Duke Cancer Network

POLICY & PROCEDURE TITLE:	DCN Monitoring of Clinical Research Activities Conducted by DCN Affiliate Sites
REFERENCE NUMBER:	CR-QM.02
EFFECTIVE DATE:	*03/10/23*
APPLIES TO:	☒ DCN ☒ DCN Clinical Sites ☒ DCN Program Development ☒ DCN Research Only Sites
DISTRIBUTION:	☒ Internal ☒ External

1. Purpose

The policy/procedure describes the *DCN Monitoring of Clinical Research Activities Conducted by DCN Affiliate Sites*. Detailed, written instructions create uniformity in conducting clinical research at Duke Affiliate sites in compliance with applicable regulations, guidelines, and Duke University, Duke University Health System (DUHS), and Duke Cancer Institute (DCI) policies.

The Food and Drug Administration (FDA), Office of Human Research Protections (OHRP), Department of Health and Human Services (DHHS), National Institute of Health (NIH), and the International Conference of Harmonization Good Clinical Practices (GCP) emphasize the need to monitor clinical research to ensure the safety and protection of human subject rights, validity of data, and compliance with the approved protocol, GCP guidelines and applicable regulatory requirements. Monitoring provides an opportunity for continued education, training, and mentoring of clinical research investigators and staff on the fundamentals of conducting clinical research with an emphasis on best practices.

2. Scope

To ensure that all individuals assisting in the conduct of clinical research are informed about the obligations and responsibilities pertaining to Good Clinical Practice (GCP), the FDA Form 1572 Statement of Investigator, the investigational plan, applicable regulations, guidance, and institutional policies. This SOP applies to all members of the DCN clinical research team involved in site research monitoring activities.

The DCN research team is responsible for monitoring research activities conducted by the DCN Program Development and Research sites. The DCN research team also conducts internal quality assurance reviews for the DCN Clinical sites.

3. Policy & Procedure

Monitoring is a systematic and independent examination of study-related activities and documents to determine whether the evaluated study was conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, contract, standard operating procedures, Good Clinical Practice, and the applicable regulatory requirement(s).

Monitoring activities will be conducted remotely, but may be done in-person at the discretion of DCN leadership, if there is inadequate access to electronic records and source documentation, or there is a need for an in-person assessment.

The DCN will conduct routine monitoring of clinical research performed at DCN Research and Program Development sites. The timeline and scope of the monitoring will follow the protocol specific monitoring requirements and applicable DCI policies.

DCN Monitoring of Duke Investigator Initiated Trials (IITs)
Routine monitoring assessments of Duke ***interventional*** Investigator Initiated Trials are detailed in the protocol and the approved *DCI Data Safety Monitoring Plan*. The DCN will follow DCI policies and procedures specific to the monitoring scope, timeline, and reporting requirements for the Safety Oversight Committee (SOC).

A formal written report will be provided to the site research team and Principal Investigator (PI). A formal written response with a detailed corrective and preventative action plan (if applicable) will be required from the site within **two weeks** of receipt of the monitoring report. The report and site response will be routed to the Duke PI, DCN Medical Director, Oncology Disease Group lead, DCI Monitoring Team, and the Safety Oversight Committee for review and assessment.

The site research team and PI will be notified of the date of SOC review. Following the SOC review, the site will be notified in writing of the SOC assessment and if additional corrective actions are required by the committee and/or the Duke PI.

The scope of routine monitoring assessments for Investigator Initiated ***non-interventional*** clinical trials will be determined at the time of study initiation. Minimal risk clinical trials may not require reporting to the SOC per Duke policy and procedures. However, the Duke PI and DCN Medical Director will be notified of any monitoring findings.

DCN Monitoring of NCI National Clinical Trial Network (NCTN) Studies
Routine monitoring visits of NCI National Clinical Trial Network (NCTN) protocols opened by Program Development and Research sites under the Duke Alliance membership will be conducted by the DCN research team. The scope and frequency of monitoring will be determined annually for each site based upon their protocol portfolio, accrual, and findings from previous monitoring visits. The monitoring plan will be discussed at the monthly meetings with the DCN to ensure that proactive monitoring activities are implemented as needed for each affiliate. These assessments will be conducted at least annually, more frequently if deemed appropriate, and will be tailored to the needs of specific sites to assure protocol and regulatory requirements are fulfilled.

A written summary of monitoring findings will be provided to the site research team and PI. A response with detailed corrective and preventative action plan (if applicable) will be required within **two weeks** of receipt of the monitoring finding. A summary report of monitoring activities will be provided to the Duke NCTN research team, the PI of the Duke Lead Academic Participating Site (LAPS) grant, and the DCN Medical Director. The site PI and research team will be notified if additional corrective actions are requested.

A. Records Review:
Monitoring assessments include, but are not limited to the review of essential documents such as regulatory documents, delegation of authority logs, financial disclosures, subject research records, relevant case histories, case report forms, and investigational product accountability and management records.

Routine protocol monitoring assessments may include:

- PI oversight and appropriate delegation of tasks
- Review of essential documents
- Site local review process
- Consent process and documentation
- Eligibility verification of clinical research subjects
- Safety of clinical research subjects
- Validity and integrity of the data
- Timeliness and accuracy of adverse event reporting
- Compliance with the approved research protocol
- Investigational product management and accountability
- Research billing practices
- Compliance with regulatory requirements
- Compliance with institutional standards and policies

B. Reporting of Non-compliance & Subject Safety Concerns:

Investigators, research staff, and any other member of the Human Research Protection Program are required to report any Unanticipated Problems to Subjects or Others (UPIRSO/UPIRTSO) and serious and/or continuing non-compliance to the study PI, sponsor, IRB of record, and FDA as applicable per institutional policy and Human Subjects Protections regulations.

Monitoring observations will be provided to the study site. The site will have the opportunity to provide additional information and/or clarifications. The site may be required to provide a corrective and preventative action plan (CAPA) and report the findings as applicable to institutional and regulatory oversight entities.

Documentation of non-compliance and subject safety issues will be completed as referenced in the DCN policy/procedure CR-REG.02: *Protocol Deviation Reporting and CAPA Review* utilizing REDCap. The documentation will clearly and succinctly state the problem identified, including the root cause. A corrective and preventive action plan will be written to provide a plan with measurable actions that will address the root cause of the problem and prevent a recurrence. Additional training and education may be provided by the DCN research team to assist the sites in meeting the goals of the corrective and preventative action plan.

For Duke IIT studies where Duke is the IRB of record, the Duke PI will be notified of protocol deviations, unanticipated events/problems, and associated corrective actions via REDCap. The PI will consider the information and determine whether prompt reporting to the IRB is required.

For studies that utilize another IRB of record, the study team will need to follow the IRB of record's reporting requirements and the site PI will need to make a determination if the protocol deviation or unanticipated event/problem, meets the requirements of prompt reporting to the IRB. REDCap will be utilized to collect information relevant to the deviation or unanticipated event/problem and the IRB of record determination.

C. Tracking of DCN Monitoring Activities

All DCN monitoring activities will be documented and records will be maintained electronically in the DCN Monitoring and QA file organized by protocol and by site. Each site will be provided monitoring updates at least monthly, which may be captured on the site specific research dashboard report. Guidelines for updating site monitoring activities are maintained in the Research Program Monitoring & QA folder on the shared drive.

4. Definitions & Acronyms:

Major Protocol Deviations or Violations: Variances from protocol specific criteria or procedures that make the resulting study conduct or data questionable are categorized as major deviations or violations. Examples of these would be enrollment and treatment of an ineligible subject, failure to obtain and document informed consent, failure to comply with IRB approval and/or re-approval guidelines, and treatment deviations such as substantial alternation or modifications of doses outside the study parameters, and/or poor quality data management, not capturing study adverse events or dose limiting toxicities, and failure to report serious adverse events (SAEs).

Minor Protocol Deviations: Deviations that do not affect the outcome or interpretation of the study data or study conduct as assessed by the protocol PI are categorized as minor deviations. An unacceptable frequency of minor deviations will be treated as a major deviation.

Non-compliance is the failure to follow federal, state, or local regulations governing human subject research, institutional policies related to human subject research, an IRB-approved research protocol, or the requirements or determinations of the IRB. This may pertain to the principal investigator, research staff, or any member or component of the Human Research Protection Program (HRPP).

5. Attachments:

Not applicable

6. References:

POLICIES & PROCEDURES:	• DCN CR-REG.02 Protocol Deviation Reporting & CAPA Review • DCN CR-REG.05 OHRP Registration Confirmation • DCN CR-REG.08 Key Personnel Requirements • DCI Data and Safety Monitoring Plan (DSMP) • DCI Policy for Monitoring Investigator Initiated Multi-Site Clinical Trials • DCI Safety Oversight Committee Process • DCI Monitoring Process for Investigator Initiated Clinical Trials • DCI Monitoring Process of Industry Sponsored Clinical Trials • DOCR - Duke Box for Clinical Research Study Monitoring • DCI-PRMC-Accrual Monitoring • DUHS IRB – Non-Compliance With the Requirements of the Human Research Protection Program • DUHS IRB – Problems or Events That Require Prompt Reporting to

	the IRB
REGULATIONS:	• Good Clinical Practice: Integrated Addendum to ICH E6(R1)E6(R2) • 21 CFR 11 Electronic Records; Electronic Signatures • 21 CFR 56 Institutional Review Boards • 21 CFR 312 Investigational New Drug Application • 21 CFR 812 Investigational Device Exemptions • 45 CFR 46 Protection of Human Subjects • 45 CFR 160 + 164 HIPAA Privacy Rule • 42 CFR 50 + 94 Responsibility of Promoting Objectivity in Research
GUIDANCE:	• FDA Guidance for Industry: Oversight of Clinical Investigations- A Risk-based Approach to Monitoring • FDA Guidance for Industry: Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects. • FDA Compliance Program – Bioresearch Monitoring • FDA Information Sheet Guidance for IRBs, Clinical Investigators and Sponsors • NCI Guidelines for Auditing Clinical Trials for the NCI NCTN Program Including NCI Community Oncology Research Program (NCORP) and NCORP Research Bases

7. Revision History

Issued: *12/01/2009*

Revised: 10/09/2011, 11/01/14, 6/5/2017, 2/21/2018, 6/20/2019, 3/10/23

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Linda Sutton, MD Date

Medical Director, Duke Cancer Network