JOHNS HOPKINS
U N I V E R S I T Y

Center for Clinical Trials

Department of Biostatistics
Department of Epidemiology
Department of International Health

Department of Medicine
Department of Ophthalmology
Oncology Center

(Thursday 5:34am) 10 August 2000

Memorandum

To: Center for Clinical Trials faculty and staff

Fr: Curt Meinert

Re: Funding good practice policies and procedures (GPPP)

Definitions

consortium funding *n* - A type of **funding** in which monies received by a designated **center** are disbursed to other centers in a **multicenter study** according to terms set forth in a **consortium funding agreement** and involving **contracts** with (typically the case) or **grants** to those other centers. rt: **indirect distribution of funds**

consortium funding agreement *n* - A **funding agreement** between the **sponsor** and a **center** in a **multicenter study** in which funds are received by that center for disbursal to one or more other centers in the study, typically via contractual agreements.

consortium funding award *n* - 1. A **grant** or **contract** awarded to a **center** in a **multicenter study** that involves a **consortium funding agreement**. The center receiving the **award** assumes responsibility for **distribution** of **funds** to all other participating centers in the study. 2. Such an award except that it is for support of only certain centers in the study; remaining centers funded in other ways.

contract *n* - [ME, fr L *contractus*, fr *contractus*, pp of *contrahere* to draw together, make a contract, reduce in size, fr *com-* + *trahere* to draw] 1. [general] A binding **agreement** between two or more parties, especially one that is legally enforceable. 2. [**business**] A legally binding, usually written, agreement between one party desiring specified goods or services and another proposing to provide such goods or services; the contract specifies the nature of goods or services to be delivered, the schedule or duration of activities, and terms of payment for said goods or services, eg, an agreement between a **sponsor** and the **business office** of an investigator's place of employment in relation to performing a specified **research project**. rt: **grant**, **subcontract**, **cooperative agreement** ***Usage note***: Both **grants** and **contracts** are used to fund **trials**, but the two mechanisms have different origins, administrative implications, and requirements, at least as applied by the **NIH** [Department of Health and Human Services, 1982; Department of Health, Education, and Welfare, 1977]. Hence, the term should not be used interchangeably or confused with grant. See notes for **grant** and **subcontract** for additional comments.

Room 5010 • 615 North Wolfe Street • Baltimore, Maryland 21205 • 410 955-8175 • Fax: 410 955-0932
E-mail: cctmail@jhsph.edu • Web site: http://www.jhsph.edu/Research/Centers/CCT

cost reimbursement *n* - A **mode** of **funding** in which actual legitimate costs are paid, even if in excess of budget projects. ant: **fixed cost**

cost-reimbursement contract *n* - A **contract** in which the amount of money paid is dictated by reasonable and allowable expenses for work performed; unlike **fixed-cost contract**. rt: **fee-for-service agreement**

direct distribution of funds *n* - **Distribution of funds** to **centers** in a **study** directly from the **sponsor** via **direct funding awards**. ant: **indirect distribution of funds**

direct funding *n* - A **mode** of **funding** in which money flows to the point of use directly from a **sponsor**; **direct distribution of funds**. ant: **indirect funding** rt: **consortium funding**

direct funding award *n* - A **funding award** (**grant** or **contract**) received directly from the **sponsor**. ant: **indirect funding award**

evaluable study patient *n* - [**trials**] A **study patient** considered suitable for inclusion in some **tabulation** or **analysis** by virtue of having had some **event** or satisfying some condition during the course of **treatment** (eg, having a recurrence of a cancer; having received the **assigned treatment** and having taken it for a specified period of time). ant: **nonevaluable study patient** ***Usage note***: See note for **evaluable study patients**.

evaluable study patients *n* - [**trials**] The **subgroup** of **study patients** considered to **satisfy** certain conditions and, as a result, are retained for **analysis**. ***Usage note***: Generally, use of the term implies a violation of a basic **analysis principle** in that the subgroup used for making **treatment comparisons** is, itself, subject to **treatment-related selection bias**. As a result, treatment comparisons are likely to be **confounded** by the **selection variable** and, hence, the **treatment difference** noted, if any, may have more to do with selection bias than with the treatment being tested. The possibility of confounding exists whenever the selection variable is observed after the initiation of treatment (as with any **treatment compliance variable** in any analysis where only those patients receiving a specified amount of the treatment are selected for analysis).

fixed cost *n* - A **mode** of **funding** in which the amount to be paid is fixed to not exceed a predetermined amount; amount fixed is independent of actual expenditures. rt: **cost reimbursement**

fixed-cost contract *n* - A **contract** in which there is an **agreement** between the **contractor** (defn 1) and purveyor of goods or services on the amount to be paid for said goods or services, regardless of actual costs incurred.

© 2001 Curtis L Meinert

funding mode *n* - The **mode** of **funding** by which **centers** in a **trial** are funded; eg, **grant** vs **contract**; **fixed cost** vs **cost reimbursement**; fixed cost vs **head payment**.

grant *n* - [general] Something given or granted; the act of granting; **grant-in-aid**; **grant application**. [**research**] 1. An **award** of monies from a federal agency to a state or local governmental unit, or to a private or public **agency**, **institution**, or foundation, to support specified **research** as described in a **grant application**. 2. An award of monies made in response to any research grant application (defn 2). 3. Materials or goods provided in lieu of money for the conduct of specified research, eg, drugs supplied by a drug company for use in a **trial**. 4. **research grant application** rt: **contract**, **cooperative agreement**, **NIH grant**, **R01 NIH grant**, **R10 NIH grant**, **U01 NIH grant**, **U01 NIH grant** ***Usage note***: The term carries the connotation of gift or giving and, hence, is best reserved for awards providing a wide degree of control of the research by the recipient of the award. A grant, as opposed to a **cooperative agreement** or **contract**, is generally made in anticipation of relatively little involvement in the work by the sponsor. Medical **research**, at least in the US, is funded via both grants and contracts. Hence, the two terms should not be used interchangeably. They have different operational implications, especially in relation to review and administration in the NIH setting [Department of Health and Human Services, 1982; Department of Health, Education, and Welfare, 1977]. In a broad sense, an NIH grant is a gift made to an investigator's **institution** to allow that **investigator** to perform research specified by the investigator. An NIH contract is a legal written agreement between the NIH and the investigator's institution to perform designated services or work under the general direction of the NIH. Normally, the grant mode of support is reserved for **investigator-initiated proposals** and for **sponsor-initiated proposals** as outlined in **requests for applications** (RFAs). The contract mode of funding is usually reserved for activities coming about via **requests for proposals** (RFPs). Normally, the mode of funding, once established, remains unchanged over the course of an activity, with notable exceptions. Institutes of the NIH do convert traditional **R01** or **R10** grants to **cooperative agreements** in some **multicenter trial** settings (eg, as happened in the Glaucoma Laser Trial). Similarly, they can change from grant to contract or contract to grant support during the life of an activity. For example, a switch from grant to contract took place during the Diabetic Retinopathy Study in relation to funding for the coordinating center for that study. In addition, the initiator role can change for activities that proceed from a feasibility phase to a full-scale phase. A case in point is the Systolic Hypertension in the Elderly Program (SHEP). The initial feasibility trial grew out of investigator initiative and was funded via grants. The full-scale phase was initiated via an RFP from the NIH and was funded via the contract mode of support. Usually the NIH will use the same type of funding vehicle for all sites in a multicenter study, but there are exceptions here as well. For example, some institutes have used grants to fund clinics in such settings and contracts for core units, such as coordinating centers. There are differences between the two modes of funding, at least as practiced by the NIH, in the amount of control and direction that is or can be exercised by the NIH. In general, use of the contract mode signals a more active hand in the design, organization, execution, and analysis of the research by the NIH than is typically the case with grant support.

© 2001 Curtis L Meinert

head payment *n* - A **payment** based on person count, eg, a fee in the amount of $2,500 paid by a drug company to an **investigator** for each person **enrolled** into a **trial** and followed for 8 weeks.

indirect distribution of funds *n* - Any system of **funding** in which **funds** flowing to a **site** from a **sponsor** are via a party other than the sponsor, as in **consortium funding**. ant: **direct distribution of funds**

indirect funding *n* - A **mode** of **funding** in which money flows to the point of use from an intermediary of a **sponsor**, eg, with **centers** in a **multicenter trial** funded via another center in the trial, eg, as in **consortium funding**; **indirect distribution of funds**. ant: **direct funding** rt: **consortium funding**

indirect funding award *n* - A **funding award** made to a **site** by another site with funds from a **sponsor**, as in a **consortium funding award**. ant: **direct funding award**

investigator-initiated research proposal *n* - 1. A **research proposal** conceived, prepared, and submitted to a prospective **sponsor**, without a formal solicitation by the sponsor. 2. An unsolicited **grant proposal** submitted to the **NIH**, such as an RO 1 **grant application**. ant: **sponsor-initiated research proposal** rt: **grant proposal** ***Usage note***: The initiating force behind a proposal is not always clear, especially in the case of large scale **multicenter trials**, even for those funded by grants not solicited by **requests for applications** (**RFA**s). Typically, investigators will not undertake the task of preparing fully developed proposals for such trials, in itself is arduous and expensive, without some indication from the **sponsor** that they will be accepted for review and that the proposed work is consistent with the general charge or scope of interest of the sponsor. See note for **sponsor-initiated research proposal** for added comments.

request for application (RFA) *n* - A document prepared and distributed by a **sponsoring agency** to solicit **applications** pertaining to a circumscribed area of work detailed in the **request**; especially such a document prepared and distributed by an agency of the federal government, such as the **NIH**, and in which said work is to be supported by **grants**. rt: **request for proposal** ***Usage note***: From the NIH perspective, both RFAs and RFPs are used as vehicles for identifying and selecting investigators and **centers** in **multicenter trials**. As a general rule (though there are exceptions), investigators have more control over the activity proposed under the NIH RFA mode of initiation and **grant** support than under the NIH RFP mode of initiation and **contract** support. The need or opportunity for NIH sponsors to assume a directive role in the activity is greater with RFPs than with RFAs. Technically, the focus in an RFP is on a defined task and on deliverables related to that task. The emphasis in an RFA is on a scientific question or issue.

request for proposal (RFP) *n* - A document prepared and distributed by a **sponsoring agency** to solicit **proposals** for execution of a specified task, especially such a document prepared and

© 2001 Curtis L Meinert

distributed by an agency of the federal government, such as the **NIH**, and in which said work is to be supported by **contracts**. rt: **request for application** ***Usage note***: Not to be confused with **request for application**. See usage note for **request for application**.

sponsor-initiated research proposal *n* - A **research proposal** prepared in response to a request by a **sponsoring agency**, as in relation to a **request for proposal** (RFP) or **request for application** (**RFA**). ant: **investigator-initiated research proposal** rt: **contract proposal** ***Usage note***: The initiating forces behind **research projects** are not always clear, even when the proposals are generated in response to RFPs or RFAs or when funding is via **contracts**. Often in the case of large-scale **multicenter trials**, the initiation process is a joint one involving people at the sponsoring agency and would-be investigators, especially in the case of **NIH**-sponsored trials. For example, the Coronary Drug Project, although funded by grants and ostensibly investigator-initiated, was, in fact, actively encouraged by the sponsoring institute. See note for **investigator-initiated research proposal** for added comments.

unit payment *n* - A **mode** of **payment** based on number of units produced, as in piecework or **head payment**.

P&P 1: Strive for relational parity in the funding structure; ie, structures in which funding mode and relationship between centers are at parity (eg, relationship to the funding agency is the same for clinics as for the CC).

Comment

Relational differences among centers, relative to the sponsor, has the potential of creating a "pecking order" that is at odds with creating and maintaining proper working environments within the trial.

P&P 2: Avoid mixed modes of funding for centers performing the same function.

Comment

The thrust of this P&P is to ensure funding parity among clinics (even if requirements for P&P 1 across types of centers cannot be met). The P&P is not achieved if some clinics are funded by grant and others by contract, if some have fixed-cost funding and others have cost-reimbursement funding, if some are funded by head payments and others are funded by fixed-cost or cost-reimbursement funding, or if some are funded by one sponsor and others by another sponsor.

P&P 3: If requirements for P&P 2 cannot be met, work to minimize the number of modes of funding used.

Comment

Every mode carries its own peculiar problems in administration and accounting. The more modes the more work and the greater the chance for mistakes and discontent.

P&P 4: In cases where trials are funded from two or more sources, establish mechanisms to create a single stream of money to the centers.

© 2001 Curtis L Meinert

Comment

The purpose underlying the P&P is twofold: (1) To establish a structure of funding consistent with P&Ps 1 and 2 and (2) To reduce the likelihood of conflicting inputs and directives to centers from different sponsors.

P&P 5: Consider the consortium mode of funding for clinics when:

- There is need to create a one stream of money from multiple streams
- Sponsor is inadequately staffed or is inexperienced in funding multicenter trials
- Sponsor is ham-strung by red-tape

P&P 6: If the consortium mode of funding is used and responsibility for management of funding is vested in the CC, Office of the Study Chair, or some other study center, vest responsibilities for management and administration in persons not involved in the day-to-day duties and function of the center; ensure that persons are properly trained to perform such functions and subject to safeguards to ensure proper use and administration of funds.

P&P 7: When considering RFPs or RFAs, be wary of proposals in which sponsors intend to fund clinics and the coordinating center via different mechanisms (eg, grants for clinics and contract for the coordinating center).

Comment

Generally, such differences are indicative of a sponsor's desire to exert more control and influence over the CC than over the clinics or that the CC is seen primarily as a service unit.

P&P 8: In regard to considering whether to respond to an RFA or RFP, forego responding if:

- Proposed trial is unnecessary or unethical
- Rationale for proposed trial is lacking
- Procedures proposed for care or treatment of patients are not sound or consistent with prevailing norms
- Funding is not adequate
- Scope of work is unreasonable given the budget
- Timetable is unrealistic
- Sponsor is naive as to the design, organization, or operation of trials
- Sponsor plans to direct the activity
- Sponsor has the right of approval for publications from the trial
- Investigator right of primacy likely to be abridged by the sponsor

P&P 9: When considering a response to an RFA or RFP or when considering whether to collaborate in development of an investigator-initiated proposal, forego response or collaboration if:

- Key CC personnel are not at par with other investigators on key study committees
- Procedures proposed for design or operation of the trial are not consistent with good practice and policy procedures of the CC

© 2001 Curtis L Meinert

- Emphasis is on service
- CC personnel are masked to treatment assignment
- The TEMC does not report to study investigators
- The TEMC is masked

P&P 10: In regard to head payments to clinics: Avoid as the sole form of payment; supplement with start-up funding and some fixed cost funding.

Comment

Head payments, because money comes after the required visits or procedures have been done, make it difficult to fund start-up efforts and to recruit and retain staff. Further, the "piece work" approach to payment may encourage shoddy, or even shady, practices.

P&P 11: If head payments are provided to clinics, do not limit payments to "evaluable patients"; provide payment for persons enrolled and followed regardless of compliance to treatment and outcome status.

Comment

Forms of payments based on "evaluable patients" are incompatible with P&Ps for followup of persons regardless of treatment status and with P&Ps aimed at maintaining some form of followup for all persons enrolled, even dropouts.

P&P 12: Opt in favor of pursuit of grant funding when faced with the option of whether to pursue contract or grant support.

Comment

The grant mode of funding is more compatible with the environment of academic institutions than is the contract mode of funding.

P&P 13: In preparing an investigator-initiated grant proposal for submission to the NIH with an annual budget in excess of $500,000 in direct costs, obtain assurance that the Institute is willing to receive such applications before submitting.

P&P 14: Do not consummate a funding agreement if the funding proposed is inadequate.

Comment

In regard to trials, it is better to walk away than to preform substandard work because of inadequate funding. The world cares only about the job done, not about excuses as to why a job was inadequate.

P&P 15: Do not hire or spend in the absence of consummated funding agreements.

Comment

If it is not over until the fat lady signs, then, likewise, it does not start until she signs. Promises of funding can disappear without a trace.

P&P 16: Commit understandings in regard to issues of funding to writing.

© 2001 Curtis L Meinert

Comment

Handshakes are fine, but there is no memory in handshakes. If the person making the commitment leaves the institution, is incapacitated, or dies the agreement may be forgotten. In any case, the likelihood of misunderstanding is reduced when things are in writing; letters signed by both parties (no e-mails, please!).

P&P 17: Avoid service as a contacting agent for the trial.

Comment

There is a tendency for CCs to be the Mikie of trials. Hence, the CC, can find itself performing the function of a procurement agent, in soliciting bids for proposals and in selecting and funding speciality centers such central laboratories, reading centers, and drug distribution centers.

All such activities take time and carry their own risks. They are likely to distract from the main duties and functions of the CC and are better done by a group or body created specifically for that purpose.

P&P 18: Avoid service as a purchasing agent for the trial.

Comment

Rationale: Same as for P&P 17.

The urge to make the CC a purchasing agent arises from the desire to streamline and standardize purchasing and the desire to "save" money by bulk purchasing (usually modest and not enough to offset the effort involved). The preferred route is for purchases to made at the sites of use.

P&P 19: Avoid service as a collection agent.

Comment

Rationale: Same as for P&P 17.

Duty in this arena arises when the CC assumes expenses for some activity or function (eg, producing and printing a patient information booklet). The way to avoid such activities is by vesting such responsibilities in a group or firm equipped for the indicated service or product.

P&P 20: Avoid service as a payment center for travel expenses.

Comment

Rationale: Same as for P&P 17.

Duty in this arena arises when monies for travel of clinic personnel to study meetings reside in the CC budget. Avoid by vesting monies for travel in clinic budgets.

© 2001 Curtis L Meinert

P&P 21: Monitor expenditures and operate within the allotted budget.

Comment

Satisfying the requirements of this P&P requires personnel dedicated to that activity and software developed specifically for that purpose. Most institutions do not have systems adequate to the task.

© 2001 Curtis L Meinert