Centrale
Commissie
Mensgebonden
Onderzoek

Recommendations for the conduct of clinical research at the time of restrictive measures due to the coronavirus

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CCMO receives many queries on problems caused by the coronavirus and its effects on the conduct of clinical research. Examples concern the delivery of study medication, subjects unable to come to the investigational site as a result of which certain study procedures cannot be carried out, the postponement of monitoring activities and the conditions for (re)start clinical research.

CCMO wishes to emphasise that in all cases the safety of research subjects and the health of healthcare professionals is paramount. As a sponsor or investigator, you should consider whether the clinical research, or parts of the clinical research, can be temporarily halted or not. CCMO realises that in many cases this is not possible with ongoing research. For example, because the subjects have to be given the study medication or because tests have to be carried out to ensure the safety of the subject. This may lead to protocol deviations, substantial modifications, urgent safety measures, temporary halt of the research or otherwise.

The advice and conditions below can be adjusted depending on the spread of the virus and the RIVM guidelines. Therefore, check the CCMO and IGJ website regularly.CCMO provides a number of recommendations in this respect, in which in some cases the review committee (CCMO or accredited MREC) and/or the competent authority must be informed:

- Set up a risk analysis on the consequences of the coronavirus on the conduct of the clinical research , whereby the safety of the participants is paramount;
- Record all deviations from the protocol and the standard procedure in writing; unless the subject's safety is at stake, these protocol deviations need not be submitted to the review committee;
- A deviation from the protocol or a protocol modification due to urgent safety measures to eliminate immediate hazards to the subject can take place without prior approval by the review committee. However, this must be reported immediately to the review committee;
- Study medication can be sent directly to the research subject by courier from the (hospital)pharmacy for reasons of subject safety; you need not inform the review committee about this, but do record this temporary procedure in writing. Consent by trial participants for using personal information is obligatory for sending IMP. Consent may be given orally and should be documented and confirmed by the trial participant via email if possible; obtaining written consent retrospectively is not required;
- CCMO does not consider logistical changes (e.g. telephone visits instead of physical visits, adjustments to schedule visits), the direct delivery of investigational medicinal

products to the trial participant and changes to the monitor plan (e.g. remote monitoring or remote SDV) as a substantial amendment which needs to be approved by a review committee;

- If the trial is (partially) suspended, for reasons of subject safety, this must be reported immediately to the review committee ; a temporary halt for other reasons should be reported within 15 days;
- If the study is terminated prematurely, this must be reported to the review committee as soon as possible, but at the latest within 15 days;
- The restart of clinical research after it was full or partial suspended due to COVID-19, has to be notified to the review committee and in case of a clinical trial with an investigational medicinal product to the competent authority as well. The (re) start of the clinical research is subject to conditions as stated in this IGJ document.
- When the restart of the clinical research involves substantial modifications, prior approval from the review committee for restarting the trial is required. In the case of a substantial amendment to a clinical trial with an investigational medicinal product, a "statement of no ground for non-acceptance" must also be issued by the competent authority;
- The procedure for submitting a substantial amendment to the review committee has not been changed. If it concerns an amendment which has an impact on the safety of research subjects and requires a fast-track assessment procedure given the emergency of the situation, you are advised to contact the review committee about the procedure to be followed. A number of review committees have a fast track procedure.
- The procedure for notifications to the Dutch competent authority both during and after the study has not been changed. The competent authority will not send a confirmation of receipt for a temporary halt and restart of the trial. However, in contrast to the normal situation, you will not receive a 'Declaration of no objection' for this type of notification during the COVID-19 pandemic;
- The obligation to submit a cover letter with a wet signature for initial applications and substantial amendments to the review committee and/or the competent authority has been suspended. Instead, a digital or scanned signature of the applicant is sufficient;
- In case a subject is unable to provide (re)consent to (continue to) participate in a clinical trial in an emergency situation, obtaining consent can be deferred under specific conditions. The applicable conditions for such a deferred consent are described in the CCMO memorandum with flow chart Deferred Consent (in Dutch). To be able to use the possibility of deferred consent it is mandatory to obtain approval by the review committee (MREC/CCMO). Please contact the review committee for information on the fast-track procedure for the review of the deferred consent procedure;
- The Dutch Health and Youth Care Inspectorate has published a document (in Dutch) with recommendations on e.g. distribution and handing over of investigational medicinal products, remote SDV and remote monitoring;
- The European Commission, the European Medicines Agency (EMA) and national Head of Medicines Agencies (HMA) have published a guidance for sponsors and investigators on how to manage the conduct of clinical trials during the coronavirus disease (COVID-19) pandemic.