Data Quality Management In Clinical Research

Intended Audience: Principal and Associate Investigators and Research Coordinators

DHHS/NIH/OD/OIR/OHSRP

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Instructions

- The audience for this course is Principal Investigators (PIs), investigators and Research Coordinators (RCs) serving on the study team of human clinical studies and trials.
- This course consists of 4 modules and a knowledge quiz.
- You must complete the entire course and successfully pass the quiz to obtain credit for this course at the NIH.
- On average this course takes 30 minutes to complete.
- Once you have passed the course, download and retain your completion certificate, and provide a copy to your Principal Investigator (PI) and/or Institutional Review Board (IRB) as requested
- Your completion record consisting of your Name, IC, and successful completion date will be retained in the OHSRP HRPP Training database: https://federation.nih.gov/ohsr/nih/investigator-training.php
- Records in this database can be viewed by the NIH community and are secured behind the NIH firewall. You have a right not to have your records included in the database, but you will be responsible for providing them upon request to your PI or IRB.

Course Overview

Purpose: This course provides an overview of data quality management practices that support valid findings from research studies.

- Module 1– Why have Data Quality Management in Clinical Research?
- Module 2 – Good Clinical Practice (GCP) Requirements and Elements of a Data Management Plan
- Module 3 – The Research File and Regulatory Binder
- Module 4 – QC/QA, Good Laboratory Practice (GLP), Monitoring and Audits
- Module 5– Bringing it All Together, Planning for Success
- Quiz

Introduction- Why have Data Quality Management (DQM)?

Investigators and institutions invest extensive resources, time and effort to conduct research likely to result in important information to improve human health or conditions. Subjects donate time and their materials to answer the questions researchers ask. Conducting research involves a myriad of details and day to day, it can be easy to lose sight of the data quality in all of this effort.

All research results in data to be analyzed which supports or refutes the study hypothesis. Poor data results in a waste of effort and resources and puts subjects and ultimately patients at risk of harm. It is for this reason that institutions, sponsors, and regulators invest such effort to ensure that research data is of high quality and validity.

- **Good Clinical Practice (GCP) and Good Laboratory Practice Guidelines (GLP)** are among the most widely recognized standards for conducting well-run trials and for managing research data and records. These standards are used by institutions, sponsors and regulatory agencies, such as the FDA, to monitor the conduct of research and data collected on trials.

What you need to know:

This course is based on FDA E6 GCP Guidelines. However, regardless of the type of research conducted, these guidelines are the basis of effective Data Quality Management (DQM).

Introduction–Monitoring in all its forms

Institutions, Sponsors and Regulators use Auditing and Monitoring to ensure quality and validity of research results. While there are many forms of monitoring (including auditing) the primary focus tends to be on data collection and management. Below we describe the forms of monitoring you may experience as you conduct research, including:

- **Safety Monitoring** – Monitoring by a Safety Monitoring Committee, a Data and Safety Monitoring Board (DSMB), a Medical Monitor or other similar entity are all forms of safety monitoring. This is a highly formalized process and often includes outside experts who are not part of the study team. The level and frequency of monitoring is related to the level of risk inherent in the research and the power of the study. These committees generally review safety data and when applicable, blinded data collected on a randomized trial or data from multicenter research.
- **Sponsor Monitoring** – Sponsors monitor the study records and processes to ensure a well run trial is being conducted and that the data being provided is of high quality and validity. If the data is not valid, the Sponsor cannot use the data to support a marketing application before the FDA. Expect Sponsor monitors to inspect your regulatory binders (including informed consents and eligibility criteria) and study data (including source documents and CRFs)
- **IC Quality Assurance and Monitoring** – The NIH is entrusted with public funds to conduct research that will enhance human health and conditions. As result of this trust, the NIH establishes quality assurance (QA) plans and conducts random and for-cause audits of the research conducted by its investigators. Additionally, ICs conduct monitoring based on level of risk (risk-based) or if asked by an IRB or IC leadership (for-cause).

Introduction – Types of Monitoring

Some other forms of monitoring/auditing include:

- **Internal monitoring:** Study teams also have a responsibility to self-monitor study processes and data, also known as quality control (QC). This self-monitoring can ensure a well-run trial and to identify and mitigate issues before they are identified by monitoring entities; which can result in time-consuming fixes. Internal monitoring includes monitoring for proper informed consent documentation/records, eligibility criteria, data quality, etc…
- **Audits by Regulatory Authorities-** Regulatory agencies such as the Food and Drug Administration (FDA) or the Office for Human Research Protections (OHRP) conduct both random and for-cause audits of protocols under their regulatory authority. Serious issues revealed by a regulatory authority can have serious consequences including stopping the study or in a worse-case scenario, debarment of an investigator.

What you need to know: While you may experience any of the types of monitoring listed above, this course focuses on internal monitoring that the study team performs to ensure the validity and integrity of the study data.

Introduction – What is the difference between Monitoring vs Auditing?

Monitoring is usually conducted by interested parties involved in the research (investigators, institutions, sponsors) to identify issues and to improve processes. The goal is quality control and quality improvement (QC/QI) and it is usually conducted on a predetermined cycle unless it is for-cause. Monitoring often identifies deficiencies that require a corrective and preventative action (sometimes referred to as a CAPA) plan.

Auditing is usually conducted by regulatory agencies to confirm that requirements are being met. This type of monitoring is much less frequent and is based on regulatory requirements or concerns. Auditing can be random or for-cause. Auditing can result in a corrective action plan but it can also result in punitive action such as stopping research or in a worse-case scenario, debarment of the PI.

What you need to know: The NIH Human Research Protection Program (HRPP) and ICs establish annual QAQI plans which are implemented throughout each year. The focus may change from year to year. It is likely that you will experience monitoring by your IC at one point or another.

If you are conducting sponsored research, you will be monitored by your Sponsor, based on your monitoring agreement.

Auditing by the FDA would only occur if you are conducting FDA-regulated research. This type of auditing normally takes place at the end of Phase II or before submission of a marketing application. If the FDA becomes aware of issues on a trial, they could conduct a for-cause audit at any time.

Introduction – What is the difference between risk-based, random and for-cause monitoring/auditing?

Risk-based monitoring: If the risks of the study interventions are more than minimal then the IC may always monitor your study, or it may put your study in a pool of more than minimal risk studies to be randomly monitored.

Random monitoring: Because monitoring and auditing is a labor and resource intensive, it is not feasible for institutions or regulatory agencies to monitor every study. Studies may be selected randomly for monitoring or audit not because a particular issue or concern has been identified.

For-cause auditing: If a sponsor, institution, IRB or regulatory agency identifies a concern about the conduct of a study or qualification of investigators, the entity will conduct a for-cause audit or monitoring visit. Continued monitoring may occur to assess if the CAPA plan was effective.

What you need to know: It is important to understand some of the terminology and types of audits a research study team could experience.

While you may experience any of the types of monitoring listed above, this course focuses on data quality management that study teams can perform to ensure a well-run protocol that will result in important information to further human health.

The next section provides some more definitions about data quality management.

Definitions

- **Case Report Form (CRF):** A CRF is a structured document for the collection of study data extracted from the source documentation. The CRF may be a paper or electronic form maintained in a clinical trial management system (CTMS) or remote data management system (RDMS).
- **Data Monitoring Plan (DMP):** The DMP describes the following: data to be collected; how and where the data are captured and stored; process for reporting and handling corrections; confidentiality and data sharing; common terminology and roles and responsibilities. The DMP should be included in the protocol but may be elucidated in a Standard Operating Procedure (SOP). Often the safety plan is combined with the DMP and is referred to as a Data and Safety Monitoring Plan (DSMP).
- **Data Quality Management (DQM):** A formal quality improvement process that ensures the validity and integrity of data during collection, aggregation, storage and analysis.
- **Quality Assurance (QA):** For the purposes of this course, QA a is planned and systematic activity implemented as part of a quality system to ensure that quality requirements (validity) of the data generated during the research will be fulfilled.
- **Quality Control (QC):** For the purposes of this course, QC is a real-time review (monitoring) of data to verify the accuracy and validity by study staff involved in the research.
- **Quality Improvement (QI):** A systematic process including the analysis and correction of gaps/issues for the improvement of a process such as data management.
- **Source Data:** Raw, unprocessed data collected from the subject throughout the course of the study including screening, H&P, laboratory, safety, procedural and survey data. These data may be held in a variety of systems and records including the medical record.

Module 1– What is Data Quality Management ?

- Data quality management (DQM) is a formal process for managing the quality, validity and integrity of the research data captured throughout the study from the time it is collected, stored and transformed (processed) through analysis and publication. This is achieved via two processes referred to as Quality Assurance (QA) and Quality Control (QC) (Module 4).
- DQM starts with a data management plan (DMP) that is specified in the protocol, as a component of the data safety monitoring plan (DSMP) and approved by the IRB and sponsor, as applicable, before the protocol starts. (Module 2)
- DQM includes the organization and retention of key study documentation, known collectively as the Regulatory File (or binder). The Regulatory File is organized and retained to support monitoring and auditing by ICs, IRBs, the HRPP, Sponsors or Contract Research Organizations (CROs) and regulatory authorities. The regulatory file is maintained by the study staff. (Module 3)

What you need to know:

- Every protocol should include a Data and Safety Monitoring Plan (DSMP)
- The DQM plan is part of the DSMP and continues throughout the conduct of the study
- For more information about Data and Safety Monitoring, see SOP 17 – Data and Safety Monitoring

Module 1– Why Do We Need Data Quality Management in Clinical Research?

- All research results in the production of data that must be processed and analyzed to support or refute the study hypothesis
- The data must be of sufficient quality and integrity to support the endpoint analyses
- The data used to support marketing applications for FDA-regulated research must be accurate and validated
- FDA E6 Good Clinical Practice (GCP) standards will be used as the basis of this course

What you need to know:

- The NIH HRPP promotes rigorous data quality management that supports the findings of NIH research studies which have important implications for the health of the public, regardless of whether the studies are FDA-regulated or not
- Quality data management is the structure that supports high-quality outcomes for clinical research
- Following best practices for data management is a continuous process that utilizes quality control (QC)/quality improvement (QI) methodology

Module 1- Regulatory and Policy Basis for Data Quality Management

Below is a list of regulations, policy and guidance regarding data quality management:

FDA GCP Guidelines: Below are a selected list of sections from the FDA E6 Guidelines that may be of interest:

- Investigator Responsibilities (4.9-4.13)
- Sponsor Responsibilities (5.1, 5.5, 5.10, 5.11, 5.15, 5.18, 5.19 and 5.22)
- Essential Documents for the Conduct of a Clinical Trial (Section 8)

NIH Policy:

- SOP 15 - Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications
- SOP 17 - Data and Safety Monitoring
- SOP 19 - Investigator Responsibilities

Regulatory Requirements for Record Keeping for FDA-regulated Research:

- 21 CFR Part 312.62 Investigator recordkeeping and record retention
- 21 CFR Part 812.140 Records
- 21 CFR Part 11: Electronic records submitted to the FDA

What you need to know:

- Investigators must abide by FDA regulation and NIH policy as applicable
- It is strongly recommended that *all* investigators follow GCP guidance for data management whether conducting FDA-regulated research or not.

Module 2- Elements of a Data Management Plan

A Data Monitoring Plan (DMP) includes:

- Specification of the data to be collected on the protocol
- Case Report Forms (CRFs) to be developed
- Establishment of desired best practices (QA) for:
  - Collecting source documentation (raw data)
  - Extracting research data from the source data to complete the Case Report Forms (CRFs)/data management system
  - Maintaining confidentiality of data
  - Plans for secure storage of data with limited data access
- Processes for Quality control (QC) of data and the specification of processes for corrections of incorrect data
- How data will be transformed (processed) to prepare it for analysis
- Quality assurance processes and timing for raw and transformed data

What you need to know:

- Data management best practice starts with the data monitoring plan (DMP) and CRF/data system structure

Module 2- DQM – Quality Assurance

- **Quality Assurance (QA)**: For the purposes of this course, QA a is planned and systematic activity implemented as part of a quality system to ensure that quality requirements (quality and validity) of the data generated during the research will be fulfilled.
  - QA procedures should be specified in the DMP
  - QA plans should establish processes or systems that prevent errors. Methods include double data entry, audit trails and real-time field-level validation.
  - QA processes should not adversely impact the power or blinding.

What you need to know:

- QA is the activity that supports the generation of quality, validated data from the research.
- Inform your PI as soon as possible if QA procedures are not preventing errors.
- Consult your biostatistician or epidemiologist for guidance as needed.

Module 2- DQM – Quality Control

Quality Control (QC): For the purposes of this course, QC is a real-time review of data to verify the accuracy and validity by study staff involved in the research.

- Quality control (QC): of data collected in source documents and CRFs
- Timeliness: QC should happen in real-time, close enough to the data collection to ensure the validity of the data if clinical (such as laboratory results) ; or as soon as feasible for complex or batched data (such as genomic or deep sequencing data)
- Validation: should happen in real-time and not after the study has ended and should be consistent with established QA processes.
- Manual Corrections: should never obscure the original data. Use strike through and write your initials for paper and audit trails for systems.
- QC of raw and transformed data should be consistent with the DMP and should not adversely impact the power or blinding. Consult your biostatistician or epidemiologist for guidance.

What you need to know:

- QC is a continuous practice that should happen in real-time, close enough to the data collection to ensure the integrity and validity of the data.
- QI requires that errors should be corrected as soon as possible following identification. Unexpected errors requiring new corrective procedures should be addressed with your PI as soon as possible.

Module 2– Who is involved in Data Quality Management ?

Data quality management involves the entire research team:

- The Principal Investigator is ultimately accountable for the quality and integrity of the data and for establishing and managing the data monitoring plan and the regulatory and research files
- Investigators are responsible for collecting and recording the data consistent with the data monitoring plan
- Research staff are responsible for implementing the data monitoring plan including quality control of data as it is collected and recorded and for maintaining the Regulatory Files
- Sponsors are responsible for monitoring data, as applicable
- Institute/Centers (ICs) are responsible for monitoring the data consistent with their QA plans
- NIH IRBs may request that the IC audit a study to investigate problems that have been brought before the Board
- Regulatory bodies such as the FDA/BIMO are responsible for auditing data in support of marketing applications or “for cause” audits

What you need to know:

- The entire research team is responsible for data quality management in one capacity or another.

Module 2- GCP Standards for Data Management

GCP Standards (FDA E6):

- provide a universal framework for data quality management that applies to all types of biomedical or social behavioral research.
- identify responsibilities for investigators and sponsors for data management:
- Investigator Responsibilities (Sections 4.9-4.13)
- Sponsor Responsibilities (Sections 5.1, 5.5, 5.10, 5.11, 5.15, 5.18, 5.19 and 5.22)
- Records management: (Sections 2.10, 4.9, 5.1, 5.21, 5.22)
- Confidentiality (Sections 2.11, 5.5.3(d))
- Quality control (Sections 2.13, 4.9.1; 4.9.3; 5.1.3)
- Monitoring/Auditing (Sections 1.25, 2.13, 4.1.4, 5.5)
- Management and contents of the Regulatory File (Sections 4.9.4, Section 8)

What you need to know:

- Even if you do not conduct FDA-regulated research, the standards above establish best practices for data management.

Module 2- GCP Standards for Investigators

GCP Standards require that all clinical trial information should be recorded, handled, and stored in a way that supports accurate reporting, interpretation, and verification (Section 2.10).

Investigator responsibilities for data management are outlined in Section 4.9:

- **Records management**: The PI should ensure the accuracy, completeness, legibility, and timeliness of the data recorded in the Case Report Forms (CRFs) and any applicable reports.
- **Data extraction**: Research data captured on the CRF, which are extracted from source documents, should be consistent with the source documents or the discrepancies should be explained.
- **Quality Assurance and Corrections**:
  - QA systems with procedures that assure the quality of every aspect of the trial should be implemented (Section 2.13).
  - Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e., an audit trail should be maintained); this applies to both written and electronic changes or corrections. The investigator should retain records of the changes and corrections. Check with your Sponsor about requirements, if applicable.

What you need to know:

- If you are a PI, you are responsible for ensuring that your investigators and research staff comply all the applicable data management standards.

Module 2- GCP Standards for Investigators

Investigator Responsibilities continued:

Confidentiality :

- Confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s) (section 2.11).
- Maintain security systems that prevent unauthorized access to the data (section 5.5.3(d).

Monitoring:

- The investigator/institution should cooperate with monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authority(ies) (section 4.1.4).

What you need to know:

- As an investigator, you are accountable for the quality and integrity of the data.
- You are responsible for complying with monitoring and auditing of the data.
- For more information see SOP 17 – Data and Safety Monitoring and SOP 19 – Investigator Responsibilities.

Module 2- GCP Standards for Sponsors of FDA-regulated Research

In FDA-regulated research, the **Sponsor** is responsible for:

- Quality Assurance (QA) and Quality Control (QC)by securing direct access to source data/documents via a written agreement with the investigator (Section 5.1)
- Trial management, data handling, recordkeeping and establishing an Independent Monitoring Committee (Section 5.5).
- Obtaining proof of IRB review from investigators (Section 5.11)
- Record Access (Section 5.15)
- Monitoring and 5.19 Auditing (Sections 5.18 and 5.19)
- Clinical Trial/Study Reports (Section 5.22)

What you need to know:

- If you are a Sponsor-Investigator on an FDA-regulated trial, you are responsible for complying with the applicable standards for Investigators in Section 4 and Sponsor requirements in Section 5 of the GCP standards.
- Here at the NIH the ICs are generally responsible for convening Data Safety Monitoring Boards (DSMBs), work with your CD if you think you need to convene a DSMB.

Module 3- The Regulatory Binder and Research Files – The Binders

The regulatory binder may be a physical binder (or set of binders) or an electronic directory containing all the essential documents, which, when taken together, support the validity, quality and integrity of the data produced in the trial and demonstrate compliance by the investigators with regulatory requirements as applicable.

GCP provides a comprehensive list of essential documents that should be retained in the regulatory binder at each phase of the study:

- Before the study commences
- During the conduct of the trial
- After completion/termination of the trial

Note that the records in the regulatory binders may contain the research subject codes instead of subject identifiers. (It is possible that external sponsors may not wish to view individually identifiable information)

What you need to know:

- Regulatory binders may be audited by the sponsor or other regulatory authorities as applicable.
- Regulatory binders may be inspected during post-approval monitoring by the IC and/or the Sponsor

Module 3- The Regulatory Binder and Research Files – Research Files

The research files contain copies of the signed informed consents and source documentation (e.g. medical records from treating physicians, outside lab results or surveys).

The consent template in use at the NIH Clinical Center (CC) informs subjects of the possibility that their private information might be seen by others outside the research team including regulatory agencies. If your research is not conducted at the CC, and there is a possibility that the protocol will be monitored (such as with FDA-regulated research) the consent document should inform subjects of this possibility.

What you need to know:

- At the NIH Clinical Center (CC), the original signed consents obtained at the CC are provided to Medical Records Department.
- Research files should also be provided to monitoring entities upon request.

Establishing the Regulatory Files: Before opening the study

Examples of documents generated before the study commences:

- IRB-approved Protocol, including initial and amended versions
- IRB-approved Informed Consent(s) and other subject information
- IRB-approved recruitment materials
- IRB approval documentation and other institutional approvals
- Regulatory notifications and correspondence
- CVs and documentation of qualifications of investigators and training records
- CRFs and lists of normal values, ranges of procedures or tests (such as lab tests)
- Standard Operating Procedures for: data, specimens, shipping/handling, investigational agents, randomization, blinding/unblinding, safety procedures, etc…
- Trial agreements, as applicable
- Investigator brochure/other prior experience w/the device, as applicable
- Monitoring plan and trial initiation monitoring report, as applicable

Maintaining the Regulatory Files: During the Study

Examples of documents generated while the study is ongoing:

- Revisions to any of the documentation listed previously
- Monitoring visit reports
- Signed/dated informed consents (may be maintained in the research record)
- Source documents
- CRFs (signed and dated) and documentation of corrections
- Reports to Sponsors such as AE and SAE reports
- Reports to IRBs such as unanticipated problems, protocol deviations or other safety information
- Continuing reviews and other interim reports to the IRBs
- Subject logs, such as screening, enrollment, and communications such as related to subjects lost to follow-up, etc…
- Drug accountability and handling logs
- Specimen and data tracking logs

Regulatory Files: After the Study Closes

Examples of documents generated after the study closes:

- Final reports to the IRB and regulatory authorities as applicable
- Final Monitoring visit and Audit reports as applicable
- Clinical study report
- Final subject identification lists and treatment allocation/decoding, as applicable
- Final drug accountability and product destruction logs, as applicable
- Final specimen and data tracking logs

What you need to know:

- The content of regulatory binders may vary somewhat depending on the nature of the study, but FDA-regulated studies must have complete information included in these files in the event of an audit or inspection. See GCP Section 8 for a complete list of documents.

Module 4 – Quality Assurance Best Practices – Planning for Successful Data Collection

Quality Assurance (QA): For the purposes of this course, QA a is planned and systematic activity implemented as part of a quality system to ensure that quality requirements (quality and validity) of the data generated during the research will be fulfilled.

- The research team should establish a data quality management plan and a quality control cycle before the research starts.
- Case Report Forms/tools should be clearly defined based on the data needed to validate the primary and secondary endpoints
- Manual Data should be captured as soon as feasible after collection to ensure accuracy and validation
- Data systems should be consistent with Case Report Forms/tools and data validation should be defined where ever possible to avoid spurious data and to promote timely data validation. For example if you are collecting HbA1c's in a data field, make sure that the field captures only numerical values. When feasible set expected ranges and force validation by the user if the data entered is out side the expected range. Ensure the data system has an audit trail or place to capture notes.

What you need to know: A well-organized and precise set of data collection tools promotes greater data accuracy and supports the interpretation of results

You can also work with your IC QA Contact to develop a plan or strategies, if you don't know who your contact is speak with your Clinical Director.

Module 4 – Quality Control Best Practices

Quality Control (QC): QC is a real-time review of data to verify the accuracy and validity by study staff involved in the research.

- QC activities should take place on a pre-determined cycle that will not jeopardize the data analysis, therefore a QA plan should be established before the protocol starts, paying particular attention to the QC cycle including who and how frequently the data will be monitored.
- **What you need to know**: Quality Control should occur on a regular basis to ensure accuracy and completeness of study data. As soon as feasible, clarify, validate, and correct any unclear or out-of-range data.

  Internal monitoring should never unblind data. Consult your epidemiologist or biostatistician if you have questions or concerns.

Module 4 – Your Responsibilities During a Monitoring Visit

You just found out your data will be monitored by your sponsor, IC or regulatory body, what is your responsibility?

- To cooperate with the monitors/auditors
- Be prepared to provide your: regulatory binders, read-only access to your database or systems, including redacting and copying some records
- To notify your IC CD and OHSRP if you are going to be audited by OHRP or the FDA
- Provide a quiet space for your monitors/auditors to work and read-only access to systems
- Be available to monitors/auditors to answer questions and provide clarifications
- Be prepared to explain your operational processes for capturing, entering and validating your data including your QC/QA and QI processes.
- Establish and implement a corrective action plan to address deficiencies identified by monitors/auditors.
- To respond promptly to any monitoring reports that identify deficiencies or issues
- To report any issues to the IRB and how they were resolved.

Module 4 – What to expect during a Monitoring Visit

What should you expect during a monitoring visit?

- You will be provided a list of records or binders to pull in preparation for and during the visit
- Expect monitoring to take place over several days and up to a week
- You may have very little notice of a visit; you may need to reschedule subjects
- You may have end-of-day and/or end-of-monitoring debriefings, the PI should be present.
- Expect the monitor/auditor to focus very closely on the completeness of your regulatory files. In particular, the signed informed consents, compliance with eligibility criteria and how complete and current your data are.
- A report of the results from the monitoring, including a list of items to be corrected or addressed ; including how soon you must respond (Note that this is called a "483" when issued by the FDA)
- If a corrective action plan is put in place that is acceptable to the monitors/auditor you may have continued monitoring to see if the plan worked.

Module 5- Bringing it All Together, Planning for Success

- Poor data results in a waste of effort and resources and puts subjects as risk of harm. If feasible work with your data manager. Keep the following best practices in mind to ensure that your research efforts result in high-quality, validated data:
  - Plan for quality data collection
  - Design case report forms/tools to capture the data needed to support the primary and secondary endpoints
  - Design the data management system to be consistent with the case report forms/tools and:
    - For standard clinical, eligibility and safety data, set in validation where ever possible
    - Consider double entry for key data variables and when manually entered
    - Use an audit trail- an audit trail runs behind the user interface and tracks all additions, removals and changes and track who made them and when
    - Allow users to capture notes about data that are out of range
    - Strive for timely data entry and real-time data validation
    - Establish a plan for validating batched data or complex data sets that are not manually entered.

Module 5- Bringing it All Together, Know Your Responsibilities

Even if your protocol has a Data Safety Monitoring Committee or Board you should still internally monitor (QC) your data frequently for completeness and accuracy.

- PI – Establish who and how frequently data will be managed.
- QA team member- establish strategies to avoid further errors in the future promptly, test and retest until you are sure you have addressed the problem
  - Promptly notify your PI and consult your statistician/epidemiologist if you identify major concerns.
  - Be careful during QC, never monitor data in such a way to unblind or otherwise jeopardize the power or data analysis, consult your statistician and PI.
- Entire research team – If issues are identified notify the PI and resolve them promptly.

What you need to know: You may not responsible for all the tasks above, but you are still responsible for understanding your role and for the quality and integrity of the data you collect, record or manage.

- Use resources available to you: consult your IC QA contact, PI, statistician or data managers for tips and best practices.

Quiz – Test Your Knowledge

1. What type of monitoring can a study team perform to identify possible issues with data quality or integrity?

   ____ a. For-cause auditing

   ____ b. Internal monitoring

   ____ c. Random monitoring

2. Some elements of Data Quality Management (DQM) include establishing a Data Monitoring Plan (DMP) in the protocol and maintaining the regulatory file. ____ True ____ False

3. Some elements of a DMP include:

   ____ a. A corrective and preventative action (CAPA) plan

   ____ b. Definition of source documentation and Case Report Forms (CRFs)

   ____ c. Plan for QC/QI of raw and transformed data

   ____ d. a and b

   ____ e. b and c

Quiz – Test Your Knowledge

4. Research staff is responsible for establishing and maintaining the regulatory files.

____ True ____ False

5. Should copies of the signed informed consents be retained in the research file or regulatory binder? __Yes __No

6. Regulatory files are not only for use by the research team, they may be inspected by monitoring entities. ____ True ____ False

7. Quality Control (QC) of study data should occur:

____ a. on a random basis by an auditor

____ b. on a regular basis by the study team

____ c. on a pre-determined basis by the IC QA monitor

Quiz – Test Your Knowledge

8. The PI should promptly notify the IRB if protocol deviations are uncovered by the monitoring of the study and what the corrective action plan is. ____ True ____ False

9. Good Clinical Practice Guidelines covers:

   ____ a. quality and integrity of study data and results

   ____ b. contents of the regulatory files

   ____ c. Rights, safety and welfare of research participants

   ____ d. all of the above

   ____ e. a and c

10. The entire research team has a role to play in Data Quality Management.

    ____ True ____ False

Data Quality Management Quiz Key

1. What type of monitoring can a study team perform to identify possible issues with data quality or integrity?

   ____ a. For-cause auditing System: Incorrect. Internal monitoring by the study team is the correct answer.

   ____ b. Internal monitoring System: Yes, that is correct!

   ____ c. Random monitoring System: (Use response to item a.)

2. Some elements of Data Quality Management (DQM) include establishing a Data Monitoring Plan (DMP) in the protocol and maintaining the regulatory file.

   ____ True System: Yes, that is correct!

   ____ False System: Incorrect, establishing a Data Monitoring Plan (DMP) is an important component of Data Quality Management.

3. Some elements of a DMP include:

   ____ a. A corrective and preventative action (CAPA) plan System: Incorrect: Defining the source documentation and the case report forms (CRFs) and planning for QC/QI of raw and transformed data are elements of a DMP.

   ____ b. Definition of source documentation and Case Report Forms (CRFs) System: Partially correct, this element and the Plan for QC/QI of raw and transformed data are both elements of a DMP.

   ____ c. Plan for QC/QI of raw and transformed data System: Partially correct, this element and the definition of source documentation and CRFs are both elements of a DMP.

   ____ d. a and b System: (Use response to item a.)

   ____ e. b and c System: That is correct!

4. Research staff is responsible for establishing and maintaining the regulatory files.

   ____ True System: That is correct!

____ False System: That is incorrect. Investigators and/or research staff *are* responsible for establishing and maintaining the regulatory files.

5. Should copies of the signed informed consents to be retained in the research files or regulatory binder?

   __Yes System: That is correct!

   __No System: That is incorrect. Copies of the signed informed consents are maintained as part of the research files or regulatory binder. At the NIH Clinical Center (CC), the original signed consents obtained at the CC are provided to Medical Records Department.

6. Regulatory files are not only for use by the research team, they may be inspected by monitoring entities.

   ____ True System: That is correct!

   ____ False System: That is incorrect. The regulatory files must be made available for inspection by monitoring entities, (e.g. IC or Sponsor monitors, or FDA inspectors/auditors.

7. Quality Control (QC) of study data should occur:

   ____ a. on a random basis by an auditor System: That is incorrect. QC is the responsibility of the study team and should take place on a regular basis.

   ____ b. on a regular basis by the study team System: That is correct!

   ____ c. on a pre-determined basis by the IC QA monitor System: That is incorrect. QC is the responsibility of the study team and should take place on a regular basis.

8. The PI should promptly notify the IRB if protocol deviations are uncovered by the monitoring of the study and what the corrective action plan is.

   ____ True System: That is correct!

   ____ False System: That is incorrect. PI's are required to report protocol deviations to the IRB, regardless of how they are identified, per HRPP SOP 16 -

Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations.

9. Good Clinical Practice Guidelines covers:

____ a. quality and integrity of study data and results System: That is partially correct. GCP also covers: contents of the regulatory file, and rights, safety and welfare of research subjects as well as other topics.

____ b. contents of the regulatory files System: That is partially correct. GCP also covers: quality and integrity of study data/results and, rights and safety and welfare of research subjects, as well as other topics.

____ c. Rights, safety and welfare of research participants System: That is partially correct. GCP also covers: quality and integrity of study data/results and contents of the regulatory file, as well as other topics.

____ d. all of the above System: That is correct!

____ e. a and c System: System: That is incorrect. GCP covers all of the following: quality and integrity of study data/results, contents of the regulatory file, and rights, safety and welfare of research subjects, as well as other topics.

10. The entire research team has a role to play in Data Quality Management.

____ True System: That is correct!

____ False System: That is incorrect, the *entire* research team as a role to play.