

VAMHCS RESEARCH SERVICE  
INVESTIGATOR GUIDELINE

GUIDELINE #HRP 07.07G

Approval date: 11/8/07

***THIS IS NOT A RESEARCH SERVICE SOP: it is not required that investigators and research staff follow the procedures below.***  
Instead, this is a **GUIDELINE** presented by the Research Service to aid investigators and research program administrators in deciding which clinical studies to accept and what to consider when budgeting for and planning the operations of a clinical trial.

GUIDELINE ON ACCEPTING A PROTOCOL

BACKGROUND:

This is based on an actual SOP that was successfully used in a former VAMHCS research Unit. That Unit conducted studies for its own investigators but also offered its services to all investigators on the UMB-VAMHCS campus. In the latter case, the Unit became a quasi-CRO, and thus had to juggle the expectations of investigators and Sponsors, often as a third party between the two.

It soon discovered the pitfalls of not clearly delineating responsibilities and expectations of all parties, of becoming locked into preliminary budgets before there was adequate time or information to develop budgets that reflected actual costs, and of not planning for hidden costs and time expenditures. It therefore developed this SOP to help its own investigators and to guide its administrators when other campus investigators approached the Unit for assistance in some or all parts of their clinical trials.

The Research Service offers this Guidance as a resource to help current investigators/research programs in their own operations: it may help to develop accurate budgets, plan for up-front costs or cancellations, anticipate questions or problems, streamline staff duties, get input from staff, etc. The ideas presented here can easily be adapted to the specifics of the investigator's situation, whether s/he works directly with a Sponsor or within a "unit" framework.

OBJECTIVE:

- To ensure that the Unit accepts only those protocols which the Unit feels it can successfully complete.
- To ensure that the Unit does not accept a protocol which competes for the same subjects as other studies for which the Unit is already recruiting.

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- To ensure that the Unit is adequately compensated for its activities in performing a protocol.
- To ensure that the Unit and the Principle Investigator (PI) are clear on each's responsibilities and division of labor.
- To ensure that the Principle Investigator (PI) is clear on the Unit's standard operating procedures with regard to his/her study and that he/she agrees to them.
- To ensure that all of this is accomplished prior to the start of the study.

### RESPONSIBILITIES:

- The Unit is responsible for:
  - an honest evaluation of the protocol to see if it is suitable for the Unit.
  - all services for which the PI/Sponsor has contracted.
  - keeping the PI apprised of progress on the study.
- The PI is responsible for:
  - working with the Unit to decide division of labor and budgetary issues.
  - keeping the Unit apprised of all protocol amendments and changes in Informed Consent Forms.
  - providing the Unit with contacts within the Sponsor or sponsoring agency as well as names and phone numbers of service providers with which the Unit will be interacting.
  - all tasks/responsibilities which s/he has retained (and therefore has not contracted with the Unit) (see #5 below and Appendix B).

### PROCEDURE:

1. The PI submits a study protocol or summary to the 'Managing Director' [or comparable person] of the Unit and has a brief conference with the Managing Director to discuss how the PI envisions the study will be carried out and which Unit services will be needed (see Appendix A for list of Unit services).

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2. The 'Managing Director' reviews the protocol and confers with the Unit Medical Director and other Unit staff to determine whether the Unit will be able to do the study well and whether the study conflicts with current Unit efforts/studies in any way.
3. If it is decided that the Unit is able to do the study, the 'Managing Director' may devise a **non-binding draft budget proposal** if strongly requested by the PI/Sponsor (for example, in order to get a very sketchy ballpark estimate of costs). The Unit will not submit a firm budget until #5-8 below have been accomplished. This is to prevent unanticipated expenses from being encountered by the Unit.
4. A final budget proposal is submitted to the PI *OR* to the Sponsor as soon as #5-8 below are accomplished. Budget negotiations proceed until a budget is agreed upon and signed by the Unit and the PI/Sponsor.
5. Simultaneously with budget talks, one or several meetings occur to discuss the logistics of the study. These meetings shall be attended by the PI, the 'Managing Director' of the Unit and other appropriate staff such as the Medical Director of the Unit, the PI's study nurse/coordinator, Unit study nurse(s)/coordinator, other providers of testing procedures. The following items must be discussed and agreed upon before a final budget proposal can be submitted and the study can begin:
  - 5.1 Unit template data collection forms (DCF's): These are the Unit's method for source documentation and will be the PI's way of following study events for his/her study subjects. Therefore it is important for the PI and his/her staff to become familiar with them and to give input on them (if s/he wishes) while they are being developed.

Alternatively, Sponsors now frequently supply "source documents" to be used for data collection. The Unit reserves the right to adapt such forms to fit the Unit's procedures or to use Unit's forms instead. Conflicts about this should be resolved before accepting the study. If necessary, a Unit SOP may be suspended
  - 5.2 Time-Event Sheets [Time-Event (TE) Sheets were this unit's master document for the conduct of their studies and were hugely important as a way of coordinating the actions of a large staff on all shifts.]: The importance the Unit places on TE sheets is communicated to the PI. The PI will be given the first draft of the TE Sheet for review and comment. Revisions will be made at the PI's request during the development process if s/he chooses to be involved. No revisions will be made once the study starts unless serious errors are discovered or unless there are substantive protocol amendments. TE Sheets will not be revised purely for convenience or appearances once the study has started; therefore it is highly advised that the PI take every opportunity during the development process to mold the TE Sheet to his/her liking by giving input at that time.

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- 5.3 The PI must keep the Unit abreast of protocol amendments. The PI must also inform the Unit of communications with the Sponsor/providers which may affect the way the UNIT envisions its role, the plan of action, the amount of time a task will take, or the cost of the task.  
For example: whether labs will be sent to the VA lab or whether shipping to a central lab will be required (demands extra time and supplies); whether specimens will be shipped to more than one lab (demands even more time, inventorying, supplies, different formats of shipping forms /instructions, etc)
- 5.4 Who is going to do what, including: admissions/discharges, notifications, tests, procedures, scheduling, shipping, storing, etc.
- 5.5 MD coverage/responsibility
- 5.6 How tenuous is lead-time for scheduling and admissions and how complicated is the set-up/scheduling for the study.  
For example, if multiple shifts of nurses need to be scheduled in advance of a planned admission and the admission is subsequently cancelled, a large amount of coordinator time has just been wasted in scheduling and phone calls for canceling shifts. This becomes a hidden and potentially significant cost to the Unit if it is not anticipated in the budget submission.
- 5.7 Cancellation fees: if the study is cancelled before subjects are enrolled but after up-front costs are incurred; if a run of the study is cancelled with "reasonable" notice; if a run of the study is cancelled with short notice; etc.
- 5.8 Is the PI planning to do the IRB submission, amendments and reporting or does s/he wish to contract with the Unit for this service? Does the PI plan to maintain the Regulatory Documents file(s)?
- 5.9 Who will be responsible for SAE reporting to the sponsor, IRB, etc.?
- 5.10 How much preparatory, "up front" work is necessary for the UNIT to be prepared for the study (Time-event sheets, source documents, staff training, obtaining/learning equipment, etc.)?
- 5.11 Is the PI/his staff planning to transcribe the Unit's DCF's (source documents) to the Sponsor's CRF's or does he/she wish to contract with the Unit for this service?
- 5.12 Is there a need to use Unit space (offices, exam rooms, desk space, inpatient Unit, storage space)? If so, is this possible to fit in with other Unit activities? The cost ("rent") that this will entail.
- 5.13 Is there a need to use Unit personnel/time (phone screeners, recruiters, chart reviewers, data entry, nurses, PCA's, nurse practitioners, etc.)? If so, is this possible to fit in with other Unit activities? The cost (wages, charges) that this will entail.
- 5.14 Is there a need to use Unit equipment (refrigerators, freezers, centrifuges, special equipment, computers, etc.)? If so, is this possible to fit in with other Unit activities? The cost (disposable supplies, rent, charges) that this will entail.

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5.15 If the Unit is to be directly involved with a significant portion of study activities or coordinating, it is recommended that selected Unit staff be sent to the protocol Investigator's Meeting at the expense of the Sponsor. Is this possible?

Alternatively, the Unit will strongly request a site initiation visit from the sponsor EARLY in the planning process, well before an initiation visit would typically occur.

5.16 The possibility of acknowledgement of the Unit in publications resulting from the study.

5.17 An understanding that the Unit conducts internal quality assurance audits on its source documents. This ensures that the PI receives consistent, complete, coherent data. This activity is included in the Unit's estimates of time needed for its conduct of the study.

6. The Unit requires access to the Sponsor as well as the PI during the planning phase. The Unit will not proceed with preparations if this is not available.

7. The Unit requires access to any VA, UM or extramural providers\* with whom the PI has contracted or whom s/he wishes to perform specific study events. This is to ensure coordination of study tasks & responsibilities and to enable the Unit to devise an accurate budget and plan of action.

\* "Provider": hospital department, physician, nurse, technician, special testing personnel/Unit, etc.

8. Once it has been decided (via the above discussions) who is responsible for each aspect of the study, a summary is drawn up in grid format (see Appendix B) and signed off by the PI, Unit management and other responsible parties as necessary. This grid becomes part of the Contract/Study Agreement that must be signed by all applicable parties before the study can begin.

9. If a study must begin emergently, the above steps must be followed as well as it is practical. Once the first logical study entity (subject, period, cohort, etc.) has reached a logical stopping point (completion of the period, interval before a follow-up visit, etc.) A MORATORIUM ON FURTHER STUDY ACTIVITY *MUST BE CALLED UNTIL STEPS 1-8 ARE COMPLETED AND THERE IS A REVIEW OF UNIT PERFORMANCE*. The study may not resume until the PI and the Unit are satisfied that a clear understanding of responsibilities and plan of action has been agreed upon.

10. The Unit must have copies of the following approvals before any study may begin: UMB IRB approval letter for protocol and amendments, IRB-approved informed consent form, VAMHCS R&D Committee approval letter, other approvals as necessary (radiation safety committee, controlled substances (DEA), etc).

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APPENDICES

- A. List of Services
- B. Pre-Study Unit -Investigator Meeting(s): Agreement on Issues, Assignment of Responsibilities, Points for Follow-Up

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**Appendix A: [List of UNIT services (List of tasks assumed by any current investigator/research staff who undertakes a clinical trial)]**

UNIT SERVICES

	DESCRIPTION	COSTS
IRB SUBMISSION	Writing, assembling in BRAAN; communication with IRB staff and Investigator staff	IRB fee; Personnel time; Number of versions>rewrites of submission due to changes in protocol; overhead
IRB AMENDMENTS	Writing, assembling in BRAAN; communication with IRB staff and Investigator staff	Personnel time; Number of versions>rewrites of submission due to changes in protocol; overhead
IRB REPORTING	Obtaining info from Investigator or UNIT DCF's; writing, assembling in BRAAN	Personnel time; overhead
STUDY MANAGEMENT/ STUDY COORDINATOR	IRB liaison, regulatory documents (see below), study start-up (see below), study coordination, source documentation (see below), planning, reUnititment & screening (see below), subject follow-up (see below), managing study procedures, sample management (see below)	Staff time, supplies, complexity of protocol, number of amendments (reorganization), level of coordination with PI staff, see other modules below
DESIGNING SOURCE DOCUMENTS	Design of documents that are GCP- compliant, protocol-specific, complete and which include SOP's of the UNIT, the Sponsor, and Investigator requirements.	Personnel time; Number of amendments/ protocol revisions which lead to revisions of DCF's
ORGANIZING REGULATORY DOCUMENTS	Creating a system for organizing regulatory documents; actual organization of documents; updates; QA of process	Personnel time; ease of obtaining current items from Investigator or other sources
STUDY START-UP	Time-event sheets; planning sessions/consultations; designing Data Collection Forms (source documents) ; inservicing/hiring staff	Personnel; Protocol amendments which lead to extensive revisions of TE's and DCF's
REUNITITMENT	Designing recruitment	Staff time, advertising, travel,

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<b>&amp; SCREENING</b>	strategies, performing recruitment & screening activities, obtaining informed consent	supplies, overhead, difficult populations/strategies
<b>INVESTIGATIONAL PHARMACY/ DISPENSING MEDS</b>	Arrangements with the VA Investigational Pharmacy for randomization procedures, storage, inventory; UNIT RN's or licensed staff to dispense study meds and document; drug accountability	Pharmacy fee, on-call fees for nights/weekends, staff time, equipment (iv pumps, nebulizers, etc), use of space (exam rooms or inpatient Unit), travel, complexity of med/administration/documentation
<b>OUTPATIENT/ TELEPHONE FOLLOW-UP</b>	Study-specified follow-ups or AE follow-ups; phone contact and documentation; outpatient or inpatient visits and documentation	Staff time – may need several calls/mailings to locate subject; documentation; late or cancelled visits; use of exam rooms or office space
<b>PHLEBOTOMY</b>	Blood drawing and other samples; lab requisitions for VA or central labs	Staff, supplies, lab charges, Late/cancelled subjects, difficult sticks, etc
<b>SAMPLE PROCESSING</b>	Processing of samples (plasma/serum, aliquotting, cultures, urine pregnancy tests, freezing, etc.) and documentation	Staff, equipment, supplies; complexity of Sponsor forms, labeling, notifications, storage
<b>SHIP SPECIMENS</b>	Invoicing and packing specimens; arranging pickups; dry ice available	Personnel, supplies; Number of separate shipments per Unit of study
<b>DATA MANAGEMENT</b>	Software or database specified by Sponsor/PI, reports and logs	Cost of software and training if not supplied by Sponsor/PI, personnel time
<b>TRANSCRIPTION TO CRF's</b>	Collating and organizing source documents; transcription to Sponsor CRF's; resolving data edits from Sponsor; presence for Monitor visits	Personnel time; quality of non-UNIT source documentation; edits due to change in Sponsor's rules for data entry
<b>USE OF EXAM ROOMS</b>	Fully stocked rooms on [location]; CPRS/DHCP access; special supplies/equipment as necessary; scheduling of visits; encounter forms; assistance with procedures	Personnel, special or excessive supplies, overhead; cancellations
<b>USE OF OFFICE SPACE</b>	Work space, computers, CPRS/DHCP access, file	Scheduling of space/times; overhead

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	space	
USE OF EQUIPMENT	Freezers, refrigerators, centrifuges, iv pumps, hoods, suction pumps, some specialty equipment	Scheduling, supplies; inservicing/training on special equipment; overhead
INPATIENT BEDS	6 patient beds or 9 healthy volunteer beds on 3A; fully staffed with RN's or PCA's; performance of study procedures according to protocol and GCP's; source documentation; charting follows requirements of VA, UNIT, Investigator and Sponsor	Personnel scheduling, shifts, training, supervision; VA bed charges, meals; <b>cancellations:</b> Set up and QA of study charts

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**Appendix B: [Current investigators/research staff should change column headings and row titles as needed (for example: “Sponsor responsibilities”, “Study coordinator responsibilities”, etc.) and signatories at the bottom.]**

PRE-STUDY UNIT-INVESTIGATOR MEETING(S):  
AGREEMENT ON ISSUES, ASSIGNMENT OF RESPONSIBILITIES, POINTS FOR FOLLOW-UP

DATE: \_\_\_\_\_ MEETING \_\_\_ OF \_\_\_ STUDY: \_\_\_\_\_

PARTICIPANTS: \_\_\_\_\_

	UNIT Responsibility	Investigator Responsibility	_____ Responsibility
IRB submission		X	
IRB amendments			
IRB reports: annual			
IRB reports: SAE			
Notification of other party of IRB approvals & amendments			
Regulatory Docs file			
Time-Event Sheet	X	Accept? Y / N Wants input into revisions? Y / N	
Design of DCF's (source documents): Screening			
Enrolled			
Maintenance of DCF's (source documents): Screening			
Enrolled			
ReUnitment activities (specify if responsibilities are split)			
Screening activities (specify if responsibilities are split)			
Enrolled activities (specify if			

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responsibilities are split)			
Registration			
Admission			
Scheduling: sbjts			
Scheduling: staff			
Contact forms			
MD coverage			
Supervision of staff			
Coordinator			
Phlebotomy			
Shipping samples			
Storing samples			
Other activity:			
Other activity:			
Acquiring equipment			
Returning (shipping) loaned equipment			
Training on new equipment			
Clerical (significant amounts of FAXing, xeroxing, mailings, etc)			
QA			
Transcription to CRF's			
Monitor visits: CRF's			
Monitor visits: Reg Docs			
Notifying Sponsor of SAE's			
Other items:			

Other items:

Question	Answer
PI allows contact with Sponsor?	Contact person(s):

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PI allows direct budget with Sponsor for UNIT portion?	Contact person(s):
How many destinations for shipped samples?	
How many shipments per sbjt/visit/etc?	
How much notice before an admission?	
Likelihood of cancellations/postponements	
Financial arrangement for cancellations:	
Financial arrangement for postponements:	
What equipment needs to be obtained?	
UNIT space needed? (cross-out those not needed; specify amount, etc of those needed)	Offices, exam rooms, inpatient rooms, storage space, other: _____
UNIT equipment needed? (cross-out those not needed; specify amount, etc of those needed)	Refrigerators, freezers, centrifuges, telephone lines, computers, special equipment: _____; other: _____
UNIT personnel needed? (cross-out those not needed; specify amount, etc of those needed)	RN's, PCA's, phlebotomists, screeners, recruiters, data managers, chart reviewers, NP's, other _____
UNIT rep to Investigator Meeting? (significant UNIT role only)	
Acknowledgement of UNIT in publications	
Sponsor must know that UNIT is an entity independent of PI	
Other providers of services which the UNIT will work with / coordinate, etc?	Names & #'s:
Other:	

We understand and agree with the items as outlined on the preceding pages. We accept the above responsibilities.

Investigator: \_\_\_\_\_ Date: \_\_\_\_\_

UNIT Representative: \_\_\_\_\_ Date: \_\_\_\_\_ Role in UNIT: \_\_\_\_\_

Coordinator(s): \_\_\_\_\_ Date: \_\_\_\_\_ (Investigator Coordinator)