Standard Operating Procedure CCTU/SOP033

Database Locking

1. Scope

The SOP applies to CCTU personnel involved in the process of locking a clinical trial database, including CIs, Statisticians, Programmers, Data Managers and Coordinators.

2. Purpose

The purpose of this standard operating procedure is to document how to undertake a database lock of a clinical trial database. It also covers the procedures required should a hard locked database need to be unlocked.

This document will cover the following principles;

1. The process is controlled
2. There must be a formal request to lock a database, and Sponsor approval to unlock a hard locked database
3. There must be procedures in place to govern how the dataset is to be made available for use i.e. what was undertaken to make it available, where it is stored and how it is to be accessed and protected
4. There is a formal declaration of when the hard lock is completed and the dataset declared 'final'
5. There is evidence of how this state of finality was achieved

3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

Common abbreviations and definitions can be found in CCTU/INF001 Common Abbreviations and Definitions.

3.1. Definitions

Term	Definition
Cambridge Sponsored	Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH); or the University of Cambridge (UoC); or jointly by CUH and UoC.
Database lock	The process whereby a dataset is readied for analysis and then its state is kept constant – i.e. locked so that the data cannot be subsequently amended
Hard lock	Refers to the process whereby a clinical trial database has data cleaned and validated and all edit permissions are revoked. Data in a 'hard locked' database is considered clean, complete (as far as is possible) and ready for analysis, and no further

	data amendments are expected. Users' edit permissions are revoked.
Soft lock	Refers to the process that precedes the Hard lock. The same procedures as a Hard lock are followed, but it is expected that some further activity may be undertaken that may result in data changes. Users' permissions may or may not be restricted during a soft lock.
Clinical trial database	A repository of data associated with a clinical trial.
Dataset	Refers to the data contained in the clinical trial database.
EDC	Electronic data capture – a system such as MACRO™
TMF	Trial Master File.
CRF	Case Report Form

3.2. Abbreviations

Abbreviation	Meaning
CI	Chief Investigator
EDC	Electronic data capture system e.g. MACRO™

4. Undertaken by

The processes are primarily the responsibility of the data management team, although the CI, Statistician, Coordinator and Sponsor may all contribute to the decision to soft and hard lock a trial database.

5. Items Required

- CCTU/SOP057 Providing a Dataset from a Clinical Trial Database
- CCTU/FRM094 Database Lock Request and Data Extract Authorisation
- CCTU/FRM096 Soft Lock Completion Confirmation
- CCTU/FRM097 Hard Lock Completion Confirmation
- CCTU/FRM072 Permission to Unlock a Hard Locked Database

6. Summary of Significant Changes

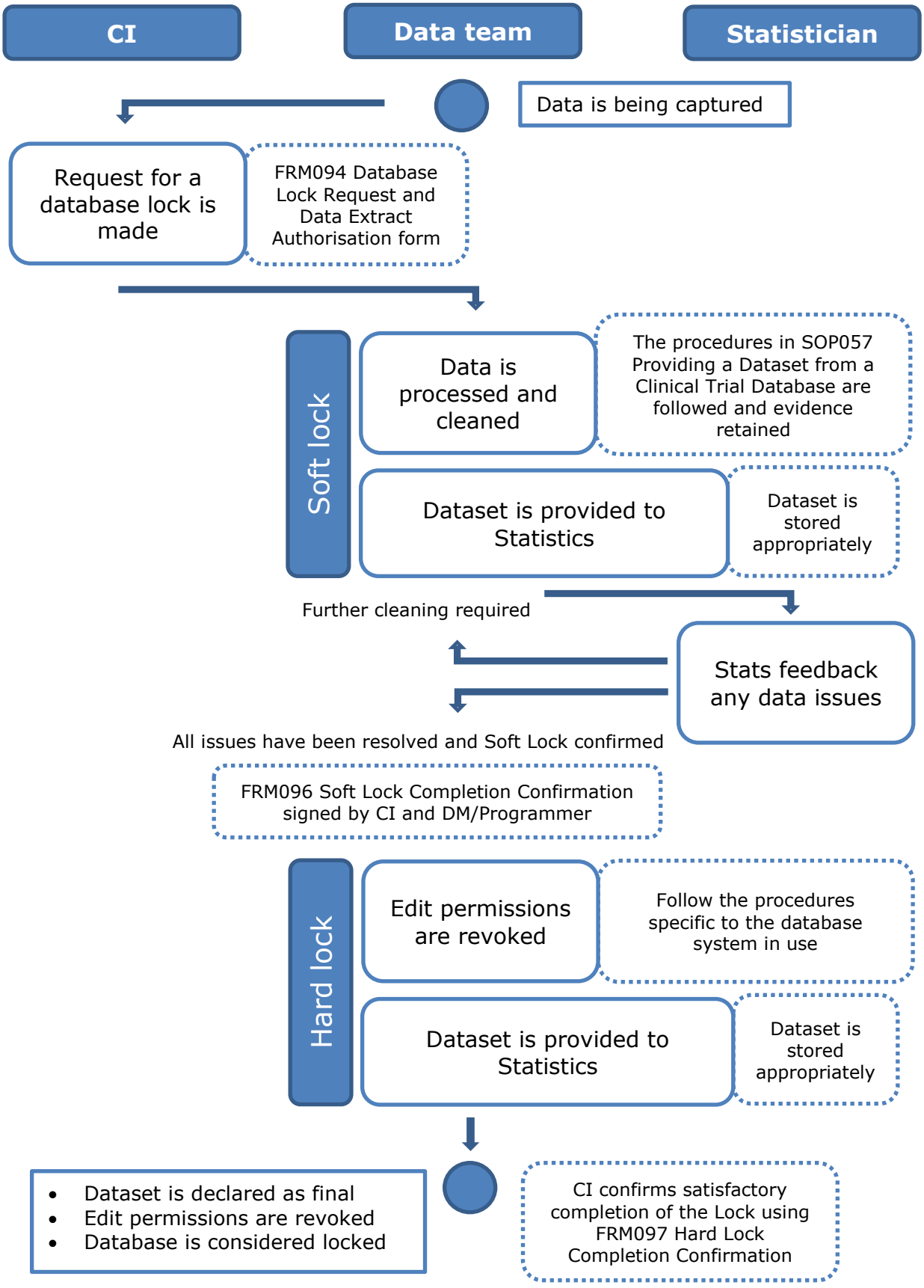
Use of new forms and flow chart to summarise process

7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

Figure 1 below shows a graphical summary;

Figure 1 - Locking process overview



In order to maintain a robust dataset it is vital that database locking is a controlled process subject to the appropriate approvals by interested parties. This is ensured by the use of approval forms.

Please note that a database lock has two parts; the soft lock and hard lock. Both are necessary in order to provide the final locked database and the associated dataset.

7.1. Initiating a hard lock

Usually the coordinator will make the request for a database lock under instruction from the CI or trial team. The request should be documented in the TMF and ultimately be instigated by the CI. Use FRM094 Database Lock Request and Data Extract Authorisation to instigate the locking procedure and provide authorisation to provide a cleaned dataset.

7.2. Locking the database

Upon receipt of a lock request, the trial team members responsible will begin the process of locking the database. A hard lock *is always* preceded by a soft lock.

7.2.1. Soft lock

During soft lock, the trial team will clean the dataset and ensure it is as complete as possible and contains accurate data. Only data directly related to previously queried data should be added and no further data should be included. This procedure is documented in CCTUSOP057 Providing a Dataset from a Clinical Trial Database which details how datasets are handled and should be followed to provide assurance that procedures are in place to govern what was undertaken to make the dataset available to the Statistician. It also details how to manage the created dataset where it is stored and how it is to be accessed and protected.

As shown in figure 1 above, the dataset may or may not require further revisions. The Statistician may highlight areas that need further cleaning and/or missing data that are required. This is an iterative process until the Statistician is satisfied. Data changes during this process should be undertaken in the same way as routine data management and data entry.

During soft lock, edit permissions are retained in order that data can be updated. It is permissible however to remove permissions from users who no longer require edit permissions e.g. for a user from a site that has had all data cleaned.

The soft lock is confirmed by completing CCTU/FRM096 Soft Lock Completion Confirmation Form.

7.2.2. Hard lock

Only when soft lock is completed and the dataset is considered final and ready for analysis can the hard lock be initiated. Evidence of procedures and processes that led to the decision that the dataset is final must be retained. This includes any correspondence, reports, checklists and assessments generated during the cleaning process.

The database should have all edit permissions revoked to prevent any amendments to the database. Use the processes associated with the EDC system used for the trial.

The dataset is managed according to CCTU/SOP057 Providing a Dataset from a Clinical Trial Database which details how to manage the created dataset where it is stored and how it is to be accessed and protected.

Once locking is complete, the CI confirms they are satisfied that the locking process has been followed by completing CCTU/FRM097 Hard Lock Completion Confirmation form.

7.3. Unlocking the database

Once locked the database cannot be unlocked without good reason. Unlocking will be limited to significant corrections that will have an impact on the reliability of the results.

In the event that a locked database requires unlocking, the CI should seek permission from the Sponsor use FRM072 Permission to Unlock a Hard Locked Database. This form must include full details of all data-points to be amended and the reason for each amendment. The justification to unlock the database, the effect on the statistical outcome and the signed approval form must be documented in the TMF prior to the unlock being undertaken.

7.3.1. Re-locking the database

Prior to re-locking, the audit trail for the database must be reviewed to confirm that only the approved changes were made. Any files, data etc. created to support this process should be retained. The outcome of the review and if appropriate, the audit trail should be filed in the TMF. If it becomes apparent that data-points not approved by the sponsor have been amended, this must be escalated to the Sponsor, CI and trial statistician immediately and appropriate steps taken to ensure data accuracy, compliance and correct documentation.

Only once all queries or issues have been resolved the re-locking process should be undertaken again as soon as reasonably appropriate.

7.4. Locking with unclean data

In some cases, the trial team may not clean every data point. In these cases, the decision to do so should be based on the requirements of the protocol (e.g. when the data is not required for the endpoints of the trial). The Statistician must be involved in this decision.

Any data that is knowingly left unclean should be documented as such, and this documentation should be available to consumers of the data.

8. Monitoring Compliance with and the Effectiveness of this Document

a. Process for Monitoring Compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

b. Standards/Key Performance Indicators

This process forms part of a quality management system. Documents are reviewed every two years

9. References

The Institute of Clinical Research, Abbreviations used in Clinical Trials.

MHRA, Good Clinical Practice "Grey Guide"

10. Associated Documents

11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

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