primarily for the convenience of the participant or treating practitioner, and not more costly than alternative services or sequences of services at least as likely to produce equivalent diagnostic or therapeutic results.

Examples:

Meets definition	Does not meet definition
Health care items and services that would, under similar circumstances, be covered by Medicare, Medi-Cal, or other health plans licensed to do business in California	<ul style="list-style-type: none"> • Hospitalization to treat an injury that can reasonably be treated on an outpatient basis • Unnecessarily duplicative tests or procedures

In order to be reimbursed, the injured subject must notify the campus in writing of any injury or illness within a reasonable time after discovery. The injured subject must also have appropriate documentation of the diagnosis or treatment costs he or she is claiming are reasonably necessary to treat the injury or illness. If the campus seeks reimbursement from The Regents, the campus must forward the claim to the Office of Risk Services at the Office of the President, where the University will review the claim to determine whether it meets the criteria of reasonably necessary medical treatment pursuant to the Presidential Memorandum. The Regents will only reimburse campuses for any costs of treatment for claims that have been presented to the Office of Risk Services at the Office of the President at the time the claim is made by the injured subject.

3. Direct Result

Definition:

A result that would not have occurred but for the subject’s participation in the trial.

Examples:

Meets definition	Does not meet definition
<ul style="list-style-type: none"> • Allergic reaction to study drug requiring hospitalization • Injury caused by investigational device malfunction • Injury caused by procedure required to implant investigational device (where the procedure would not have been performed but for the study) 	<ul style="list-style-type: none"> • Injury resulting from procedures or interventions that the subject would have undergone regardless of his or her participation in the study • Injury due to disease progression and not participation in the study

4. Authorized University Activity

Definition:

An activity that (1) is conducted (i) on UC property; or (ii) by a UC employee acting within the course and scope of his or her UC employment; and (2) has been approved by a UC IRB or by a central, independent, or collaborating institution's IRB with which the applicable UC IRB has a reliance arrangement pursuant to an appropriate written agreement. In multi-site studies, activities performed at remote sites under the supervision or direction of other institutions' faculty members or investigators are not considered authorized University activities.

Examples

Meets definition	Does not meet definition
<ul style="list-style-type: none">• A study pursuant to an agreement between the University and a sponsor, where UC is a study site, and the study is conducted in a UC facility.• A study (or study activities) conducted at a remote site, where a UC investigator is actually performing or directly supervising the study at that site.	<ul style="list-style-type: none">• A University investigator is conducting a study as a consultant and not on UC property.• A study (or study activities) conducted at a remote site under the supervision or direction of another institution's faculty members or investigators.• A study (or study activities) conducted at a remote site and by an investigator granted an unpaid UC faculty appointment.

5. Designed to Benefit the Subject Directly

Definition:

A procedure or intervention that involves the delivery of health care items or services with an intent to diagnose or treat subjects. *Note: language in an informed consent document designed to avoid the therapeutic misconception by notifying subjects that they may receive no benefit from participation does NOT create a presumption that a particular procedure or intervention administered in connection with the study (even if investigational) is not intended to benefit subjects directly; there may be therapeutic intent even though no promise or guarantee is made that the experimental or investigational intervention will be advantageous to subjects.*

Examples:

Meets definition	Does not meet definition
<ul style="list-style-type: none">• A study that administers an investigational drug, with the purpose of determining whether the study drug improves subjects' prognosis, survival, or quality of life.• An investigational chemotherapy regimen administered in a study enrolling cancer patients, even though the safety or efficacy of the regimen is not yet established.• A medically necessary MRI performed to facilitate clinical management of the study participant.	<ul style="list-style-type: none">• A study that involves only data collection or other observational tasks.• An approved drug administered to healthy, normal volunteers for pharmacokinetic testing.• An MRI performed solely to collect study data or endpoints but not otherwise necessary in the clinical management of the study participant.

Operating Requirement No. 95-5

This Memorandum provides guidance on the meaning of the highlighted terms in [UC Operating Requirement No. 95-5](#):

In cases where a proprietary drug or device is to be tested under the **private sponsor's protocol**, an agreement between the sponsor and The Regents must be signed by a University official who has

been delegated authority for contracts and grants. Such an agreement should be in process prior to the protocol being submitted to the IRB for review. In any case, IRB final approval will be contingent upon completion of an appropriate signed agreement between the University and sponsor. The agreements are subject to applicable policies and procedures, including those promulgated by in the University of California Contract and Grants Manual, and must be reported in the Corporate Contracts and Grants System.

The agreement must make explicit that the sponsor assumes responsibility for **reimbursing the University** for the **reasonable cost of medical treatment** for injuries **directly resulting** from participation in the study. It is not acceptable for such agreements to require billing of third party insurance companies in lieu of recovery of such costs from the sponsor, nor is it appropriate to accept provisions restricting participation of human subjects on the basis of medical insurance coverage status or on the subject’s ability to pay.

1. Private Sponsor’s Protocol

Definition:

A human clinical trial initiated by or on behalf of a pharmaceutical, biologic or device company in which the company provides the study protocol to the University or contracts with the University to develop a protocol on its behalf.

Examples:

Meets definition	Does not meet definition
<ul style="list-style-type: none"> Pharmaceutical company authors the protocol, asks the University to sign a Confidential Disclosure Agreement prior to submitting the protocol to the investigator for review, and then seeks to use the University as a site for the trial. UC investigator authors the protocol (even as a consultant) at a device company’s request, and then the sponsor uses the protocol for a clinical trial. 	<ul style="list-style-type: none"> A UC investigator authors the protocol on his or her own initiative. <i>The fact that a sponsor may provide some financial or other support for the study (e.g., by furnishing free drugs or devices or supplies) does not by itself render the study sponsor-initiated.</i> A UC investigator participates in an academic consortium through which the protocol is authored. <i>If a pharmaceutical company initiated the protocol through the consortium, the protocol would be considered sponsor-initiated.</i>

Considerations in negotiation: determining whether a study is sponsor-initiated:

In determining whether a study is sponsor-initiated, officers should consider:

- Who authored the protocol, and the sponsor’s role, if any, in authoring and developing the protocol;
- Funding provided by the sponsor;
- The intellectual property demanded by the sponsor;
- Sponsor’s proposed or anticipated use of data;
- Who secures the IND or IDE, if applicable;
- Who registers the trial, if applicable;
- Reporting that must or may be made to the sponsor and/or to FDA under any clinical trial agreement.

2. Reimbursing the University

Definition:

Costs incurred directly by the University, other health care providers, or the study subject.

Examples:

Meets definition	Does not meet definition
<ul style="list-style-type: none">• Facility and professional fee charges associated with treatment of subject injuries at University facilities or by University faculty or staff members.• University reimbursement of third-party providers for their charges in connection with treatment of subject injuries.	<ul style="list-style-type: none">• Costs incurred by a subject and not submitted to the University for payment.• Costs for services that are not actually performed.

Considerations in negotiation:

1. The Sponsor is obligated to reimburse for injuries treated outside the University.

Claims for treatment outside of the University may be paid pursuant to the sponsor’s indemnification obligations. For example, the following language would be acceptable:

If a Study participant incurs medical expenses for medically necessary items or services provided by a healthcare provider other than Institution, or its campuses, then Sponsor will cooperate with Institution to resolve any claim made by the participant or the third party provider for reimbursement from the Institution of those costs. Sponsor will reimburse any such claim in accordance with its indemnification obligations pursuant to this Agreement.

2. The Sponsor is obligated to reimburse the entity or individual incurring the cost of treatment.

Operating Requirement No. 95-5 does not preclude the University from seeking sponsor payment directly to a non-UC facility for treatment provided by the non-UC facility. Similarly, the University may also require the sponsor to directly reimburse the subject for any costs of treatment the subject has directly incurred.

3. Reasonable Cost

Definition:

The fair market value of the items or services provided to treat a subject injury.

Examples:

Meets definition	Does not meet definition
<ul style="list-style-type: none">• Payments consistent with a medical center’s established rates for corresponding services.• Payments consistent with discounted rates that the medical center agrees to make available to the sponsor.	<ul style="list-style-type: none">• Payments for services provided at a UC medical center in excess of the medical center’s full charges.• Payment less than the cost to the University to provide such items and services.

Considerations in negotiation:

Contract language must ensure that the University will not experience a financial loss. Below are some examples of subject injury reimbursement language to consider and to avoid:

- **CONSIDER:** “Payment for healthcare items and services shall be consistent with the fair market value of the services provided and shall not exceed the Institution’s established rates.”

- AVOID: “Payment for healthcare items and services shall not exceed the Institution’s actual costs and expenses.” *Healthcare items and services are not priced in this manner and it is therefore difficult to prove what is or is not “actual”; this language would not actually assure that the campus would avoid a financial loss on the study.*
- CONSIDER: “Payment shall be consistent with the Institution’s established research rate, which shall not exceed XXX% of the Institution’s established rates.” [Or: “Payment shall be consistent with the Institution’s established research rate, which shall not exceed XXX% of Medicare rates.” *Consult with your local hospital or professional fee billing directors for an acceptable rate to use in agreements.*]
- AVOID: “Payment shall be consistent with the prevailing Medicare rate.” *This rate most likely will not adequately cover the costs to the University of treating a subject injury or illness. Consult with your local hospital or professional fee billing director for an acceptable rate to use in agreements.*

Further, because the University cannot control the “reasonable cost” of treating a subject injury at another facility, the University cannot agree to cost language with respect to such charges. However, the University can agree on language that the sponsor will cooperate with the University to resolve any claims made by a subject for reimbursement for the University of these costs. For example, the following language would be acceptable:

If a Study participant incurs medical expenses for medically necessary items or services provided by a healthcare provider other than Institution, or its campuses, then Sponsor will cooperate with Institution to reimburse any claim made by the participant (or from the third party provider) for reimbursement from the Participating Institution of those costs. Sponsor will resolve any such claim in accordance with its indemnification obligations pursuant to this Agreement.

4. **Medical Treatment** (See No. 1 in discussion of Presidential Memorandum, above)
5. **Directly Resulting** (See No. 3 in discussion of Presidential Memorandum, above)

Considerations in negotiation:

The policy requires the sponsor to reimburse for:

- **Injuries that extend beyond those caused by a study drug or device:** Injuries *directly resulting* from participation in a study include injuries that result from both use of the study drug or device as well as procedures required by the protocol. Sponsor reimbursement of medical treatment should not be limited to injuries caused by the drug or device, as this allows “cause” to be determined by the sponsor, possibly limiting recovery, and also prevents the subject from being reimbursed for injury caused by procedures required by the protocol – procedures the subject would not have endured absent participation in the study. Sponsors have similarly sought to limit reimbursement to injuries resulting from a defect or malfunction in the drug or device. This language does not follow University policy, as it precludes reimbursement for injuries that may result from a properly functioning device or drug. Such language also leaves the sponsor with the ability to deny reimbursement based upon its assessment as to the functionality of a drug or device.
- **Injuries that may result from failures of the subject to follow protocol procedures, or the study subject’s negligence:** Sponsors may seek to limit their liability to the extent an injury is attributable to the failure of a study subject to follow the Investigator’s or University’s instructions. Such limitations create obligations between the sponsor and subject, who is not a party to research agreements. This language also creates a mechanism for the sponsor to circumvent its obligation to reimburse the University for all injuries directly

resulting from subject participation. Any language that creates a carve-out for a sponsor's subject injury obligations should be tied to the University or investigator's acts or omissions, not those of the subject.

However, sponsors are not obligated to reimburse the University for the following injuries or illnesses, **to the extent the injury or illness** is due to the:

- Failure of the University or its employees to follow a sponsor's protocol or the sponsor's written instructions regarding use of the study drug or device or the conduct of the study.
- Failure of the University or its employees to comply with FDA or other government requirements with respect to the conduct of the study.
- Negligence or willful misconduct of the University or its employees.
- Natural progression of the subject's disease or a preexisting condition.

It is the responsibility of the institution, not the sponsor or the investigator, to determine whether an injury or illness is the "direct result" of participation in a clinical trial. The Subject Injury Program, managed by the Office of the President, Office of Risk Services, will not necessarily accept a determination made by the investigator or the sponsor. Language that enables the sponsor or investigator to determine whether an injury is the "direct result" of clinical trial participation may result in direct liability to the campus, school, or department that entered into an agreement.

For example, the following language may be acceptable, depending upon campus policies:

- *Silence*: "Sponsor shall reimburse Institution for the diagnosis and treatment of any or illness that is a direct result of Study Subject's participation in the Study."
- *Consultation with Sponsor*: "Sponsor shall reimburse Institution for the diagnosis and treatment of any or illness that, as determined by Institution and in consultation with Sponsor, is a direct result of Study Subject's participation in the Study."
- *Mutual agreement*: "Sponsor shall reimburse Institution for the diagnosis and treatment of any or illness that, as mutually agreed by Institution and Sponsor, is a direct result of Study Subject's participation in the Study."