

- Q. How does IRC assure compliance of investigators after approval is granted?  
A. IRC cannot assure compliance but we can and do take some actions toward that goal.

## PREMISE

IRC believes that our clients are innocent at least until there is some reason to believe they are not. (Or as one reviewer said, "Never assume malice when ignorance is the probable cause.") Our investigator application form requires an investigator signature attesting (a) that the information presented is complete and honest and (b) to their intention of following the protocol.

21 CFR 56.108 each IRB shall (b) Follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of ... and (2) any instance of serious or continuing non compliance with these regulations or the requirements and determinations of the IRB.

## MISCONDUCT AND SERIOUS OR CONTINUING NON-COMPLIANCE

On occasion IRC has discovered that a study is not being conducting as the IRB believed it would. This has resulted in several actions.

Investigation: a query letter, a site visit,

Corrective action: further education, a CAPA or explanation may be all that is required.

Notice: notice to the sponsor, and the funding or regulatory agency regarding the findings and actions.

## PASSIVE SITE MONITORING METHODS

### 1. IRB Phone Number on the Consent Document:

Our subject contact number, 1-800-IRC-3241 is on every consent form unless an appropriate alternative is proposed in the protocol. IRC's President or the Director of IRB Operations takes such calls and serves as subject ombudsman. Subjects may need to leave a message on an answering machine.

The practice has been to answer all questions possible, to attempt to encourage direct communication with the principal investigator, to attempt to resolve problems and to report such calls, with the caller's permission, to the investigator, the sponsor, and the IRB. (Note: About half the calls received are about not getting paid as expected.)

### 2. Education of investigators and staff and of their subjects.

As of January 2002 all investigators (except those for registry studies) are expected to complete continuing education courses on the ethical conduct of research. Our web site is intended to assist in our educational outreach and has a list of educational opportunities.

### 3.3.2 MONITORING

#### 3. Accessing routine monitoring

The Principal Investigator Application Form and the Continuing Review form ask about audit and monitoring history and results.

### ACTIVE SITE MONITORING METHODS

#### 1. Calling the site, keeping in contact

Staying in contact with the site personnel and being ready to answer questions can prevent many problems. The site numbers given on the consent forms are called at odd times to determine that they work.

#### 2. Perusing the Press

IRC staff and IRB members read a variety of trade and popular press items and often bring in interesting tidbits about IRC clients. These are discussed at the following meeting.

#### 3. Web information

The web contains a wealth of information and may be searched as needed. We often search client sites.

#### 4. On site monitoring

IRC has the authority to conduct random or targeted inspection either directly or through contract with independent monitors

### IS IT SERIOUS? IS IT CONTINUING? IS IT NON-COMPLIANCE?

#### And what next?

#### 1. The wrong consent form

At the time of continuing review the investigator submitted, as requested, a copy of the last consent form signed. It was found to be the version approved prior to the most recent modification. The staff recognized the problem and probed further and found that the 3 most recent (out of 20) subjects had signed the old form. They had been recruited after the last modification was approved.

Serious? Probably serious. It mentioned a new theoretical risk. But none of the three evidenced the symptoms.

Continuing? Yes, three mistakes. No, they have corrected the available forms.

Non compliance? Yes

Penalty: Report to sponsor? Yes Report to FDA? Perhaps

Find out: Did the sponsor know of this and not tell the IRB?

### 3.3.2 MONITORING

#### 2. Adverse events not reported

A sponsor monitor, during a visit, asks if reports of ten serious adverse events were submitted to the IRB. The coordinator (who is new on the job) cannot tell from the records so the IRB is called. The IRB received only one report.

Serious? Yes

Continuing? Yes

Non compliance Yes

Penalty? Questions about whether they are truly serious?

Corrective Action Plan required?

Corrective action plan for monitor?

#### 3. Data was collected after the expiration date

During data cleaning it was noticed that subject visits and data collection had occurred after IRB expiration.

Serious? Regulatorily, yes,

Continuing? No, study complete

Non compliance Yes

Action? Assess safety?

Deny use of data?

