Decentralised Elements in Clinical Trials (DCT)

Decentralised clinical trials (DCT) are a natural evolution of the methods we already use for clinical trials of medicinal products. One of their benefits is that patients do not have to attend the clinical trial unit as often, or in some cases at all.

Guidance document from the DCT working group, with members representing Uppsala Clinical Research Center, Region Stockholm and the pharmaceuticals industry, and with support from Swetrial.

Revised 2026-03-26.

Table of contents

Abbreviations/Glossary

AE	Adverse Event
CTIS	Clinical Trial Information System
CRF	Case Report Form
DCT	Decentralised Clinical Trial
DTP	Direct to Patients
eConsent	Electronic informed consent
EU-CTR	European Clinical Trials Regulation
GDPR	General Data Protection Regulation
ICH-GCP	International Council for Harmonisation – Good Clinical Practice
PI	Principal Investigator
RBC	Regional Biobank Centre
RWD	Real-world Data
SAE	Serious Adverse Event
SmPC	Summary of Product Characteristics
SOP	Standard Operating Procedure
TMF	Trial Master File

Expert Working Group on DCT

Mats Thoring, pharmacist,
Global DCT Advisor, Bayer

Sandra Funning Schedin, pharmacist,
clinical trial project manager, Roche

Gabriella Seger, clinical trial coordinator,
Uppsala Clinical Research Center

Anna Åhlander, research nurse,
clinical project manager, Uppsala
Clinical Research Center

Susan Öman, nurse, line manager for
project leaders working in the
Nordic Baltic region, Sanofi

Elham Hedayati, associate professor and
senior consultant, Karolinska Institutet/
Södersjukhuset

Jonas Oldgren, professor and senior
consultant, Uppsala University/Uppsala
University Hospital

Introduction

Clinical trials depend on patients and trial participants being willing, and able, to take part. Trials therefore need to be made accessible to as many people as possible, whilst ensuring that they are scientifically robust and that they make efficient use of resources and funding. One of the common challenges in traditional clinical trials is that all the participants are required to visit the trial unit, often multiple times.

Decentralised clinical trials (DCT) are a natural evolution of the methods we already use in clinical trials of medicinal products. One of their benefits is that patients do not have to attend the clinical trial unit as often, or in some cases at all. Many of the trial activities can be carried out closer to the patient.

Incorporating decentralised elements into clinical trials can ease and improve implementation, thereby increasing choice and flexibility for both patients and investigators. Decentralisation helps participants adapt a clinical trial to their own lifestyle. Advances in technology and the use of IT and digital infrastructure now offer good scope for decentralising elements of clinical trials in Sweden.

One reason for the growing need for DCT elements in trials is the increase in precision medicine, which sees trials conducted with relatively few patients who have rare medical conditions. If patients are able to mostly avoid long, time-consuming journeys, their recruitment becomes that much easier. In a large, sparsely populated country such as Sweden, there are particular advantages to having some or all stages of a trial conducted remotely.

A decentralised trial is defined by the medical regulators in Sweden and other countries as a clinical trial in which activities are carried out at a location other than the traditional trial site. In a decentralised trial, therefore, not everything needs to be carried out remotely. Many decentralised trials are likely to require the patient to visit the clinic at least once.

The latest GCP guidelines, ICH E6(R3), emphasise flexible and risk-based approaches, i.e. conducting a risk analysis that weighs risks against benefits. The guidelines also encourage innovation in study design, implementation and technology. There is a strong focus on ensuring that all aspects of a clinical trial are fit for purpose, meaning that every step, process and system must be designed to support the trial's objective.

A trial that is easy for patients to participate in is more fit for purpose because it reduces the burden on participants, increases compliance and thereby improves the quality and reliability of the data collected in the study. Decentralised elements can often help to make a trial more fit for purpose. However, as with all the other elements, they must genuinely benefit the trial's objectives and not pose disproportionate risks. It can also be argued that if a decentralised element would make the trial more effective but is not used, this impairs the quality of the trial.

A key issue is to assess the benefits, opportunities and challenges of a DCT compared with a traditional clinical trial for the project in question. Not all clinical trials are suitable for implementation as a DCT, and a hybrid combining a traditional trial with DCT elements may be a viable solution. This is also crucial in determining which main trial unit is selected and what is required of it, as well as for ensuring good investigator oversight.

In this guidance document, we refer to the activities within a clinical trial that can be carried out remotely as DCT elements. Common elements include:

1. Investigator oversight

2. Involvement

3. Main trial unit

4. Distance unit

5. Home health visits

6. Digital consent

7. Video calls

8. Medicines delivered directly to patients

9. Sampling and measurements in the home

In principle, there are no regulatory barriers in Sweden to the use of any of the DCT elements. However, it is important to have a good understanding of the applicable regulations, particularly around the digital management and sharing of data, so that DCT elements can be used correctly and safely. As there is relatively little established practice in the field of DCT, it is especially important to describe in detail, in study protocols and applications, any elements that differ from traditional clinical trials. This makes it easier for the authorities to assess new approaches when evaluating a DCT.

As the authors of this guidance document, we have extensive experience of working with clinical trials. We also have experience of incorporating various DCT elements into clinical trials. Our working group includes representatives from academia, the healthcare sector and industry. We have deliberately chosen to write in this document about clinical trials that include individuals with a specific diagnosis and specific investigational medicinal products. However, the concept can of course also be applied to clinical trials involving healthy individuals. Furthermore, the concept can be applied to other clinical studies that are not trials, where appropriate.

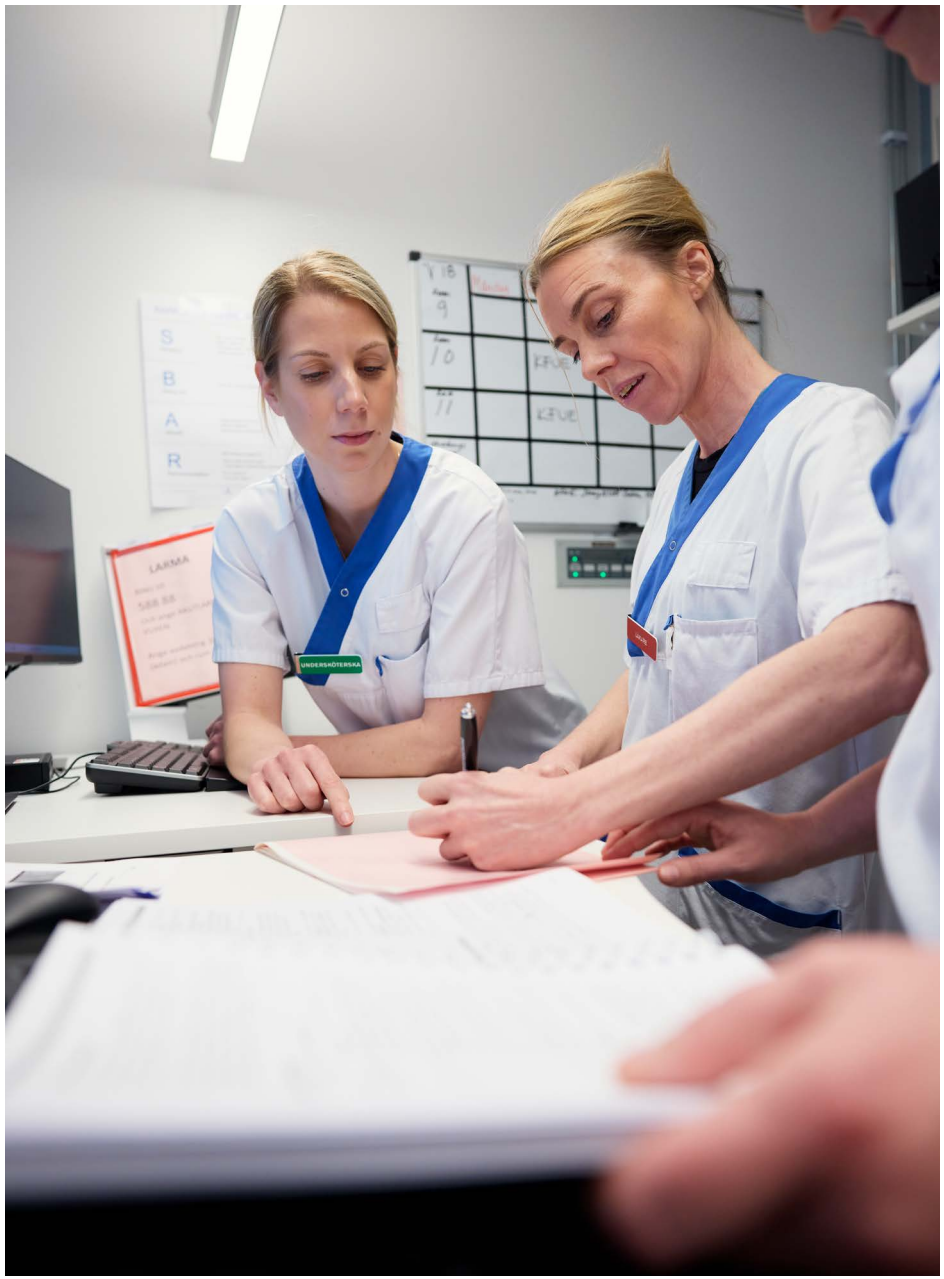
In this rapidly evolving field, the aim of this DCT guide is to provide support for relevant stake-holders across various roles within clinical trials.

Sweden is well placed to become a pioneer in trials with DCT elements, and such a development could also make Sweden more attractive for international research investment. This guide should be viewed as a current summary of our experiences and does not claim to be exhaustive.

In our endeavour to make this guide as readable as possible, whilst using established terminology and maintaining consistency, we have chosen to use the following vocabulary:

- Clinical trial/trial: Most aspects relating to DCT tend to also be relevant to other types of clinical studies.
- Hospital/clinic/healthcare provider: This also includes research centres that do not provide healthcare outside of research.
- In this guide, we usually use the term ‘Patient’ for study participants, as this is the term commonly used in most contexts. The terms ‘Subject’ and ‘Research Participant’ are also used.

Below, the guide describes the various DCT elements mentioned above and what different stakeholders need to consider when DCT elements are used in a clinical trial.



Investigator oversight

All visits and procedures during the trial are primarily the investigator's responsibility – and this remains the case in decentralised trials. The term 'investigator oversight' is used to refer to the overall responsibility that the principal investigator has for everything that happens in the trial. All activities relating to investigator oversight must be documented, and the documents must be available to the relevant authorities on request.

In a DCT, it is particularly important to have a documented plan setting out how the investigator can meet their overall responsibilities and demonstrate that they have done so. The reason for this is, firstly, because much of the performance of a DCT differs from traditional trials and, secondly, because the patient visits the trial unit and meets the investigator less frequently, if at all.

If home health visits form part of the trial or if patients are required to visit a distance unit, the investigator also bears overall responsibility for these. It is reasonable to expect that ensuring the investigator's supervision of the DCT is carried out correctly and documented will take longer the first time, at least until a more established routine is in place for the DCT elements.

Expectations

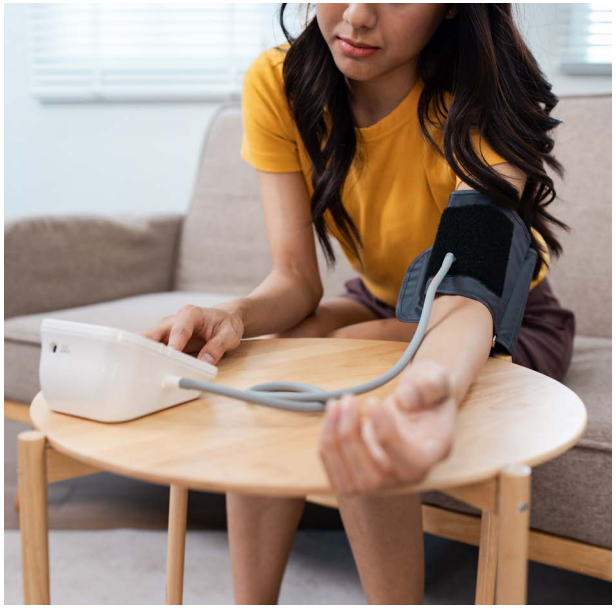
For the investigator to be able to fulfil their overall responsibility, a certain degree of oversight is required for all the activities included in the trial.

The level of oversight required for different stages and activities in the trial depends on various factors, such as the properties and safety of the investigational medicinal product, how it is administered, and how extensively the investigational medicinal product has been studied already. The type of activity and who performs it also influence the level of supervision required.

The extent to which the investigator should exercise oversight in the trial-related activities is therefore determined by the nature of the activity and must be proportionate to the importance of the activity for the quality of the data collected and the level of risk to which the research participant is exposed.

The investigator is responsible for ensuring that the people carrying out tasks within the trial have the right competence and sufficient knowledge of the parts of the study protocol that are relevant to their tasks. Documentation must be in place showing which people or parties have been delegated to carry out study-related tasks. If the tasks are to be carried out as part of clinical practice, no such delegation is required.

We provide some examples of how the oversight may be organised and carried out later in the chapters on the Main trial unit, Home health visits and Distance units.



Checklist

Ensure that

- clear agreement and communication is established between the principal investigator and the staff conducting home health visits (home health staff)
- all activities relating to investigator oversight are documented
- the trial unit and the home health staff are in contact prior to each home visit to a patient
- the trial unit is available, by telephone or video call, to the home health staff during ongoing home health visits
- source data collected during home health visits is made available to the trial unit as soon as possible
- if home health staff suspect an AE/SAE during a home health visit, they contact an investigator as soon as possible for an initial assessment.

Involvement

Experience from decentralised clinical trials clearly shows the importance of involving patients, healthcare providers and trial units early on, continuously and in a structured manner for a DCT to be feasible, safe and accepted. DCTs require robust processes to ensure data quality and participant engagement as research moves into the home.[1]

Clinical trial units need to be involved right from the planning stage.To successfully implement DCT elements, trial units must be included early on in the work on digital maturity, development of workflows, allocation of responsibilities and support requirements. Starting the dialogue early reduces the risk of technical barriers, start-up problems and a greater workload than is necessary, which in turn can increase the acceptance of decentralised processes.[2]

It is essential to involve patient and family representatives to ensure that the decentralised study elements are practically viable in the home.

Ethical analyses stress that the investigator's responsibility towards patients is higher in a DCT, and that tools, procedures and data collection must therefore be designed in collaboration with users in order to maintain safety and understanding.[3]

Studies also show that patients' preferences vary – many appreciate the flexibility of participating from home, whilst others value the option of in-person appointments. This argues in favour of using hybrid models, and suggests that investigators must take patients' perspectives into account when choosing distance units, digital platforms, home sampling and virtual visits.[4] The principle of 'making it easy to do the right thing' is particularly important when study activities are carried out in the patient's domestic setting.

Involvement of healthcare providers

The participant's regular healthcare provider plays a central role in DCTs, particularly when some of the assessment or follow-up takes place close to or within primary care.

Factors that strengthen the healthcare provider's involvement:

Training and information: Healthcare providers should receive a clear introduction to the protocol, criteria, digital tools and DCT-specific elements.

Clear communication: Easily accessible channels of communication should be established between the trial team and the healthcare providers.

Collaboration: Implementation is improved if the investigators engage in dialogue with the healthcare providers regarding their practical experiences and needs.

Resources and support: Ensure that the healthcare providers have access to technical platforms, training material and support.

Feedback and follow-up: Give the healthcare providers continuous feedback, as this increases their engagement and makes it easier to implement improvements.

Involving patient and family representatives, healthcare providers and trial units in a structured manner enables DCTs to be conducted more efficiently and equitably, with higher participant acceptance and better data quality.

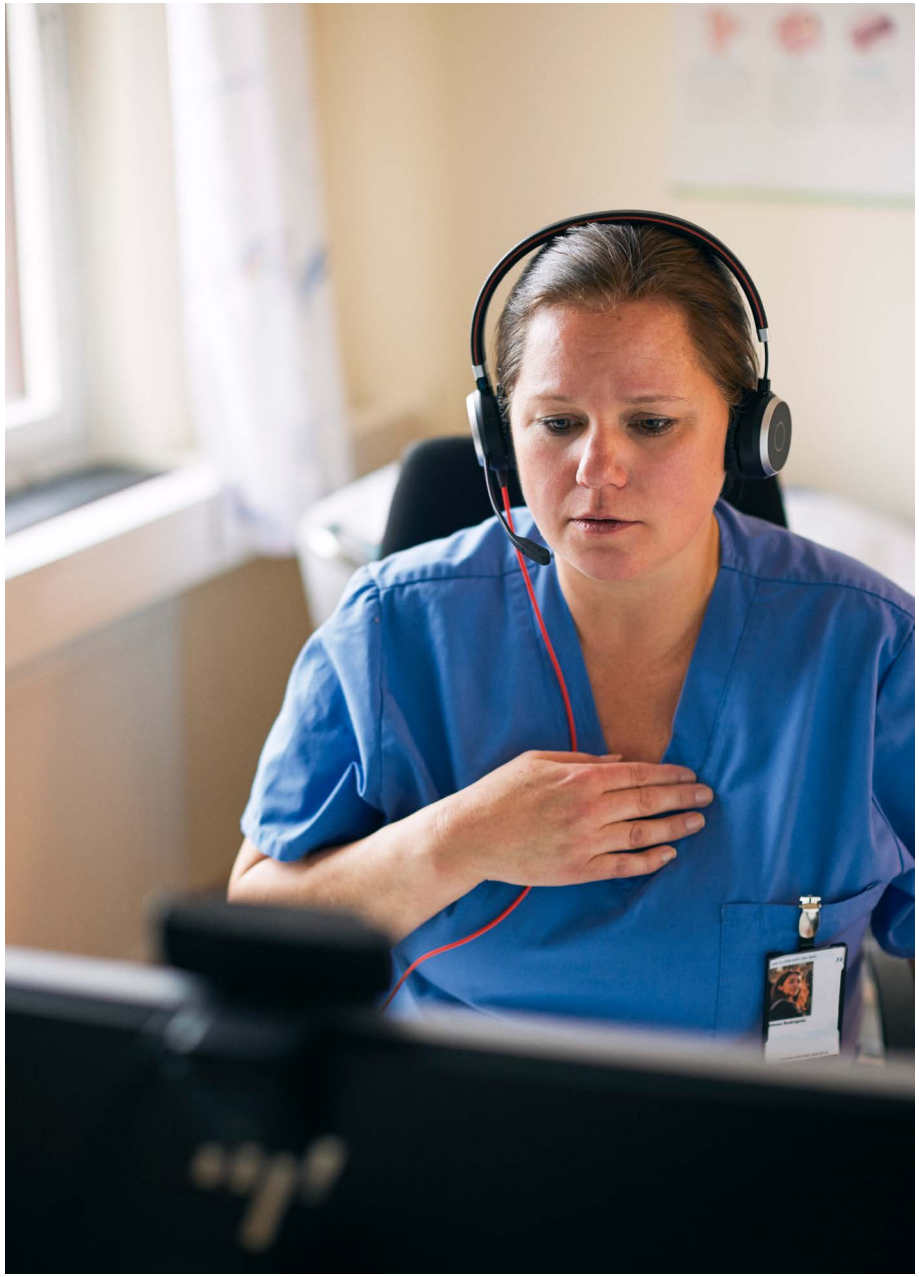
References

1. Holstein SA. Home Is Where the Research Is: The Promise of Decentralized Clinical Trials. Clin Pharmacol Ther. 2025;118(5):979–981.

2. Lipinska K, van Weelij D, Lagerwaard B, et al.; Trials@ Home consortium. Selecting and Preparing Clinical Sites for the Successful Conduct of Decentralized Clinical Trial Activities – Findings From the RADIAL Trial. Clin Pharmacol Ther. 2025;118(5):1057–1066.

3. Vayena E, Blasimme A, Sugarman J. Decentralised clinical trials: ethical opportunities and challenges. Lancet Digit Health. 2023;5(6):e390–e394.

4. Kopanz J, Lagerwaard B, Veldwijk J, et al.; Trials@Home consortium. Do people prefer to take part in a clinical trial from home or come to site? A discrete choice experiment in type 2 diabetes. BMJ Open. 2025;15:e107737.



Main trial unit
(primary investigation site)

The main trial unit is a central research centre that can conduct a clinical trial remotely, regardless of the research participant's location. The main trial unit's tasks include offering digital solutions to recruit trial participants, distributing the trial intervention – such as a medicinal product or a medical device – to the research participant, monitoring, collecting data and communicating with the research participant remotely.

The main trial unit should ensure that it has dedicated project managers, trial coordinators and data managers with expertise in DCTs. The trial unit should, in collaboration with the sponsor, develop standardised processes for DCTs – including the use of digital and technical systems, either internally within its organisation or via an external system provider – and develop risk management strategies and contract templates for home visiting staff, remote laboratories, home delivery of investigational medicinal products and other DCT elements.

In the planning phase of a DCT, the main trial unit and the principal investigator must agree that the trial design, including any planned distance visits such as video calls, sampling and measurements, data collection, and communication channels, is sufficient to ensure patient health and safety, and investigator oversight over the course of the trial. The DCT elements must be clearly described and justified in the protocol. There should also be a clearly described risk-benefit assessment covering the choice of DCT and DCT elements.

Responsibilities of the sponsor and principal investigator

The sponsor and principal investigator have the same responsibilities in a DCT as in traditional trials. See the Swedish Medical Products Agency's information on EU Regulation 536/2014 (Clinical Trials Regulation, CTR).

There must be a plan in place for communication between the principal investigator, the main trial unit, any distance units, and other staff who interact with the research participants, such as home health staff. The plan should also include a distribution of responsibilities and, where necessary, communication channels between the main trial unit and the patient's regular GP or attending physician.

Safety reporting

- Just as in a traditional clinical trial, the principal investigator is responsible for
  - assessing potential (S)AEs
  - documenting (S)AEs in the CRF
  - reporting SAEs to the sponsor within the required timeframe.
- Participants report (S)AEs to the main trial unit during scheduled contacts or on an ad hoc basis by contacting the unit directly, or systematically via questionnaires.
- Trial staff may come across relevant information at any time, and this must be made available to the principal investigator. This includes all obvious (S)AEs, such as those that occur during home health visits or where participants spontaneously report an (S)AE during a home visit.

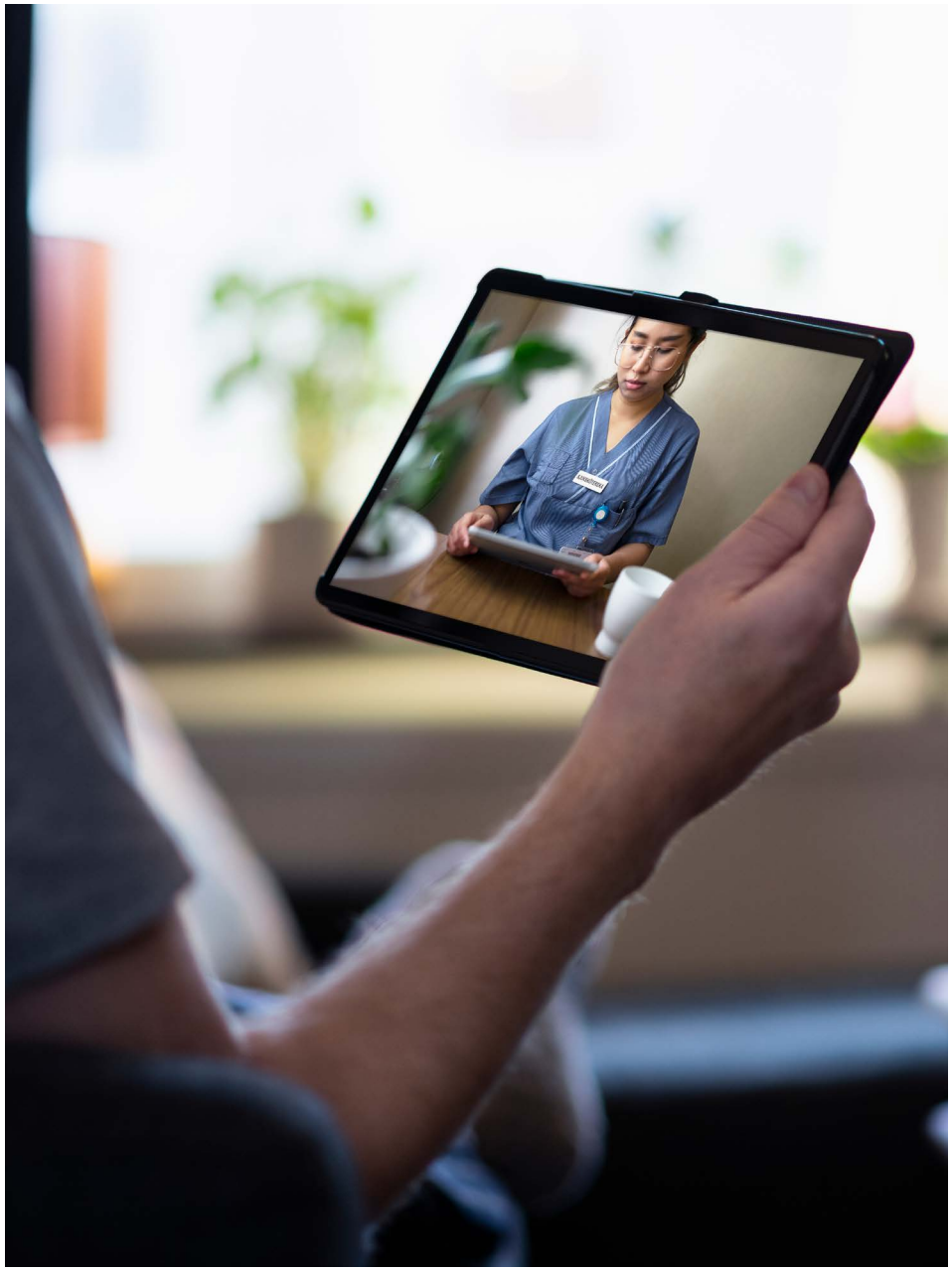
Checklist

Ensure that

- the investigator's overall responsibility is clear
- there are processes in place for safety reporting and follow-up
- there is a documented division of responsibilities between the main trial unit, distance units and home healthcare
- there is a communication plan between all the parties involved
- there is a clear division of responsibilities and clear lines of communication between the main trial unit and the attending physician.

References

https://www.lakemedelsverket.se/en/permission-approval-and-control/clinical-trials/medicinal-products-for-human-use/clinical-trials-regulation-eu-536-2014/sponsor-and-investigator#hmainbody1



Distance unit
(satellite site)

To make a clinical trial accessible to participants who are geographically distant from specialist healthcare and to increase their opportunity to participate in clinical trials, a visit to a distance unit such as a primary care provider or other healthcare facility may be an option. The term ‘satellite site’ may also be used, but there is no actual definition of this concept. Cooperation between the main trial unit and distance units generally benefits research, as it enables more healthcare facilities across the country to participate in clinical trials and gain knowledge about new treatment options.

According to the Swedish Medical Products Agency, visits to a distance unit may be used if the sponsor can demonstrate that the efficacy and safety data collected will be of the same quality as in traditional trial visits, and that patient safety is not compromised. The sponsor should carry out an assessment, in consultation with the investigator, to determine whether the use of a distance unit is appropriate for the trial in question.

Once a suitable distance unit has been identified, the investigator should consult with the sponsor, the patient and the distance unit to determine which specific trial activities that are suitable to be carried out remotely.

The division of labour between the main trial unit and the distance unit has been described by Clinical Trials Sweden (kliniskastudier.se). We therefore refer you to their guidance setting up and working with distance units in a context where most of the activities take place at the distance unit but the main trial unit retains overall responsibility.

Examples of activities that may be carried out at a distance unit, where deemed appropriate for the trial, include follow-up visits, dispensing of investigational medicinal products, blood sampling, and delivering samples to the laboratory, as well as other assessments such as measuring weight and blood pressure.

Applications and implementation

If the principal investigator chooses to use a distance unit in the trial, with registration of samples directly in the sponsor's biobank, the same application procedure applies as in other trials.

It is important that the study protocol submitted to the regulatory authorities and the patient information for the clinical trial clearly state that distance visits will form part of the trial. The principal investigator must demonstrate their oversight of any remote service provider (ICH E6(R3) 2.3).

The principal investigator who delegates tasks to a distance unit must ensure that the delegated tasks are performed correctly and that the quality of the reported data is accurate (ICH E6(R3) 2.3).

The level of the investigator's oversight and decision-making regarding trial-related activities depends on the nature of the activities and should be proportionate to the risks to participant safety and data reliability. Oversight should ensure that documents meet the relevant requirements, including ensuring that trial results are reliable, participants are kept safe and decision-making is appropriate.

Safety assessment and reporting

For safety monitoring of individual trial participants (see ICH E6(R3) Annex 1, Section 2.7.1), the investigator should review and assess information on participants' health status from a range of sources, including home health visits, distance unit visits or digital monitoring devices. See ICH E6(R3) Section 3.9 and Annex 1, Section 3.13.2 for details on how this information should be made available to the investigator.

Investigational medicinal product

In accordance with applicable regulatory requirements, the sponsor may arrange for investigational medicinal products to be sent directly to the participant, for example to the patient's home – see the specific section in this document titled 'Medicines delivered directly to patients' and ICH E6(R3) 3.15.3. If investigational medicinal products are to be sent between the main trial unit and the distance unit, there must be a written description of how the investigational medicinal products are transported between these sites. The sponsor's SOPs must also be followed in this regard.

In cases where investigational medicinal products are stored at the distance unit, there must be a clear description of how the medicinal products are stored and how any temperature logs are to be completed, as well as reporting pathways and a contingency plan for any deviations or unforeseen events. If a pharmacy manual exists for the trial, it must be followed.

Remote data collection

Remote data collection in clinical trials with decentralised elements – e.g. the use of distance visits and digital instruments such as wearable devices, or the retrieval of data from electronic patient records – requires the investigator to pay particular attention to vulnerabilities regarding data security (see ICH E6(R3) Annex 1, Section 4.3.3). This includes factors such as cybersecurity and data protection (see ICH E6(R3) Section 3.7).

Some of the considerations regarding real-world data (RWD) in section 3.5.1 may also apply when data are collected remotely in clinical trials.

Agreements and delegation

We recommend that the main trial unit draws up a written delegation plan or a clear delegation from the principal investigator. (Clinical Trials Sweden has supporting templates for this).

The written plan or delegation of authority must be kept in the investigator site file at the main trial unit and in the Trial Master File (TMF) held by the sponsor (see also examples in Appendices 1–3).

Both the main trial unit and the distance unit must keep records, which must be available in the event of an audit or inspection. These records must clearly show that the principal investigator has maintained regular contact with the distance units (see also the section on the investigator's oversight/ responsibilities). An agreement regarding remuneration must be drawn up in the form of a financial agreement, either directly between the main trial unit and the distance unit, or by the sponsor drawing up such an agreement directly with the distance unit.

Training and documentation maintenance

Staff at the distance unit must have the formal and practical competence to perform the tasks required for the trial in question. The staff listed in the delegation list must receive the training required for the trial, with the principal investigator and the sponsor responsible for ensuring compliance with this.

The distance unit must keep records in the usual manner regarding the participant's visits to the distance unit. The written work description from the main trial unit must specify which trial documentation the investigator expects the distance unit to maintain.

In accordance with GCP, the distance unit must report any AE/SAE to the main trial unit if they learn from the participant that such an event has occurred (see safety reporting under the section Main trial unit).

Documentation must be kept at the main trial unit and, to a certain extent, also at the distance unit. Depending on the tasks and investigations carried out at the distance unit, the following documents may be available at the distance unit if needed:

- the study protocol and any amendments to the protocol
- regulatory approval and biobank approval
- Investigator's Brochure or SmPC
- Delegation Log & Source Data Location List
- documentation on the distance unit's processes, standard operating procedures (SOPs) or job descriptions
- medication logs + temperature logs
- requisitions for ordering medicinal products
- required system manuals
- relevant correspondence
- contact details for the main trial unit.

Study initiation, monitoring and close-out visits

The sponsor must make a 'selection visit' to the distance unit in accordance with applicable regulations and the sponsor's SOPs if the scope of the study requires this. The visit involves checking the premises, equipment, how medicinal products are stored and other matters that may be relevant. It may also be beneficial for the sponsor to conduct a 'remote start-up visit' according to the same principle.

The question of whether the investigator needs to conduct monitoring visits and close-out visits at the distance unit depends on the scope of the research being conducted and on whether medicinal products are stored at the distance unit.

The sponsor must comply with the regulations and internal requirements set out in the sponsor's SOPs, as well as the monitoring plan drawn up for the trial.

Participant recruitment via referring units

Referring units are sometimes used as a way to enable more people to participate in clinical trials, and to increase the chances of achieving the desired number of participants for the trial. A referring unit may, for example, be a clinic at a hospital, a primary care provider or another healthcare facility that sees a specific patient group relevant to the trial in question.

The referring unit's role is to identify patients and ask for their consent to be contacted by the main trial unit for information about an ongoing trial. Once the patient has consented to being contacted, the main trial unit takes over and is responsible for providing study information, obtaining remote informed consent, and carrying out other study-related activities.

The referring unit may subsequently provide supplementary information, such as medical records, but does not perform any study-related tasks. No protocol training or delegation of tasks is therefore required for staff at the referring unit.

Key aspects:

- Secure processing of personal data is essential. Avoid insecure communication channels, such as email, for the transfer of sensitive information.
- A cooperation agreement is usually drawn up between the main trial unit and the referring unit. In some cases, the referring unit may receive a small fee for the work it carries out.

References

ICH: E6(R3): Guideline for good clinical practice – Step 5, Clinical Trials Information System, European Medicines Agency (europa.eu)

Decentralised clinical trials, Swedish Medical Products Agency (lakemedelsverket.se)

Clinical trials, Clinical Studies Sweden Research Guide – Biobank Sweden

Checklist

- The investigator may use a distance unit if the trial is suitable and if this has been preceded by a discussion between the parties concerned.
- For a study conducted via a remote unit to be successful, the investigator must ensure that the patient is comfortable with occasionally attending the distance unit. Ensure that distance visits are described as an option in the protocol and in the information provided to participants, and that approval has been obtained from the relevant authorities to use a distance unit.
- It is important that staff at the distance unit receive the training they need to carry out the work, that they have the necessary equipment, and that there is a delegation of authority from the principal investigator.
- The distance unit must also be made aware of what they are required to document within the scope of the trial.
- Furthermore, clear and well-defined written reporting and communication channels must be established between the distance unit and the main trial unit.

Home health visit

In this context, a home health visit means that trial staff visit the patient at a location other than the trial unit, usually the patient's own home. The staff carrying out the home health visit may be the trial unit's own staff or a contracted organisation specialising in home health visits.

Before the investigator decides to include home health visits in the trial, they must carry out a documented risk assessment. The investigator should balance the benefits to the patient of home visits against the need for equipment and facilities and access to such resources, not least proximity to the trial unit or other healthcare facility.

Home health visit process

The process described below is an example of how this can be carried out in cases where trial staff who do not belong to the trial unit and who specialise in conducting home visits to patients have been engaged.

Make a written agreement between the trial unit and the organisation that will carry out the home visits. The agreement should include the division of responsibilities between the trial unit and the organisation, communication channels, and assurances that the staff carrying out the home visits have the relevant skills (see Appendix 1 for an example of a written agreement). This agreement thus governs the collaboration between the trial unit and the home health visit organisation and contains no financial terms. An outsourcing agreement containing financial terms must be drawn up between the sponsor and the home health visit organisation.

If an agreement has been drawn up between the trial unit and the home health visit organisation, similar to the one in Appendix 1, the home health staff do not need to be listed in the trial unit's delegation log. The agreement must be drafted in such a way that it constitutes a delegation in itself and clearly states that the home health visit organisation is responsible for ensuring that staff have the training, education and experience required for the tasks. The investigator must be able to access documentation of this at any time. The home health staff must carry out tasks specific to the trial and must therefore be trained in these duties and the relevant sections of the study protocol, as well as GCP.

Whatever tasks the home health staff are expected to perform, they must be familiar with the procedures applicable to AE/SAE reporting.

Before any home visit is carried out, the home health staff should meet with the staff at the trial unit to discuss what is to be done with the patients, the division of responsibilities and how they are to communicate with one another. Prior to the patient visit, the home health staff and the trial unit should check in with each other for a briefing. This may include relevant information about the patient that has emerged during scheduled video calls or other contact with the patient, and whether there is anything in particular to bear in mind ahead of the home visit.

During the home visit, the trial unit should be available in case the home health staff need to contact it. The home health staff must document all activities and relevant observations. This documentation constitutes source data and must be transferred to the trial unit as soon as possible. One option is for the home health staff to be connected to the same healthcare information system or trial platform as the trial unit. If this is not possible, and the documentation is done on paper, it should be posted to the trial unit as soon as possible. In such cases, it is advisable for the home health staff and the trial unit to make telephone contact immediately after the home visit, to avoid any delay in relevant information about the patient reaching the trial unit. Medical records and other identifiable patient data must not be sent by email.

If the patient informs the home health staff about an AE/SAE, or if such an event is apparent to the home health staff during the home visit, the home health staff must contact the trial unit as soon as possible – preferably during the home visit in question. The investigator must then contact the trial patient as soon as possible and assess the AE/SAE. Naturally, the same procedures for reporting AEs/SAEs apply to DCTs as to traditional trials.

An alternative to having healthcare staff carry out home visits may be to engage healthcare facilities close to the patient to perform tasks of a less specialised nature. These may include taking blood samples, measuring blood pressure and similar tasks. The investigator can then engage a healthcare provider with good geographical coverage in the location in which trial participants are to be recruited (see also the section on Distance units).

Considerations when planning the trial

- Plan for open and clear communication between the trial unit and the home health staff.
- The home health staff should be informed of anything specific they need to bear in mind ahead of each home visit.
- The home health staff must be able to contact the trial unit before, during and after each home visit to obtain information and to provide the trial unit with relevant information about the patient.
- The home visit organisation must have insured staff. The PI needs to ensure that this is the case.
- Establish a process for transferring source data to the trial unit and document the process.
  - This can be done by writing the visit notes on paper and then posting them to the trial unit.
  - If the home health staff and the trial unit are connected to the same IT platform, the home health staff can enter visit notes into this system, provided that the trial unit has full access to the notes. If specified in the study protocol, the simplest approach is for the data to be entered directly into the CRF.
- It is common to take samples during home visits to a patient. Under the Biobank Act, newly collected samples may be registered directly in the sponsor's biobank without the need to apply to the RBC or the principal of the biobank for biobank access. The sponsor is responsible for documentation and for ensuring compliance with the Biobank Act. Gaining access to existing samples such as biopsies requires an application for access and an agreement with each relevant biobank.

Considerations during recruitment and implementation

- Inform the patient that healthcare staff will be visiting their home, and explain how many visits there will be and what procedures will be carried out at home.
- Ensure that the patient's home is suitable for the intended procedures.
- All visits during the course of the trial are primarily the responsibility of the investigator. The investigator must be able to ensure and demonstrate their overall responsibility for the trial (investigator oversight).
- Maintain clear and frequent communication with the home health staff.
- The source data generated during the home visit must be made available to the trial unit as soon as possible.
- The patient may feel excluded as they do not physically meet the staff at the trial unit. Therefore, make it possible for the patient to contact the trial unit if they wish to do so throughout the trial, just as in all clinical trials.

References

The Swedish Medical Products Agency on DCT: https://www.lakemedelsverket.se/sv/tillstand-godkannande-och-kontroll/klinisk-provning/lakemedel-for-manniskor/decentraliserade-kliniska-lakemedelsprovningar#hmainbody1

EMA Q&A on GCP: https://www.ema.europa.eu/en/human-regulatory-overview/research-and-development/compliance-research-and-development/good-clinical-practice/qa-good-clinical-practice-gcp

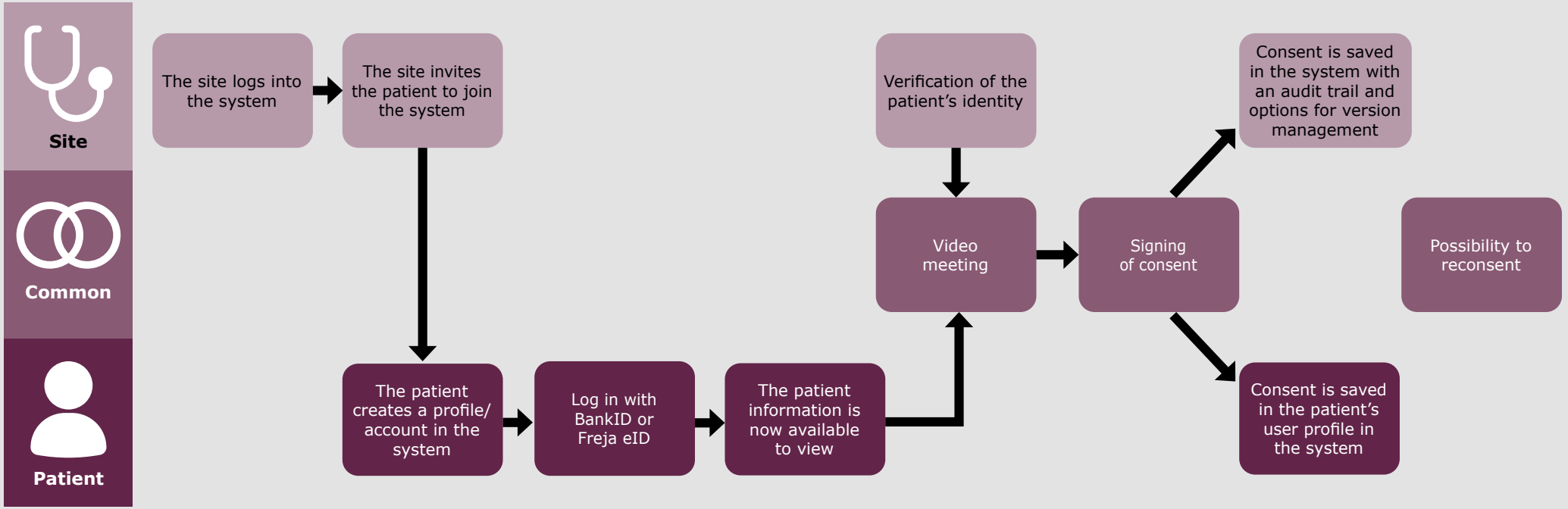
EMA Recommendation paper on DCT: https://health.ec.europa.eu/system/files/2023-03/mp_decentralised-elements_clinical-trials_rec_en.pdf

Digital consent

Electronic informed consent at a distance
(Remote eConsent)

In order to conduct a decentralised trial, where the participant is not physically present at the trial unit when recruited, the investigator must obtain informed consent remotely.

The same requirements regarding informing the participant and giving them the opportunity to ask questions apply in this context as in an in-person meeting. The investigator must be able to verify the participant's identity and assess whether they have taken in and understood the information. It is therefore most appropriate to conduct such a meeting via a video call between the investigator and the participant. The Swedish Medical Products Agency deems that a telephone call alone is not sufficient.



Using an electronic consent system allows researchers to streamline the process of obtaining consent. The participant may also find it more practical and convenient to give their consent electronically.

The requirements for electronic patient information are no different from those applicable to traditional trials. However, it is important to describe the process and the DCT elements included in the trial with particular clarity.

Make sure there is a process in place for archiving the electronic consents securely, to ensure compliance with laws and guidelines and for any future audit.

Once the investigator has collected all electronic consents from the research participants, the entire consent database needs to be exported, for example as a CSV file.

The downloaded consent database should contain:

- participant's name and personal identification number
- date on which the participant signed the consent form, including specific electronic signature
- status of the consent (valid/withdrawn)
- healthcare facility
- date on which the study doctor signed, including specific electronic signature
- research participant information, both versions and content
- monitoring status.

Once the consent database has been exported or downloaded, it must be delivered on a suitable storage media to a pre-designated person for archiving. The investigator is responsible for this, but may delegate it to another person.

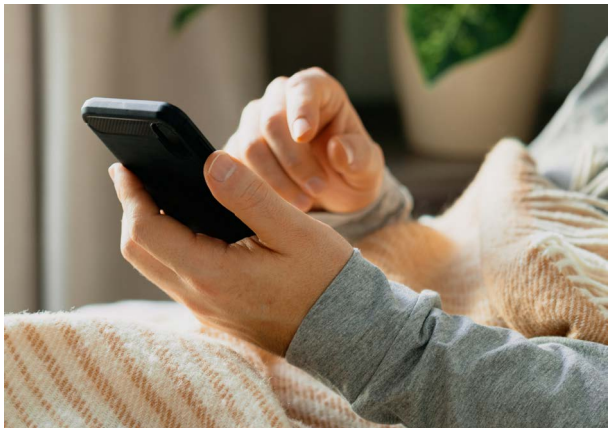
It is important that data intended for long-term storage remains readable even after a long period of time. Such data must therefore be transferred, regularly and as required, to media or systems for continued storage. The study sponsor must be notified of any changes to the person responsible for the archive.

Choice of electronic system

It is the sponsor's responsibility to ensure that the electronic system to be used is suitable and validated for the task, and that it complies with applicable laws and security requirements, in order to protect participants' privacy and personal data.

It is common to use some form of trial platform where a profile can be created for the participant, containing personal details and a unique login. There are several systems that handle the signing of digital consents. The example above is from a system that we in the working group have previously used.

The participant's identity must be verified via BankID, Freja eID+ or two-factor authentication – that is, using both a personal password and a



personal code generated at each login and sent to the participant by email or text message. This is to ensure that the consent and the associated signature come from the correct person.

The video call may take place in the same system as the signing of the consent form – for example in a trial-specific platform – or in a separate system, such as the hospital's medical records system.

References

The Swedish Medical Products Agency on DCT: https://www.lakemedelsverket.se/sv/tillstand-godkannande-och-kontroll/klinisk-provning/lakemedel-for-manniskor/decentraliserade-kliniska-lakemedelsprovningar#hmainbody1

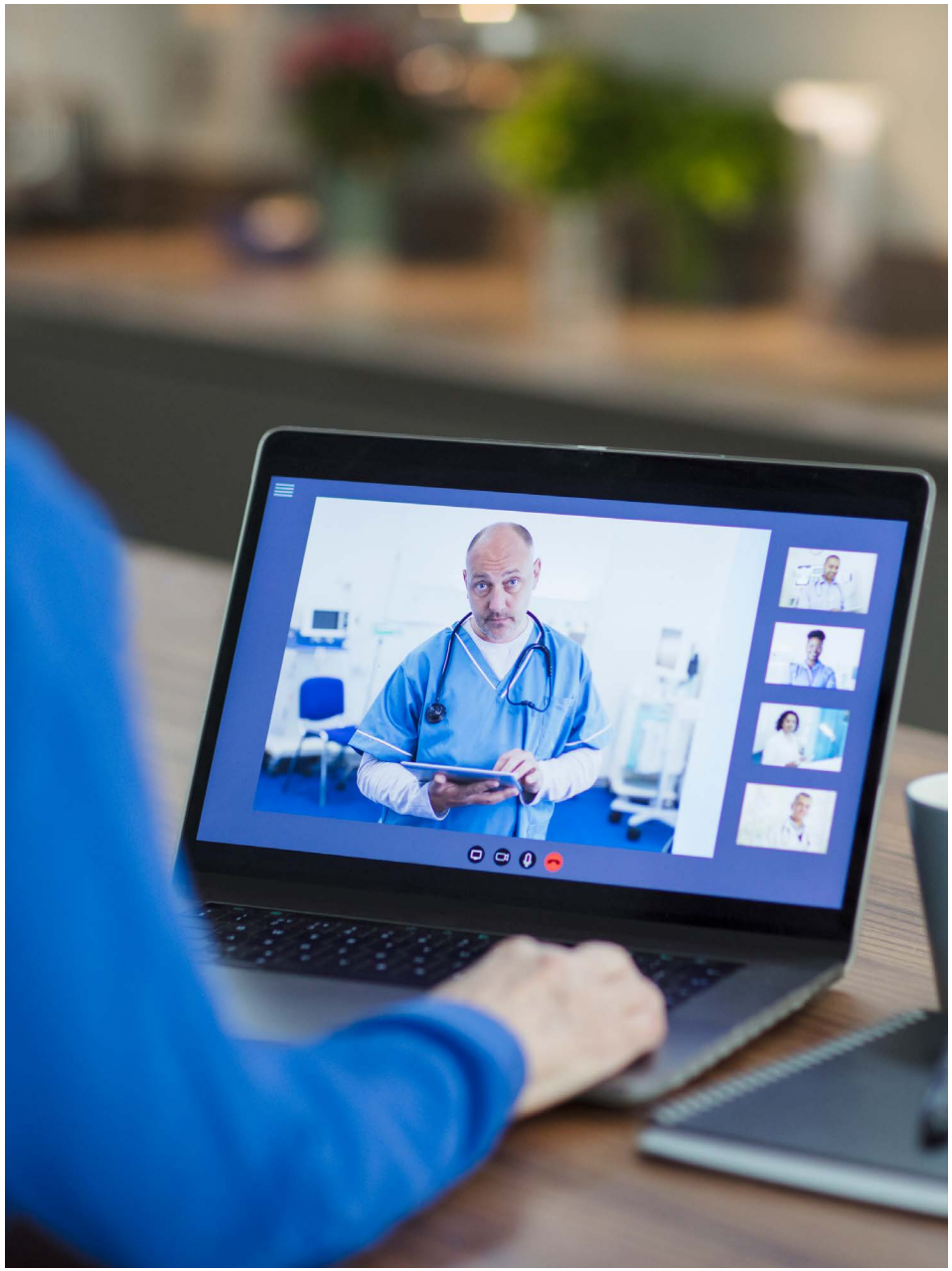
EMA Q&A on GCP: https://www.ema.europa.eu/en/human-regulatory-overview/research-and-development/compliance-research-and-development/good-clinical-practice/qa-good-clinical-practice-gcp

EMA Recommendation paper on DCT: https://health.ec.europa.eu/system/files/2023-03/mp_decentralised-elements_clinical-trials_rec_en.pdf

Checklist

Ensure that

- you use a validated system – this is a requirement
- the participant and the investigator identify themselves via BankID, Freja eID+ or two-factor authentication
- the study protocol describes how consent will be obtained electronically
- the meeting with the participant is a video call – a telephone call is not sufficient
- email is not used for signed consent
- records are retained for 10 or 25 years, depending on the type of study
- care is taken with version management.



Video calls

By video calls, we mean communication via mobile phone, tablet or computer where the parties can communicate with each other using both audio and video.

Generally speaking, a video call can always replace a telephone call, but not the other way round, as seeing the other party provides additional information, such as body language and facial expressions. For this reason, obtaining informed consent by telephone is not acceptable, but it may be acceptable to do so via a video call.

For this to be the case, the transmission of audio and images must be secure. Major providers of video call systems, such as Zoom and Microsoft Teams, encrypt the data transmitted between the parties. If the trial unit routinely uses a compliant system for video calling patients, this may be a good option.

Check whether the clinic or hospital has any guidelines on which systems they are permitted to use for video calls with patients. In industry-sponsored trials, it is common for the sponsor to use a telehealth platform, which must then be validated by the sponsor.

Video calls are primarily suitable for remote follow-ups with trial patients and during the consent process. It is also possible to carry out simple visual assessments during a video call, but this depends entirely on the requirements for such assessments in the trial. Otherwise, the suitability of video calls is determined by the trial population, the type of medicinal product or medical device being studied, and the phase of development the trial is in. If an AE/SAE is detected or reported by the patient during the video call, it must be assessed and documented. It is important that a video call is designed such that it entails no increased risk to the patient or to the quality of the data collected, compared with a physical visit to the trial clinic. If it is not possible to meet these requirements, the investigator should instead consider a physical visit to the trial unit or to another healthcare provider, or a home health visit.

When patients are recruited into the trial, the investigator must inform them that consultations will be conducted via video call.

The investigator must also ensure that the patient has suitable equipment for video calls and is able to use it. The sponsor should be able to provide equipment if the trial participant does not have any or does not wish to use their own. It is also beneficial if the patient can be in a suitable room where they will not be disturbed during the video call.

There are generally very few guidelines and recommendations regarding video calls in clinical trials. This is perhaps because clinical trials have long relied on follow-up telephone calls, and video calls can be considered to serve a similar function but with a slightly greater scope.

References

EMA recommendation paper: https://health.ec.europa.eu/document/download/2ccc46bf-2739-4b9a-ab6b-6f425db78c61_en?filename=mp_decentralised-elements_clinical-trials_rec_en.pdf

EMA Guideline on computerised systems and electronic data in clinical trials: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-computerised-systems-and-electronic-data-clinical-trials_en.pdf

Q&A: Good clinical practice (GCP): https://www.ema.europa.eu/en/human-regulatory-overview/research-development/compliance-research-development/good-clinical-practice/qa-good-clinical-practice-gcp

Swedish Medical Products Agency: https://www.lakemedelsverket.se/en/permission-approval-and-control/clinical-trials/medicinal-products-for-human-use/decentralised-clinical-trials#hmainbody1

Medicines delivered directly to patients

In Sweden, medicinal products for clinical trials must be distributed via pharmacies. The sponsor cannot send the medicinal product directly to the clinic or to the patient's home. However, only one pharmacy needs to be contracted for the trial in Sweden.

An agreement must be made between the sponsor and the pharmacy, specifying conditions such as quality and transport requirements, and it must follow the handling instructions for the investigational medicinal product.

The investigator/institution is responsible for investigational medicinal products at the trial unit, in accordance with ICH-GCP(R3) 2.10.1 (Annex 1).

The general requirements regarding responsibility for medicinal products, as described in ICH-GCP(R3), also apply

if investigational medicinal products are sent to the patient's home. This might involve documentation confirming which batch was sent, how many packs were sent, when they arrived at the home, and the temperature of the medicinal product during transport.

It is important to contact the pharmacy in the early stages of the trial to discuss the specific requirements for the investigational medicinal product in question and how it should be stored, as well as the options available to the pharmacy to engage a transport company or courier to transport the medicinal product. It is recommended that the pharmacy enters into an agreement with the transport company or courier to avoid the sponsor becoming involved with the patient's contact details. The transport company or courier must be able to meet the transport requirements and maintain patient confidentiality, and this must be specified in the agreement between the pharmacy and the transport company or courier.

It may also be advisable to check with the pharmacy early in the process regarding the requirements for distributing compounded medications across regional boundaries in the specific regions where the trial is to be conducted.

During the trial

Here is an example of a process for transporting medicines directly to a patient in a trial:

1. The investigator prescribes the investigational medicinal product and other relevant medicines in accordance with the local procedure at the trial unit or the trial-specific procedure.
2. The trial coordinator orders the medicinal product from the pharmacy.
3. The pharmacy organises delivery to the patient's home with the help of the trial coordinator.
4. The pharmacy arranges for a courier and provides the patient's address and contact details. The sponsor must not have access to the patient's address. The pharmacy ensures that the patient's details and confidentiality are strictly maintained, and this must be set out in the agreement between the sponsor and the pharmacy. The pharmacy contacts the patient to organise the delivery, and confirm they will be at home to receive it.
5. The pharmacy should discuss a back-up option with each patient, such as a relative, in case the patient is not at home when the parcel arrives. There should be a back-up plan in place for each patient.
6. The home health staff confirm the handling of the investigational medicinal product in transit and on delivery, as well as its quality and quantity, at the next visit before the patient begins treatment. If the patient handles the investigational medicinal product themselves without any trial visits to their home, they must have received instructions on how to store the investigational medicinal product and what documentation requirements apply.
7. If you use a mobile team of home health staff, returns can be handled by the home health staff, who can carry out drug accountability before any surplus medicinal product is transported back to the pharmacy. In this case, the trial coordinator should contact the courier to collect the investigational medicinal product for delivery back to the pharmacy. If no home health staff are being used in the trial, the patient may return medicinal products themselves via a courier or by post, in which case a tracked postal option should be chosen.
8. Prescriptions for other medicines are handled electronically by the investigator. In accordance with standard practice, electronic prescriptions are sent to all the pharmacies that the patients may visit to collect their medicines.

Document management

Drug accountability logs and documentation must be kept at the clinic and at the pharmacy for monitoring purposes, as the monitor cannot visit the patient's home for reasons of confidentiality.

Checklist

Ensure that

- there is an agreement in place between the sponsor and the pharmacy
- transport conditions and confidentiality are set out in an agreement
- checks are carried out regarding distribution across regional boundaries
- the patient has a back-up contact who can receive home delivery of medicines
- the patient and any home health staff are trained in how to handle the investigational medicinal product
- investigational medicinal product handling is documented in line with ICH-GCP, including in the patient's home.

References

ICH-GCP (guidance for good clinical practice E6(R3), EMA/CHMP/ICH/135/1995

EU-CTR 536/2014 HSLF-FS 2021:10

Sampling or measurement at home

There are several ways to carry out tests or measurements at home. For example, digital measuring devices and communication tools are commonly used in DCTs for collecting patient data remotely. However, patients can also take their own blood samples at home. The trial designer should consider whether a self-managed solution adds any extra value for the trial participant or for the trial itself.

The trial designer should also consider whether the technical solutions are appropriate for the population participating in the trial, and whether they are suitable for answering the scientific question. The technical solutions may include apps on

a mobile phone or tablet, electronic diaries or questionnaires, or portable measuring devices such as heart rate monitors.

It is important that the instruments are easy to use, that data collection is straightforward for the participant, and that good support is available if they need it. One risk of overly complicated sampling procedure or technical solutions is that the trial participant may become frustrated and avoid using them.

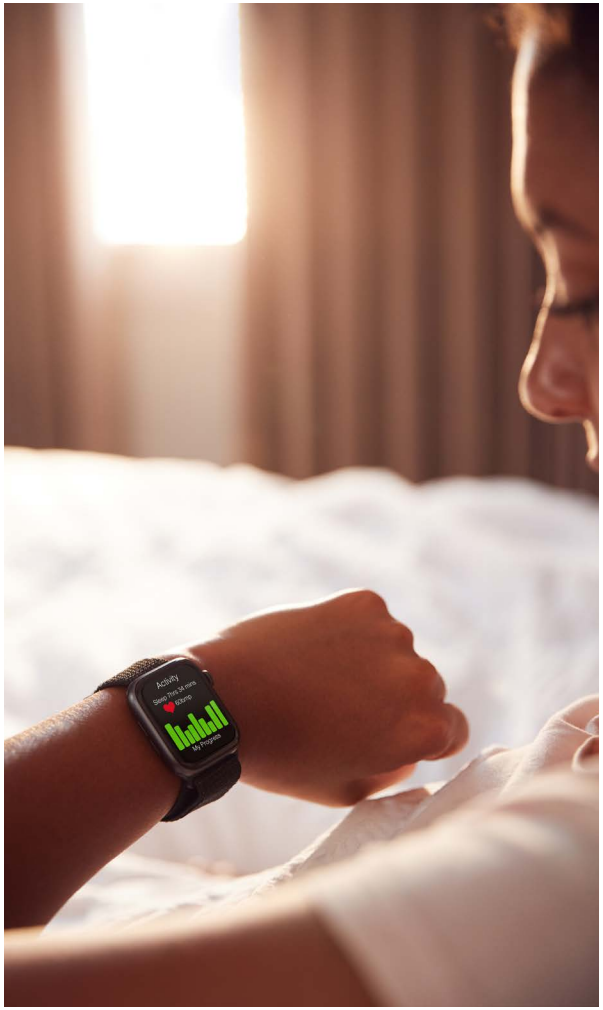
If the trial uses an app, an agreement is required with the app developer regarding data sharing and how data is to be handled in the trial, as well as the confidentiality of patient data. The sponsor is not entitled to direct access to the data. All digital measuring instruments must be validated and CE-marked for the purpose in question. If they are not CE-marked, a separate trial for the medical device may be required.

Further information on the requirements for medical devices, validation and other related matters can be found on the Swedish Medical Products Agency's website.

Checklist

Ensure that

- the use of sampling procedure in the home is tailored to the specific trial and patient group
- the measuring equipment is validated and CE-marked for the purpose
- data management is set out in an agreement with the party or parties supplying the sampling equipment
- support for the digital measuring instrument and clear instructions for self-sampling are available.



Appendix 1

Example of agreement between trial unit and home healthcare provider

Between **Trial unit**
with Principal Investigator

and **Mobile care provider** (hereafter referred to as" Provider")

The Trial unit and Principal Investigator have been engaged by the Sponsor, to conduct the study "Study title" with the protocol number xxxxx. Provider has been engaged by Sponsor to support The Trial unit and Principal Investigator in delivery of the study.

Provider and the Trial unit shall perform tasks set forth in this Delegation Agreement in accordance with Good Clinical Practice, applicable laws and regulations and the Clinical Trial Protocol. Principal Investigator authorizes Provider to assume the study tasks listed below, for which Provider and Provider's staff are qualified by training, education, and experience.

Tasks to be carried out by Provider and The Trial unit:

The Trial unit	**Provider**
Request patient visits by provider in accordance with agreement with the participants	Schedule off-site visit with participant and inform the Trial unit
...	Perform and communicate Handover visit with the Trial unit
...	Perform trial assessments
...	...

As observed during the visit, Provider staff shall, in accordance with the Protocol, alert the Principal Investigator (or medical designee) of any observed changes to the trial subject's health, safety, and any observed or trial subject-reported Adverse Events, Serious Adverse Events, Serious Adverse Drug Reactions, and Unexpected Adverse Drug Reactions, as these terms are defined in ICH Harmonised Tripartite Guideline: Guideline for Good Clinical Practice E6(R3) (ICH GCP). Provider staff shall be available to communicate directly with the Principal Investigator (or medical designee) in the event of safety or any Adverse Event or Adverse Drug Reactions reporting.

Provider will adequately document the activities conducted at the study visits and source documentation will be provided to The Trial unit to be part of The Trial unit's source documents. Source documentation should comply with ICH-GCP requirements and be attributable, legible, contemporaneous, original, accurate, and complete.

Provider shall report to The Trial unit any protocol deviations or potential serious breach incidents.

Principal Investigator shall always retain all responsibilities regarding identification, classification, assessment, documentation, and reporting of all safety issues, and all safety events, including Adverse Events, Serious Adverse Events, Serious Adverse Drug Reactions and Unexpected Adverse Drug Reactions, as these terms are defined in ICH GCP and required to be reported as per applicable regulations, ICH-GCP, and the Protocol.

Principal Investigator understands and agrees, that delegation of these tasks to Provider, in no way alters the responsibilities of the Principal Investigator for this study as defined by ICH-GCP.

Provider accepts delegation of these tasks and agrees Provider and Provider's staff will conduct the tasks as directed by Principal Investigator and in accordance with this Agreement, the Protocol, all applicable laws, industry standards, regulations and guidelines including ICH GCP, and data protection regulations for the duration of the study. Provider agrees that Provider staff are qualified by training, education, and experience to conduct these tasks. Provider staff will provide their CV, documentation of qualifications, training, and experience to The Trial unit on request.

Provider retains responsibility for any liability related to professional malpractice or individual misconduct resulting in damage to the trial subject. Provider acknowledges that an insurance policy is in place to cover any potential damages to the trial subject. Such insurance policy can be provided upon request by The Trial unit.

Provider acknowledges that all payments for services rendered as a result of this agreement are to be paid by Sponsor and, therefore, The Trial unit will have no financial obligations with Provider under the Terms of this Agreement.

Trial subject's confidentiality shall be maintained in accordance with applicable personal data protection regulations, ICH-GCP and the clinical trial informed consent form.

The Parties shall otherwise comply with the confidentiality and data privacy provisions concerning Sponsor and/or trial subject information as provided for in the respective Clinical Trial Agreement.

ACKNOWLEDGED AND AGREED:

THE TRIAL UNIT:	PROVIDER:
Name:	Name:
Title:	Title:
Signature:	Signature:
Date:	Date:
Name:	Name:
Title: Principal Investigator	Title:
Signature:	Signature:
Date:	Date:

Appendix 2

Principal Investigator(PI) plan for overseeing the conduct of the clinical study at the satellite sites.

- The PI needs to prepare a plan for overseeing the conduct of the clinical study at the satellite site(s).

The plan addresses:

- Storing and transferring of study documents, Investigational Medicinal Products (IMP), Non-IMP and medical devices, and supplies
- Communicating information in a timely manner (e.g., notification of screened/randomized study participant, faxed and mailed lab results from the Central Laboratory, safety events, updates, and clarifications)
- Handling/shipping laboratory specimens
- Attending to clinical emergencies (e.g., notifying PI, obtaining unblinding information, communicating with the study participants)
- Any other study specific information

Appendix 3

Example of a delegation clause to specify that the Principal Investigator (PI) oversees a distance unit/satellite site

- With this contract Principal Investigator ((PI), XXX will delegate tasks to YYY who will act as a Designated Satellite Investigator (DSI) at hospital XXX.
- DSI, YYY, will have his own delegation list at XXX hospital and delegate tasks to his/her investigational staff.
- PI XXX and XXX hospital will be responsible for oversight of the study at the Satellite Site as well as for XXX hospital. Including from day XX -to XX -day- YYYY during the conduct of the study responsibility for subject eligibility, training, leading and supervising study site staff as described in the established Clinical Study Agreement with the sponsor.

Biographies

Mats Thoring
A pharmacist who has been working in clinical trials since the mid-1990s. Has led Bayer's clinical trials organisation in Scandinavia for 16 years. He has been involved in the planning and launch of decentralised trials, participated in Bayer's project to develop DCT, is a member of a working group within IMI Trials@Home, has been involved in the Swedish Medical Products Agency's DCT project, and acted as a stakeholder for the European Medicines Agency (EMA) during the drafting of the Recommendation Paper on DCT. He now works on supporting Bayer's trial managers and study teams around the world in implementing projects with DCT elements.

Sandra Funning Schedin
A pharmacist with 16 years' experience working in the pharmaceutical industry, primarily in clinical trials. She currently works as a project manager and is responsible for the review of trials within Clinical Operations at Roche AB in Sweden. Has experience of planning and applying for approval of a fully decentralised oncology trial in Sweden, and it was here, alongside other trials involving decentralised elements, that she gained her experience of decentralised trials.

Gabriella Seger
A nurse who has worked for around 20 years on clinical trials and medical devices at various trial units in Sweden. She has worked in several trials where use has been made of one or more DCT solutions. She currently holds the position of Clinical Research Associate and Study Coordinator at Uppsala Clinical Research Center, where she is involved in clinical trials and DCT projects.

Anna Åhlander
A nurse who has worked on clinical trials at Uppsala University Hospital and Uppsala University for around 10 years. She has taken on various roles in a number of trials where use has been made of one or more DCT elements, including one of the pilot studies included in the Swedish Medical Products Agency's DCT project. For just over three years, she has been working as a Clinical Project Manager at Uppsala Clinical Research Center (UCR), focusing on trials with DCT elements.

Susan Öman
A nurse with a background as a research nurse at Karolinska University Hospital in Huddinge. Has been working on clinical trials at Sanofi AB for the past 25 years. Has held various positions within clinical trials, but currently leads a team of 13 project managers who run Sanofi's trials in the Nordic and Baltic regions, where DCT elements are playing an increasingly significant role. These days, one or more DCT elements are included in all the clinical trials run by Sanofi.

Elham Hedayati
Associate Professor and Consultant in Oncology at Karolinska Institutet and Södersjukhuset. Clinical researcher who early on established an independent line of research focused on personalised breast cancer treatment and trials investigating side effects and long-term complications of conventional breast cancer therapy. Founder of True Dose AB.

Jonas Oldgren
Professor of Coagulation Research and Consultant in Cardiology at Uppsala University and Uppsala University Hospital. Has conducted clinical and randomised trials in cardiovascular diseases, with grant support from the Swedish Research Council (VR), the Swedish Foundation for Strategic Research (SSF), the Swedish Heart-Lung Foundation and the NIH, or in collaboration with industry. Head of Uppsala Clinical Research Center (UCR) 2014–2022, currently general secretary for clinical research at the Swedish Research Council. Aims to enable more patients to participate in clinical trials through the development of pragmatic trial designs such as DCT, in order to reduce resource requirements and workload for both patients and investigators, while maintaining quality.

Decentralised Elements in Clinical Trials

Decentralised clinical trials (DCTs) are a natural evolution of the methods we already use in clinical trials of medicinal products. One of their benefits is that patients do not have to attend the clinical trial unit as often, or in some cases at all.

SweTrial

De forskande läkemedelsföretagen

Region Stockholm

UCR

Guidance document from the DCT working group, with members representing Uppsala Clinical Research Center, Region Stockholm and the pharmaceuticals industry, and with support from Swetrial.