Regulatory and ethical requirements in medical device studies

Norway
SECTIONS

A. Type of research
B. Definitions/ Legal basis
C. Insurance
D. Sponsor
E. Investigators
F. Competent Authority
G. Ethics Committee
H. Data Protection
I. Healthy volunteers/Patients
J. Specific requirements
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We have differentiated 8 types of research:

- Medical device alone with CE mark use within label
- Medical device alone with CE mark use outside label
- Medical device alone without CE mark
- Medical device combined with medicinal product with CE mark use within label
- Medical device combined with medicinal product with CE mark use outside label
- Medical device combined with medicinal product without CE mark
- Observational studies with medical device
- Registries
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Definitions in Norwegian law

- For medical device alone with CE mark use outside label, the legal requirements relating to clinical investigations in Norway conducted in order to establish support for CE marking are set out in:
  - Act of 12 Jan 1995 relating to medical devices
  - Regulations of 15 Dec 2005 relating to medical devices
  - NS-EN ISO14155 Clinical Investigations of medical devices for human subjects
  - Clinical activities involved in such investigations are subject to Act of 30 March 1984 No.15.
B. Definitions/Legal basis

Definitions in Norwegian law

- Law on Medical Devices
  For registry studies only:
  - [www.helseregistre.no](http://www.helseregistre.no)
  (Website is in Norwegian only)
B. Definitions/Legal basis

Conventions/ Guidelines / laws to apply – Medical Devices alone with CE Mark within label:

- Declaration of Helsinki
- NS-ENISo14155 Clinical Investigations
- NS-ENISO14971 Risk Management
- NO-EN-ISO 14155:2001 Good Clinical Practice
B. Definitions/Legal basis

Conventions/ Guidelines / laws to apply — Medical Devices alone with CE mark outside label and medical devices alone without CE mark

- Declaration of Helsinki
- NS-ENISo14155 Clinical Investigations
- NS-ENISO14971 Risk Management
- NO-EN-ISO 14155:2001 Good Clinical practice
- Regulation on medical devices 15 Dec 2005 nr 1690
**B. Definitions/Legal basis**

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**Conventions/ Guidelines / laws to apply** – Medical Device combined with medicinal product with CE mark use outside label: AND without CE Mark

- Declaration of Helsinki
- NS-ENISO14155 Clinical Investigations
- NS-ENISO14971 Risk Management
- European Directive 2001/20/EC
- Regulation on medical devices 15 Dec 2005 nr 1690
B. Definitions/Legal basis

Conventions/ Guidelines / laws to apply – Observational studies

- NS-EN- IS0 14155
- Regulation on Medical devices 15 Dec 2005 nr 1690
B. Definitions/Legal basis

Conventions/ Guidelines / laws to apply – Registry studies

- NS-EN- ISO 14155
- Regulation on Medical devices 15 Dec 2005 nr 1690
- Declaration of Helsinki
 Acts to apply

• For all types of studies listed;
  • Hospital Act
  • Data Protection Act

For medical device alone without CE mark, medical device combined with medicinal product without CE mark and for observational studies the following apply in addition to the above:

• Law on medical devices 12 Jan 1995 nr 6
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• For all types of studies listed with the exception of observational and registry studies, it is necessary to cover insurance for

- Patients and healthy volunteers
- Sponsor
- Manufacturers

• A mandatory compensation sum per trial is required for all types studies with the exception of observational and registry studies.
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D. Sponsor

- **A. Type of research**
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It is mandatory to have a sponsor in all the interventional studies listed below:

- Medical device alone with CE mark use within label
- Medical device alone with CE mark use outside label
- Medical device alone without CE mark
- Medical device combined with medicinal product with CE mark use within label
- Medical device combined with medicinal product with CE mark use outside label
- Medical device combined with medicinal product without CE mark
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There are no specific requirements/regulations for GCP training of the investigators in Norway for any of the study types. NS-EN ISO14155 applies.

There are specific requirements/regulations for qualifications of investigators for all study types with the exception of registries and medical device combined with medicinal product with CE mark use within label.
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F. Competent Authority

www.helsedirektoratet.no

Norwegian Competent Authority

Helsedirektoratet

Universitetsgata 2

0130 Oslo
### F. Competent Authority

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<tr>
<td>Observational and Registry studies</td>
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F. Competent Authority – Initial submission

- The sponsor is responsible for the submission
- No submission fee
- The submission is national - You only have to submit one dossier to the national competent authority

- Standard application form for:
  - Medical devices alone with CE mark use outside label
  - Medical device alone without CE mark
F. Competent Authority – Initial submission

- English documents are accepted.
- Submit form and attachments
  - by email to medisinsk.utstyr@helsedir.no
  - by mail/post to the Norwegian Directorate of Health, Pb 7000 St. Olavs plass, 0130 Oslo, Norway
- Approval timeline: 60 days following notification
- Can submit anytime – no deadlines
- If the manufacturer is not based in Europe the name, address, telephone, fax and email of the authorised representative must be provided.
F. Competent Authority – Initial submission

Main documents required for submission (1 of 2)

For all types of studies except Medical Device alone within CE Mark use within label, and registry studies:

- Submission letter
- *Clinical Trial application form (*Only for medical device combined with medicinal product with CE mark use outside label, and medical device combined with medicinal product without CE mark )
- Clinical Investigation Plan/ Protocol signed
- Clinical Investigation Plan/Protocol summary
- CRF draft
- Informed consent form
- Subject information leaflet
**Main documents required for submission: (2 of 2)**

- Investigators Brochure or CE certificate
- Instructions for use/Technical manual
- Performance evaluation
- Pre Clinical evaluation
- Insurance certificate
- **Signed and dated CV of Investigators** (Not needed for observational studies)
- Product training of investigators
- Proof of payment of submission fees
- Copy of local Ethics Committee opinion - including aspects covered by it’s opinion.
F. Competent Authority - Vigilance

• It is mandatory to declare AEs, ADE, SADE and SAEs to the Norwegian Competent Authority for all study types except:
  • Medical devices with CE marks used within label – including those combined with medicinal products, and registry studies.
  • The sponsor is responsible for declaring AEs to the Competent Authority.
  • AEs are declared using Meddev 2.7/3 forms.
  • There are specific timelines for declaring AEs.
**F. Competent Authority - Vigilance**

<table>
<thead>
<tr>
<th>Events mandatory to declare to the Competent Authority:</th>
<th>AE</th>
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<tr>
<td>Observational studies with medical device</td>
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AE: Adverse Event (Non device related)
ADE: Adverse Device Effect (Device or procedure related)
SADE: Serious adverse Device Effect (Device or procedure related)
SAE: Serious Adverse Event (Non device related)
F. Competent Authority - Vigilance

- No specific Norwegian definition of SAEs.
- SAE definition corresponds to MEDDEV 2.7/3 and directives 90/385/EEC and 93/42/EEC.
- The sponsor is responsible for declaring adverse events to the Competent Authorities in the specific countries
- No annual safety report required.
F. Competent Authority – Substantial amendment

- There is a specific procedure for submitting a substantial amendment to the Norwegian Competent Authority

This is ‘notification’ of the amendment and must be done for all studies except for:

- Medical device alone with CE mark use within label
- Medical device combined with medicinal product with CE mark used within label.
- Medical device alone without CE mark
- Registry studies
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G. Ethics Committee

- Norwegian Medicines Agency:
  post@noma.no
  T. +47 22 89 77 00
  http://www.legemiddelverket.no

- Clinical Investigations of medical devices where human subjects are involved must be approved by a regional medical research ethics committee.

- Details of regional ethics committees available on: www.etikkom.no/en/I-English/
G. Ethics Committee

- Favourable opinion/approval is required for all the study types listed.
- Sponsor is responsible for submission for Observational and Registry studies.
- Sponsor or PI are responsible for submission for all other types of studies.
## G. Ethics Committee

<table>
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G. Ethics Committee – Initial submission

• The submission has to be:
  - Online

• English documents are accepted.

• No submission fee.

• No specific application form.

• Guidance available on The Norwegian is: https://helseforskning.etikkom.no

• Deadlines for submissions to EC.

• When both Competent Authority approval and Ethics Committee positive opinion are required, it is NOT possible to request the two in parallel.
Main documents required for submission:

- Submission letter
- Clinical Trial application form
- Clinical Investigation Plan/Protocol signed
- Clinical Investigation Plan/Protocol summary
- Informed Consent Form
- Signed and dated CV of Investigators
- Conflict of interest statement from investigator
- Study approval from administration department
- *GCP training certificate for investigators (*not necessary for device with CE mark being used within label.)
G. **Ethics Committee - Vigilance**

- Sponsor is responsible for AE declaration to Ethics Committee

- Timelines vary depending on the regional ethics committee

More information on https://helseforskning.etikkom.no/ikbViewer/page/frister/

- The sponsor also has to declare events to the Ethics Committee in the specific countries
<table>
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<tr>
<th><strong>G. Ethics Committee - Notification</strong></th>
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- No specific requirement to notify EC re the first patient enrolled
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The Norwegian Data Protection Agency:

[https://www.datatilsynet.no/English/](https://www.datatilsynet.no/English/)
<table>
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<tr>
<th>Section</th>
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<tr>
<td><strong>H. Data Protection</strong></td>
<td>• Submission in English is accepted by the Norwegian data protection agency</td>
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<td>• No submission fee</td>
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## I. Healthy volunteers/Patients

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| I. Healthy volunteers/Patients | - In Norway there are no specific requirements/regulations for children
- No national healthy volunteers registry in Norway
- There is no obligation to inform the patients on the outcome of the clinical trial – no specific Norwegian requirements only adherence with the Declaration of Helsinki Guidelines. |
| J. Specific requirements | |
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- There are no specific requirements to publish both positive and negative results of clinical studies in scientific journals.

- There are specific requirements/regulations to provide devices, without CE mark or used outside the intended use, for free.

- There are specific requirements/regulations regarding devices emitting radiation - see www(nrpa.no)

- ICF - Use ISO 14155 which provides guidelines
J. Specific requirements

• There are specific requirements/regulations regarding archiving of documentation (not detailed here).

• Specific requirements regarding blood/tissue samples (not detailed here).

• No specific requirements for data management of Clinical investigations.

• No specific strategies for monitoring of medical device studies.
### J. Specific requirements

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- Registration at clinicaltrials.gov may be a requirement for publication in certain journals

- For national registration of clinical studies, write to: Kliniskestudier.helsenorge.no

- No accreditation process for research centres but this may be in place for certain laboratories.