EU Clinical Trial Regulation (536/2014)
- Informed Consent -

Centrale
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Mensgebonden
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CTR training EMA – HMA - COM

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Overview – Informed consent

1. General rules (art. 28,29)
2. Cluster trials – simplified means (art. 30)
3. Incapacitated persons and minors (art 31, 32)
4. Deferred consent (art 35)

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General rules – informed consent (IC)

- subject information sheet (minimum requirements: art 29)
- interview by qualified member study team (qualified person: up to national law)
- adequate time for subject to consider participation
- verification that subject has understood information
- written, dated and signed by subject and qualified person performing the interview (IC by electronic means – according to national law)
- subject unable to write: alternative means (e.g. oral) in the presence of at least one impartial witness. Impartial witness has to sign and date the ICF
- subject unable to give consent: IC by legal representative (legal representative: according to national law)

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Cluster trials

CTR, considerans 30

..... clinical trials where the methodology of the trial requires that *groups of subjects rather than individual subjects are allocated to* receive different investigational medicinal products. In those clinical trials the *investigational medicinal products are used in accordance with the marketing authorisations*, and the individual subject receives a *standard treatment regardless of whether he or she accepts or refuses to participate in the clinical trial*, or withdraws from it, ...

Such clinical trials, which *serve to compare established treatments*, should always be conducted within *a single Member State*.

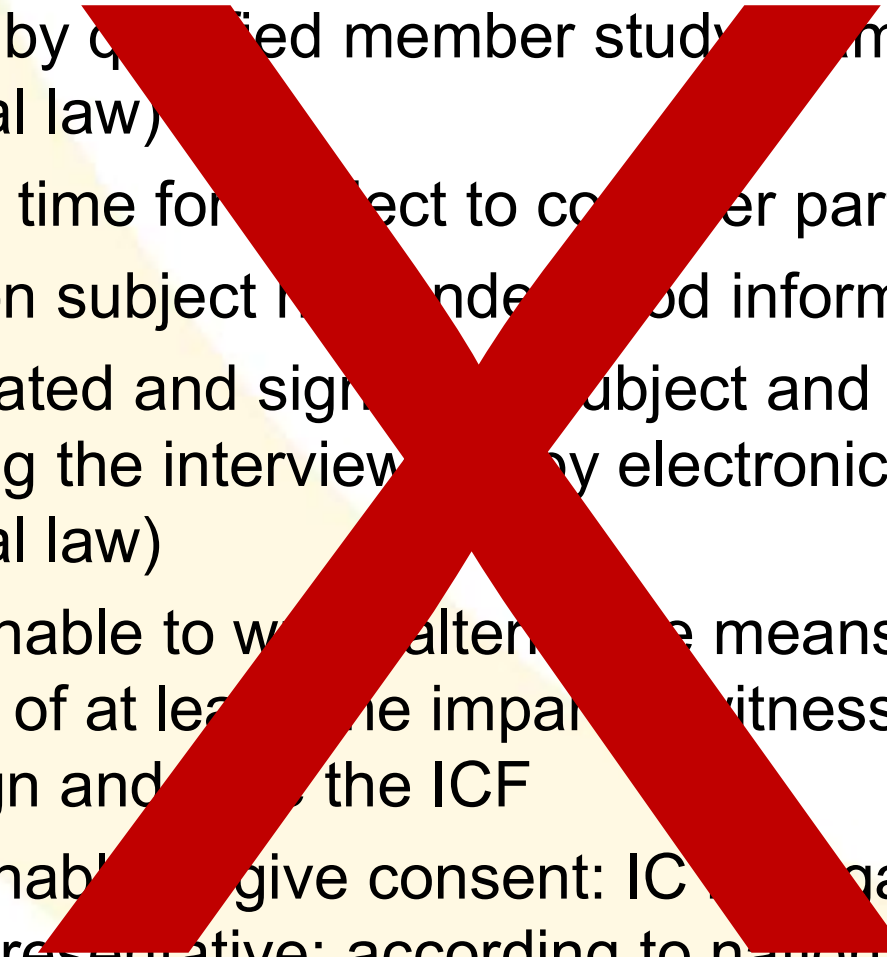
Cluster trials – IC by simplified means

Conditions all to be fullfilled:

- clinical trial to be conducted in one single MS
- the simplified means for obtaining IC are according to national law in the Member State concerned
- the methodology of the clinical trial requires that groups of subjects rather than individual subjects are allocated to receive different investigational medicinal products in a clinical trial
- the clinical trial is a low-intervention clinical trial and the investigational medicinal products are used in accordance with the terms of the marketing authorisation
- there are no interventions other than the standard treatment of the subjects concerned
- the protocol justifies IC with simplified means and describes the informed consent process

General rules – informed consent (IC) in cluster trials not mandatory

- interview by q[illegible]ied member study t[illegible]m (qualified person: up to national law)
- adequate time for [illegible]ject to co[illegible]er participation
- verification subject [illegible]nde[illegible]od information
- written, dated and sign[illegible]ubject and qualified person performing the interview [illegible]y electronic means – according to national law)
- subject unable to w[illegible]alter[illegible]e means (e.g. oral) in the presence of at lea[illegible]he impar[illegible]itness. Impartial witness has to sign and [illegible] the ICF
- subject unab[illegible]give consent: IC [illegible]gal representative (legal representative: according to national law)



Cluster trials – IC by simplified means

How?

- Information to be provided on
  - the nature, objectives, benefits, implications, risks and inconveniences of the clinical trial
  - the subject's rights, e.g. to refuse to participate or to withdrawn at any time without any resulting detriment and without having to provide any justification;
  - the conduct of the trial
  - follow-up measures if participations is discontinued
  - applicable damage compensation
  - EU trial number and summary of results in EU database
- information should be comprehensive, concise, clear, relevant, and understandable to a layperson
- no objection to participate (instead off written IC)

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Incapacitated persons, additional conditions IC:

- incapacitated subject has not refused to give, informed consent before the onset of their incapacity
- informed consent from their legally designated representative
- legally designated representative: according to national law
- incapacitated subjects will receive information about their rights and the clinical trial in a way that is adequate in view of their capacity to understand it
- explicit wish of an incapacitated subject who is capable of forming an opinion and assessing the information to refuse participation in, or to withdraw from, the clinical trial at any time, is respected by the investigator
- the subject shall as far as possible take part in the IC procedure
- both signatures on ICF: of legally designated representative(s) and the incapacitated person (assent) – according to national law

Minors, additional conditions IC (1):

- informed consent from their legally designated representative
- legally designated representative: according to national law
- the minors will receive the information on their rights and clinical trial (taken into account age and mental maturity)
- information given by qualified member study team trained or experienced in working with children;
- explicit wish of minor who is capable of forming an opinion and assessing the information to refuse participation in, or to withdraw from, the clinical trial at any time, is respected by the investigator
- the minor shall as far as possible take part in the IC procedure (taken into account age and mental maturity)
- both signatures on ICF: of legally designated representative(s) and the minor (assent) – according to national law

Minors, additional conditions IC (2):

- during a clinical trial the minor reaches the age of legal competence to give informed consent as defined in the law of the Member State concerned:
  - informed consent shall be obtained before that subject can continue to participate in the clinical trial

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Deferred consent – clinical trials in an emergency situation

considerans 36

..... emergency situations ..... relate to cases where for example a patient has suffered a *sudden life-threatening medical condition* due to multiple traumas, strokes or heart attacks, *necessitating immediate medical intervention* ..... in certain emergency situations, it is *not possible to obtain informed consent prior to the intervention* ..... such patients may be enrolled in the clinical trial under *very strict conditions* .....

Clinical trials in an emergency situation and deferred informed consent (art 35)

Conditions all to be fullfilled:

- subject is unable to provide prior informed consent and to receive prior information on the clinical trial due to urgency of the situation
- the clinical trial will have the potential to produce a direct clinically relevant benefit for the subject
- therapeutic window too short to obtain prior IC from legally designated representative
- the clinical trial relates directly to the subject's medical condition
- the clinical trial is of such a nature that it may be conducted exclusively in emergency situations
- minimal risk and burden in comparison to standard treatment

Deferred informed consent (art 35)

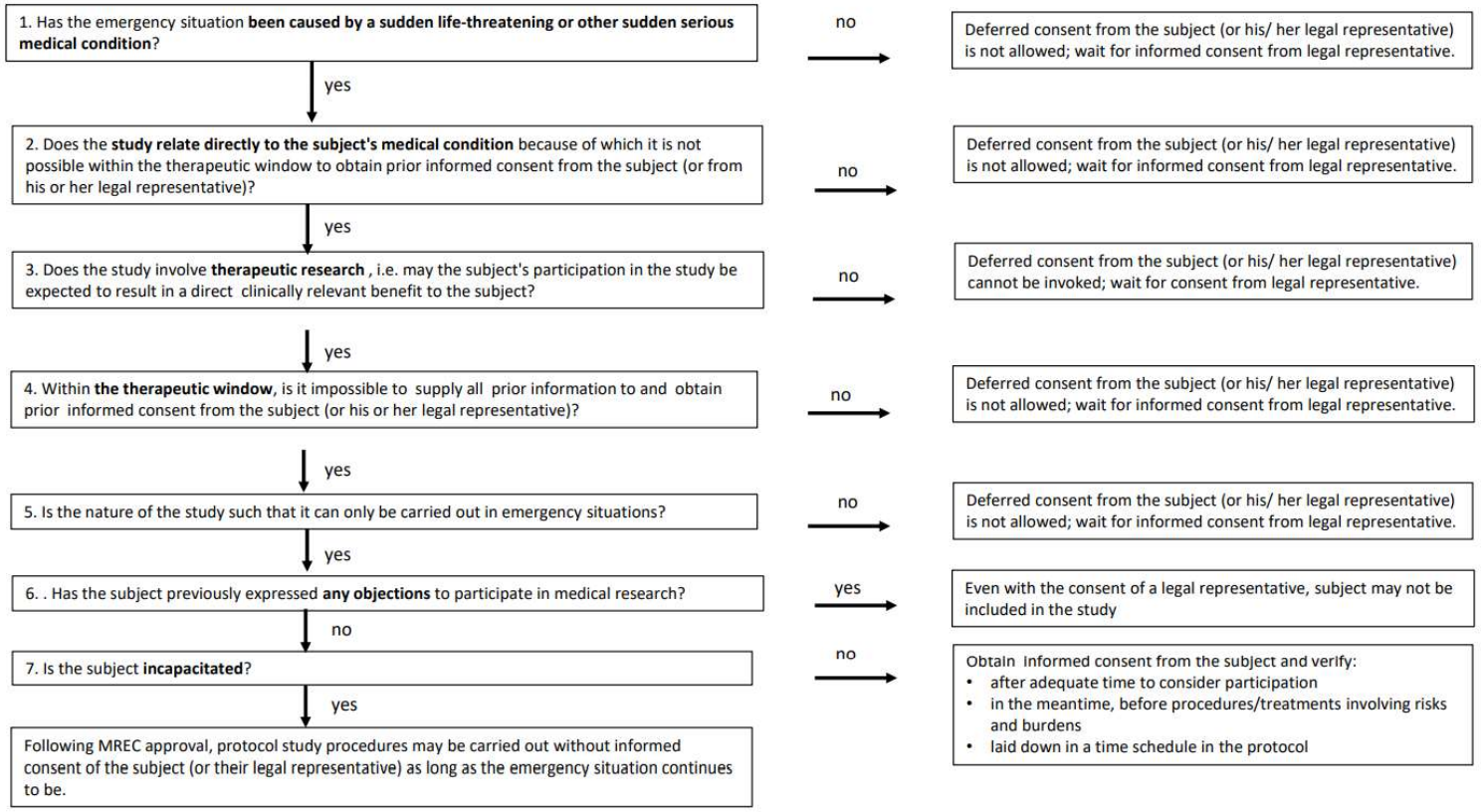
- no objections to participate in the clinical trial previously expressed by the subject;
- following CT intervention – IC shall be sought from legally designated representative(s) and/or subject without undue delay
- In case subject is not a minor or subject is capacitated to form an opinion: informed consent to continue the participation in the clinical trial shall be obtained from the subject as soon as he or she is capable of giving informed consent.
- no informed consent from subject or legally designated representative (if applicable) : subject shall be informed of the right to object to the use of data obtained from the clinical trial
- subject dies before informed consent from legally designated representative: data collected during the study may be used. No IC is needed.

Clinical trials in an emergency situations

Flow charts deferred consent and obtaining informed consent afterwards

https://english.ccmo.nl/investigators/publications/publications/2020/04/07/ccmo-memorandum-flowcharts-deferred-consent-for-medical-research-in-emergency-situations

Flowchart 1: deferred consent for medical research in emergency situations



Clinical trials in an emergency situations

Flow charts deferred consent and obtaining informed consent afterwards

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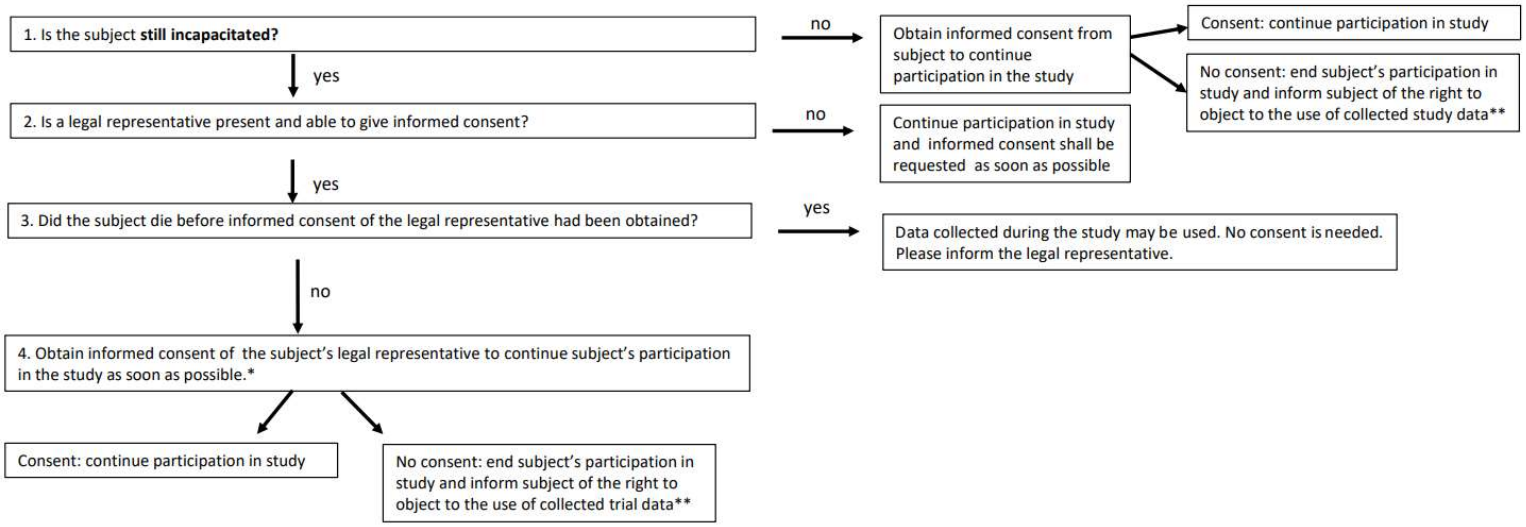
Flowchart 2: Obtaining informed consent in medical research in emergency situations after inclusion incapacitated subject*



* This concerns obtaining informed consent to continue participation in the study. If the study has already been completed before it was possible to obtain written informed consent, there is no longer any need for informed consent. However, the subject (and/or his legal representative) must be informed about the study.

** See text in note on whether the objections should be honoured.

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information

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