



University of Colorado Denver

Campus Guidelines

Title: Clinical Trials, 4-1

Source: Office of Grants and Contracts

Prepared by: Director of the Office of Grants and Contracts

Approved by: Vice Chancellor for Research

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Replaces: July 1, 2007, UCD Fiscal Policy for Clinical Trials, 4-1

Applies: All Campuses

A. Introduction

1. The purpose of this policy is to establish guidelines and procedures for the management of clinical trials.
2. It is the responsibility of the various account administrators throughout the UCD to comply with this policy.
3. It is the responsibility of the UCD Director of Grants and Contracts and the UCD Controller to ensure compliance with this policy.

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C. Policy Statement

A clinical trial is the prospective evaluation of a technology or product (pharmaceutical, surgical procedure, medical device, vaccine, diagnostic test or technique) beginning with pre-clinical animal pharmacological and/or toxicological studies and extending through phase I, II, III, and IV human studies. Inherent in this definition is the exclusion of discovery or early research and development endeavors relating to technology or product.

Clinical trial agreements must be processed for review and approval in the same manner required for sponsored program grants and contracts. Clinical trial agreements must provide reimbursement for Facilities and Administrative costs incurred by UCD.

All clinical trials shall be performed in conformance with generally accepted standards of good clinical practice with the Protocol, and with all applicable local, state and federal laws and regulations governing the performance of clinical investigations including but not limited to the Federal Food, Drug, and Cosmetic Act and regulations of the Food and Drug Administration.

UCD requires a written clinical trial agreement with sponsors of proposed clinical trials as set forth by the requirements of this policy.

D. Procedures

1. Clinical Trial Agreements

Clinical trial agreements are processed for review and approval in the same manner as required for other sponsored program grants and contracts. Routing and documentation requirements, along with human subjects, animal research, and biohazard approvals, are required for clinical trials consistent with UCD Fiscal Policy 4-5, *Application and Proposal Approval Process for Sponsored Projects*.

2. Facilities and Administrative Costs

All clinical trial agreements must provide reimbursement for Facilities and Administrative Costs (F & A) incurred by UCD. The off-campus research F & A rate will be charged to sponsored clinical trials when a majority of the activity is conducted off-campus, i.e., at one of the hospitals affiliated with the UCD. Waivers or reductions of the F & A rate must be formally requested and processed through the UCD waiver approval process. F & A will not be assessed against COMIRB fees associated with protocol review.

3. Intellectual Property

To commercialize intellectual property, the University retains ownership of patents and copyrights arising from contracts, materials transfer agreements and other research agreements, and offers sponsors a nonexclusive license for *internal* uses or a first right to negotiate an exclusive license for commercial uses. Clinical trial agreements should include language regarding ownership of intellectual property rights in accordance with the University of Colorado Administrative Policy Statement, *Intellectual Property Policy on Discoveries and Patents for Their Protection and Commercialization*.

If University representative(s) have been unable to negotiate intellectual property terms that conform to the policies of the University, the principal investigator may request that the University accept the Sponsor's terms by submitting a completed Request for Intellectual Property Variance form. See, Exhibit A. This form should be completed by the principal investigator, executed by the principal investigator and department chair, and routed to the CU Technology Transfer Office for final signature.

4. Study Data Access, Use and Notices

Where a sponsor has the regulatory requirements for monitoring a study, the parties will use their best efforts to include provisions in the clinical trial agreement which outline the sponsor's monitoring obligations and require the sponsor to promptly notify the PI and/or UCD. During a clinical trial, UCD will expect the sponsor (including its employees or agents) to use reasonable efforts to provide notice when it identifies information that can affect safety, medical care, or continued participation (including willingness to participate) of research participants, or discovers information that may influence the conduct of the study or alter the IRB's approval to continue to the study. For post study results or interim findings that could affect human subjects protections, the sponsor will use best efforts to provide notice to study subjects when it identifies information that can affect safety or medical care or continued participation (including willingness to participate) of current or former research participants.

For dissemination of the study results, the sponsor will be required to report post-study results in accordance with FDA regulations. The clinical trial agreement will seek to include language addressing the PI's access to final study data and analysis and should provide for maintenance of a copy of the data generated at UCD by the PI for record retention purposes. The clinical trial agreement can provide that data generated by the study is confidential except for academic publications in accordance with the University of Colorado Administrative Policy Statement, *Restricted, Proprietary and Classified Research*.

If COMIRB or the PI suspends, terminates or places an administrative hold on a protocol, COMIRB will notify the Office of Grants and Contracts so that they may notify sponsor in accordance with terms negotiated in the clinical trial agreement and in accordance with federal regulations.

5. Termination Dates and Extensions

Clinical trial projects will be set up in the UCD financial system for three years unless a different end date is specified in the contract. If the trial is not completed within three years, the department must send an update to Grants and Contracts documenting the status of the trial and request an extension for the appropriate period of time. Depending on the agreement and sponsor, documentation may be in the form of information from the sponsor that identifies estimated completion date or it may be a formal modification to the agreement that has been prepared by the sponsor, or, if appropriate, the Office of Grants and Contracts. The Office of Grants and Contracts must receive fully completed documentation at least 10 days prior to the termination date.

6. Invoicing and Financial Reporting

It is the responsibility of the department conducting the research to complete invoices and/or financial reports that are sent to the sponsor for non-federal clinical

trials. (For federal clinical trials, please contact Grants and Contracts.) Sponsors will be notified in contracts that payments are to be sent to the Grants and Contracts lock box address. The sponsor will be directed to include the UCD Grants and Contracts proposal number with the remittance address as well as the first and last initials of the principal investigator's name to ensure that payment is reconciled with the correct clinical trial project.

7. Hospital/Patient Care Charges

a. Budgets for Patient Care Charges

Projects that include plans to utilize institutional facilities that are external to UCD for patient care (i.e. University of Colorado Hospital, The Children's Hospital, health care clinic, etc.) are required to include the costs for such activities in the proposed budget. The department conducting the research study is responsible for contacting the external institution directly to ascertain the anticipated costs for carrying out proposed patient care activities. Please note that certain patient care activities are exempt from F & A. See Exhibit B for more information. In accordance with applicable law and regulation and institutional policies, all non-routine patient care costs must be supported by the study budget and not charged to the patient subjects and/or their medical insurers. Routine care is that which is medically reasonable, necessary, and ordinarily furnished (absent any research study), appropriate to the medical condition of the patient. The study budget must also specify who will be the responsible party for the cost of routine patient care services that may not be covered by third party health insurance payors due to the patient's study participation, limits on insurance coverage and/or eligibility exclusions.

b. Billing for Patient Care Charges

Patient care items/services in clinical trials should be charged appropriately to the clinical trial or medical insurance carriers according to federal and state regulations and medical insurance carrier's requirements. Refer to UPI, University Hospital, and/or the billing policies of other affiliates as appropriate for specific requirements.

Principal Investigators should include anticipated standard of care, data collection and analysis expenditures in their clinical trial budgets. Items/services performed only for data collection and analysis should only be charged to the clinical trial project.

Patient subjects should only be billed for patient care expenditures in a manner that is consistent with the informed consent document. The unit completing the research is responsible for ensuring appropriate patient bills are paid.

c. Medicare Billing

In September 2000, HCFA (now known as the Centers for Medicare and Medicaid Services) issued a National Coverage Decision (NCD) which contains requirements for qualifying clinical trials for coverage and provides that routine patient care items/services can be billed to Medicare as long as the items/services are:

1. covered by a Medicare benefit category, not statutorily excluded and not governed by any national noncoverage decision on the specific items/services;
2. typically provided without a clinical trial (e.g., medically necessary conventional care);
3. required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent);
4. required for the clinically appropriate monitoring of the effects of the investigational item or service, or the prevention of complications;
5. required for reasonable and necessary care arising from the provision of an investigational item or service -- in particular, for the diagnosis or treatment of complications arising from the provision of an investigational item or service.

AND the items/services are not:

1. provided by the sponsor in the budget and award amounts. If the items/services have been budgeted and awarded by the clinical trial sponsor, these items/services **cannot** be billed to Medicare. This includes items/services that are designated as standard of care;
2. performed solely for data collection and analysis and not used in the direct clinical management of the patient;
3. the investigational item or service itself; performed to determine the patient's eligibility in the clinical trial.

8. Time and Effort

Faculty members and staff who dedicate time and effort to the conduct of clinical trials should have a proportionate amount of their compensation charged to the clinical trial through the University of Colorado Human Resource system. In addition to or in lieu of effort being reflected on the program/project, patient care expenses incurred at the University of Colorado Hospital, Colorado Psychiatric Hospital, or any other facility, are to be billed by UPI to the project or to the appropriate payer (please refer to UPI billing procedures). Exhibit C, *Clinical Trials Required Form, Effort Commitment and Certification*, must be completed for all clinical trials and submitted along with the application/proposal at the time of UCD routing/approval.

Physician time spent on clinical trials at the University of Colorado Hospital or Colorado Psychiatric Hospital and/or billed through UPI will be reflected as effort in under the section entitled "Other Institutional Activities" on the electronic Personnel Effort Reporting form. Patient care provided at hospitals other than the University of Colorado Hospital or Colorado Psychiatric Hospital that is associated with a clinical trial will also need to be reported in the "Other Institutional Activities" section of the electronic Personnel Effort Reporting form.

Faculty effort should be allocated to clinical trials for which they are performing services. The effort can be allocated by either one of the following or a combination of both:

- (a) allocating a percentage of the faculty member's compensation to the clinical trial project in proportion to the faculty member's time and effort on the project; or
- (b) billing through UPI to the clinical trial project for the professional services provided by the faculty member to patients who are participating in the clinical trial.

As a general rule, supervisory or on-going activity on a clinical trial should be handled by allocating a portion of the faculty member's salary against the clinical trial; short term clinical trial support may be handled by billing services through UPI.

UCD faculty and staff conducting a study may not receive direct personal payments from the sponsor, other than institutional salary support in the study budget, for their performance of the study.

9. Positive Cash Balance Requirement

Departments are required to maintain a positive cash balance in their clinical trial accounts at all times. Sponsors will need to be prepared to provide "up-front" funding at the start of the program/project so the department can initiate appropriate expenditures to undertake the program/project. The amount of up-front funding should be at least the minimum amount necessary to cover start up costs through receipt of initial sponsor payment(s) for UCD invoices for services or deliverables provided to the sponsor. Departments may incur expenditures against the clinical trial program/project provided the program/project maintains a positive cash balance. Expenditures will not be allowed on programs/projects that are in a negative cash balance status and departments will be required to resolve negative cash balance projects as soon as possible. Resolution may include obtaining additional up-front money, invoicing for services/deliverables already provided that have not yet been invoiced, contacting the sponsor for payment of unpaid invoices, and/or transferring expenditures to other suitable funding when no additional funds will be forthcoming from the sponsor.

Departments are generally permitted to create program/project encumbrances that are in excess of the cash balance. Departments must ensure that cash will be available to pay the encumbrance when it becomes payable.

10. Residual Balances

There may be circumstances in which the amount of sponsor support for a clinical trial exceeds the full, actual costs of conducting the research. If residual balances exist, the principal investigator must make certain that all direct costs of conducting the clinical trial have been charged to the clinical trial program/project. In the event that adjustments are necessary, they must be made before residual balances are used for other purposes. Once the clinical trial is concluded and research deliverables are complete, full appropriate F & A charges will be assessed and then the residual balance in the clinical trial can be transferred to the auxiliary fund if allowed by the clinical trial sponsor.

For clinical trials which are conducted in contract segments, the procedure outlined above shall be followed after the end of each contract segment. Residual balances which remain following the end of the contract segment may be transferred to the auxiliary fund if allowed by the clinical trial sponsor.

11. Principal Investigator Records Retention Responsibilities Specific to Clinical Trials

In addition to the UCD records retention requirements of Fiscal Policy 5-4, *Accounting and Financial Records Retention and Access*, clinical trials produce important non-financial, non-accounting records that are maintained by the Principal Investigator for future reference and review. At a minimum the investigator's file must include the original signed consent form and a list of participating patient names with the patient's hospital number.

Other suggested items for maintenance in the investigator's file include the following: case history records, case reports, study protocol and amendments, patient care data, objectives and purpose of the study, selection criteria, clinical procedures, FDA forms, serious adverse events reports, study design and other documentation relating to study protocols. The investigator's file does not need to include medical information/materials which are also maintained in official patient medical record. Exhibit D, *Clinical Trials Records Retention Schedule for Principal Investigators*, sets forth various non-financial, non-accounting documents produced during a clinical trial, the type of document that should be retained (i.e., the original document or a copy of the original document), and the period of retention.

12. Indemnification

Clinical trial agreements should include language that describes the party responsible for providing and paying for medical care for research related injury. Grants and Contracts will use best efforts to include the following terms when negotiating contracts with sponsors research involving an investigational drug, biologic or device, or where the clinical or preclinical study data and/or IP may be utilized for such products in the future:

- A. Studies in which a commercial sponsor holds the IND or IDE and also controls the protocol must provide indemnification coverage and defense of UCD for performing the study, including its trustees, officers, agents, faculty, employees and students, for all claims arising from the institution's conduct of the study that are not due to an institution's negligence or willful misconduct. If the indemnification terms specify types of claims to be covered, the contract must, at a minimum, cover claims arising from (1) study subject injury or illness caused by the product or protocol, (2) institutions' proper conduct of the protocol, and (3) sponsor's use of study data and intellectual property assigned to the sponsor.
- B. Commercial sponsors holding INDs or IDEs are encouraged to fund medical care costs for any study related injury. Clinical trial agreements may exclude medical care costs for illnesses primarily due to a participant's underlying medical condition, or known risks of routine patient care portions of the protocol.
- C. Commercial entities providing product for investigational studies that are initiated by a non-commercial investigator (e.g., faculty at UCD or a collaborating noncommercial entity holding the IND or IDE and controlling the protocol) are required to provide indemnification or to be responsible for their actions in the study (i.e., design, manufacture, and shipment of the product) and for the sponsor's use of the data and any intellectual property assigned to sponsor.
- D. Investigator-initiated investigational studies do not require provision of medical care costs by the commercial entity providing the investigational product. Non-commercial entities sponsoring and/or providing investigational products are not required to provide indemnification or medical care costs.
- E. Commercial sponsors of non-investigational clinical trials and preclinical studies will be required to provide indemnification for their use of data and any assignment of intellectual property to them.

13. HIPAA

Clinical trial agreements for research projects that involve disclosing protected health information (PHI) to the sponsor must comply with Health Insurance Portability and Accountability Act of 1996, 45 CFR 160, 164, (HIPAA) and UCD Privacy and Security Policies and Procedures.

14. Informed Consent

The terms of the clinical trial agreement are expected to be consistent with the informed consent document that the IRB has approved. If during the term of the contract, the informed consent document is modified the COMIRB office will provide Grants and Contracts an updated document. If sponsor requires specific terms in the clinical trial agreement that varies from the standard practice and may affect statements within the informed consent document, Grants and Contracts will notify the COMIRB office and will work together to ensure the clinical trial agreement and informed consent document contain appropriate and consistent language.

E. References

1. *Sponsored Projects Application/Proposal Approval Process*, UCD Fiscal Policy 4-5
2. *Facilities and Administrative Costs and Distribution of Recovery*, UCD Fiscal Policy 4-4
3. *Medicare Reimbursement for Medical Services Related to Clinical Trials*, Health Care Financing Administration, National Coverage Decision (NCD), September 19, 2000