

Process Summary for Research Compliance Assurance Human Subject Reviews

To protect the rights and wellbeing of clinical trial research subjects, the Duke Office of Audit, Risk and Compliance (OARC) Research Compliance Assurance (RCA) section conducts confidential reviews of research protocols approved by the Duke University Health System (DUHS) Institutional Review Board (IRB). Reviews can be either routine or directed (for cause).

Routine protocol selections are based on risk metrics geared toward high subject enrollment, studies with limited oversight or monitoring, investigator-initiated investigational drugs or devices, federally funded studies, high degree of risk (based on adverse events, type of study or vulnerable populations), phase I studies or studies that involve Medicare populations. Directed reviews can be requested by the department, Clinical Research Unit (CRU), IRB, an institutional official or as a result of any official complaint.

In reviewing DUHS clinical trials, the RCA section examines clinical trials methodology, processes and systems to assess whether the research is conducted according to the protocol approved by the DUHS IRB. The primary purpose of the review is to verify that the standards for safety of human subjects in clinical trials and the quality of data produced by the clinical trial research are met. Reviews serve as confidential quality assurance measures internal to the institution. An additional goal of these reviews is to detect both random and systemic errors occurring during the conduct of clinical research.

'Passing' an RCA review does not guarantee the absolute integrity of the data scrutinized nor the ability of the clinical trial research to stand up to a U.S. Food and Drug Administration (FDA), or other agency, sponsor or institutional audit or review.

The steps involved in a routine review include: the opening meeting, active protocol review, closing meeting (if necessary) and final summary of review findings.

All reviews are performed at a previously determined scheduled location Monday through Friday during regular business hours. Length of reviews vary depending on protocol-specific elements (e.g., number of case report files to be examined, overall state of protocol documentation and staff preparedness).

On the first day of review, if possible, an opening meeting occurs. Attendees include the RCA compliance auditor, the principal investigator (PI), the lead study coordinator and any additional key personnel the PI wishes to invite.

The active portion of the protocol review begins with an assessment of the overall conduct of the study, division of responsibilities for particular portions of the protocol, documentation of the degree of delegation of authority and appropriateness of this delegation of authority (certification/training), the 'informed consent process,' assessment of how the data was recorded and how the research test article (such as the drug, device or biologic) was accounted for and maintained, and review of the quality of systems if the research article was produced and/or manufactured at DUHS.

In both routine and directed reviews, RCA requests and/or reviews protocol-specific regulatory binder and IRB documentation, case report forms, signed informed consents, research test

article accountability, storage and destruction logs, record retention and storage, and overall data quality.

If needed, a closing meeting is held after all review assessments have been performed. At this meeting, all action items assessed during the review are discussed with the appropriate parties. A confidential summary is presented to the PI; this is a draft of the observations that may appear in the Final Compliance Review Summary and a copy of this document is left with the PI, who has five business days after the closing meeting to clarify any of the noted observations.

A Final Compliance Review Summary is generated from the draft closing meeting summary, incorporating any additional information provided by the PI during the five business day clarification window, by the reviewer(s) who conducted the protocol-specific review. This confidential Final Compliance Review Summary is issued by the RCA section and sent (electronically with return receipt) to the PI, with a copy to the IRB. If protocol deviations are extensive, a copy may also be sent to the department chair.

When the reviewer is satisfied that all corrective actions have been implemented and all action items are resolved, OARC will send an email to the PI confirming review closeout. This email is also sent to all parties previously notified in the review process including the Duke University chief compliance officer. If action items are not addressed in the agreed-upon timeframe, the review will remain 'open.'