



IRB INTERACTION WITH COMPLIANCE OFFICES

07/18/2008

It is the policy of the Duke University Health System Institutional Review Board (DUHS IRB) to conduct internal Quality Assurance (QA) reviews on a regular basis to ensure compliance with federal regulations, state and local laws, and IRB and institutional policies and procedures. Toward that end the DUHS IRB relies upon and works cooperatively with the Duke School of Medicine Clinical Trials Quality Assurance (CTQA) Office to conduct routine review of IRB-approved protocols and to investigate allegations of misconduct in human subject research. As defined in 42 CFR Part 93.103, *research misconduct* means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Research misconduct does not include honest error or differences of opinion. The DUHS IRB, working through its relationship with CTQA, is interested in investigating instances of failure to adhere to an IRB-approved protocol, instances of research misconduct, and allegations of non-compliance with federal regulations, state and local laws, and IRB and institutional policies and procedures.

The IRB also relies on the DUHS Compliance Office to evaluate concerns about clinical trials billing and program procedures for all Duke entities involved in clinical trials. As noted above for CTQA, the IRB is interested in investigating instances of failure to adhere to an IRB-approved protocol, instances of research misconduct, and allegations of non-compliance with federal regulations, state and local laws, and IRB and institutional policies and procedures.

Both offices promptly report to the IRB any allegations or findings of non-compliance with federal regulations, state and local laws, and IRB and institutional policies and procedures as they relate to research with humans.

About the CTQA Office

The CTQA Office, a component of the Duke University School of Medicine Compliance Office, was declared a peer review board on 21 April, 2004 by the DUHS IRB. The office exists as a *functional* extension of the IRB while being completely separate, organizationally, to maintain objectivity. The CTQA Office has the authority to review both IRB records and IRB conduct.

The purpose of CTQA review is: 1) to verify that the rights and welfare of human subjects are safeguarded; 2) to verify that the clinical trial is conducted in a manner consistent with the approved protocol and regulatory requirements; 3) to assure that the reported study data are accurate, complete and verifiable from

the source documents; and 4) to investigate complaints and/or allegations of noncompliance with federal regulations, applicable laws, or institutional policies.

The CTQA staff conducts both routine, proactive, on-site reviews (audits), and directed, reactive, "for-cause" reviews of IRB-approved protocols. Additional services provided by the CTQA Office include assistance in preparing for external audits; providing consultation to research personnel; and conducting regulatory training and incident resolution. The CTQA staff also helps provide information to faculty and staff on regulatory compliance and Good Clinical Practice (GCP) guidelines concerning human subjects, data collection and data management.

CTQA review includes but is not limited to the following: the protocol-specific regulatory binder and IRB documentation; case report forms and source documentation (for about 10 to 20% of the total subjects enrolled); test article accountability and storage; record retention and storage; and overall data quality. To that end, CTQA auditors have full read-only access to all electronic IRB files, including the eIRB, and all paper files held in the IRB Office or its off-site storage.

Selection of Protocols for Review

Studies are commonly selected for review based on routine monitoring by the CTQA Office of the IRB database for information such as:

- Absence of external monitoring or oversight
- Investigator initiated IND or IDE (includes both investigator and sponsor regulatory responsibilities for study conduct and reporting)
- Degree of risk ---- based on expected adverse events, type of study, or vulnerable population(s)
- Credible allegations of human subjects violations or noncompliance with Federal regulations
- Investigator inexperience
- Failure to submit a progress report and application for continuing review to the IRB before the expiration of IRB approval;
- Failure to respond to IRB deferral issues or to respond to the IRB requests for information or modifications in a timely manner.

However, the DUHS IRB and other DUHS compliance groups may also suggest or request CTQA review of a particular study for any credible reason, including on the basis of a complaint from a research subject (or family member) or an individual internal or external to DUHS. Both the IRB and the CTQA office have the authority to interview relevant research personnel in response to an allegation of research misconduct.

Distribution of the Reports of Review Findings

Upon completion of the CTQA review, the CTQA staff will promptly draft a final report which will include any necessary corrective actions and a deadline for receipt of a written response from the investigator.

Depending upon whether the review is a directed, for-cause review or a routine review, copies of the final report will be distributed to the following individuals or entities:

- Principal Investigator and Co-PI ^a
- Department Chair ^b
- IRB Executive Director ^a
- Vice Dean for Research ^a
- Associate Dean for Research Support Services ^a
- Associate Dean of Compliance ^a
- Regulatory and/or Funding Agencies ^b

^a All reviews

^b Directed reviews and if major problems are identified requiring agency notification

Exchange of Information between DUHS IRB and CTQA

The IRB Office receives copies of all final reports of reviews conducted by the CTQA Office. All findings and allegations of non-compliance discovered on study audits are promptly reported to the IRB for review. Upon review by the IRB Executive Director, the CTQA reports are maintained electronically in a secure location by the Executive Director. If the CTQA Office has reported a finding or allegation of non-compliance, or the IRB Executive Director concludes from the review of a CTQA report that an assessment for non-compliance is needed, the policy titled “Non-Compliance with the Requirements of the Human Research Protection Program” will be followed.

In addition to the full report, referenced above, the CTQA staff also prepare an IRB Item Follow-Up Report which is used to report observations that require corrective actions on the part of the PI and notification to or approval by the DUHS IRB Office. In cooperation with the IRB, the CTQA staff monitor all corrective actions required of the research team to ensure that all such actions have been adequately addressed. After all corrective actions have been resolved by the investigator, the CTQA Office issues a recall letter, a copy of which is sent to all individuals or entities that received the final report.

A CTQA Office designate may attend any convened IRB meeting as a non-voting observer and representative of the School Of Medicine Compliance Office. When

this occurs, the representative is granted the same access to the agenda items as the attending IRB members.

The Executive Director of the IRB, CTQA personnel, the Chief Compliance Officer and the Associate Dean for Research Support Services meet quarterly to review summaries of CTQA audit results and discuss concerns regarding the conduct of research involving human subjects within DUHS. In addition, the IRB Office provides CTQA with quarterly reports concerning IRB submissions. These reports are based on mutually agreed-upon parameters consistent with institutional risks, such as submissions with INDs/IDEs, submissions targeting vulnerable populations, and number of protocols with IRB approvals that have lapsed more than 5 days.

Monitoring/Observation of the Informed Consent Process

The IRB has the authority to observe or appoint a designee to observe the informed consent process in IRB approved research. The CTQA Office has the expertise and the authority to conduct this activity on behalf of the IRB. The CTQA plans to add additional staff in the future and conduct monitoring of the informed consent process on a more routine basis. Monitoring the actual informed consent process may be particularly applicable to protocols involving vulnerable populations such as fetuses, pregnant women, prisoners, children, or the cognitively impaired.

Monitoring of Protocols at External Sites

Directed audits and routine periodic compliance reviews may also be conducted by CTQA at non-Duke University Medical Center (DUMC) and non-DUHS sites, especially those sites for which the DUHS IRB serves as the IRB of Record; and/or a Duke P.I. holds an IND and is shipping drug to external sites.

In lieu of a site visit, sometimes CTQA will ask for the case report forms and source documentation for subjects enrolled at non-Duke external sites, and will perform a QA review on the requested documents.

REFERENCES

45 CFR 46
21 CFR 50 and 56
42 CFR 93.103