Clinical Research Informatics Policy

Number: **CRI.POL-003**	**Title: Clinical Research Informatics Data Management Lifecycle (DMLC)**	
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1.0 Purpose

This policy specifies and establishes the procedural controls for the Data Management Lifecycle (DMLC), i.e., the operations performed on research data from origination to disposal. The DMLC is one of the core process areas covered by the CRI Quality Management System (QMS) established by CRI QMS policy CRI.POL-001. The DMLC is critical to meeting the CRI mission -- to support knowledge generation toward improvement in human health and well-being through provision of data, information systems, and related services to clinical investigators and research teams. Together the Software Development Lifecycle (SDLC), the DMLC encompass the processes that achieve the CRI manifesto.

(1) Data are handled in a manner compliant with applicable laws, regulations, and other requirements including research contracts and that privacy and confidentiality are maintained;

(2) Data are available when needed for use such as management of study operations, in human subject protection, and institutional oversight;

(3) Data are capable of supporting study conclusions and other intended decision-making;

(4) Data are documented sufficiently to support reuse, research reproducibility, and replication; and

(5) Software and other computer programs developed or offered by CRI function as intended or as specified.

It is not uncommon for data lifecycle to span decades. Data often originate or are processed outside the controls of the CRI QMS. The goals of compliant, safe, rigorous, and reproducible research must be met regardless of the data source or location of data processing. Doing so requires implementing appropriate controls across the data lifecycle. This policy specifies these controls.

2.0 Scope

This policy applies to all new research-related endeavors for which data are managed by Clinical Research Informatics (CRI) at the University of Texas Health Science Center San Antonio (UTHSA). The DMLC spans from origination to archival or disposal of data.

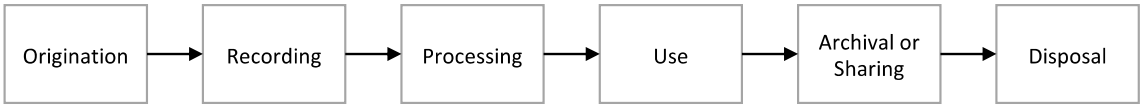

Figure 1: Research Data Management Lifecycle

3.0 Responsibility

3.1 The CRI Directors are responsible for maintaining and implementing this policy.

3.2 Through this policy, the CRI Directors will ensure that DMLC SOPs and Data Management Plans (DMPs) are sufficient to provide full traceability of operations performed on data.

3.3 The Lead Clinical Research Informatics Specialist (CRIS) for a study is responsible for the creation and maintenance of the DMP, when required, covering the CRI scope of work for a project or program.

3.4 CRI's faculty, staff and subcontractors performing data management tasks are responsible for adhering to CRI policies, SOPs and Work Instructions (WIs) and will notify a CRI Director when adherence will not be likely or has lapsed.

3.5 CRI's Faculty, staff and subcontractors performing data management tasks are responsible for adhering to study- and program-specific procedures documented in DMPs and will notify the Lead CRIS for the study or program when adherence will not be likely or has lapsed.

3.6 The lead CRIS is responsible for associating DMP documentation with shared or archived study data.

4.0 References

4.1 ICH E 6, Good Clinical Practice E6(R2), March 2018

4.2 The following regulations are used as the basis for the CRI QMS:

- 4.2.1 Title 21 CFR Part 11, Electronic Records, Electronic Signatures
- 4.2.2 Title 21 CFR Parts 50 and 56
- 4.2.3 Title 21 CFR Part 312 and 314
- 4.2.4 Title 21 CFR Title 21, Parts 800-1299
- 4.2.5 Title 45 CFR Part 46, the Common Rule
- 4.2.6 Title 45 CFR Parts 160, 162, and 164, The Health Insurance Portability and Accountability Act (HIPAA)

4.3 Office of The Director National Institutes of Health (OD) (2020). NOT-OD-21-013 - Final NIH policy for data management and sharing. HHS.

4.4 Office of The Director National Institutes of Health (OD) (2020). NOT-OD-21-014 - Supplemental information to the NIH policy for data management and sharing: elements of an NIH data management and sharing plan. HHS.

4.5 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008 Apr;61(4):344-9. PMID: 18313558

4.6 Benchimol E, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, RECORD Working Committee, The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med . 2015 Oct 6;12(10):e1001885. doi: 10.1371/journal.pmed.1001885.

4.7 Lebedys E, Famatiga-Fay C, MPH, Bhatkar P, Johnson D, Viswanathan G, Zozus MN, (2020) Data management plans, in Society for Clinical Data Management (SCDM) Good Clinical Data Management Practices (GCDMP). Data Basics, 26(1). Available from https://scdm.org/gcdmp.

5.0 Acronyms and Definitions

Term	Definition
Auditability	Whether adherence to a process can be independently and objectively verified.
Audit trail	Secure, time-stamped and immutable records generated by a computer system that independently record the date and time of operator entries and actions that create, modify, or delete electronic records and do not obscure previously recorded information. (Title 21 CFR Part 11)
CAPA	A Corrective And Preventative Action is one or more steps planned and undertaken in response to a quality problem with the intent of correction, remediation, prevention or mitigation of future instances of the problem.
CRI	Clinical Research Informatics
CRIS	Clinical Research Informatics Specialist
DMP	Data Management Plan; comprehensive documentation of data and its handling from definition, collection and processing to final archival or disposal. (ICH E6(R2), March 2018)
External data	With respect to the Clinical Research Informatics division, data originating or processed outside the CRI QMS are referred to as “external data”. Examples of external data may include data collected from clinical investigational sites where the medical record is the source, Electronic Health Record (EHR) data obtained from other organizations, data from devices provisioned by others, and data processed at external core labs or reading centers.
GCDMP	Good Clinical Data Management Practices
IND	As defined by the Food and Drug Administration (FDA), an IND, or investigational new drug application, is a request for authorization from the FDA to administer an investigational drug or biological product to humans in a clinical study to collect safety and effectiveness data required to support a New Drug Application (NDA) for marketing authorization.
IDE	As defined by the Food and Drug Administration (FDA), an IDE, or investigational device exemption, is a request for authorization from the FDA for an investigational device to be used in a clinical study to collect safety and effectiveness data required to support a premarket approval

	(PMA) application or a premarket notification [510(k)] submission to the FDA.
Managerial controls	Administrative procedures usually involving selection, credentialing, training, and oversight of personnel including performance expectations and corrective action for inadequate performance. Within CRI, managerial controls also include project management.
Procedural controls	Standard procedures specifying process tasks, their sequence, and the roles responsible for performing them. SOPs and WIs are procedural controls.
Process documentation	Records created by or in the performance of a process such as signatures, dates, and computer system audit trails that provide objective evidence against which adherence to procedures can be assessed
program	When referring to program-specific procedures, program means a group of studies for which procedures are similar enough to be documented in the same DMP
Qualified Designee	An individual designated by an individual in the responsible role and directly overseen by the individual in the responsible role or equally qualified by training, education or experience according to the Training SOP to perform a responsibility of the designating role.
QMS	Quality Management System; a formal system that documents the structure, processes, roles, responsibilities and procedures required to achieve effective quality management (ASQ Glossary)
SCDM	Society for Clinical Data Management
Source	As defined in ICH E6(R2) the Source is, "All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial". The source is the original recording of the data.
SOP	Standard Operating Procedure; text that communicates an organization's requirements for a process including what will be done (process tasks), when (their sequence and timing), and by whom (the institutional roles responsible for performing and overseeing the tasks). In regulated industries, SOPs also commonly specify the documentation generated by a process (process documentation), and how the quality of a process will be controlled.
Substantive changes	Changes to tasks, their sequence, timing, documentation or the roles designated as responsible for tasks.
Technical controls	Functionality in computer systems that constrain operations performed, their sequence and the roles that can perform them.
Unexpected quality problem	Any deviation from the fitness for use of data or computer programming that (1) were not anticipated, i.e., for which detection and control mechanisms were not planned or do not exist, or that (2) occur with a greater severity or frequency than anticipated in such plans.
UTHSA	University of Texas Health Science Center San Antonio

Work Instructions	WIs; Detailed step by step directions for accomplishing process tasks.

6.0 Policy

6.1 The CRIS will explicitly define, with study investigators, the data sources for a study and the associated workflow and data flow.

6.1.1 Data that originate or are processed outside the controls of the CRI QMS will be clearly indicated.

6.1.2 The acceptance criteria for data quality, i.e., level of data quality needed for the study, will be documented together with the study statistician.

6.1.3 Available data collection and processing options for each type and source of data that are capable of meeting the requisite data quality will be enumerated and an indication of relative cost of each will be discussed with the Investigator to support decision-making.

This ensures that investigators have information for informed decision-making about the methods and approach to data collection and management for their study, that methods are matched to the requisite data quality and available resources where possible, and where not possible, that the investigator is aware of the risks and steps to mitigate them.

6.2 The level of quality needed and the data collection and processing methods ultimately selected are Investigator decisions.

6.3 The fitness of the data for project use and claims made based on analysis of the data remain the responsibility of the Investigator.

6.4 CRI will manage study data to achieve the agreed level of data quality and, in all cases, will report known and encountered problems with the data to the Investigator as agreed and encountered. These problems may include instances where data processing methods prove incapable or not cost effective to meet the needed data quality level necessitating alternate methods or quality control measures.

6.5 Control of the DMLC

6.5.1 For data collected and processed within the CRI QMS, procedural control and traceability of the DMLC are achieved through a combination of Standard Operating Procedures (SOPs) and, where required, a project- or program-specific Data Management Plan (DMP).

6.5.2 The following DMLC process areas will be controlled through one or more Standard Operating Procedures (SOPs).

- Data Management Plan Creation and Maintenance
- Data Definition
- Data Collection Form Design and Form Change Control
- Bulk Data Acquisition

- Manual Data Collection and Processing
- Computer-aided Data Collection and Processing
- Data Encryption
- Data Surveillance and Reporting
- Database Lock
- Data Release
- Data Archival and Public Data Sharing

6.5.3 To minimize documentation burden on projects, where possible, procedures are specified in SOPs that are referenced by project- or program-specific DMPs. Similarly, process documentation (also called process artifacts or process evidence Fig. 1 in QMS.POL-001) specified by SOPs, Work Instructions and in DMPs are often a by-product of processes. Examples include signatures on approval forms and records in information system audit trails.

6.5.4 DMLC SOPs specify project- or program-specific documentation comprising project- or program-specific DMPs and call out those requiring approvals.

6.5.5 A DMP is required for clinical studies meeting one or more of the following criteria:

6.5.5.1 Studies run under an Investigational New Drug application (IND) or an Investigational Device Exemption (IDE)

6.5.5.2 Studies for which traceability of operations performed on data is contractually required

6.5.5.3 Studies where a DMP is contractually required by the study funder or sponsor or otherwise necessary as a condition of application or award

6.5.5.4 Studies conducted for the purpose of generating generalizable knowledge

- Investigator-initiated or pilot studies, if intended for publication to demonstrate study design or feasibility, do not often meet this requirement because of their small sample size. In such cases, pilot studies do not require a DMP unless otherwise required.
- Hypothesis generating studies based on secondary analysis of existing data and not intended for publication do not often meet this requirement and do not require a DMP unless otherwise required.
- Studies that incorporate quasi-experimental or experimental design elements intended to generate or strengthen evidence toward causal statements would meet this requirement but do not require a DMP (unless otherwise required) if the study is conducted with existing data and for which the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) or Reporting of studies Conducted using Observational-Routinely collected Data (RECORD) reporting requirements comprehensively document operations performed on data.

6.5.5.5 Studies for which a commitment has been made for data sharing should strongly consider but are not required to have a Data Management Plan because the DMP documents the shared data.

6.5.5.6 In all other cases, except where documented by a waiver obtained from a CRI Director, a DMP will be developed and maintained.

6.5.6 Where contractually specified, a DMP drafted and maintained by another organization may be used with approval in writing from a CRI Director.

6.5.7 The DMP for a study or program of studies will cover all sources of data for the study or program of studies and will specify those data originating or processed within CRI (and falling under the CRI QMS) and all operations performed on data by CRI. As such the DMP establishes traceability.

6.5.8 DMP components are listed in the DMP Table of Contents (maintained in the DMP SOP) and are included according to the CRI scope of work for the study.

6.5.9 As comprehensive documentation of all data management operations performed on data, either through direct specification in the DMP or through reference to CRI SOPs, DMP documentation is considered essential documentation under section 8 of ICH E6(R2), Good Clinical Practice. For this reason, DMP components are version-controlled and archived with study data at project close.

6.5.10 DMP components used as specifications for data system development will be available prior to the start of data system development. DMP components documenting data processing will be available prior to the start of the specified data processing.

6.5.11 DMPs are maintained throughout the active data collection and processing phase of a study to reflect current procedures. Thus, DMP components often have multiple versions.

6.5.12 Because DMP documentation establishes traceability, the DMP is customarily provided with shared data.

7.0 Deviations

7.1 Deviations from this policy

7.1.1 Deviations from this policy are handled according to section 7.0 in the CRI QMS Policy (CRI.POL-001).

7.2 Planned Deviations to Study-specific Procedures Specified in DMPs

7.2.1 There are no planned deviations to study-specific procedures specified in DMPs.

7.2.2 Study-specific procedure changes should be reflected prior to implementation as revisions to the appropriate DMP.

7.3 Non-Planned Deviations to Study-specific Procedures Specified in DMPs

7.3.1 When instances of non-compliance with policies, SOPs, WIs or study-specific procedures specified in DMPs are discovered, they must be reported using the Deviation or Incident Report and Corrective and Preventative Action (DIR-CAPA) form (Attachment 4 to CRI.POL.001: Deviation or Incident Report and Corrective and Preventative Action Plan (DIR-CAPA) Form).

7.3.2 Deviations from project-specific procedures, i.e., those specified in the DMP, must be reported by the CRIS or qualified designee leading the informatics work on the project. Preventing harm to research participants and study results should be prioritized over reporting with reporting occurring as soon as possible thereafter. Section 8.0 of the CRI QMS Policy specifies reporting requirements.

7.3.2.1 Reporting of all deviations and unanticipated quality problems as defined in section 8.0 of the CRI QMS Policy (CRI.POL-001) should occur at least verbally by the end of the following business day to a CRI Director, the Principal Investigator of the research project, and the project Statistician.

7.3.2.2 CRI operational faculty and staff should seek guidance from a CRI Director as soon as possible following problem detection if unsure whether an incident or problem requires reporting.

7.3.2.3 The initial version of the DIR-CAPA form should be provided within one week of root cause determination.

7.3.3 Non-planned deviations from CRI policies, SOPs, WIs and study- or program-specific procedures documented in DMP components for research projects that do not impact the CRI QMS must be filed with the Data Management Plan documentation.

7.3.4 Non-planned data- or information system-related deviations also meeting the definition of reportable safety events on clinical studies, non-compliance, or reportable Unanticipated Problem Involving Risk to Subjects or Others (UPIRSO) may also be subject to additional reporting requirements (i.e., reports to the reviewing Institutional Review Board or UTHSA Institutional Compliance and Privacy Office) separate from and in addition to the non-planned deviation.

8.0 Review and Revision of This Policy

8.1 Review and revision of this policy is handled according to section 7.0 in the CRI QMS Policy (QMS.POL-001).

9.0 Attachments

none

10.0 Revision History (Since Last Version)

Version No.	Revision Date	Description of Revision
0.0	07/09/2020	This is a draft procedure for trial use.
1.0	05/17/2022	This is the approved policy for dissemination
2.0	06/01/2022	Effective date changed