

**Research Compliance Assistance Program
Pediatric Clinical Translational Research Center (CTRC)
(UCHSC & TCH)**

Staged Assistance Plan

I. Rationale

The Research Compliance Assistance Program (RCAP) is designed to assist CTRC-supported investigators achieve compliance with State and Federal regulations and guidance, and good research practice standards. The focus is upon assisting investigators in conducting research and documenting their compliance activities in such a way that should an investigator undergo an audit by local or national entities the investigator will be found to have been in compliance with all applicable regulations and standards. The program is structured such that assistance can range from minimal to significant depending upon the needs of the investigator and the type of protocol.

II. The Role of the Research Subject Advocate (RSA)

NCRR guidance specifies that the CTRC Research Subject Advocate (RSA) will be responsible to facilitate compliance with applicable regulations and standards in the conduct of all research supported by a CTRC. In the Pediatric CTRC this is not interpreted to mean that the RSA has the responsibility to police regulatory or standards compliance but rather to provide the assistance, resources and expertise necessary for the investigator to achieve compliance with the applicable regulations and standards. The RSA, however, must document that protocols are compliant with the applicable regulations and standards.

III. Levels of assistance

The aim of the program is not to duplicate the efforts of others charged with compliance enforcement or to create another layer of oversight of clinical research but rather to document that the existing requirements are met and the oversight is being conducted. Thus, there will be several levels of assistance which are available across a range of activities.

1. Exempt Status:

This level of assistance is aimed at protocols which have been approved by the COMIRB as consent-exempt which generally will not require the sort of compliance assistance provided by this program.

2. Minimal assistance:

This level of assistance is aimed at protocols that have significant oversight activities in place for the protocol. Included in this level are protocols with industry sponsors who hold INDs, or are conducting a phased clinical trial, and, have formal monitoring bodies empanelled. Also included are foundation- and NIH-funded research which have independent Data and Safety Monitoring Boards (or equivalent) for a single- or multi-site study. Also included are studies without industry, foundation, or NIH support for which the investigator has arranged for an independent DSMB for the study.

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This includes any protocol monitored by the Pediatric Coöperative Data and Safety Monitoring Board.

The National Institutes of Health is increasing its vigilance with regard to investigator adherence to its 1998 guidance regarding Data and Safety Monitoring. It is now mandatory that all NIH-supported protocols contain a Data and Safety Monitoring Plan. For protocols monitored by a Data and Safety Monitoring Board specific information must now be contained in the DSMP. This information must provide details about the following: 1) the identity of the entity or group constituting the DSMB, 2) the composition of the DSMB, 3) the frequency and character of the meetings, and 4) the format of the meeting. Greater detail regarding these items is contained in the guidance, *Information for Investigators – Minimum Assistance*.

Assistance provided and documentation required:

Upon application for CTRC support, the RSA will communicate with the investigator and provide guidance in the formulating and writing of a DSMP for the protocol, or assistance in documenting that a plan exists in a form different from the CTRC format. The RSA will assist the investigator in identifying the documentation that he/she must obtain and provide to the CTRC which details any monitoring entities associated with the protocol, members' names, meeting schedule and reports to be provided to the CTRC on an on-going basis. The RSA may provide other types of assistance requested by the investigator as feasible.

3. Intermediate Assistance:

This level of assistance is aimed at protocols which have only minimal or no contact with human subjects and do not meet any of the criteria of the minimal assistance level and pose little if any risk to the subjects. Protocols included in this level may, for example, involve the collection and de-identified use and storage of tissue and fluid samples, or questionnaire data, or accessing data collected for clinical purposes.

Assistance provided and documentation required:

Upon application for CTRC support the RSA will provide guidance to the investigator in formulating and writing the DSMP for the protocol. In addition, the RSA will communicate with the investigator about labeling conventions for storing samples, databases for storing protocol data, design of source documents and regulatory binders (if applicable). The RSA will provide other assistance as requested by the investigator as feasible.

4. Significant Assistance:

This level of assistance is aimed at protocols which have more than minimal contact with human subjects but do not meet the criteria for minimal assistance. This level will include many investigator-initiated studies.

Assistance provided and documentation required:

This level of assistance is designed to provide the practical and logistical support that is vital to the successful conduct of investigator-initiated studies. This includes support in achieving regulatory and standards compliance. Examples of the type of assistance that has been provided to investigators to date include: assistance in setting up regulatory binders and research databases, designing source documents, development of standard language, advice and assistance in writing HIPAA authorization and informed

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consent forms, formulation of Data and Safety Monitoring Plans, advice on protocol amendments, and methods for enhancing human subject protection. The RSA may also assist investigators in resolving documentation and protocol issues raised by outside entities.

Generally, the RSA (or designee) will meet with the investigator upon approval by the SAC for CTRC support to assist in the protocol initiation. This will, in large, part include the operationalizing of protocol provisions relevant to the safety of subjects and the integrity of the data. The RSA (or designee) will meet with the investigator again at 3 months post-CTRC-approval or after enrollment of 10% of the research participants (whichever occurs first). At this time the RSA and investigator will evaluate how well the initial protocol initiation assistance has worked and formulate operational changes or changes to the protocol that may be necessary. The RSA will complete a compliance assistance checklist at the protocol initiation meeting and the 3 month visit which will serve as documentation that the protocol is compliant with the applicable regulations and standards. Subsequently, this checklist will be completed on a yearly basis, contiguous with the deadline date for COMRIB continuing review submission. At any time, investigators may (and are encouraged to) seek additional assistance from the RSA in addressing compliance or good research practices issues and concerns.

IV. Procedures for addressing deficiencies in compliance to regulations or adherence to good research practice

1. Deficiencies discovered by the RSA which do not qualify as regulatory non-compliance, and, do not involve research subject safety:

The RSA will provide investigators with recommendations, where applicable, for improving compliance activities and research practices. Further, every effort will be made to identify or provide all the available resources and expertise to accomplish the recommended improvements.

2. Deficiencies discovered by the RSA which qualify as regulatory non-compliance, or, involve research subject safety:

The RSA will clearly identify and articulate any areas of non-compliance or deficiencies in human subject protection for the investigator and assist the investigator in formulating a plan to correct deficiencies. The RSA will also advise the investigator on how to proceed with informing COMIRB or other oversight/funding entities if applicable. If the investigator fails to act to correct deficiencies in a timely and appropriate manner, the RSA will consult with the CTRC Program Director to discuss the appropriate course of action.

Rationale and aims of the program:

I have chosen this particular approach for several reasons.

1. It takes seriously the NCCR guidance that the RSA is “to facilitate” and not police regulatory compliance.
2. It does not duplicate the provisions in place for studies which have adequate or excellent oversight and monitoring. Investigators involved in such studies

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will have very little more to do on account of this program. In fact, these investigators are already providing the documentation required as part of their DSMPs. We will need to step up efforts in obtaining more timely DSMB reports.

3. Likewise, the program will require very little additional work for investigators involved in studies which have little or no invasive human subject contact. These would include our cord blood studies. Much of the compliance work would be done up-front by way of assisting the investigators in setting things up adequately.
4. This approach focuses upon the types of studies which, historically, have caused investigators and institutions the largest compliance difficulties. In the Peds CTSC these investigators are already receiving more of my attention but in a retrofitting fashion. Many of these protocols are being monitored by our DSMB.
5. This approach also serves a strong education aim for inexperienced investigators. There is more intensive assistance at the initiation of the protocol, a close follow-up interval, and then yearly continuing review all of which, hopefully, will assist these investigators in developing good compliance and research practice habits which will, ultimately improve the quality and impact of their research.
6. This approach incorporates (but does not duplicate) Research Institute activities.