# 1 PURPOSE

The purpose of this procedure (Standard Operating Procedure - SOP) is to describe how to ensure good quality by adequate risk management throughout all phases of a clinical trial, from planning to publication.

The SOP should ensure that national and international laws and regulations and ICH Guideline for Good Clinical Practice (ICH GCP) specified in the reference document are followed.

# 2 SCOPE

The SOP is valid for all clinical drug trials in which the sponsor institution has included the NorCRIN SOPs in their quality system.

Quality management includes an adequate trial protocol, an expedient tool for data capture and processing, as well as a thorough risk evaluation and appropriate handling of the risks identified through all phases of the trial. A required part of the risk handling in clinical drug studies is the monitoring plan, which should reflect the risks identified for the trial.

# 3 RESPONSIBILITIES

Sponsor has an overall responsibility to implement a system to ensure quality in all phases of the trial according to this SOP. Sponsor should ensure all aspects of the trial are feasible. Unnecessary complexity should be avoided. The protocol, data capture system, monitoring plan and other trial documents should be clear, concise and consistent. This task is delegated to the Principal Investigator in single center trials / National Coordinating Investigator in multi center trials.

# 4 APPROACH AND RESPONSIBILITIES

A well written protocol is the first step to ensure the quality of the trial. It is recommended to use the Transcelerate's template, see guidance document available at norcrin.no, as this will include all required topics to be included in a protocol, as well as valuable instructions for aspects to be considered in a clinical trial.

The protocol should take into account all processes and critical data to ensure the well-being of the trial participant and the reliability of the study results. Study specific procedures may also be required to complement the protocol e.g. on how to handle biological samples.

Next step of the quality management is to ensure an adequate data capture system is available for the study. A paper based tool is acceptable, but not recommended; a description of different web based electronic data capture systems (eDCS) is available at norcrin.no. For single centre studies, the institution might have other eDCSs available.

A risk assessment should be performed by the sponsor or designee (i.e. Principal Investigator in single center trials / National Coordinating Investigator in multi center trials) before the trial is initiated and thereafter on a regular basis throughout the trial. It is recommended that an interdisciplinary group of involved study personnel and support functions participate in the risk assessment. A useful template to be used for risk assessment is attached to this SOP; Risk Assessment Tool. This template also includes a Study Organizational Tool.

The purpose of the risk assessment is to identify specific processes critical to ensure trial subject's protection and the integrity of the data to be collected in the trial. The risk assessment should also include an evaluation of the following parameters:

- Likelihood
- Consequence
- Risk for not detecting

The parameters should be graded into low, medium and high. Further, the assessment should also include a consideration whether the risk is acceptable or not, and if acceptable; an assessment of the need for threshold values, e.g. how much deviation / how many deviations can be accepted before certain measures or actions should be taken.

As an outcome of the risk assessment, national coordinating investigator in a multi center trial / principal investigator in a single center trial will decide upon different solutions and actions to be performed and by whom, to prevent or reduce the risk for events and deviations to occur. These should all be documented in the Risk Assessment Tool.

Before the study is initiated, a Monitoring Plan for the study will be written. This should take into account the risk assessment already done and mitigate risks identified which can effectively be discovered and corrected by monitoring. Examples of risks that can be mitigated by monitoring is lack of adherence to protocol, inadequate consenting procedure, deviation in collection of primary and secondary endpoints or safety data, missing essential and required study documents and inappropriate facilities and equipment.

A regular review of the risk assessment is required. This can be done annually, e.g. at the time for submitting the annual report to the Competent Authority. A more frequent review may be required. The regular review should also include a check that previously solutions and actions agreed upon are completed accordingly.

All quality management activities should be documented and communicated to the concerned parties.

The quality management implemented for the trial should also be summarized in the study report, together with important deviations.

# 5 NON-COMPLIANCE MANAGEMENT

All non-compliance should be handled according to the procedures for handling non-compliance of the individual health trust / institution and to SOP Issue Management.

# 6 REFERENCES

## 6.1 EXTERNAL REFERENCES

- ICH Guideline for Good Clinical Practice (GCP) E6 (R2)

## 6.2 INTERNAL REFERENCES

# 7 ATTACHMENTS

- Template Risikovurdering
- Template Monitoring Plan

# 8 DEFINITIONS

Definitions

# 9 CHANGES FROM PREVIOUS VERSION

Version 3.1. This SOP replaces SOP 1.10 version 3.0 and is written in English. The sponsor's responsibility is described in more detail. Added that the monitoring plan should reflect the risk evaluation. Monitoring Plan template added as attachment.