MRC Clinical Trials Unit

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UCL

DATABASE LOCK SOP

VERSION 4.0

APPROVALS

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All appropriate approvals must have been completed prior to uploading to SOPbox.

UPLOAD TO SOPBOX

Name	Position	Signature	Date uploaded to SOPbox
Nancy Tappenden	SOPbox Administrator	Nancy Tappenden Digitally signed by Nancy Tappenden Date: 2019.08.16 14:08:46 +01'00'	16 Aug 2019

The effective date of this SOP is the day on which it is uploaded to SOPbox and is available to use. This is the date associated with the signature of the SOPbox Administrator.

For the Revision History please see the Version History Summary in SOPbox.

DATABASE LOCK

TABLE OF CONTENTS

Note: Glossary of terms, acronyms and abbreviations will be provided in a separate document for all SOPs and associated documents

The following symbols may be used in this SOP:

Indicates a link to a related document

Indicates instructions to document trial-specific processes elsewhere

Throughout this document 'MRC CTU' will be used to refer to the MRC Clinical Trials Unit at UCL (MRC CTU at UCL).

1 PURPOSE

The purpose of this SOP is:

- To outline the procedures for locking databases containing trial data at MRC CTU :
    - to meet regulatory requirements
    - to provide evidence of data quality of data used in final or published analyses
    - to provide traceability of data used in final or published analyses
- To define the MRC CTU roles and responsibilities involved in the database lock procedure
- To highlight the use of database lock procedures in platform trials
- To describe the process of providing a copy of site data to sites in eDC trials after final database lock

2 RESPONSIBILITY AND ROLES

The following table lists the roles relevant to this SOP and a brief description of their responsibilities.

This SOP will be circulated for Read and Understood to all appropriate roles identified in the training matrix.

ROLE	RESPONSIBILITIES
Trial Statistician	• Works with other trial team members to specify the data quality checks required for database lock in the Data Management Plan (DMP) • Works with CPM, TM and/or DM to complete data quality checks required for database lock as specified in the DMP prior to requesting database lock • Ensures that the Statistical Analysis Plan (SAP) is signed off prior to requesting database lock • Requests the database lock (request goes to the DSPM) • Reviews and signs off the Database Lock document
Trial team members: Clinical Project Manager (CPM), Trial Manager (TM) and/or Data Manager (DM) - varies by trial team	• Work with the Trial Statistician to complete data quality checks required for database lock as specified in the DMP • Review the Database Lock document • For eDC studies, work with sites to arrange receipt and verification of site data copies
Data Management Systems Project Manager (DSPM) or Database Programmer	• Prepares the database lock document when a database lock request has been received • Performs the database lock as per the database lock document once the Database lock document is signed off
Information Services (IS)	• Produce copies of exported site data on encrypted media for sending to site in eDC studies if required

3 PROCEDURES

Database lock is a procedure that documents the quality of data used for statistical analysis, and ensures that the database the data were extracted from for that analysis is preserved unchanged. All access rights to insert, delete, or update data in the database are removed as part of the lock procedure (although read-only access can be maintained).

3.1 WHEN SHOULD A DATABASE LOCK BE PERFORMED?

A database lock must be performed:

- before unblinding, if applicable
- before the final analysis of the primary outcome as defined in the protocol
- before any analysis of the results which are to be reported as final to an external audience (at conferences, in publications, Clinical Study Reports for industry collaborators, etc.)

The procedure, with the programs and logs produced during analysis, allows traceability from the CRF data as held in the database to the reported results. It also provides evidence to support peer review of published data, and patent or submission support based on data from a locked database.

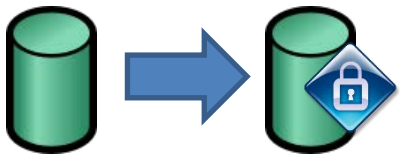
A database lock does not need to be performed for every interim analysis. However, a database lock should be performed before any analysis the results of which may cause a change in trial design or progress. Examples of these include:

- planned interim analyses with formal stopping rules
- multi-arm/multi-stage (MAMS) design decision points
- platform designs allowing analysis and publication of some comparisons within the trial while other comparisons are ongoing
- if it is expected that the Independent Data Monitoring Committee (IDMC) could make a decision to stop the trial for futility, change sample size or change primary outcome measures

Although in most of these cases the trial continues, the database lock procedure allows documentation of the quality of the data in the database that the decision was based on, and ensures that a copy of the locked database is retained in that state.

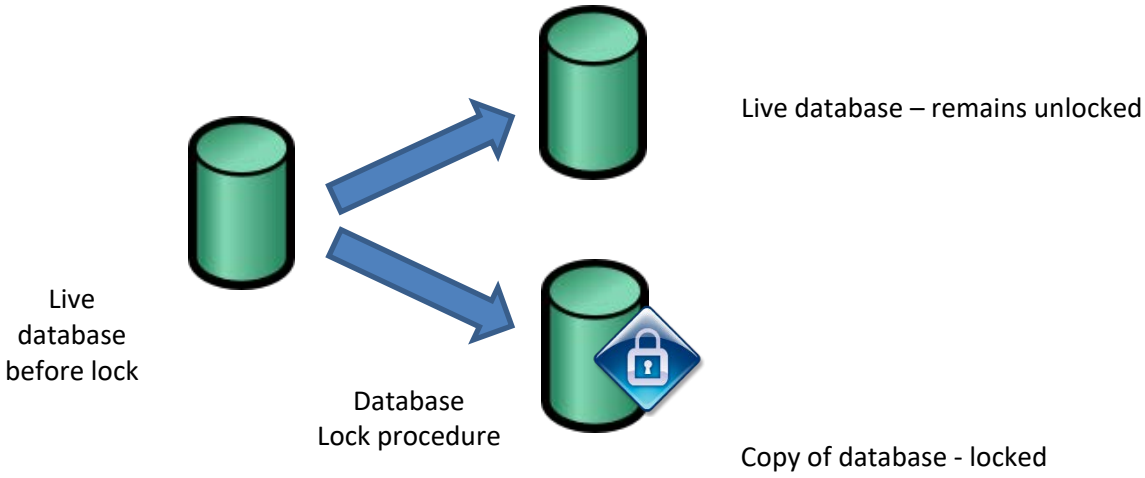
3.2 WHAT IF THE DATABASE NEEDS TO REMAIN OPEN AFTER LOCK?

When a database is not expected to be used after lock (i.e. at the end of a trial), the live database undergoes the database lock procedure and becomes the locked database:



Live database | Database lock procedure | Locked database

However, in some cases it may be the database needs to remain open after the lock – for example, to collect data for secondary endpoints, substudies, or long-term follow-up, or if the lock was done prior to a critical (but not final) analysis. The database lock procedure should still be completed to provide evidence of data quality checks and to preserve a copy of the locked database from which analysis files have been extracted. However, in these the lock is done on a copy of the database, so that access rights in the live database remain to allow further data collection :



3.3 BEFORE REQUESTING A DATABASE LOCK

The trial statistician and other trial team members should be in regular communication with the DSPM to forecast a potential database lock well in advance, to allow sufficient preparation time. The DSPM can also advise as to when a database lock should be planned, including those situations when the database will need to remain open after the lock has been completed (see section 3.2).

Tasks that must be completed before requesting the database lock:

3.3.1 DATA QUALITY CHECKS

The trial statistician is responsible for providing evidence that the data are clean enough to analyse. The Database Lock Quality Checklist should contain a description of priorities and thresholds for data quality. The results and location of these checks and justifications need to be detailed in the Database Lock Request.

See Data Cleaning and Quality SOP for more information on data quality levels

3.3.2 SAP SIGN-OFF

The trial statistician is responsible for ensuring that the SAP has been completed, reviewed, and signed off before requesting database lock. This is required for any database lock, not just the final analysis. A database lock being performed for pre-planned protocol-required analyses, such as for an analysis of selected comparison(s) in a platform trial, must have a signed off SAP to refer to.

3.4 REQUESTING A DATABASE LOCK

The trial statistician should request a database lock be performed in writing, using the Database Lock Request Form.

Database lock should be requested by the statistician using the Database Lock Request Form

The Database Lock Request Form contains details of:

- Which database system(s) are to be locked. Platform trials in particular may have multiple databases to be locked.
- Effective lock date
- Results of data quality checks as decribed above, including the acceptable quality thresholds, review and justification
- SAP sign-off date
- Database access needs post-lock

In most cases, the only database access mode that will be available to users post-lock is read-only. However, if there is a need to use the database for other purposes after this database lock, this should be detailed in the Database Lock Request Form. (See section 3.2 for more detail). The signed Database Lock Request Form is stored in the DMS Master File.

3.5 PREPARING THE DATABASE LOCK DOCUMENT

Upon receipt of a Database Lock Request Form, the DSPM will prepare a Database Lock document to detail the proposed database lock procedure, after consultation with the trial team.

The DSPM prepares the Database Lock document upon receipt of the Database Lock Request Form

Specific details will vary depending on the database system, but are likely to include:

- Scripts or procedures to document the last data inserted, updated, or deleted in the database
- Proposals for removing access permissions, and recording this in the Database Delegation Log. If the database will continue to be used post-lock, then the removal of access permissions is for the locked copy only (not required to update Database Delegation Log)
- Proposals for extract of frozen data set, if required
- Proposals for database backup and archiving, if required

The Database Lock Document should be reviewed by the trial statistician and other members of the trial team as required; review should be documented in the revision history.

3.6 PERFORMING THE DATABASE LOCK

Once the Database Lock Document has been reviewed and agreed, the DSPM can proceed to implement the database lock as detailed in the document, with the assistance of the database programmer if required. The final version of the document is printed and signed once the lock has been implemented, and is stored in the DMS Master File.

3.7 CONSIDERATIONS IF THE DATABASE NEEDS TO BE USED POST-LOCK

If the database will need to be used post-lock, the typical solution is to:

- Make a copy of the live database from a backup
- Perform the database lock as described above on the database copy
- This includes having a backup of the locked database
- Access rights should remain as existed before the lock on the live database

The Database Lock Request document should detail exactly what these needs are, and the Database Lock document details exactly how this is to be done. Normally the trial team will no longer need access to the locked database, but if required, view-only access that can be arranged by assigning the appropriate user roles.

3.8 REQUEST TO UNLOCK A LOCKED DATABASE

If a final database lock has been performed (i.e. the database is not expected to be used post-lock), the trial statistician may wish to request that a database be re-opened (if, for example, new data or corrections have come to light). This request must be made in writing and needs to be signed by the Project/Programme Lead.

A locked database will not be re-opened when the lock was not for final analysis. Any new data received after the lock must be entered into the live database, not the locked database. This is because the live database will continue to have data added and edited post-lock. If new data received is critical for the analysis, a new database lock (including repeat of all data quality checks) must be requested.

The Database Unlock Request Form is written by the Statistican and needs approval by Project Lead, Programme Lead, or Head of Research Theme

The request form should contain details about:

- which database system(s) are to be re-opened
- user access required
- reasons for re-opening

The request should be discussed with relevant members of the trial team

3.8.1 PREPARING THE DATABASE UNLOCK DOCUMENT

Upon receipt of a request for a database to be unlocked, the DMS Project Manager will prepare a document to detail the proposed database unlock procedure, after consultation with the trial team.

The DSPM prepares the Database Unlock document upon receipt of the Database Unlock Request Form

Specific details will vary dependent on the database system, but are likely to include:

- proposals for granting access permissions, and recording this in trial database delegation log
- report of details of what data points have changed after unlock

The Database Unlock Document should be reviewed by the trial statistician and other members of the trial team as required prior to implementation.

3.8.2 PERFORMING THE DATABASE UNLOCK

Once the Database Unlock Document has been agreed, the DSPM can proceed to implement the database unlock as detailed in the document (with the assistance of database programmer or system administrator as required). Once the database unlock has been applied, the database unlock document should be printed and signed by the DSPM and the trial statistician.

To re-lock the database, the procedures detailed in sections 3.2-3.6 should be performed again.

3.9 PROVISION OF DATA TO SITES AFTER FINAL DATABASE LOCK IN EDC STUDIES

Following final database lock in an eDC study, each site must be provided with a copy of the data for that site as extracted from the study database. Site must retain read-only access to the locked database until the extract has been produced and received, and the site has confirmed it is satisfied with that copy.

Copies of site data for retention at site are produced according to the procedures for the database system used. For example, MACRO has an export module to produce site data files. A copy of these files will be retained in the S:\Database_Archive share. Study teams should discuss the appropriate method with DMS.

The CPM or TM will work with DMS and IS to produce copies of the site data onto encrypted media (typically CD or USB stick). The CPM or TM will then manage the remainder of the process, which should consist of:

- sending these copies to site, by guaranteed delivery
- documenting the receipt of the media at site
- documenting that the media can be read at site
- documenting that the site confirms that it is satified that the media contains the data in the database for that site
- documenting site procedures for providing long-term access to the data on the disk and to backing up the data

See Site Confirmation of Data Receipt Form in SOPbox

If sites raise any concerns with the data provided to them, the study team should work with them to resolve the issues. Once the signed form documenting all of these steps has been received, read-only access to the database can be revoked and the delegation log updated.

For platform studies which use eDC, the point at which the data is provided to sites should be discussed within the TMT.