1 PURPOSE

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures for application for approval and start-up of clinical trials.

For transition of trials approved according to the directives 2001/20/EC and 2005/28/EC (old legislation) to the Clinical Trial Information System (CTIS) according to Regulation 536/2014 see Working Instruction Transition from outgoing legislation to Reg 536/2014.

This SOP ensures compliance with ICH Guideline for Good Clinical Practice (ICH GCP) and national and international laws and regulations, specified in the SOP Legislation and Guidelines.

2 SCOPE

This SOP is valid for all clinical drug trials sponsored by hospitals that have implemented the NorCRIN SOPs.

3 RESPONSIBILITIES

Sponsor is responsible for ensuring that for all clinical drug trials approvals are obtained and that the trials are started in accordance with this SOP.

For multicentre trials, the sponsor has overall responsibility for ensuring written agreements with cooperating healthcare companies / other partners.

The sponsor's responsibilities shall be described in the quality system of his/her institution. Tasks are delegated according to SOP Roles and Responsibilities in clinical trials implemented in the institution.

The sponsor is responsible for obtaining approval of a clinical drug trial by ethics committees and competent authorities and other concerned bodies.

The sponsor may transfer any or all of the sponsor's trial-related duties and functions to a third-party vendor such as a Contract Research Organisation (CRO), but the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. The sponsor should ensure oversight of any trial-related duties and functions carried out on its behalf. Transfer of duties shall be specified in a written agreement.

4 PROCEDURES

The application for a clinical trial consists of Part I and Part II. Part I contains general study documents i.e. study protocol, study drug documentation, etc. Part II contains site specific documents and patient facing material (e.g. informed consent). In Norway, Part I will be assessed by both the Norwegian Medical Products Agency (NoMA/DMP) and Regional komité for medisinsk og helsefaglig forskningsetikk (REK), Part II by REK only.

Genetically modified organisms (GMO-IMPs)
For clinical trials with investigational medicinal products (IMPs) that contain or consist of genetically modified organisms (GMO-IMPs) for use in humans, application must be sent both in CTIS and to (see Clinical trials with GMOs in medicinal products - Norwegian Environment Agency).

Genetically modified micro-organisms (including viruses, viroids, animal, and plant cells in culture) may have to

be carried out under containment until given to the patient, to limit contact of these organisms with the environment. Such activities include or example the process of genetic modification, the use, storage, transport, destruction and disposal of GM microorganisms. NoMA (DMP) will involve the Health Directorate to assess whether approval for contained use is required. For details see Genterapi - Helsedirektoratet

4.1 Application in the EEA

4.1.1 Low intervention studies

Low intervention studies have reduced requirements for traceability of IMP and monitoring. Sponsor must justify why the clinical trial is a low-intervention clinical trial in the application.

Studies can be regarded as low intervention studies if they fulfil the following conditions:

(a) The IMPs are authorised;

(i) the IMPs are used in accordance with the terms of the marketing authorisation; or

(ii) the use of the IMPs is evidence-based and supported by published scientific evidence on the safety and efficacy of those IMPs in any of the MSC, and

(b) The additional diagnostic or monitoring procedures do not pose more than minimal additional risk or burden to the safety of the subjects compared to normal clinical practice in any MSC

4.1.2 Required documents

Annex I of REGULATION (EU) No 536/2014 lists the required documentation. The European commission has also prepared a Q & A document to complement the regulation. For international trials, see also working instruction International Trials.

The submission documents are listed in the table below. In addition, the following documents are useful when preparing the submission:

- SOP Investigational Medicinal Product (IMP) at Trial Start
- Language requirements for Part I documents can be found in the Q & A document, Annex II
- The European Commission has provided guidance for submission of Part II documents, Part II Document Harmonisation Guidance.

Special attention should be brought to the Informed consent and patient recruitment procedure (template)

- If hospital records (patient journals) are to be reviewed to identify potential trial subjects this must be described in the recruitment procedures. The EC will then grant waiver from confidentiality. Without this such review of records cannot be done. Review should follow institutional procedures.
- The trial subject should not be in a dependent relation to the person who asks for the subject consent, e.g. have treated the subject for a while. Preferably the information should be given and the consent obtained by a study member who does not have a relation to the subject. In cases where this is not possible to avoid, e.g. small institutions, voluntary participation must be secured by other means, like substantial time to make the decision. This should be described in the application under Recruitment arrangements.

- Subjects that do not understand Norwegian should in general not be excluded from inclusion and should be given written and oral information in a language they master. For translations, see Oversettelsestjenester - Sykehusinnkjøp (sykehusinnkjop.no). REK does not need to approve the translations.

For guidance on special subject groups, see Veileder til helseforskningsloven.

Insurance:
In Norway insurance should be purchased through Legemiddelansvarsforeningen (LAF). The coordinating investigator will ensure payment of the premium before the trial is initiated, and then every year for as long as the patients are undergoing trial specific procedures.

Naming and version control:
All documents must have an "ID" (e.g. acronym) and version number and date stated in the header or footer of the document. The document CTCG Best practice guide naming of documents issued by the Clinical Trial Coordination Group (CTCG) must be followed. During document upload, make sure to change the name of the document according to the naming convention, and the date and version number must correspond with the date and version number of the actual document (not version date of template). Part I documents are coded B to J, and Part II documents K to R.

Redaction of personal information

The purpose of redacting documents and structured fields is to comply with GDPR.

Some trial documents and structured data will by default be published in EU Clinical Trials as soon as the application is approved. Special attention should be given to the inclusion of personal information, which should be redacted. Revised transparency rules for CTIS have been adopted, but updates in CTIS to reflect these changes will not be in place before spring 2024. Sponsors are therefore advised not to use the deferral option and to limit uploading of "for publication" documents, see section 3.4.

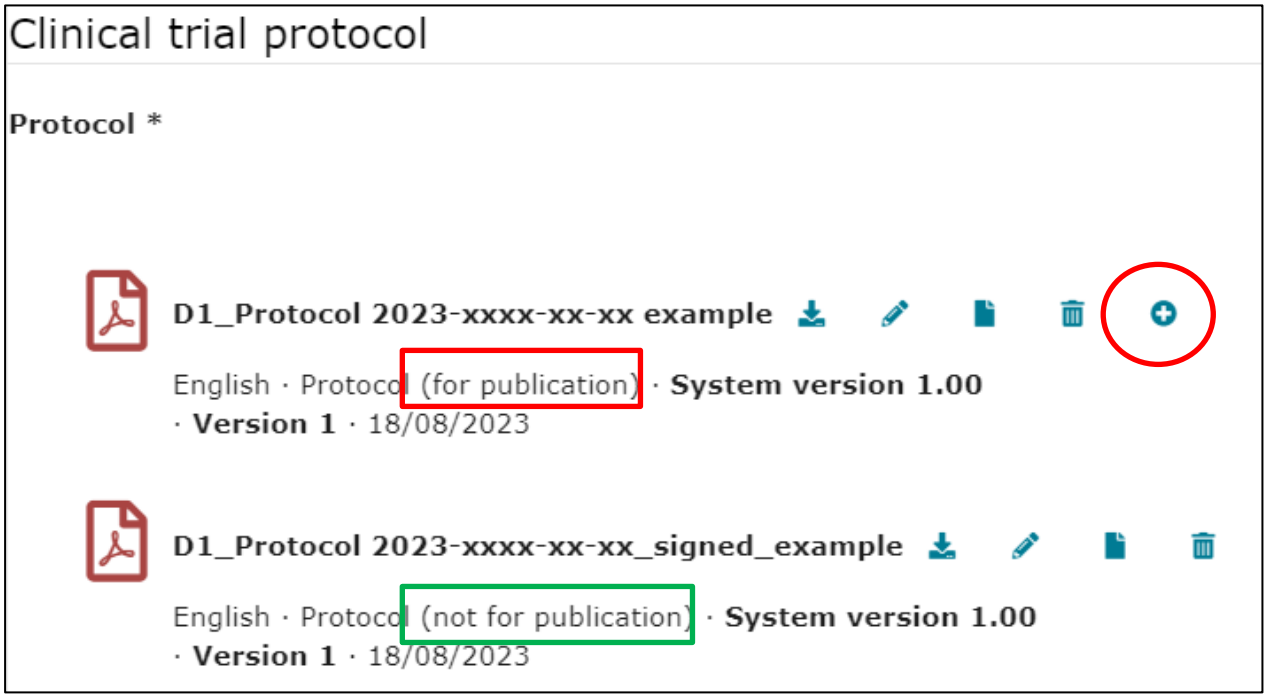
- The personal information that should be published is the name and work-related contact information/affiliation of:
  - the principal investigators
  - the Qualified person for GMP compliance documentation if applicable
  - the members of the DSMB if applicable
  - sponsor staff such as contact point for union, scientific contact point and public contact point. All three functions may be held by the coordinating investigator, or not
  - the person issuing the Site suitability form
  - the person issuing the GDPR compliance statement
- No signatures should ever be published. Documents with wet ink signatures should be uploaded as "not for publication". The first upload will per default be "for publication", the second "not for publication". Only the Qualified person for GMP compliance documentation and the person signing the site suitability form requires a signature in the "not for publication" document.
- All personal data included in metadata of a file should be removed, see Guide on CTIS common features
- All data from trial participants (e.g. patients) must be anonymised in "for publication" documents and in structured fields.

For further information, see Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS)

Although technically possible, it is recommended not to apply for deferrals and insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document and the required document as "not for publication", see tables 4.1.1.3 and 4.1.1.4 for more details.

Signatures:
Signed versions of the documents must be archived in the Trial Master File/Investigator Site File (TMF/ISF). Redacted or unsigned versions of the same documents should be uploaded in CTIS. Norwegian authorities do not require signed documents in CTIS, but authorities in other countries might. If signed documents are uploaded in CTIS, they should be uploaded as "not for publication" using the "add document" button.

Example:



The tables below refer to the different sections in the CTIS application portal and includes links to templates. If the templates are not used, a separate document should describe where the different items are covered.

Table 4.1.1.1 Forms

Templates/ Links		Application section	Naming convention codes	Comment
1	Cover letter	Initial application details	B1_ Cover letter EU CT number	The cover letter must list all documents submitted with version number
2		Proof of payment of fee		Not required for academic trials in Norway.

3	Compliance Norwegian Requirements on Data Protection (mononational trials) Template statement on compliance Regulation (EU) 2016/679 (multinational trials)	Compliance with requirements on Data Protection	Compliance on the collection and use of personal data	See comment in table 4.1.1.4 Part II, row number 38.
4	Transparency publication of clinical trial information contained in CTIS (europa.eu)	Deferral publication dates		It is not recommended to apply for deferral as new rules have been adopted although the technical updates in CTIS are not expected to be implemented before Q2 2024.

Table 4.1.1.2 Member state concerned (MSC)

Application section		Comment
5	Member states concerned	State here participating countries, number of subjects per country, and suggest RMS for multinational studies.

Table 4.1.1.3 Part I

Templates/Links		Application section	Naming convention codes B-J	Comment
6	Individual Participant Data (IPD) Sharing Statement	Trial information		Should be consistent with the study protocol and Informed Consent Form. See also; Data Sharing Statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors
7	Protocol template	Protocol information	D1_ Protocol EU CT number	SOP Protocol
8	Protocol synopsis	Protocol information	D1_ Protocol synopsis_MS EU CT number (*include MS* NO for Norway *in title)*	Must be written in local language for each participating country. Language requirements

Templates/Links		Application section	Naming convention codes B-J	Comment
				for different countries are listed in Q&A Annex II
9		Protocol information	D1_ Master protocol EU CT number and name and sub-protocol name and specific number/ID	Applicable for complex CT only.
10		Protocol information	D2_ Protocol modification nr number EU CT number	If applicable. In case of SM as separate doc.
11	DSMB Charter template	Protocol information	D3_ DSMB Charter EU CT number	If applicable. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
12		Protocol information	D4_ Patient facing documents e.g. questionnaire or diary	Subject questionnaires may also be included in the study protocol. The uploaded questionnaires should be in English. For trials conducted in Norway only, where the questionnaire does not exist in English, it is acceptable to have a Norwegian version.
13		Products	E1_ IB product name	If used as Reference Safety Information (RSI). Usually used for non-marketed IMPs. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
14		Products	E2_ SmPC product name	If used as Reference Safety Information (RSI) Usually used for marketed IMPs.
15		Products	F1_ Marketing/importing authorization MIA product name abbreviated name manufacturer/importer	If applicable, provided by IMP manufacturer. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for

Templates/Links		Application section	Naming convention codes B-J	Comment
				publication" document
16		Products	F2_ QP declaration product name abbreviated name manufacturer/importer	If applicable, provided by IMP manufacturer. Should be signed in "not for publication" document. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
17		Products	F3_ Other statements/licences *(e.g. import license)* product name abbreviated name manufacturer/importer	If applicable, provided by IMP manufacturer. Should be signed in "not for publication" document. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
18		Products	G1_ IMPD_Q product name	See Q&A, question 2.15 in case IMPD is provided by pharmaceutical company
19		Products	G1_ IMPD_E-S product name	If applicable, provided by IMP manufacturer. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
20		Products	G1_Simplified IMPD_Q product name	See Reg 536/2014, Annex 1, Table I
21		Products	G1_Simplified IMPD E-S product name	See Reg 536/2014, Annex 1, Table I. If the SmPC is needed, and has already been uploaded under line 12, please refer to that document. Insert WI-LM-

Templates/Links		Application section	Naming convention codes B-J	Comment
				3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document.
20		Products	H1_ AxMPD product name	If applicable (not marketed in the EEA), provided by IMP manufacturer.
		Trial Details	I1_ Scientific advice summary name organization	If applicable. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document.
21		Trial Details	I1_Scienfitic advice Quality name organisation	
22		Trial Details	I2_ PedCo opinion	If applicable. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document.
23		Trial Details	I3_ EMA PIP decision name agency	If applicable. Only applicable for companies that will apply for marketing authorization. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document.
26		Products	J1_ Label IMP_MS product name (*include MS* NO for Norway *in title)*	If applicable. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document.
27		Products	J2_ Label AxMP_MS product name (*include MS* NO for Norway *in title*)	If applicable. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for

Templates/Links		Application section	Naming convention codes B-J	Comment
				publication" document.

Table 4.1.1.4 Part II

Templates/Links		Application section	Naming convention codes K-S	Comment
28	Recruitment and Informed consent procedure template	Recruitment Arrangements	K1_ Recruitment arrangements	See details section 4.1.1
29		Recruitment Arrangements	K2_ Recruitment material description	
30	Hjem - Insights (rekportalen.no)	Subject information and informed consent form	L1_ SIS and ICF description (e.g. SIS and ICF adults, SIS and ICF 12-16 yr)	SOP Preparing Written Information and Consent Form In Norway, if the REK template is not used, attach documentation confirming that all requirements in Regulation (EU) No 536/204 are covered.
31		Subject information and informed consent form	L2_ Other subject information material description (e.g. information leaflet adults)	
32	Investigator CV	Suitability of the investigator	M1_ CV Investigator name investigator and clinical trial site (use abbreviations)	To be issued by PI. To be uploaded in the Suitability of the investigator section. Does not need to be signed or to have EU CT number added. PI must be a physician or a dentist. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
34	Declaration of Interest	Suitability of the	M2_ DoI	To be issued by PI.

Templates/Links		Application section	Naming convention codes K-S	Comment
		investigator	Investigator name investigator and clinical trial site (use abbreviations)	Update header/footer with study specific details. Delete instruction text. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
35	Site and Facilities Suitability	Suitability of the facilities	N1_ Site suitability form name clinical trial site	To be issued by the head of the clinic/institution or equivalent, according to institutional procedure (i.e. Level 2, Head of Clinic, or equal). Update header/footer with study specific details. Delete instruction text. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
36		Proof of insurance cover or indemnification	O1_ Trial participant insurance certificate	Not required in Norway. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
37		Proof of insurance cover or indemnification	O2_ Proof of coverage sponsor or investigator name sponsor/trial site (if not covered by O1)	In Norway this is confirmation from Legemiddelansvars-forsikringen (LAF). Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
38	Financial and other arrangements	Financial and other arrangements	P1_ Compensation trial	Update header/footer with study specific details Delete instruction

Templates/Links		Application section	Naming convention codes K-S	Comment
			participants, investigator, funding, and other arrangements	text in template.
39	Compliance Norwegian Requirements on Data Protection	Compliance with national requirements on Data Protection	R1_ Compliance on the collection and use of personal data	In mono national studies this document can also be uploaded under Forms (see table 4.1.1.1, row number 3). Update header/footer with study specific details. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document
40	Compliance with applicable rules for biological samples	Compliance with use of biological samples	S1_ Compliance on the collection, use and storage of biological samples	Update the version number/date in header/footer of the templates to a study specific version number/date. Delete instruction text in template. Insert WI-LM-3-06-02-vedl-02-template-for-documents-no-longer-subject-to-publication-rules as "for publication" document

Table 4.1.1.5 Evaluation

Evaluation		Comment
40	Validation	Lists responses to RFIs and confirmed validation of the application.
41	Assessment Part I	Lists responses to RFIs and confirmed approval or rejection of the application.
42	Assessment Part II	Discloses responses to RFIs and confirmed approval or rejection of the application.

43	Decision	Final decision given jointly by competent authority (e.g. NoMA) and ethics committee (e.g. REK-KULMU) per country

Table 4.1.1.6 Timetable

Timetable		Comment
44	CTIS Evaluation Timelines (europa.eu)	All tasks / events are shown in European Central Time (CET). Please note that the due dates for tasks in the future are indicative and might get updated. After the RMS has been selected, all projected tasks / events will be updated based on the RMS calendar. Part II assessment project timeline is based on each respective MSC calendar

4.1.3 Application process

For submission of application for clinical trials in all EEA-countries, Regulation 536/2014 applies.

4.1.3.1 Roles

Coordinating Investigator (CI) must follow the institution's procedure to get an EU CT number and applicable roles in Clinical Trial Information System (CTIS).

The Coordinating Investigator must request "CT admin" rights in CTIS to be able to assign roles to other qualified persons as appropriate for the trial. This is done while logged into CTIS Sponsor workspace and selecting "user administration" in the top menu, and then click on "Assign new role".

To be assigned a role in CTIS for a specific clinical trial, each user must have an EMA account (ensure the correct organization name and ID for the sponsor is selected).

To request a role, a user will need to:

1. Get an EMA account. See EMA Account Manager.
2. Log on to CTIS, click https://euclinicaltrials.eu/home
1. Select name at the upper right corner, then click "Personal profile" – "Update employer information" - choose the appropriate institution. Check the institution's procedure to ensure the right organization name, number and address is chosen.
2. Select name at the upper right corner, then click "My roles" "Request role", select your organization, scope= specific trial, enter EU CT number provided by CT Admin, select appropriate role. Several roles can be requestedThe CT admin will then need to log on to CTIS and approve the roles (select "User administration" on the blue line Search select persons for whom roles should be approved Approve Confirm)

Alternatively, the CT admin can assign roles without the users requesting them. User IDs must first be shared

with the CT admin.

Roles can be assigned for different parts of the application and further correspondence within CTIS: Part I, Part II, notifications, CT (both parts and notifications), Q-IMPD (the manufacturing part of the IMPD). Roles are also assigned at different levels; viewer, preparer (will also be able to view) and submitter (will also be able to view and prepare).

To be able to submit Annual Safety Reports (ASRs), a specific "ASR submitter" role must be applied for. CTIS – M03 Registration of a new CTIS user – YouTube

If the trial is to be conducted in several institutions, CI should require that the unregistered institutions get registered in the EMAs OMS database, see Clinical Trials Information System (CTIS) – Sponsor Handbook, section 3.2.1. The registration process can take up to 10 days.

As CTIS is a closed system that does not send information by emails, it might be useful to add a user whose task is to monitor the system for replies or requests for information (RFIs).

1.1.1.2 Application

See EMAs Training program, especially module 10.

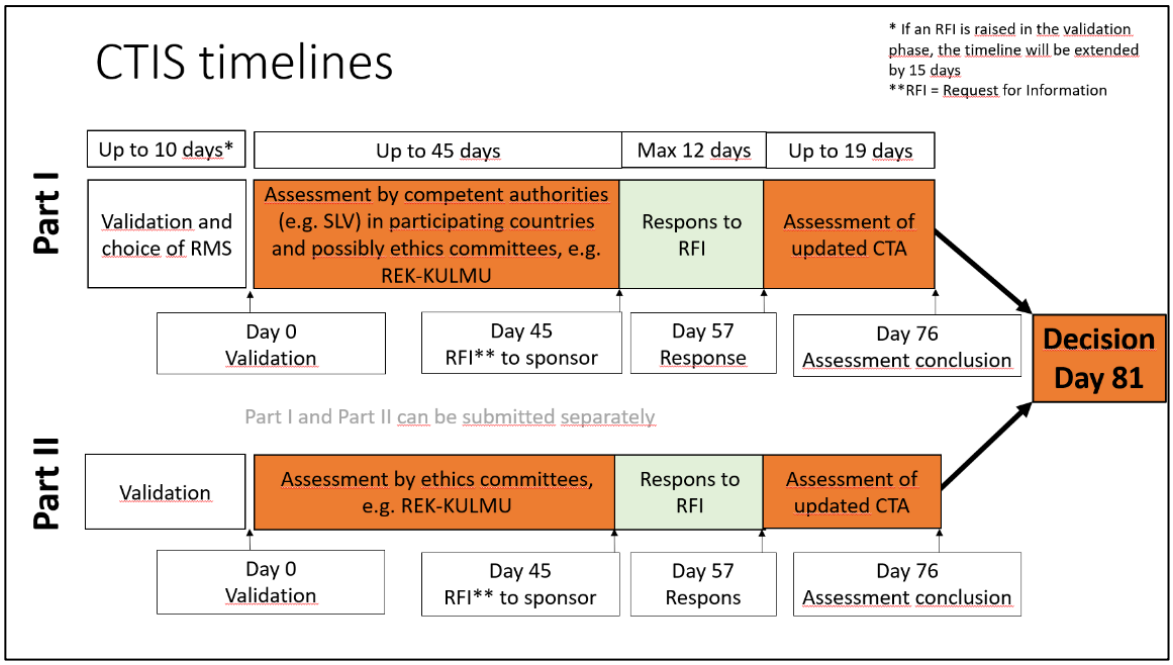
The submission information is under four different tags: Form, MCSs, Part I and Part II.

Common rules:

- All fields with an asterisk should be filed in.
- The lock should be closed when editing (and open when submitting the application). Additional structured fields and request for documents may appear when the lock is closed.
- Documents should be uploaded as PDFs
- Most documents will be made publicly available. It is specified in CTIS for each single section. Deferral from publication dates can be applied for (see table 4.1.1.1 Forms, row 4)
- Documents "not for publication" can be uploaded by clicking the "add document" button 
- To comply with GDPR, the use of personally identifiable information such as date of birth, signature, home address, children names, photographs etc. should be avoided. Use of Investigator CV (template) is recommended
- If the timelines are not met, the application will be cancelled in CTIS
- Within 2 years from notification date, if no subjects have been included the authorisation shall expire in the MS
- The CI should propose one of the member states concerned as reporting member state (RMS). For national trials the Norwegian Medicines Agency (NoMA/DMP) shall be the RMS. For a low-intervention clinical trial, where the IMP is not used in accordance with the terms of the marketing authorisation (MA) but the use is evidence-based, a member state where the use is evidence based, should be proposed as RMS.

- If a commercial company has provided documents such as e.g., an Investigator's Brochure to be used in the application, the CI should ask/review the contract with the company to check whether the company requires deferrals (request for postponing publication) for their documents (see table 4.1.1.1 Forms).
- The authorities may answer earlier than stipulated in the flowchart. In Norway, the authorities have agreed not to send RFIs before Day 26. The authorities may also give the sponsor less than 12 days to respond. This is unusual unless the sponsor agrees to it.

Flowchart:



1.1.1.3 Responses to RFIs

For applications where RMS is Norway, the first RFI is expected to be issued at the earliest 26 days after validation of initial application.

Relevant videos:

- How to manage the workload in CTIS – RFI tab: where to find RFIs and sort them
- How to respond to RFI considerations and submit an RFI response; how to respond, uploading supporting documents and submission
- How to change a Clinical Trial Application as part of an RFI response

See also FAQs.

How to respond to an RFI

- in cover letter; explain if changes have been made in the submitted documentation, and list new/revised documents with version date and version numbers
- revised documents should be submitted with track-changes and a clean version using the "update"

button inside the trial dossier

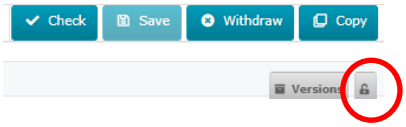
- The "Add document" button Add document is used only for adding fully new documents, e.g. missing documents requested by the MS during validation. The System version will be 1.00. Please use document codes and titles as explained earlier.

- in the dossier;
  - use the "change application" functionality if changes are made to the dossier (IMPD, protocol, IB etc.)
  - On the top of left side of the RFI (just above "Supporting documentation"), click on MSC: Norway Submission date:
  - Then, on the right side of the RFI the button "Change application" Change application will appear.

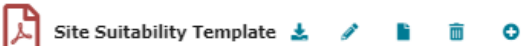
    Changes should be done in the applicable section by using the "update" button . This will ensure correct versioning and publication in accordance with deferral/transparency rules.

How to make changes inside the dossier:

1) Click on the lock (upper right side of the window) to open the application



2) Additional options will appear next to the document you want to update, delete or add.



Download document

Edit document title, version date and number

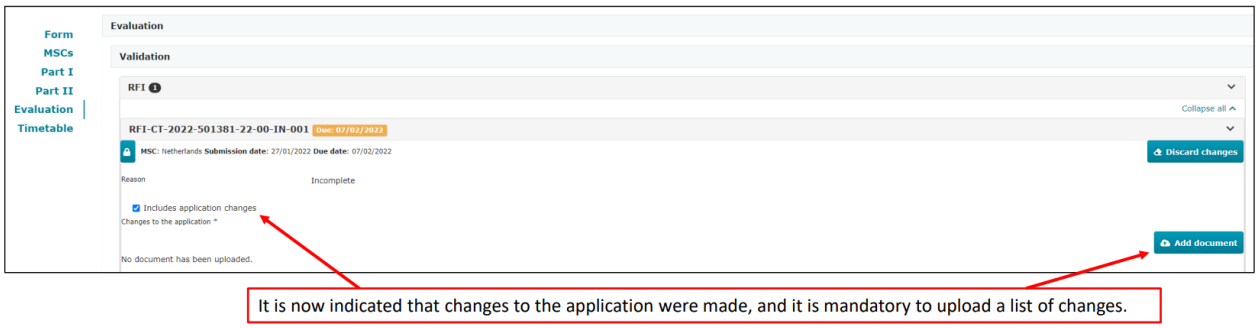
Update document. Upload new version of the document, e.g. protocol v2 with changes requested by the MS. You are asked to enter the version number and date, but the document title in CTIS cannot be changed

Delete uploaded document

Add e.g. a version with tracked changes. The document will be listed as "not for publication".

All responses to RFIs need to be summarised in a cover letter (ref. link to template in table 4.1.1.1) that is uploaded at the top of the RFI. The cover letter should detail all changes made to documents and especially information given in the consideration answers and not included in other documents, as well as list all included documents with version date and number. The "Submit" option only appear at the end of the RFI when the "cover letter" is uploaded and all locks are open (except the lock for the cover letter that should be closed).

When finished adding new/changed documents to the application, navigate back to the RFI response.



4.2 Application outside EEA

Similar documentation will be required in non-EEA countries as in EEA-countries. CI should seek information about application process.

Information should be gathered by using the Feasibility Questionnaire Template. See also Working Instruction International Trials. See also Working Instruction for international trials.

4.3 Registration

The trial should also be published on the hospital's website once the trial is approved and ready for recruitment, according to local procedure.

CTIS is a registered data provider for the World Health Organization (WHO). Data from authorised trials published on the CTIS website - excluding trials with category 1 deferrals of the main characteristics - is now included in the WHO's International Clinical Trials Registry Platform (ICTRP). This applies to relevant clinical trial data, as required by WHO, published on CTIS since launch of the system on 31 January 2022. CI should verify that the trial is published on ICTRP before start of recruitment.

Clinical trials with any type of deferrals and a decision issued after mid-August 2022 are currently not published on the CTIS website. Therefore, these trials will not be included in WHO's ICTRP. This is a system failure that hopefully will be fixed.

4.4 Start-up

Approval from the competent authority and ethics committee is a pre-requisite for initiation of the trial. It is recommended that the Start-up Meeting Checklist and the template Start-up Meeting Agenda are used to ensure that all requirements are complied with and all decisions are documented.

2 DOCUMENTATION

In the regulatory section of TMF and ISF the following should be archived;

- Cover letter(s) for initial application and submitted RFIs, if applicable.

- Decision letter

The approved documents should be archived in their respective section of the TMF/ISF (see SOP Study Files).

3 NON-COMPLIANCE MANAGEMENT

Non-compliance should be handled according to the procedures for handling non-compliance of the individual institution. Protocol deviations should be reported according to the study protocol or the Protocol Deviation Handling plan.

4 REFERENCES

4.1 External References

- ICH Guideline for Good Clinical Practice (GCP) E6 (R2) – in particular section 3.1, 4.1, 4.4, 5 and 6
- EudraLex-Volume 10.
- CTIS
- REGULATION (EU) No 536/2014 of The European Parliament and of the Council on clinical trials on medicinal products for human use, in particular chapter II and Annex I
- Data Sharing Statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors
- Veileder til helseforskningsloven (Guide to the Health Research Act; in Norwegian)
- Lov om produktansvar [produktansvarsloven] - Lovdata, LOV-1988-12-23-104 (Laws on product liability; in Norwegian)
- EMAs training program
- How to manage the workload in CTIS – RFI tab: where to find RFIs and sort them
- How to respond to RFI considerations and submit an RFI response; how to respond, uploading supporting documents and submission
- How to change a Clinical Trial Application as part of an RFI response
- Part II Document Harmonisation Guidance, which includes information about:
  - Investigator CV
  - Declaration of Interest
  - Site and Facilities Suitability
  - Informed consent and patient recruitment procedure
  - Compliance with applicable rules for biological samples

4.2 Internal References

- SOP Protocol
- SOP Preparing Written Information and Consent Form
- SOP Investigational Medicinal Product (IMP) at Trial Start

- SOP Study Files
- Working Instruction International Trials

5 ATTACHMENTS

- Sponsor Checklist Planning of Clinical Trial
- Start-up Meeting Agenda
- Start-up Meeting Checklist
- Cover Letter CTIS Application template
- Compliance Norwegian Requirements on Data Protection
- Financial and other arrangements

6 DEFINITIONS

SOP Definitions.

Abbreviation	Term
ASR	Annual Safety Report
CRO	Contract Research Organisation
CTIS	Clinical Trial Information System
EC	Ethics Committee
EEA	European economic area
EMA	European Medicines Agency
GCP	Good Clinical Practice
GMO	Gene Modified Organism
ICH	International Conference on Harmonisation
IMP	Investigational Medicinal Product
IMPD	Investigational Medicinal Product Dossier
MA	Marketing Authorisation
MS	Member state

NoMA	Norwegian Medical Product Agency, Direktoratet for medisinske produkter
IMPD	Investigational Medicinal Product Dossier
Q & A	Question and Answer
REK	Regional komité for medisinsk og helsefaglig forskningsetikk
RFI	Request for information from authorities to sponsors in CTIS
RMS	Reporting member state
SOP	Standard Operating Procedure

7 CHANGES SINCE LAST VERSION

CT SOP version no 1.11

Main changes from version 1.10: Link to Individual Participant Data (IPD) Sharing Statement inserted in table 4.1.1.3 Part I