DANISH NATIONAL
CENTER FOR ETHICS

Experimental programme on new informed consent processes in decentralised clinical trials (DCT)

Danish National Center for Ethics // Section for the Medical Research Ethics Committees

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Contact information

Please send all questions or requests related to the contents of this document to kontakt@dvmk.dk.

Preface

Decentralised clinical trials in relation to drug development is a field characterised by fast progression. A driving factor behind this development is the idea that the geographic and demographic diversity of trial participants ought to be increased. One way of doing this is to reduce the need for visits at the research site and perform trial activities in the home of participants, thereby decreasing the total burden of participating in clinical trials. Moreover, DCTs also have scientific advantages. For instance, decentralised study designs make it possible to obtain data with better temporal resolution, to make detailed surveillance of adverse events, and to run clinical trials with a lower cost. In lieu of the Danish life science strategy and the formation of the Medical Research Ethics Committees (MREC) as a section under the Danish National Center for Ethics, it was decided to establish an experimental scheme to test decentralised elements in clinical trials, especially concerning the informed consent process. Moreover, the handling and reconfiguration of clinical trials during the corona crisis has already established the relevance of several decentralised elements. However, many of these elements remain understudied, and their introduction into clinical trials has mostly been on a temporary basis. This experimental scheme aims to remedy some of these shortcomings. Therefore, the *Executive Order on Clinical Trials with Medicinal Products* now describes a possibility of using these decentralised elements in connection to the informed consent process to further innovation and support understanding. In particular, this experimental scheme intends to gather knowledge about one central but understudied element of DCTs: the provision of oral participant information solely by pre-produced video material.

Background

Many different decentralised elements will be used in clinical trials in the future, especially in so-called hybrid trials, where specific trial activities are performed outside traditional research sites. These activities include monitoring of physiological parameters, answering questionnaires, and blood sampling performed by qualified healthcare professionals. The functionality of many of these elements are already tested in clinical trials, including oral participant information via video calls before authorising consent, or are used as part of normal treatment practice (telemedicine). However, there are still decentralised elements where the available knowledge is extremely sparse. In addition, the ethics committee system has refrained from approving the use of decentralised elements, because there has not been any clear legal authority. For instance, before the introduction of this experimental scheme, it has not been possible in Denmark to replace the classic oral participant information, which is characterised by being simultaneous, specific to the given participant, and dialogue-based, with a video-based information material informing the participant about the trial without the involvement of an investigator. Introducing this possibility enables a situation where participants, who do not feel the need to ask clarifying questions, can agree to participate in a trial without prior dialogue with the investigator or other members of the research team.

The experimental programme

MREC wants to contribute to the collection of knowledge that is a prerequisite for a meaningful and evidence-based discussion of new types of informed consent in clinical trials. In this experimental programme, it will be possible to get approval for clinical trials, in which

(1) non-simultaneous, oral information is provided via pre-recorded video material before consent is authorised through electronic signature, if
(2) a possibility of clarifying questions is offered to the participant, if
(3) the investigator otherwise ensures that the participant information is understood correctly, and if
(4) the ethics committee finds the model suitable for the given experiment.

The experimental programme is limited to low intervention clinical trials with minimal risk to the participant, as defined in the EU Regulation on clinical trials on medicinal products for human use. These are trials using already authorised medicinal products in accordance with the terms of the marketing authorisation. Only trials performed only in Denmark have the opportunity to be evaluated under the experimental programme. The overall framework for the consent process in the experimental programme described in the points above will from hereon be referred to as the *non-synchronous consent process*. The experimental programme is established for a two-year period.

The application process and guidance

To inform investigators, sponsors, and participants about the ethical conduct of DCTs, MREC has published a guidance paper, wherein basic ethical principles are applied to different DCT elements.

In the application process, MREC will offer supportive guidance either by telephone or e-mail. Investigators and sponsors, who wish to have their application assessed under the experimental programme, must contact MREC at kontakt@dvmk.dk with the trial protocol or a protocol summary that enables a full overview of the desired consent process and other decentralised elements. If the trial is suitable for assessment under the experimental programme, the application must be submitted via the pan-European Clinical Trial Information System (CTIS). If there is application material (e.g. video material) that cannot be submitted via CTIS, the MREC assessor and applicant will agree on how this material can be submitted directly to MREC and linked to the same case number.

The following information is considered relevant to the application:

- Notices and advertisements on physical or digital media used to make the first contact with a potential trial participant.
- Pre-screening questions and communication about the suitability of the potential trial, which is done before the participant information and consent process is initiated.
- Participant information in the form of text, illustrations, and video material that is disseminated to the possible trial participant, including a clear overview of personal data transfer throughout the trial and the geographical location of any central assessors.
- Presentation of the user interface of dedicated apps used on mobile phone, tablet, or computer, as well as a list of what data that the app has access to and retrieves from the trial participant's device.
- Procedure for how trial participants who want additional information (such as dialogue with the investigator) can receive this.
- Procedure for how to ensure that the trial participant has understood the participant information, including risks of the trial, as well as the extent of the activities that the trial participant is expected to perform throughout the trial.
- Procedure for how to validate the identity of the trial participant, including assessment of whether the trial participant is suitable for giving an informed consent.

- The full informed consent process, including a description of other types of consent used in the trial, e.g. dynamic consent, where the participant must consent repeatedly to participate throughout the trial.
- Additional information that will be communicated to the trial participant during the trial, e.g. insight into the progress of the trial and communication intended to increase the trial participant's motivation to remain in the trial.
- Procedure for communicating the results of the experiment to the trial participant.
- Instructions for deleting trial app and information on what types of non-trial related data (if any) that is saved despite this deletion process.

Another prerequisite in the experimental programme is that the application comply with the Danish Medicines Agency's expectations related to the implementation of other decentralised elements in clinical trials. Further information is available in the Danish Medicines Agency's guidance on the implementation of decentralised elements in clinical trials with medicinal products.

Feedback requirements

In addition to the abovementioned framework for the type of clinical trials that can be approved under this experimental programme, MREC wishes to set requirements for the trial design to ensure that useful knowledge is gathered about the non-synchronous consent process *compared to* the classic consent process. This knowledge should be made publicly available afterwards. Therefore, feedback is required in the following areas:

- Recruitment and retention, including recruitment time and conversion rate, and what media have been used to create awareness about the trial
- The demographic composition of the trial participants
- The trial participants' understanding of the information and satisfaction with the consent process, as well as the relevant professional expertise in relation to this topic (e.g. qualitative studies) has been included in the design and execution of the study.

In addition to a general feedback that summarises the experiment with a focus on the abovementioned points, the experimental scheme requires that one or more endpoints are defined in the protocol that directly quantify one or more of the abovementioned points *compared to* the classic consent process. It must also be stated in the protocol that the method and expected number of trial participants can yield high-quality qualitative or quantitative data to provide knowledge about the non-synchronous consent process. In relation to quantitative analyses, it is assumed that the trial can achieve a relevant statistical power in relation to the chosen endpoint. Moreover, trial results should be published in relevant journals or databases and thereby contribute to the common knowledge base on the non-synchronous consent process.

MREC will use the submitted material to evaluate the experimental scheme and summarise the gathered knowledge about the non-synchronous consent process in reports or publications. This summary will be part of the decision on whether the non-synchronous consent process should remain a possibility when the current experimental scheme expires. It will also be used as a knowledge base for the broader discussion with national and international stakeholders about the value of decentralised elements in clinical trials, not least concerning the informed consent process.