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SECTION 1

BACKGROUND AND PURPOSE OF THE RTOG AUDITING PROGRAM

A. INTRODUCTION

Quality assurance is any method or procedure for collecting, processing, or analyzing study data that is aimed at maintaining or enhancing their reliability and validity. Quality assurance includes prevention, detection, and action from the beginning of data collection through publication of the results. Practitioners of clinical trials have an obligation to take appropriate steps to protect both the integrity of science and human subjects who participate in research studies. Vigilance to detect honest errors, systemic or random, as well as data falsification, is especially important to clinical trials since independent replication of most trials is not feasible. The goals of our quality assurance program include preventing problems, detecting problems and taking appropriate action in a timely and effective manner. A well-designed and implemented quality assurance program should serve as a valuable educational vehicle. The Radiation Therapy Oncology Group (RTOG) audit team will use the opportunity of every audit to share with the research staff good clinical practice techniques and data management and quality control systems that have been successfully implemented at other institutions. The facility can use the results of the on-site audit to identify operational areas where improvements can be made.

B. BACKGROUND

As one of the oldest Clinical Trials Cooperative Groups, RTOG was established in 1968. Funding from the National Cancer Institute (NCI) began in 1971. As the world’s largest sponsor of clinical trials of investigational antineoplastic agents and cancer clinical trials, the NCI must ensure that research data generated under its sponsorship are of high quality, reliable and verifiable. The NCI’s quality assurance and monitoring policies for clinical trials have been in evolution since 1955. In 1982, the NCI made on-site monitoring a requirement for the Clinical Trials Cooperative Group Program, cancer centers, and other investigators conducting clinical trials under its sponsorship.

The RTOG is a multi-institutional cooperative organization, the principal objectives of which include: 1) increasing the survival of patients with malignant diseases in which control of the local-regional tumor is a major determinant of outcome; 2) demonstrating the contributions of new modalities to the therapy of cancer, adjunctive to the established modalities of surgical resection, radiation therapy and chemotherapy; 3) improving the quality of life of patients by preserving structure and function while maintaining or increasing survival, and providing palliation and preserving dignity for patients who are not cured; 4) preventing second and subsequent malignant tumors among patients cured of cancer, and 5) seeking greater understanding of the biology of several types of cancer.
C. PURPOSE AND OBJECTIVES

The purposes of the NCI-sponsored audit are:

1) To verify adherence to regulatory requirements, including those for protection of human subjects and those for the handling of investigational agents;
2) To enhance the delivery of accurate and reliable clinical trials data and results according to Good Clinical Practice;
3) To verify the accuracy of submitted data and to monitor protocol compliance using source documents on-site;
4) To provide educational support to the clinical trials sites regarding issues related to data quality, data management and other aspects of clinical research quality assurance.

The RTOG Quality Assurance Program strives to improve institutional procedures. The scope of this program is to audit member institutions with the purpose of: protecting human subjects with regards to Informed Consent; validating that data submitted to RTOG can be supported by material in the institution’s source documentation; verifying that quality control procedures mandated by the Group and by the NCI, especially those related to investigational drugs, are being followed; and confirming that policies designed for the protection of human subjects are in effect.

The RTOG Quality Control auditors are dedicated to providing educational support, not only at the exit interview, but also at any time in the conduct of the Group clinical trials or with preparation for an audit.
SECTION 2

AUDITING COMPONENTS

A. INSTITUTIONAL REVIEW BOARD (IRB)

The purpose of the IRB is to protect the rights and welfare of human subjects of research. Review of IRB procedures are based on the Office of Human Research Protection (OHRP) Guidelines. This review includes the initial IRB approvals for chosen RTOG and CTSU protocols to which you have registered cases. IRB approval must precede any case registration. Documentation of annual re-approvals or renewals within 365 days of the last approval will be checked. Documentation of the review and/or approval of all protocol amendments and safety report submissions within 90 days of broadcast will also be confirmed. If your local IRB policy does not mandate reporting of external safety reports, a copy of the Standard Operating Procedure (SOP) must be present for review at the time of the audit. Each protocol must have annual IRB approval even if it is closed to accrual until the study has been terminated by RTOG (notification by broadcast). Also, a study may be terminated with the IRB if no patients have ever been accrued to the protocol OR if both of the following conditions are met: all patients are deceased and written verification by RTOG that all data and queries have been submitted, reviewed and resolved. The auditor also checks that internal Serious Adverse Events (SAE’s) are reported appropriately per individual protocol requirements.

IRB approvals letters should contain all of the following information:

- The date of the convened meeting and IRB approval.
- The protocol identification (number and title)
- What is being reviewed and approved (initial approval, annual renewal, protocol amendment, SAE, safety report)
- “Approval” or “disapproval.”
- Type of review (full board or expedited)

All institutions should maintain their own copies of IRB approvals and documentation for RTOG protocols even if they utilize the IRB of another institution.

The proper use of the expedited review as per the OHRP guidelines is as follows: an expedited procedure may be used for the continuing review of research previously approved by the convened IRB (1) where the protocol is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions; OR (2) where no subjects have been enrolled and no additional risks have been identified; OR (3) where the remaining research activities are limited to data analysis. OHRP guidelines highly recommend that documentation for continuing reviews conducted under an expedited review procedure include the specific permissible categories justifying the expedited review. The local IRB always has the right to require Full Board approval.
The following descriptive terms as per the Clinical Trials Monitoring Branch (CTMB) guidelines are used in our audit reports.

1. **Delayed Re-approval**: protocol re-approval by the full IRB delayed up to one year.
2. **Expired Re-approval**: protocol re-approval by the IRB delayed for greater than one year (365 days).
3. **Missing Re-approval**: Missing documentation of protocol re-approval (e.g., letter from IRB, IRB minutes, letter without sufficient information, etc.).

You will receive an IRB Review Form with your audit confirmation letter. This form will list all of the protocols which will be reviewed during the site visit.

If the NCI Central Institutional Review Board (CIRB) is utilized as the IRB of record, the following documentation is required to be reviewed at the audit:

- CIRB Acceptance Form
- All copies of CIRB approvals (including the date of the approval just prior to the Acceptance Form)
- All copies of Facilitated Review approval letters.
- Written SOP for facilitated reviews.
- External Safety Report (ESR) submissions or SOP for ESR's.

**B. INFORMED CONSENT CONTENT (ICC)**

The auditor will review each protocol’s IRB-approved consent forms for all components required by Federal Regulations and check that informed consent forms have been revised and include the necessary changes required by protocol amendments. All versions of approved Informed Consent forms must be available at the audit.

Basic elements of the informed consent required by Federal regulations and which shall be provided to each subject include:

1) A statement that the study *involves research*, an explanation of the *purposes* of the research and the expected *duration* of the subject’s participation, a description of the *procedures* to be followed, and identification of any procedures which are experimental.

2) A description of any reasonably foreseeable *risks* or discomforts to the subject.

3) A description of any *benefits* to the subject or to others, which may reasonably be expected from the research.

4) A disclosure of appropriate *alternative procedures* or courses of treatment.

5) A statement describing the extent to which *confidentiality* of records identifying the subject will be maintained.

6) An explanation as to whether any *compensation* and an explanation as to whether any medical treatments are available if injury occurs and what they consist of or where further information may be obtained.

7) An explanation of whom to *contact* for answers to pertinent questions about the research and research subjects’ rights and whom to contact in the event of a research-related injury.
8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time.

C. INVESTIGATIONAL DRUG ACCOUNTABILITY

Investigational drug review will occur if patients have been accrued to any protocol that includes an investigational agent provided by the Pharmaceutical Management Branch (PMB) of the National Cancer Institute and/or an agent provided free of charge from a pharmaceutical company. The consent form must include a statement that the drug will be provided free of charge.

As of February 15, 1983, the NCI has required that the NCI Drug Accountability Record Forms (DARFs) be maintained by all institutions conducting clinical trials with PMB distributed Investigational New Drugs (INDs). This form (Appendix I) is available on the CTEP web site under Drugs/Agents. RTOG has provided individual protocol DARF's that may be used for specific protocols in which the pharmaceutical companies provide the agent. These forms are available on the RTOG web site although the NCI DARF may be utilized for all protocols. You may also use the NCI DARF for these protocols.

Drug accountability includes the review of DARFs, shipment forms, transfer forms, destruction forms and/or return of drug forms. To facilitate the drug portion of the audit, we request that copies of all drug accountability record forms as well as the other above stated forms be provided at the beginning of the audit in order to calculate and match the required dispensed doses for each patient, verify the drug was not used for any other purpose, verify that the DARF is properly maintained and verify commercial drug was not substituted. This will precede the actual visit to the pharmacy at which time the auditor will review the original drug logs, check for storage and security compliance, compare pharmacy shelf count with DARF log count, and check expiration dates of the agents.

If any drugs have been dispensed to a satellite, those records will also be audited as well as the handling procedures. If a dispensing area (other than the central pharmacy) receives a multiple day or overnight storage supply of an IND, a satellite record must be maintained. These satellite records should also be provided at the beginning of the audit.

All unused, unopened, nontransferable agents provided by PMB must be returned to the NCI within 2-3 months of notification of a closed protocol when all patients have completed active treatment and there are no appropriate open protocols to which to transfer the agent. The area in which the drugs are stored should be a separate, secure, limited-access area; and the drugs must be stored at the correct temperature and must be identified by protocol number.

A copy of the PMB Policy and Guidelines for Investigational Agents is found on the RTOG web site under the auditing section.

D. PATIENT CASE ASSESSMENT

The patient case assessment portion of the audit includes six separate components for review: Informed Consent, Eligibility, Protocol Treatment, Disease Outcome, Toxicities/Adverse Events and Data Quality.
The original signed and dated informed consent should be present at the audit for review. Documentation of the consent process should be found in the patient’s chart. If consent is obtained on the same day as the start of treatment, documentation must be in the patient chart that consent was obtained prior to randomization and prior to the start of treatment. A copy of the consent document must be given to the patient.

Source documentation for the patient case review may include any of the following: research charts, inpatient and outpatient medical records, diagnostic reports, lab oratory data, special study reports, pathology and operative reports, radiotherapy and chemotherapy flow sheet and prescriptions, medication logs, dated and signed H&P’s, assessments and progress notes (physicians, nurses, research associates, therapists, etc.) and subject diaries/calendars.

A patient case checklist has been provided for your use (Appendix II).

Please note: Hard copies of all source documentation and electronic medical records **MUST** be provided for an RTOG Audit at the present time. If there is any future change to this requirement, a broadcast will be sent.

Source documentation identified as missing at the time of the audit and requested by the auditor, must be supplied within **one week** of the audit to clarify patient case findings. This grace period only applies to the patient case review. All regulatory (IRB and Informed Consent) and pharmacy review material must be present at the time of the audit.

E. **EXIT INTERVIEW**

At the completion of the audit, the auditor or auditing team will conduct an interview with the facility’s principal investigator and research staff to summarize and discuss the findings of the audit. Time is also given to discuss site performance standards; explain the requirements for response, present recommendations from the auditor or audit team for a corrective action plan; and to answer questions that the staff may pose. This is an **educational time**. It is important to take advantage of this time to seek the assistance of the auditors for ideas and suggestions to improve your program, or to share your suggestions and implemented ideas that can be used at other facilities to improve their programs. This interview provides opportunity for education, dialogue, immediate feedback, and clarification.

If your Principal Investigator cannot possibly be present for the exit interview, his or her representative is acceptable. This representative should be familiar with RTOG policies and procedures. Any and all members of your staff may attend and participate in the exit interview.
SECTION 3

SCHEDULING AND PREPARATION

A. SCHEDULING THE SITE VISITS

In compliance with the NCI’s requirement for periodic on-site audits, any institution which accrues patients to RTOG protocols or CTSU clinical trials is eligible for an audit at least once every thirty-six months. However, all institutions may be audited at any time. New full member institutions are audited within 18 months of membership approval. New affiliates and joint centers will be audited between 18 and 36 months of the date the first case is accrued.

RTOG’s audit team, on a yearly basis, identifies institutions that are candidates for audit. Institutions are selected by date of last visit, previous audit score, geographic location, patient accrual, and/or date of membership activation. All membership categories, full, CCOP, provisional, affiliate and joint centers are selected and audited in the same manner. Institutions will remain eligible for audit even if their membership in the Group is withdrawn or terminated since they have made a commitment to long-term follow-up of patients on study with provision of good quality data according to the study schedule.

When possible, a letter notifying the site that they are eligible for an audit in the upcoming year is sent (Appendix III). The institutions to be visited are contacted by a member of the auditing team at least one month in advance of the visit. Approximately two to four weeks before the scheduled visit, the institution receives a patient case list, a protocol list for the regulatory review and a drug list (if applicable) along with a confirmation letter (Appendix IV) with instructions for preparation. Unannounced cases will be identified for review when the auditor arrives at the institution. While most cases are selected from accruals since the last audit, all cases are eligible for selection. Correspondence is sent electronically. It is important to keep RTOG headquarters informed of current e-mail addresses and any and all changes in contact information to assure this important audit information is received.

In most instances, the on-site audit will take place in one day; however, full members/large CCOP’s and institutions with exceptionally large accrual may require 2 to 3 days. The audit team is composed of one or more RTOG Quality Control auditors. On selected audits, a physician auditor, a CTSU auditor, or an NCI representative may accompany the auditor(s). The RTOG Quality Control auditors are responsible for planning and conducting the audits as well as preparing all audit reports for submission to the NCI. This ensures uniformity in the audit process and in report preparation.

B. PROTOCOL AND PATIENT CASE SELECTIONS

A list of all patient cases and their respective protocols to which patients have been accrued since an institution’s activation or last audit are obtained from the RTOG database. This list is used to predict the length of the audit (1, 2 or 3 days). The list of patient cases to be audited is randomly selected. Our policy is to include as many different protocols and disease sites as possible. The selection is primarily random; however, patient cases in which eligibility is pending are automatically included.
Protocols and patient cases which have been randomized through the CTSU are selected by a CTSU staff member.

An audit packet is then prepared. This packet consists of printouts from your submitted data. Also included are any unanswered queries that you have received from our Data Management department. Individual protocol requirements such as eligibility criteria, mandatory pre-tests, and treatment and follow-up schedules are also included. Protocol activation dates, amendment, update, safety report and broadcast dates as well as NCI approved consents also make up part of our audit packet.

C. INSTITUTIONAL PREPARATION

The best time to begin preparing for an audit is just prior to registering a patient to a study. Confirm that your IRB has approved the protocol prior to registration. Confirm that the patient has signed the IRB approved consent form (making sure it is the correct, most updated version). Verify that all eligibility criteria have been met, all required pre-tests have been completed within the protocol directed time frame, treatment is provided directed in the protocol, adverse events are documented accurately and reported, follow-up evaluations are completed and documented, and data is accurate and submitted on time.

Schedule or reserve a conference or meeting room that provides a quiet, well-lit, spacious work area for the auditor or audit team.

Confirm that all primary source documentation is available to verify all information pertinent to each protocol and patient case. Order department charts, medical records, diagnostic reports, etc. as soon as you receive your case list. If the original medical records are not available, legible copies may be used. Remember, RTOG data forms are not considered primary source documentation.

Notify the IRB Chairperson that your site is scheduled for an audit so that if IRB minutes are needed, they can be available. Schedule a time with your Pharmacist so that all Investigational Agent records and storage areas can be reviewed.

If your institution stores study information on a computerized database or has an electronic medical record, hard copies must be provided and available at the beginning of the audit.

It is not necessary for any member of your research team to sit with the auditor(s) during the review. A member of your team should be available at intervals during the visit to answer questions or locate source documentation.

There is no RTOG requirement regarding the organizational system for your research charts. The more organized your source documentation is when you first register and follow your patients, the less time you will need to prepare for an audit.

If you know of a particular deficiency or problem that occurred in a patient case or with your IRB, pharmacy, etc., let us know prior to the audit or upon arrival to save time and, more importantly to allow sufficient time for discussion of recommendations to prevent repeated deficiencies.
SECTION 4

SCORING AND COMPLETING THE AUDIT

A. AUDIT SCORES

All Cooperative Groups, Community Clinical Oncology Program (CCOP) Research Bases, and CTSU use a common set of terms or examples of MAJOR and LESSER deficiencies, a common system for assessing each component of an audit, and a standard audit report format using the Clinical Trials Monitoring Branch (CTMB) Audit Information System. A lesser deficiency is one that is judged to not have a significant impact on the outcome or interpretation of the study. Multiple lesser deficiencies may be treated as a major deficiency in determining the final assessment of an audit.

The scoring of an audit is divided into three major components: the regulatory (IRB/ICC), drug accountability and patient case findings. Each of these three components are independently assigned an assessment of either Acceptable, Acceptable Needs Follow-Up, or Unacceptable.

- **Acceptable**: No deficiencies identified; compliance with all regulatory and investigative drug assessments; few lesser deficiencies identified; major deficiencies or non-compliance items identified during the audit that were addressed and/or corrected prior to the audit for which documentation exists and no further action is required.

- **Acceptable Needs Follow-up**: Multiple lesser deficiencies identified, major deficiencies identified during the audit not corrected and/or addressed prior to the audit.

- **Unacceptable**: Multiple major deficiencies and/or non-compliant categories identified; a single major flagrant deficiency found; excessive number of lesser deficiencies identified; multiple lesser deficiencies of a recurring nature found.

- **Unacceptable, Requires NCI Follow-up**: Audit findings reveal suspected scientific misconduct, findings suggestive of scientific misconduct, fraud, or intentional misrepresentation of data and/or disregard for regulatory safeguards. Immediate NCI and/or OHRP notification is required.

Unacceptable scores in any and all components require a re-audit within twelve months. If a participating institution is deemed unacceptable for the same audit component on two consecutive audits, the institution will be placed on probation and a site plan must be developed and provided for submission and approval of the NCI’s Clinical Trials Monitoring Branch (CTMB). If improved performance is not documented at the time of the second re-audit, the institution may be terminated from the Group.
B. THE FINALIZATION PROCESS

When the auditor returns to RTOG headquarters after a site visit, the audit report is entered into the NCI Audit Information System (AIS) Database. This begins the finalization process. A copy of this audit report, along with a formal cover letter, is sent electronically to the Principal Investigator (with a copy to the Data Manager of record). This letter now includes a detailed list of deficiencies that require follow-up (Appendix V).

The institution’s response (if required), a corrective action plan is due at RTOG headquarters within two weeks after receiving a copy of the final audit report. The Corrective Action Plan (CAP) should be started as soon as the audit is complete as all deficiencies have been disclosed at the exit interview. Also, any required revisions of submitted forms or IRB approval letters should be sent along with the corrective action plan.

The institution’s response is reviewed by the Senior Quality Assurance Auditor and, if complete, is submitted to the NCI for their review and approval. The NCI may request additional information or a more detailed action plan. If so, the site will be notified for a second response or addendum.

Based on the October 2006 Cancer Trials Management Branch (CTMB) Guidelines, if an audited institution fails to provide a corrective action plan for one or more audit components rated as “acceptable needs follow-up” or “unacceptable” within the required time limit, the following actions will be imposed by RTOG:

1) Written notice will be provided to the Principal Investigator at the institution that the response/corrective action plan is overdue and a five working day grace period will be granted for the submission of the response.

2) The Group will immediately suspend patient registrations from that institution if the response or complete corrective action plan is not received during the five day grace period,

3) All new patient registrations will be suspended from both the Full Member/CCOP and the affiliate/CCOP component if the audited institution is an affiliate of a Full Member institution or a component of a CCOP.

A report of all audit site visits and results are provided to the RTOG Quality Control Committee at each RTOG semi-annual meeting.

C. CORRECTIVE ACTION PLAN

A Corrective Action Plan (CAP) is a prospective plan to describe the process to prevent the identified deficiencies from recurring. Submitting revised forms or delinquent IRB approval letters to RTOG headquarters may be required, but they alone do not constitute a Corrective Action Plan. All major deficiencies or multiple lesser deficiencies must be addressed individually. This response must be dated, on institution letterhead, and signed by the principal investigator. This Corrective Action Plan must be acceptable, both to the RTOG auditing staff and the NCI. We have developed a sample copy of a corrective action plan (Appendix VI).
D. MAIL AUDITS

Mail audits are usually conducted for institutions that have resigned from RTOG membership AND have accrued only one or two patient cases since the last audit AND there have been no patients accrued to protocols with NCI/PMB supplied agents. At the RTOG auditing team’s discretion, a mail re-audit may be conducted on an active member. The institution will be notified when the mail audit will be conducted. The audit information will be mailed to the site listing a DUE DATE. This date is usually one week prior to the date of the audit. This audit date is entered into the NCI database as the date that the audit will take place at headquarters. Copies of required IRB, informed consent and patient chart documents must be mailed to RTOG headquarters. The RTOG suggestion is to send the requested information earlier than the due date in case there are additional documents that are needed to complete the audit and meet the deadline.

E. CTSU AUDITS

Sites which have enrolled patients through the Clinical Trials Support Unit, (CTSU) are also eligible for RTOG audits. CTSU works with RTOG to select CTSU cases and specific data items that will be audited. If less than 3 CTSU patients are selected for an audit, RTOG auditors will conduct the audit by including these patients in their case list. If three or more CTSU patients are selected for an audit, CTSU auditors may accompany the RTOG auditor (or team) to review the CTSU cases. The regulations, guidelines and requirements do not differ from those of any cooperative group auditing standards.
## APPENDIX I

### Drug Accountability Record Form

<table>
<thead>
<tr>
<th>Line No</th>
<th>Date</th>
<th>Patient's Initials</th>
<th>Patient's ID No.</th>
<th>Dose</th>
<th>Quantity Distributed or Received</th>
<th>Balance Forward to Dispenser</th>
<th>Manufacturer and Lot No.</th>
<th>Recorder's Initials</th>
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</thead>
<tbody>
<tr>
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<td>02/14/94</td>
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<td>0412</td>
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</table>
APPENDIX II

RTOG SITE VISIT PATIENT CASE CHECKLIST

Study Number
Case Number
Patient Name

CONSENT
- Was the consent protocol-specific?
- Was the consent the current IRB-approved version?
- Has Informed consent been signed and dated by patient?
- Was consent signed prior to protocol entry?
- Was consent signed prior to protocol treatment?
- Is consent timed if protocol entry and treatment occurred on the same date as consent?
- Are all required signatures present?
- Is consent process documented?

ELIGIBILITY
- Do all elements in Sections 3, 4 and 11 have primary source documentation (including performance status score)?
- Are there copies of all pre-treatment lab results?
- Are there copies of pre-treatment radiographic reports?
- Is there a copy of the pathology report?

PROTOCOL TREATMENT
- Was treatment provided as per protocol?
- Is the radiation treatment record complete?
- If applicable, were treatment times recorded?
- Are the patient's height, weight and body surface area recorded?
- Are there drug administration records for each cycle of chemotherapy?
- Are copies of the required blood tests available?
- Is there source documentation to verify toxicities?
- Are copies of subsequent operative reports and pathology reports available?
- Have required pre and post-operative assessments been completed?
- Was any non-protocol treatment given?

DISEASE OUTCOME/RESPONSE
- Is the follow-up current?
- Is there source documentation that corresponds with the dates of follow-up reports?
- Are there copies of all pertinent lab and radiographic reports?
- Are all films that evaluate tumor status available for review?

TOXICITY/ADVERSE EVENTS
- Can all reported toxicities be verified?

DATA QUALITY
- Is all submitted data accurate?
- Is all data submitted on time?
December 15, 2009

RTOG Member PI, M.D.
RTOG Member Institution (#9999)
1818 Market Street
Yourstown, USA  19103

Dear Dr. ___:

As part of the NCI and RTOG Quality Control requirements, your institution is due to be audited in 2010. An RTOG auditor will contact you to schedule your audit.

The primary purpose of these NCI-mandated visits is to verify the accuracy of the data submitted to RTOG Headquarters. In addition, consent/IRB procedures and the management of investigational drugs will be evaluated for compliance with NCI and OHRP regulations. Additionally, we hope you find this experience to be educational.

Prior to your institution’s audit, we will provide you with the list of cases to be surveyed and instructions regarding the materials to be prepared.

Thank you for your participation in RTOG.

Sincerely,

Elaine M. Boyle, R.N.
RTOG Senior Quality Control Auditor

cc:   Member RA
      L. DiFerdinando (CTSU)
      W. Curran, M.D.
      R. Rabinovich, M.D.
      RTOG Auditor
December 15, 2009

RTOG Member PI, M.D.,
RTOG Member Institution (#9999)
1818 Market Street
Yourtown, USA 19103

Dear Dr.______:

This is to confirm that the NCI-mandated RTOG Quality Control Committee Site Visit is scheduled for (add date) 2009. The auditor will arrive between 9:00 and 9:15 am.

The surveyor will be, R.N. from RTOG Headquarters. Attached is your audit packet. The link to the RTOG Institution Audit Manual can be found on the RTOG web under Memo Info - RA corner then Item# 10 - Institutional Audit Manual.

The audit will consist of three components: Regulatory, including IRB and informed Consent reviews; Pharmacy review for NCI supplied agents, as well as Corporate Pharmaceutical supplied agents (if applicable); and Patient Case Reviews.

The regulatory component of the audit will be comprised of a review of your initial IRB approvals, annual renewals, amendment approvals, submissions of safety reports, and internal SAE’s. Copies of Informed Consents will be reviewed.

The Pharmacy reviews (both NCI supplied agent and Corporate supplied agents) will include a visit to the Pharmacy. Please arrange for copies of all DARF’s shipment forms, transfer forms and return of drug forms to be available for the auditor to review before the visit to the Pharmacy. Please notify the pharmacist of the visit.

Materials necessary for the patient case review include but are not limited to the following:

1. Signed and dated Informed Consent Form
2. Inpatient and outpatient medical charts.
3. All diagnostic reports, laboratory data, special study reports and consults.
4. Pathology and operative reports
5. Radiation and chemotherapy flowsheets, medication logs
6. Dated and signed H&P’s, assessments and progress notes (physicians, nurses, therapists, research associates, etc)
7. Subject diaries/calendars

Hard copies of all source documentation and electronic medical records must be present at the audit.

Upon completion of the site visit, the surveyor will meet with you to discuss his or her findings.

If you have any questions regarding the site visit or the material needed, please feel free to contact the auditor at RTOG Headquarters at (add auditor telephone number).

The auditor will be available by cell phone only on the day prior to your audit as well as the day of your audit for any pressing issues or questions; (add auditor name), R.N. (cell phone #).

Sincerely,

Elaine M. Boyle, R.N.
RTOG Senior, Quality Control Auditor

cc: Inst. RA
    W. Curran, M.D.
    R. Rabinovitch, M.D.
    RTOG Auditor
November 18, 2009

Overall Evaluation:
Acceptable With Follow-Up

Dr. #
Inst. and Address

Dear Dr.:

I have reviewed the data from the institutional audit performed on February 24, 2009. In tabulating the results, I found the Informed Consent review fully acceptable. There were no major deficiencies found in the IRB, Pharmacy and Patient Case Reviews. These deficiencies are described in the enclosed audit report.

A Corrective Action Plan is required from your institution describing the procedure your staff will follow to eliminate future deficiencies.

IRB assessment:
- Late protocol amendment approvals.
- Late annual renewals

Pharmacy:
- NCI drug accountability form not used for investigative agents.

Patient Case Review:
- Lack of documentation of all eligibility criteria.

Required follow-up for each of the points listed above is due **within 2 weeks** of receiving this audit report to be sent to RTOG headquarters to the attention of

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*Note: The footer text is not relevant to the main content.*
Elaine M. Boyle, R.N. Electronic submission is encouraged, if possible (eboyle@phila.acr.org). This corrective action plan should be on official letterhead and signed by Dr Kumar.

Your site will be scheduled for an audit again within 36 months.

Thank you for your continued support of and participation in RTOG.

Sincerely,

Elaine M. Boyle, R.N.
RTOG Senior Quality Control Auditor
1818 Market Street Suite 1600
Philadelphia, PA 19103
215-574-3161
Fax: 215-574-0300
eboyle@acr-arci.org

cc: RA
    W. Curran, M.D.
    R. Rahmovitch, M.D.
APPENDIX VI

SAMPLE CORRECTIVE ACTION PLAN

Elaine M. Boyle
Radiation Therapy Oncology Group
1816 Market Street, Suite 1600
Philadelphia Pa 19103

Dear Ms. Boyle:

RE: Audit Report

I would like to thank you for your efforts in the audit of our Clinical Trials Protocol Office and would like to reply to this Audit of April 2, 2008. Our corrective action plan is as follows.

IRB Review:
- Untimely and missing protocol amendment approvals:
  The Clinical Trials Protocol Office will implement a new amendment tracking system to insure the timely completion and follow up of amendments. The supervisor of the Clinical Trials Protocol office will be responsible for this new amendment tracking system ensuring that all amendments are processed in a timely fashion. Then any deviations incurred due to the IRB review will be handled.
- Missing safety reports:
  The IRB does not require or mandate the reporting of external safety reports within 90 days. Documentation of their SOP is enclosed which describes our policy that all external safety reports are submitted/reviewed by the PI within 90 days and to the IRB for review as indicated in the SOP.

Informed Consent Review:
- Missing required component in the Informed Consent form:
  There will be a new process implemented using a two person approach during consent processing. The supervisor of the Clinical Trials Protocol Office will review the pertinent details, note any changes necessary then process the consents. This will then be reviewed by the CRA in charge of each trial to ensure all items are included in the consent.

Pharmacy Review:
- Systematic incorrect DARF entries:
  Investigational pharmacist will educate and demonstrated to all appropriate staff the proper method of DARF completion.
- Storage/security non-compliant:
  Investigational pharmacist will educate and provide PMB guidelines to all appropriate staff.

Patient Case Assessment:
- Eligibility criteria not met or not documented:
  All eligibility criteria will be double-checked by 2 Protocol Office staff prior to randomization
- Delinquent data submission:
  The supervisor of the Clinical Trials Protocol Office will use a flow chart database to ensure that documents are processed timely to eliminate any delay.

Signature
Principal Investigator