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1  Introduction

This document describes the policies of the Radiation Therapy Oncology Group (RTOG) on complying with the National Institutes of Health (NIH) Final Statement on Sharing Research Data, released February 26, 2003.

RTOG is an NCI funded Cooperative Group conducting clinical trials in cancer research. Each RTOG study has a formal protocol document, which includes a statement of the objectives of the study. Patient consent and Health Insurance Portability and Accountability Act (HIPAA) authorization are obtained to collect the individual patient data required for addressing the study objectives. Data from study forms are sent from the treating or enrolling institution to the RTOG Statistics and Data Management Center (SDMC), where it is processed, entered into the RTOG database, and validated. The Data may be submitted on paper or electronically. Not all information submitted on paper becomes part of the electronic database. Digital radiation therapy data is sent from the treating or enrolling institution to the Image-Guided Therapy Center (ITC) at Washington University in St. Louis, Missouri where it is processed and accessed by the SDMC. The electronic database is used as the basis for the analysis of RTOG studies, with the analyses performed by the RTOG SDMC.

The procedures described here do not cover requests from the National Cancer Institute (NCI), Food and Drug Administration (FDA) or other federal agencies for information required by federal regulations or by the terms of the RTOG grant awards. Such requests do not require internal review or approval, and will be honored as expeditiously as possible.
This document also does not cover requests for collection of additional data. Requests for additional data usually require Institutional Review Board (IRB) review at each participating site and may require obtaining additional patient consent and/or authorization. Consequently, the information obtained is often incomplete. Retrospective collection of data is expensive and time consuming and therefore rare.

The data requested by an investigator may include data generated from RTOG laboratory correlative studies. However, only requests for existing data are covered by this document. Requests for use of tissue and/or other biospecimens are covered by a separate review procedure that is compliant with National Cancer Institute Group Banking Procedures. Instructions and a request form are available at www.rtog.org/tissue/main.html.

2 Request Procedures

While most analyses of RTOG studies are performed at the RTOG Department of Statistics, RTOG also makes research data available to other investigators (i.e., those conducting research outside the RTOG) as required by the policies of the NIH. An investigator who wishes to use “final research data,” as that term is defined by NIH, from one or more RTOG studies must make a formal request which is reviewed by the RTOG Publications Committee. Specifically the scientific merit and feasibility of each request will be evaluated. In accordance with NIH guidelines requests will only be considered once the primary study analyses have been published. Any release of data will take into consideration individual patients’ rights to privacy as well as the source of funding. Use of data from a phase III study, prior to general release of the data by the RTOG Data Monitoring Committee (DMC), requires approval of the RTOG DMC.

Most data requests involve only electronic records. Issues relating to requests for data available only in the paper records are discussed in Section 3.

There are several different types of requests that can arise. Different review procedures apply to different types of requests.

2.1 Requests from Statistical Centers of Other Cooperative Groups

Requests for data only on cases registered by the requesting group on RTOG-coordinated Intergroup studies. These requests are automatically honored, and no review is required, although a brief proposal (approximately 2 pages) indicating the project objectives and analysis plan must be submitted to the RTOG Group Statistician and the RTOG Publications Committee (RTOG_Publications@phila.acr.org). RTOG does reserve the right to limit the frequency of such requests, and release of data from phase III studies is subject to review by the RTOG DMC. The requesting group’s IRB approval is assumed to cover the use of the data. No fees will be assessed as long as the requesting group has a reciprocal policy.

Requests for data on cases entered from groups other than the requesting group. These requests are processed as described in Section 2.2 below.

2.2 Requests for Data for Use in Health Related Research Projects

To request existing data for use in health-related research projects, a brief proposal (1 to 2 pages) must be submitted using the Request for Data by Non-RTOG Investigators form available at http://www.rtog.org/publications/main.html. The proposal must indicate the objectives of the project and briefly describe how the project will be conducted, including a summary of the statistical analysis plan. The proposal must state which cases are to be included in the data set, e.g. list the study numbers and describe any exclusion criteria, and
state the data elements required. Proposals should be submitted to RTOG Publications at RTOG_Publications@phila.acr.org.

The proposal will be reviewed by the appropriate RTOG disease site chair, the senior statistician for the disease site, and the RTOG Publications Committee. The RTOG Publications Committee will review the recommendations from the disease site chair and the responsible senior statistician. All reviews will consider the scientific merits of the project, whether there is sufficient data to provide adequate information for analysis, the availability of the required data, and the potential costs.

Investigators will be notified of the final decision in writing, and provided with an estimate of potential fees, if appropriate. Release of the data is subject to the conditions stated in Section 5.

2.3 Requests for Data to Illustrate Statistical Methodology

Requests for data sets to use for illustration of statistical methods in papers intended for publication in the statistical literature should be submitted in writing to the RTOG Group Statistician and the RTOG Publications Committee (RTOG_Publications@phila.acr.org). A brief proposal describing the nature of the project and the data required should be provided. If the data set has previously been used for illustrative analysis in statistical papers, and the data set appears to be appropriate for the project, then the Group Statistician can approve the request without further review. Release of the data is subject to the conditions stated in Section 5. Typically no fees will be assessed for use of an existing data set. If the data have not previously been used in a statistical paper, then the request will be reviewed by the RTOG Publications Committee, as described in Section 2.2.

2.4 Grants and Protocols

Special projects, especially but not limited to laboratory correlative projects, sometimes involve submission of grant applications for separate funding. Grants submitted with requests to use data or tissue from RTOG cases must be reviewed by RTOG Clinical Trials Administration prior to submission and may only be submitted with RTOG’s approval. Such projects may involve sending clinical data to other locations, such as to the institution performing the lab work, for analysis. If the specific data required and a summary of the analysis plans were clearly described in the grant at the time of RTOG review, and RTOG and the funding agency have approved the grant, then data requests for these projects will be approved without further review. The release conditions in Section 5 still apply. If the data requested or the planned analyses go beyond what RTOG had agreed to at the time the grant was reviewed, then the request must be reviewed by the RTOG Publications Committee, as described in Section 2.2 above.

Similar considerations apply to specialized analyses written into RTOG protocols. It may sometimes be necessary to send data outside the RTOG SDMC for these analyses. As long as the details, including the location where the work is to be performed, the data needed for analysis, and a summary of the analysis plan, have been included in the protocol, and provided the protocol has received all required approvals, then further review of the data request is not needed. The release conditions in Section 5 still apply.

2.5 Pharmaceutical Companies

Data provided to pharmaceutical companies is generally for regulatory rather than research purposes. Provided that a contract has been executed covering the request, further review is not required. Data may also be made available to pharmaceutical companies for planning purposes, with the approval of the RTOG leadership and RTOG DMC, if necessary.
3 Data Abstractions

It will sometimes be the case that all data requested for analysis will not be entered into the RTOG database but will be available in the paper case report forms at the RTOG headquarters. In this case, the data must be abstracted from the case report forms. Data abstractions can only be performed if both adequate funding to support the abstraction and adequate staff are available.

One option is that the investigators or their representatives or contractors could perform the abstraction at the RTOG headquarters. Some funding for clerical support at the headquarters may be required. While it would also be possible to copy the case report forms and send them to the investigator, the case report forms necessarily contain potentially identifiable patient data, so this creates a considerably higher risk to patient confidentiality. RTOG therefore will not send copies of paper case report forms to other locations. In the rare cases where this might be considered, more stringent regulatory approvals and data use agreements will be required.

4 Regulatory Considerations

All research use of data collected on human subjects from Cooperative Group studies is subject to applicable Office of Human Research Protections (OHRP) regulations and to applicable regulations of the Privacy and Security Rules of the Health Insurance Portability and Accountability Act (HIPAA). Generally, patients have only consented to have their health information used for the objectives of the clinical trial in which they participated. Use of the data for other research projects is allowed only if an IRB has determined that use of the data in the project meets the minimal risk criteria for conducting the research without the patients' consent, if the use of the data in the project is exempt from consent requirements, or if the project does not constitute human subjects research. The required level of review or approval will generally depend on the degree to which the data have been rendered fully anonymous, de-identified, or coded. Guidance on these matters can be found in the OHRP document “Guidance on Research Involving Coded Private Information or Biological Specimens” (http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf) and at the NIH HIPAA Privacy Rule Information for Researchers site (http://privacyruleandresearch.nih.gov/clin_research.asp). The criteria for de-identification of data under HIPAA are given in the Code of Federal Regulations, Part 46, Section 164.514. It should be possible to conduct most projects using coded data (as described in the OHRP Guidance) that meet the criteria for a limited data set that can be released under a data use agreement (as described in Part 46 of the CFR, Section 164.512 and in the NIH HIPAA guidance documents), without obtaining additional patient consent or authorization.

The RTOG Department of Statistics is overseen by the Institutional Review Board (IRB) of the American College of Radiology. The ACR IRB requires that documentation be provided that the investigator’s local requirements for conducting the research have been met prior to releasing the data. Usually this consists of one of the following:

a) An approval or waiver from the local IRB for conducting the research without obtaining the patients’ consent.

b) Documentation of an exemption issued by their local IRB (note, it is generally up to IRB officials, not individual investigators, to determine if research is exempt).

c) A statement from a local IRB official that the project does not constitute human subjects research (for example, because of anonymization or de-identification), and therefore does not require review.
For research projects using only data from existing databases (that is, with no additional patient contact or data collection), it is usually possible to obtain a waiver through an expedited review, but that is subject to the policies of the local IRB. Generally b) and c) are only appropriate if the data set to be provided can be fully de-identified. Data sets that contain no identifiable information and no patient specific dates may qualify as de-identified.

5 Release Conditions
Release of data for research purposes is subject to the following conditions. RTOG may require a signed letter of agreement or a formal data use agreement covering the relevant conditions.

a) Investigators must agree to use the data only for the approved research project. If the investigator later wishes to use the data in a new project, a new proposal must be submitted.

b) Investigators must agree to keep the individual patient data confidential. The data may only be shared within the team conducting the analysis project. Requests from other individuals for access to the data should be referred to RTOG.

c) The regulatory requirements discussed in Section 4 must be met.

d) Applicable fees must be paid.

e) Copies of all manuscripts arising from the project must be sent to RTOG Publications at RTOG_Publications@phila.acr.org. Approval of the manuscript is not a condition for use of the data, however.

f) There is no expectation of RTOG representation on the authorship unless members of RTOG have made substantial contributions to the project.

g) Release of data collected in a clinical trial conducted under a binding collaborative agreement between the NCI Cancer Therapy Evaluation Program (CTEP) and a pharmaceutical / biotechnology company must be in compliance with the terms of the binding collaborative agreement and must be approved by CTEP and the company. Release of the data is also subject to the terms of any contracts between the Group and other entities, which cover any of the requested data.

h) In releasing the data, the Group makes no representations and extends no warranties of any kind, either expressed or implied. There are no expressed or implied warranties of merchantability or fitness for a particular purpose, or that the use of the data will not infringe any patent, copyright, trademark, or other proprietary rights. No indemnification for any loss, claim, damage, or liability will be intended or provided.

6 Fees
Routine costs associated with preparing standard data sets are viewed by NCI as covered by the RTOG grant. For complex data sets where substantial work is involved, fees may be charged for preparing and documenting the data set. Any fees will be limited to the actual time, effort, and materials required for preparing and documenting the data set.

7 Appeals Process
If a request for data is denied, the applicant may appeal the decision. The appeal will be reviewed by the Group Chair or his/her designee, the NCI’s program officer and an outside statistician. The statistician will be named jointly by the Group Chair and the program officer.