# document Summary Sheet

|  |  |
| --- | --- |
| Document: | Data Handling Plan |
| Purpose: | This DHP template may be used for clinical studies at CTU, unless another template has been agreed upon. |
| Audience/User: | Clinical Data Managers and study teams of clinical studies at CTU |
| Details: | The template should be customised to the protocol, the studies’ special needs / circumstances, and the requirements of the data capture system. Sections may be edited or deleted as needed. |
| Best Practice Recommendations: | * Instructions to the users in red (delete before final). * Suggested texts in blue (edit and change the colour of the text before final). * References to “Sponsor” may refer to the sponsor or other person who has been delegated some sponsor duties depending on the context of the sentence and on the decisions at the time of DHP development. Update the template at the time of implementation to refer to the appropriate party. * Please note that according to EU regulation 536/2014 the definition of a “clinical study” at CTU is a clinical trial or a non-interventional study. * Please update the DHP Template identifier in the lower left hand section of the footer. * **Remove this Tool Summary Sheet prior to the use of this template.** |

Document Revision History:

|  |  |  |
| --- | --- | --- |
| **Version Number** | **Version Date** | **Summary of Revisions Made:** |
| **0.1** | 26AUG2014 | **Draft version** |
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| **1.0**  **2.0** | 08APR2018  29NOV2023 | **Revision of SOP and templates**  **Revision of SOP and templates** |

|  |  |
| --- | --- |
| **study DESCRIPTION** | |
| **EU CT no (ID)/REC No.** |  |
| Study Name |  |
| Study Short Name |  |
| Protocol version and date |  |

|  |  |  |
| --- | --- | --- |
| **Version Control** | | |
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|  |  |  |
| --- | --- | --- |
| **Signature List** | | |
|  | **Name and Role** | **Date and Signature** |
| **Approved by** | [Name],  Sponsor/ Cordinating Investigator / Project Leader/ Principal Investigator/ |  |

|  |  |  |
| --- | --- | --- |
|  | **Name and Role** | **Date and Signature** |
| **Created by** | [Name], Clinical Data Manager |  |
| **Reviewed by** | [Name], Clinical Data Manager |  |

List of Abbreviations  
Edit accordingly.

| **Abbreviation/term** | **Explanation** |
| --- | --- |
| aCRF | Annotated Case Report Form |
| ATC | Anatomical Therapeutic Chemical (ATC) classification system |
| CDM | Clinical Data Management / Clinical Data Manager |
| CDMD | Clinical Data Management Documentation |
| CI | Coordinating Investigator |
| CM | Centralised Monitoring |
| CTU | Department of Research Support for Clinical Trials, Clinical Trials Unit |
| DEI | Data Entry Instructions |
| DHP | Data Handling Plan |
| DHR | Data Handling Report |
| DMC | Data Monitoring Committee |
| DSMB | Data and Safety Monitoring Board |
| DVP | Data Validation Plan |
| eCRF | Electronic Case Report Form |
| EDCS | Electronic Data Capture System |
| IMP | Investigational Medicinal Product |
| ITT | Intention To Treat |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MM | Medical Monitor |
| PI | Principal Investigator |
| PP | Per Protocol |
| PL | Project Leader, studies that requires Regional Committees for Medical and Health Research Ethics (REC ) approval |
| PROM | Patient Reported Outcome Measurements |
| QC | Quality Control |
| Safety population | Subjects who received at least one dose of study treatment (even if it is a placebo) |
| SAE | Serious Adverse Event |
| SAS | Statistical Analysis System language |
| SOP | Standard Operating Procedure |
| Sponsor | An individual, company, institution or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial |
| SUSAR | Suspected Unexpected Serious Adverse Reaction |
| UAT | User Acceptance Testing |
| TMF | Trial Master File |
| .CSV | A comma separated values file |
| .sas7bdat | SAS datasets |
| .sav | SPSS data file |

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# Introduction

## Purpose

The purpose of this document is to describe the plan of action for all Clinical Data Management (CDM) tasks for the [short name]. The CTU will be responsible for the CDM process from DDMMMYYYY (1st version of demo mode on Viedoc training server) to the end date as agreed upon in the cooperation agreement (data handling report / archiving). This plan also identifies the documents and deliverables that will be produced as part of the CDM activities. This document is managed by the Clinical Data Manager (CDM).

# Electronic data capture system

Electronic data capture system (EDCS), Viedoc version 4.77 has been used in the development of the study specific electronic Case Report Form (eCRF). The eCRF has been developed and tested according to SOP DM04 Electronic Data Capture (EDC) system.

## Audit trail

All changes made to trial data are audit trailed and stored in the database. The audit trail is created automatically by the Electronic Data Capture system and describes the data change, when the change was made, by whom, and the reason for the change. The audit trail is available to all the users in Viedoc and is included in the archive PDFs. The audit trail is stored on the Viedoc server until the study is decommissioned from the server, usually few months after the final study database lock and approval from the sponsor.

## Electronic Data Capture System Access

The user roles and associated rights will be defined and configured in the Viedoc designer module by the CDM. The CDM is responsible for creating EDC user access which has been requested/validated by the CI or designee during the setup and conduct phase using the Temp DM01.03 Personnel log.

## Access Security

All eCRF users require a unique account, which uses the user’s email-address and a self-chosen password.

The following security measures are included in the EDC system Viedoc:

* Log in attempts: if the user fails to log in more than 3 times, the account is locked. In such circumstances, the user should use the “forgot password” link on the login page to unlock and reset the password. The reset password link is valid for 3 hours.
* Inactivity: if the user is inactive for more than 20 minutes, the user will be automatically logged out from the system.
* Password expiration: the user is required to change the password every 90 days, and the new password should be different from the latest 10 previous passwords.

# Laboratory data

All standard laboratory samples will be analysed at [Hospital, clinic] local labs and the result will be entered into Viedoc.

The units and reference ranges for each local laboratory are effective from DDMMMYYYY and will be loaded into Viedoc for each site. If the reference ranges change during conduct, the study team should notify the CDM, and a new set of reference ranges will be uploaded into Viedoc with a new effective date. The new set of reference ranges can only be uploaded and published into Viedoc by the Reference Data Source Manager (usually CDM).

Abnormal results should be assessed as clinically significant or not.

Other special analysis should also be covered in this section.

# PROMs in ViedocMe

Viedoc will be used for the Patient Reported Outcome Measurements (PROMs).

If paper PROMs are used the data will be entered manually into Viedoc by site personnel.

Please note that if so, the paper PROMs are the source data.

# Data Validation

Data Validation performed by CTU will be limited to automatic data checks programmed in Viedoc, to prevent entering of invalid/illogical data. All data checks are listed in sheet “Data checks” in the Configuration Report. Further data validation will be performed by the study team.

*or*

Data validation will ensure data accuracy and validity and will be performed according to the SOP DM05 Data Validation and documented in the Data Validation Plan (DVP) and Data Validation Document (DVD). The DVP is a document specifying all data checks performed during the study, and the frequency of these procedures.

# Randomisation

The CDM will complete the Temp DM07.01 Specification for Randomisation according to protocol and send the form to the study statistician. Randomisation will be generated by [name of study statistician] using [name of stat program]. CDM will upload the randomisation list to Viedoc and the list will be saved in a secured area with restricted access. The research subject allocation will be performed in the eCRF and the CDM will test the allocation solution with a test list.

*or*

The CDM will complete the Temp DM07.01 Specification for Randomisation according to protocol and send the form to the unblinded statistician with a notification that the recipient of the randomisation list should be the unblinded CDM. Randomisation will be generated by [name of study statistician] using [name of stat program]. The unblinded CDM will upload the randomisation list to Viedoc and save the list in a secured area with restricted access.The research subject allocation will be performed in the eCRF and the CDM will test the allocation solution with a test list.

*or*

There will be no randomisation in this study.

*or*

Randomisation will be generated by using https://icostatistics.shinyapps.io/randlist/

Copy relevant information about blinding/not blinding from paragraphs above.

# Internal and external testing of the EDC system

The study specific application will be tested by CDM, the internal quality control (QC) CDM and by the study team according to SOP DM04 Electronic Data Capture (EDC) system.

The QC is based on a needs assessment, and the findings are documented in [Study short name]\_Internal QC. Appropriate corrections according to findings are implemented in the EDC system and documented accordingly.

The external quality control is performed by the study team. The testing will be documented in the User Acceptance Testing (UAT) document and archived in the CDMD folder. The corrections made to the eCRF after UAT are checked by the QC CDM. The test data will be locked and kept as documentation of the QC performed by the study team.

Before the eCRF is moved into production mode, Temp DM04.03 eCRF Approval Form will be completed and sent to CI/Project Leader or designee for approval.

# Training for site personnel

The CI/Project Leader or designee is responsible for the training of site personnel. Standardised eLearning are available in Viedoc and can be made mandatory or optional in cooperation with the CI/Project Leader or designee. The mandatory eLearning might prevent access to the system before the training is completed and signed.

## Data Entry Instruction

The CDM may create a study specific data entry instruction (DEI), which will be complementing the e-Learning. The DEI will be accessible in the Documentation & Training section in the eCRF.

# Medical coding

Medical coding will be performed by the CDM consecutively according to separate procedures and approved by CI in the EDC system.

| **Coded items and coding dictionaries** | |
| --- | --- |
| **Coded data items** | **Coding dictionary** |
| Adverse Events | MedDRA version 25.0 (version at study start) |
| Medical History | MedDRA version 25.0 (version at study start) |
| Concomitant Medication | WHO DDD ATC 2022 |
| Diagnoses | ICD version xx or  DSM version xx |

# Changes to the eCRF during the study

If the final version of the eCRF is changed after it has been set in production mode, the changes will be tracked in a separate document named [Study short name]\_Changes eCRF.

If the CDM considers the changes as major, it will require an updated and signed eCRF Approval Form from the CI/Project Leader and, if applicable the study statistician, before made effective. The new versions of the changed eCRF forms and an annotated CRF (aCRF) will be sent for archiving in the TMF.

# Importing external data

Describe the format and frequency of the data uploading, including the process for uploads and corrections to previously received data, should be agreed upon with the source organisation and the study group. The process should be documented.

*or*

Not applicable.

# Interim analysis/Data Monitoring Committee

Interim analysis is planned of clinical safety and efficacy data obtained for at least [number of subject] subjects who have completed up to xx, every [number] month. The data must be validated as if the database was to be locked, and if applicable, medical coding must be performed and approved. The data will be submitted as agreed upon. CDM should stay blinded during the process and the unblinded CDM will inform the unblinded statistician about the treatment code.

*or*

No interim analysis is planned in this study.

*and/or*

Data Monitoring Committee (DMC) meeting is planned of clinical safety data obtained for at least [number of subject] subjects who have completed up to xx, every [number] month. Safety data should be monitored and validated, and if applicable, medical coding must be performed and approved, before submitted to the DMC. The data should be submitted to DMC at least [number] week(s) prior to the meeting. CDM should stay blinded during the DMC process and the unblinded CDM will inform the unblinded statistician about the treatment code.

If both interim analysis and DMC are planned, please edit the section accordingly.

# Handling of Suspected Unexpected Serious Adverse Reaction (SUSAR)

Check the cooperation agreement concerning who will report SUSARs.

If the cooperation agreement specifies that the sponsor will handle the SUSAR reporting:

Sponsor must ensure that any suspected unexpected serious adverse reaction (SUSAR) that occur during the study/trial is reported as individual reports (reports for each subject) via the EudraVigilance database.   
Sponsor must report the SUSAR via the EudraVigilance database within 7 days for life-threatening and/or fatal criteria or 15 days for non-fatal criteria.

*or*

If the cooperation agreement specifies that Forskningsstøtte will handle the SUSAR reporting:

Sponsor must ensure that any suspected unexpected serious adverse reaction (SUSAR) that occur during the trial is reported as individual reports (reports for each subject) in the EudraVigilance database.

*The report must be sent to* [SUSAR@ous-hf.no](mailto:SUSAR@ous-hf.no) *on a Council for International Organizations of Medical Sciences (CIOMS) form or an equivalent form. As a general rule, CIOMS forms should be unblinded.  The CIOMS form should be transmitted in a secure way protecting sensitive personal data within 3 days for life-threatening and/or fatal criteria or 5 days for other criteria.*

*or*

Not applicable

# Clinical data management documentation

CDM will create the CDMD according to SOP DM01 Clinical Data Management. All CDMD and other applicable documents created during the study will be stored in the electronic study folder. The electronic study folder will contain a copy of the TMF/eTMF documents for this study delivered from CTU. The CDM documentation will be sent to the study team for archiving in the TMF consecutively. / The CDM documentation will be saved in the eTMF consecutively.

## eCRF documentation

The eCRF documentation consists of the following documents:

* [Study short name]\_ConfigurationReport version 1.0
* [Study short name]\_Annotated CRF (aCRF) version 1.0

The configuration report will specify the complete set of data variables to be collected. It describes functions and conditions, source data verification (SDV), alerts, roles, forms, items and groups, data checks and code lists. It will also give a study overview of all study events, including all unscheduled and common events (described in the sheets “Study workflow-Events/ Study workflow-Activities/ Study workflow-Forms”). It will be created by using the Viedoc export functionality.

The aCRF documents all the forms with complete code lists used in the eCRF.

# Database lock

The CI/PL is responsible for informing the relevant CTU personnel about the planned date for last patient last visit (LPLV) in the trial, or any other milestone that triggers a database lock. CTU staff should be notified six months in advance of database lock.

The database lock process will include tasks such as approving medical coding, performing SAE reconciliation, resolving queries, completing monitoring visits and validating data. All forms must be signed by CI or designee. The DB will be locked when all outstanding issues are agreed upon, the SAP and Temp DM06.02 Database Lock Approval Form has been signed by the CI/PL. The CDM will send the signed form to the study team for archiving and a copy will be kept in the CDMD folder.

Before the database lock, if agreed upon, STAT will create a listing of all research subjects included in the study and their allocation to the different populations according to the protocol (e.g. safety, ITT and PP)

*or*

Before the database lock, if agreed upon, the CDM will create a listing of all research subjects included in the study and their allocation to the different populations according to the protocol (e.g. safety, ITT and PP), using Temp DM06.01 Analysis population allocation form. The list will be sent to CI/PL for approval.

For assessment of allocation the research subject CRF, monitoring reports, status of any open or pending queries, protocol deviations, medical coding, and the outcome of the SAE reconciliation should be investigated. If the subjects are not included in a population, the cause should be listed.

## Partial Database Lock

Primary and secondary endpoint analysis is to be expected after last subject has completed the x, x and x year visit.

*or*

There will be no partial database lock in this study.

## Complete Database Lock

Complete database lock will be performed as described above after x years follow-up.

## Database Unlock

If any error that requires correction is discovered, the database may be unlocked to correct these errors after approval from the CI/study statistician according to Temp DM06.03 Locked Database Correction Form.

**If the study is blinded, edit item 17 accordingly. If no blinding, please delete items 17.1 and 17.2.**

# Unblinding

## Unblinding before DB lock

Emergency unblinding can be performed in the eCRF by accessing the eCRF as an Emergency Unblinder. The eCRF will require a reason for unblinding and this must be provided without revealing the IMP given to the subject. In this study this role is assigned to CI/Project Leader /PI/Investigator [name of the unblinder].

*or*

In this study all investigators have access to the Emergency Unblinder functionality.

*or*

In case of emergency unblinding, [name of the unblinder], has access to the randomisation list and will provide the subject caregiver with the information what IMP is given to the subject

*or*

Not applicable.

## Unblinding after DB lock

After all subjects have been checked for correct allocation according to the randomisation list, the unblinding will be performed according to SOP DM07 Randomisation and unblinding. If any violation from the allocation is revealed during this process the study statistician and CI will be notified and the violation will be reported in the analysis population allocation form and the DHR. If the analysis is performed blinded the CDM should not receive the randomisation list from the unblinded CDM before the analysis is finalised. Temp DM07.02 Code Breaking Form will be completed and the signed off form will be sent to TMF / saved in eTMF for archiving and a copy will be kept in the CDMD folder.After the CDM has received the randomisation list from the unblinded CDM the code will be broken by merging the randomisation list with the DB and the outcome is thoroughly checked.

*or*

Not applicable.

# Audit

The study team/sponsor will be responsible for any internal audit.

# Database export

## Export format

Formats available for export from the database are CSV – comma –separated values with SAS script / Excel / CDISC ODM – XML.

The clinical datasets delivered to the sponsor after database lock are specified as .csv / .sas7bdat (SAS datasets) / .sav files (SPSS) / [name of other files].

Please adjust the table according to the study.

| **Exported files** | |
| --- | --- |
| **Form Name** | **Form ID** |
| Adverse Events | AE.[file] |
| Clinical chemistry | CC.[file] |
| Comments | CO.[file] |
| Demographics | DM.[file] |
| Eligibility | EI.[file] |

## Export

**If data is uploaded in Viedoc CTU Admin / CTU Transfer by CDM:**

After database lock, the exported datasets will be temporarily saved on a secured Oslo University Hospital server, before being uploaded in Viedoc CTU Admin / Viedoc CTU Transfer.

The clinical datasets will be subject to quality control according to SOP DM08 Electronic Data Transfer.

*Or*

**If data is exported from Viedoc by the Sponsor/CI/PI:**

After database lock, the Sponsor/CI/PI will get access to download the locked data if this access has not already been given.

*Or*

**If data is exported to a secure Oslo University Hospital server by CDM:**

After database lock, the exported datasets will be temporarily saved on a secured Oslo University Hospital server.

The clinical datasets will be subject to quality control according to SOP DM08 Electronic Data Transfer.

# Archiving

Files for electronic archiving will be delivered through a secure solution in Viedoc. The downloaded files will contain the complete audit trail and all queries, and will be split by site. Sponsor will receive complete files for all sites. The file formats will be PDF, CSV and Excel files.

*Or*

Files for electronic archiving will be saved in a designated secured area on an Oslo University Hospital server.

The downloaded files will contain the complete audit trail and all queries, and will be split by site. Sponsor will receive complete files for all sites. The file formats will be PDF, CSV and Excel files.

*Or*

The site will get access to download the subject data entered into Viedoc after database lock. The downloaded files should contain the complete audit trail and all queries, and should be split by site. Sponsor should keep a complete archive for all sites.

The file formats should be PDF, CSV and Excel files.

CDMD documentation that are not sent to the study team consecutively will be sent for archiving in the TMF at the end of the study. The TMF structure used in this study/trial is described in NorCRIN SOP LM 2.09, template Trial Master File (TMF), attachment LM2.09.05 (single center)/attachment LM2.09.01 (multicenter) or Drug Information Association (DIA) TMF Reference Mode.

# Data Handling Report

Deviations from the clinical data management process described in the DHP and study specific procedures implemented during conduct, will be described in the Data Handling Report (DHR).

# References

Legg inn alle referanser til SOP’er – med versjonsnummer!

The following versions of SOP’s will be used in this study:

|  |  |  |
| --- | --- | --- |
| SOP | Version | Approval date |
| SOP DM01 Clinical Data Management | 2.0 | 29NOV2023 |
| SOP DM04 Electronic Data Capture (EDC) system | 3.0 | 29NOV2023 |
| SOP DM05 Data Validation | 2.0 | 29NOV2023 |
| SOP DM06 Database Lock | 2.0 | 29NOV2023 |
| SOP DM07 Randomisation and unblinding | 2.0 | 29NOV2023 |
| SOP DM08 Data Transfer | 2.0 | 29NOV2023 |
| SOP DM09 SAE Reconciliation | 2.0 | 29NOV2023 |
| SOP DM10 Medical Coding | 2.0 | 29NOV2023 |
| SOP DM11 Configuration of PROMs | 2.0 | 29NOV2023 |
| SOP DM12 Centralised Monitoring | 0 | 18MAR2019 |