Use of Investigational Products When Subjects Enter a Second Institution - Information Sheet

Guidance for Institutional Review Boards and Clinical Investigators

Several issues are raised when a subject who is participating in a research study at one institution is admitted to another facility. To help illustrate, the following will serve as the model for this information sheet: Regional Medical Center (RMC) has developed a research protocol; the study has been reviewed and approved by the RMC institutional review board (RMC-IRB); each subject receives a test drug for a 16 week period (4 weeks inpatient, 12 weeks outpatient); some research subjects will live in a distant town with a local health care facility, Memorial Hospital (MH). For these subjects, participation at RMC will involve considerable travel time and costs. While several examples can be imagined, the three scenarios below may help to illustrate some key points.

1. The least complex (first) scenario is when a subject's treatment/hospitalization is not related to the research. Procedures should be in place for rapidly identifying test drugs and devices (e.g., an emergency contact number and unblinding procedure). For this example, we will assume that hospitalization at MH is medically necessary and that the local physician has determined that it is appropriate to continue the subject (now patient) on the test drug. In this case, MH is providing incidental medical care and is not participating as a research site. Therefore, MH staff are not investigators and the MH-IRB does not need to review the protocol. The usual procedures for dealing with drugs prescribed out-of-facility would be followed (often, this is a pharmacy department policy). The investigator at RMC remains responsible for test drug administration and follow-up and therefore, should be aware of the hospitalization. The RMC investigator may need to report the event as an unexpected adverse incident, if it is possibly related to use of the test article. The RMC-IRB remains the IRB of record.
2. For the second scenario, the involvement of MH is reasonably foreseen and is an anticipated part of the study protocol (e.g., the need for inpatient care is anticipated for the condition under study, or the need for subjects to return home and receive medical follow-up). The RMC-IRB should be aware that other institutions and/or providers will be providing medical care/follow-up and should ensure that adequate reporting and safety systems are in place before approving the study. In this example, the protocol allows the test drug to be sent to the subjects' regular health care providers. Even though the test article is being given at MH, only routine medical monitoring is conducted by the local provider with little or no reporting to the RMC

investigator, who remains responsible for the test drug administration and collects research data when the subject returns to RMC. The involvement of MH is incidental to the study (i.e., research data are not collected) and thus, it is not participating as a research site.

In the first two scenarios, prior to continuing the investigational drug, the local physician should obtain from the clinical investigator the information necessary to safely continue the investigational drug. The information conveyed might include a description of treatment procedures, warnings of possible adverse reactions, emergency procedures, a copy of the signed informed consent document (which is a research summary as well as documentation of consent).

3. For the third scenario, MH is designated as an extension of the research milieu. In this instance, the second institution (MH) is responsible for a portion of the research protocol. For this example, a physician at MH has been identified in the protocol as a sub-investigator for subjects residing in that local catchment area. As sub-investigator, this physician is responsible for conducting examinations of subjects to monitor status and measure effects of the test drug (data collection). These research data are systematically reported to the RMC investigator.

Because MH is conducting research, it is responsible for complying with the applicable research regulations. The MH-IRB may review, approve and be responsible for monitoring the portion of the research conducted at MH just as it would for any other research in the facility or, MH may agree to accept the RMC-IRB as the responsible IRB. If the RMC-IRB is to accept responsibility for other sites, it should consider the rationale for transferring or referring subjects to another institution; the circumstances under which responsibility will be shared; the instructions that will be given to the sub-investigators; the monitoring procedures that will be followed; and the informed consent process.

Informed Consent

Although not specifically discussed in the FDA regulations, requiring the subject to sign a second research consent document for the secondary facility should be avoided when feasible. In the first and second scenarios, research is not being conducted at MH and therefore, no research consent is needed for the second facility (however, consent for medical treatment may be required). Since the medical need in the first scenario is unexpected, the informed consent document would not describe such involvement. In the second scenario, because MH involvement is planned, the informed consent document should describe the activities to be carried out at MH. When some of the research activities are carried out at a secondary location, the investigator and the IRB should consider whether any additional information, such as a local emergency contact number, needs to be included in the informed consent document.

The third scenario is the most complex. Because MH is involved in research, the informed consent process should include a description of this activity. As appropriate, this could be included in the consent document presented to all subjects, or a separate informed consent document could be prepared for those subjects entering MH. If the RMC-IRB is accepting responsibility for other sites, it would review and approve the informed consent document(s). If MH does not agree to cooperative review, however, MH-IRB may accept the RMC informed consent document if it adequately describes the involvement of MH (i.e., not require a second document). MH-IRB may also decide to develop its own informed consent document. In this case it is important that the subject not receive conflicting information and the two IRBs should work to resolve such issues. If there are two consent documents, generally the RMC document would cover the overall study and the MH document would only detail the specific procedures involved while at that facility.

Also see this FDA Information Sheet:
"**Cooperative Research (/RegulatoryInformation/Guidances/ucm126422.htm)**"

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