I. Introduction

NRG Oncology has developed an audit program in compliance with the guidelines of the Clinical Trials Monitoring Branch (CTMB) of the National Cancer Institute (NCI). The audit program, which is under the direction of the Statistics and Data Management Center (SDMC), ensures the integrity of the data on clinical trials, compliance with federal regulatory and Good Clinical Practice requirements and protocol adherence, while educating institutional staff.

The NRG Oncology Audit Program is directed by the Associate Head of Quality Assurance and Operational Support, who interacts with the areas of Data Management, Regulatory, Information Technology, Membership and Administration.

II. Program Overview

A. Site Selection

Each active NRG Oncology site is audited at least once in every three-year cycle. In general, audits are conducted at the “parent” institution (NRG designated Main Member, NCORP office, LAPS office hereafter referred to as Main Member Site). All members, including those following patients but not actively accruing, are at risk for being audited at any time. New and reactivated Main Member Sites are audited within 18 months of the first patient enrolled. Occasionally, special audits may be arranged by NRG Oncology or by the NCI in cooperation with NRG Oncology if warranted by significant data irregularities. The primary consideration when scheduling audits is the time elapsed since the prior audit. Other considerations include:

- a prior audit designated as “acceptable needs follow-up” or as an “unacceptable audit” that requires a re-audit before the regular cycle;
- indication trials requiring more frequent audits;
- questionable data reports or decrease in data quality necessitate an early audit;
- geographic proximity to other sites which are due for an audit (this is considered in order to conserve costs);
- accrual since the prior audit;
- site status (i.e., active or inactive);
- early audit is requested by the site; or
- site is targeted for a multi-group audit

B. Notification

In general, the Main Member Site Contact Principal Investigator (PI) and Lead Research Associate (RA) are notified, via email, of a site visit audit two to four months in advance of the date determined by NRG Oncology.
C. Audit Team

The audit team is determined by the size of the audit and special requirements (requiring physicians). The team consists of NRG Oncology staff and volunteer auditors. Volunteer auditors are current or former NRG Oncology members, experienced in the conduct of NCTN trials and knowledgeable in NCI Guidelines, GCPs and federal regulations. A team leader is designated to oversee the overall audit process, conduct the exit interview, submit the preliminary report and draft the final report.

All auditors sign an NRG Oncology confidentiality agreement.

D. Selection of Regulatory, Investigational Agent, Patient Cases for Review

1. Regulatory

Per individual site (as determined by separate audit report required by CTMB), a minimum of 4 protocols is chosen for review of regulatory documents. Whenever possible, this selection includes a treatment protocol, prevention/cancer control protocol, advanced imaging protocol and registration trial for trials with cases credited to NRG Oncology. Review includes protocol and amendment approvals, safety update submissions, informed consent content and if applicable, delegation of task logs.

2. Investigational Agent

NCI Drug Accountability Record Forms and/or logs for imaging/radiopharmaceutical agents for all control and satellites are reviewed for all protocols for which any agents were used since the prior audit.

3. Patient Cases

For each individual site, identified by a unique institution CTEP ID, a minimum of 10% (rounded up) of cases enrolled since the prior audit is selected for each of the following categories: NRG Oncology treatment trials, NRG Oncology prevention/cancer control trials, NRG Oncology registration trials, NRG Oncology advanced imaging trials. In addition, 10% of other NCTN Lead Protocol Organization (LPO) protocol cases credited to NRG Oncology are selected for each of these categories. In some cases, additional cases beyond the minimum are selected for designated protocols.

E. Audit Conduct

In general, regulatory and drug accountability records are reviewed remotely prior to the audit at the NRG Oncology SDMC. On site, source documentation and adherence to protocol and regulatory requirements are reviewed, and the pharmacy is visited for storage, security and shelf counts. Patient cases are reviewed for informed consent, eligibility, treatment, adverse events, disease outcome/response and general data quality. Cases are reviewed for protocol adherence and reported data are compared to source documentation. Auditors interact with site staff throughout the day.

Audit findings are categorized by severity (critical, major or lesser) in accordance with CTMB guidelines. At the conclusion of the audit, an exit interview takes place with the team leader explaining deficiencies and general audit findings. The Main Member Site Contact PI and
Lead RA (or designees) are to attend and all appropriate staff are encouraged to attend and participate in the discussion. Recommendations and positive findings are discussed.

At any time during the audit, if research misconduct is suspected or critical deficiencies are found, the Associate Head of Quality Assurance and Operational Support is immediately notified, who in turn notifies the Clinical Trials Monitoring Branch (CTMB), the NRG Oncology Group Chairs, the SDMC Chair, the Deputy Group Chair for Membership and Research Integrity, and the NRG Executive Director.

Per 42CFR93.103, research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

F. Assessing Findings/Reports

Within 1 business day of completing the audit, a Preliminary Report of Audit Findings is uploaded to the CTMB audit system. Each area of review (Regulatory, Accountability of Investigational Agents and Patient Case Review) is given one of the following assessments: Acceptable; Acceptable, needs follow-up; or Unacceptable. In addition, it is determined if a re-audit is required for any of these three categories. A re-audit within 12 months is required for an Unacceptable assessment. If applicable, the report includes directions regarding submission of a Corrective and Preventive Action Plan (CAPA).

If an institution receives two consecutive unacceptable assessments for the same category, the institution is placed on probation. In addition to the CAPA, a Site Improvement Plan is required, addressing key infrastructural issues contributing to poor performance. Sites on probation are closely monitored for accrual and data submission and may be assigned a mentor.

Depending upon the severity of deficiencies identified, sites can be suspended from enrolling new patients. Suspension will result if any critical deficiency is found or if it is determined that there was scientific misconduct.

Final reports are drafted by the team leader and submitted to the Associate Head of Quality Assurance and Operational Support for review, final assessment and submission to CTMB. CAPAs, required from the institutions within two weeks of report submission, are reviewed by the Audit Program Manager and submitted to CTMB after review/resolution of any questions within 45 days of final report submission. Site Improvement Plans are reviewed by the Audit Program Manager as well as the Associate Head of Quality Assurance and Operational Support and submitted to CTMB within 45 days of final report submission.