Clinical trials - questions and answers

Updated October 7, 2022

NOTE – Applies only to clinical trials with medicinal products that have been applied for under EU Directive 2001/20/EC. For trials applied for under the new EU regulation for clinical trials with medicinal products, we refer to the Danish Medicines Agency's page for the regulation as well as guidance in EudraLex Vol 10 for the regulation .

Information about trials and results

1. How is my trial registered in the EU Clinical Trials Register?

The EU Clinical Trials Register meets the requirements of the International Committee of Medical Journal Editors (ICMJE), which requires clinical trials to be pre-registered in a recognized public database before the editors can accept articles about the trial for publication.

The EU Clinical Trials Register obtains information from the EudraCT application form, which must be submitted in connection with the application for permission for the trial at the Danish Medicines Agency. Once we have registered that there is permission for an experiment from both the Danish Medicines Agency and the scientific ethics committee system in the database, data about the experiment will be published.

It deserves the **EU Clinical Trials Register** .

2. Where can I find information about clinical trials with medicines in Denmark

All trials in the EU can be found in the common European database of clinical trials in the EU: **www.clinicaltrialsregister.eu** You can search for trials in Denmark by typing 'Denmark' in the search field on this website: **https://www.clinicaltrialsregister.eu /ctr-search/search** The European Medicines Agency (EMA), which hosts this database, has prepared a guide for a more specific search:

Contact

General questions about clinical trials:

send a mail

Questions about PASS studies:

send a mail

Questions about the inspection of clinical trials (GCP inspection:

send a mail

https://www.clinicaltrialsregister.eu/doc/How_to_Search_EU_CTR.pdf

3. How should I report my results to the Danish Medicines Agency

You must enter your trial results in EudraCT as soon as possible and no later than 1 year after the end of the trial. Data will then be published on www.clinicaltrialsregister.eu . This replaces the test result having to be submitted to us. You can read more on the EudraCT website under 'update': eudract.ema.europa.eu/ and generally about the end of trials in our guidance section 13 . The public GCP units have produced a guide which can be found here: www.gcp-enhed.dk/eudract-vejledninger/rapportering-af-resultater/

4. How do I search for trials where results have not been published in EudraCT/clinicaltrialsregister.eu?

You can search at https://www.clinicaltrialsregister.eu/ctr-search/search at, for example, the relevant hospital. Here it appears which trials (Trial protocol, DK) have been registered as completed (completed) and if results are missing, it is listed Trial results: *No results available*

(However, you must be aware that department etc. must be spelled correctly in the original EudraCT form in order to be able to search. It can therefore be an advantage not to search too specifically).

5. What requirements apply to the composition of subjects in clinical trials?

There are no fixed standards or requirements for the distribution of test subjects in terms of gender, age, ethnicity or health profile, since the composition of test subjects in a clinical trial depends on which target groups the specific drug and its indication are aimed at. However, the legislation dictates that it must always be justified if the trial protocol contains exclusion criteria which may contribute to a distortion in the distribution of test subjects. This is supported by the EMA guidelines, which states that there must be a fair distribution of test subjects, and when the pharmaceutical authorities assess the results of clinical trials as part of the approval process, they look closely at whether there is sufficient documentation of effect and side effects in specific target groups. It must therefore be clearly described and documented in the application that the composition of test subjects is representative, so that the results cover all relevant recipient groups.

Drug trial or not?

1. Which clinical trials must the Danish Medicines Agency give permission for?

We must give permission for clinical trials with medicines and medical devices that are not CE marked for the purpose for which they are being tested. (please see **www.medicinsudstyr.dk**).

2. What is a clinical trial with a drug?

A clinical trial is defined as any trial on humans that aims to:

- Uncover or verify the clinical effects of one or more experimental drugs and/or
- Uncover or test the pharmacological and/or other pharmacodynamic effects of one or more experimental medicinal products and/or
- Investigate the absorption, distribution, metabolism and excretion of one or more experimental drugs (pharmacokinetics) and/or
- Identify side effects of one or more investigational drugs

with a view to assessing the safety and/or efficacy of investigational medicinal products.

We recommend using our **guide to assess whether a trial is defined as a drug trial** .

Permission for these trials must be applied for from the Danish Medicines Agency.

3. What is a non-interventional trial (non-interventional trial)?

This is a non-intervention attempt when:

- The medicine or medicines in the study are prescribed as usual in accordance with the conditions of the marketing authorisation
- The decision to prescribe the drug in question is clearly separate from the decision to include the patient in the study
- The treatment itself does not take place according to an experimental protocol, but follows common practice
- No extra diagnostic or control procedures are carried out (questionnaires are not considered extra procedures in Denmark)
- Epidemiological methods must be used to analyze the collected data.

Non-intervention trials do not have to be reported to the Danish Medicines Agency, unless they are specific types of non-intervention PASS studies - see these.

We recommend using **our guide to assess whether a trial is defined as a drug trial** .

Reference is also made to the Commission's questions and answers:
http://ec.europa.eu/health/files/eudralex/vol-10/ctqa_v10.pdf - see Annex: Decision tree

4. When can a drug be defined as a tool in trials?

- The drug (tool) is not the subject of the study and is used as a tool to achieve a well-known physiological response.

Examples:

- Pupil-dilating eye drops are used to examine the physiology of the eye

- Radioactively labeled tracer (drug) during a PET scan to get an image of e.g. oxygen uptake or glucose metabolism in the body

- The therapeutic, diagnostic or preventive effect or safety of the medicine (tool) is NOT uncovered/verified.

- Data is NOT collected regarding the drug's pharmacological effects, including pharmacodynamics and/or pharmacokinetics.

A clinical trial in which a drug/drugs is used exclusively as a tool does not have to be reported to the Danish Medicines Agency. **Read more about the legislation** .

5. Do I have to report trials where medicinal products are used as a tool to the Danish Medicines Agency?

No, this type of trial is not covered by the application requirement.

6. Can I get an assessment of whether the Danish Medicines Agency should grant permission for a specific trial?

We recommend using **our guide to assess whether a trial is defined as a drug trial** .

If, after the assessment, there is doubt as to whether a clinical trial must be notified to the Danish Medicines Agency, you can send an inquiry about the application obligation.

The inquiry must contain the protocol for the trial and data on the preparation that is to be examined. If the protocol is not finished, we can assess it based on a synopsis, where the purpose, effect targets and a description of how they are achieved must appear.
You can send your inquiry to **Send an email** .

If there is any doubt as to whether the substance to be tested is a medicine or not, you can get help here: **The distinction between medicines and other products** .

Application

1. How can I send my application to the Danish Medicines Agency?

An application to the Danish Medicines Agency can be sent digitally via, for example, Eudralink or direct e-mail.

- Application digitally via e.g. EudraLink Applicants can send the application and associated documentation digitally e.g. via EudraLink. Eudralink is the European Medicines Agency's (EMA) system which can send files securely (secure file transfer system). Alternatively via our **mailbox for clinical trials** .

Read more about **Application for clinical trials via EudraLink**

2. How do I enter billing information?

Invoicing information must be stated in the covering letter (if public institution EAN no.

See also checklist for applications: **Guide to applying for permission for clinical trials with medicinal products on humans** - appendix 10 - click on appendix 10. **Read more about fees and invoicing information for clinical trials here** .

3. When must I submit notifications/notify the Danish Medicines Agency?

The Danish Medicines Agency must be notified of the following:

- Extension of the experiment in relation to the date specified in the Danish permit.
- New centres/change of centers (incl. updated xml file).
- Change of principal/coordinating investigator (incl. updated xml file)
- Change of CRO/applicant (incl. updated xml file if the xml file has changed)
- When the trial ends in Denmark.

The Danish Medicines Agency does not have to approve these changes.

Only substantial changes/amendments must be submitted to the Danish Medicines Agency. You can read more about this under **Application for significant changes to clinical trials**

4. What must the power of attorney give access to for representatives from foreign authorities

who must control the experiment and how long is it valid for?

A power of attorney is only required if inspection is carried out by representatives from foreign health authorities to control the trial.

In the power of attorney, the subject must grant access to his entire patient record for a specifically defined number of years.

If data from the trial is expected to be used for the approval of a medicine, the number of years during which access to the patient's record is given must take into account the expected time leading up to approval.

We draw your attention to the following minimum requirements regarding the power of attorney declaration:

It must be clear from the heading or sub-heading that this is a proxy statement.

The wording "I give power of attorney to..." must be used. Linguistic formulations such as "I give permission to..." or "I am informed about..." are thus not accepted.

The power of attorney must cover the entire patient record. Access to the record must therefore not be limited to parts or relevant sections of the record.

The purpose of the power of attorney must be stated (inspection/control)

It must be stated that access to the patient record applies during and after the trial for a period of up to a minimum of 5 years after the end of the trial. Both a period and a number of years must be specified.

It is recommended that no statutory reference is given, as the power of attorney rests on a contractual legal basis.

Power of attorney regarding the transfer of data to third countries does not belong in the power of attorney declaration, but falls under the Danish Data Protection Authority's legislation. Information to test subjects about transfer can instead appear in the participant information.

The power of attorney can be included as part of the consent, but we recommend that the consent and power of attorney are two separate documents.

We would also like to draw your attention to the fact that it must be stated in the participant information that the Danish Medicines Agency and the sponsor have access to the entire patient record for purposes of control and inspection.

Read more: **Guidance for applying for permission for clinical trials with medicinal products on humans** -

see section 10.

PASS studies

1. What is a PASS study?

- A PASS study (Post Authorization Safety Study) is:
  a study of a marketed drug which aims to identify, characterize or quantify a safety risk or verify the safety profile of a drug. It can also be carried out with the aim of assessing whether risk-minimizing measures are effective.
- Is a study in which the medicine is used in accordance with the conditions of the marketing authorisation. It can be both an intervention trial and a non-intervention trial (also called a non-intervention safety study).

A PASS study can be initiated by the marketing holder voluntarily, or on the basis of a condition in the marketing authorization for the medicinal product, and can be carried out in one or more European countries.

Further details on PASS studies can be found in this European **Guideline on good pharmacovigilance practices (GVP)**

2. Should PASS studies be registered in the EU?

Yes PASS studies must be registered in the electronic register for post-authorisation studies (EU Pas Register). The protocol must be entered in the register before the start of data collection. The Danish Medicines Agency must first have information about PASS studies when they are registered in the EU-PAS register.

Read more in the **EU PAS Register Guide**

3. When must PASS studies be approved by the Danish Medicines Agency?

It depends on whether the PASS study is initiated voluntarily by the marketing holder, or whether it is initiated on the basis of a condition in the marketing authorization issued by the Danish Medicines Agency or on the basis of conditions in a European marketing authorisation.

- Non-intervention PASS studies which are initiated on the basis of a condition in a marketing authorization issued by the Danish Medicines Agency must be approved by the Danish Medicines Agency if the study is only to be carried out in Denmark.

- Non-intervention PASS studies that are initiated on the basis of a condition in a European marketing authorization are assessed, approved and monitored by the European Pharmacovigilance Risk Assessment Committee (PRAC), which belongs to the European Medicines Agency (EMA). The Danish Medicines Agency does not approve these studies Read more about **PRAC**

- Non-intervention PASS studies which are initiated voluntarily by the marketing holder do not have to be approved by the Danish Medicines Agency.
- Intervention PASS studies must be approved by the Danish Medicines Agency.

Further details on PASS studies can be found in this European guideline: **Guideline on good pharmacovigilance practices (GVP)**

4. In which cases must I inform the Danish Medicines Agency about non-intervention PASS studies?

The Danish Medicines Agency must be informed and have submitted documentation for non-intervention PASS studies when:

- Non-intervention PASS studies are initiated on the basis of a condition in a marketing authorization issued by the Danish Medicines Agency.
- Non-intervention PASS studies are initiated on the basis of a condition in a European marketing authorization if the study takes place in Denmark. The documentation must be submitted after the PRAC (Pharmacovigilance Risk Assessment Committee) has approved the study.
- Non-intervention PASS studies are initiated voluntarily by the marketing holder if Denmark is the reference country or rapporteur for the medicine.

Læs mere i **Annex to GVP module VIII - Post-authorisation safety studies**

5. What documentation for non-intervention PASS studies must I submit to the Danish Medicines Agency?

The Danish Medicines Agency must have submitted the following documents:

- Cover letter containing information about:
- Date of registration in the EU-PASS register and registration number
- The study is initiated voluntarily or on the basis of a condition in the marketing licence

- Denmark is the rapporteur/reference country for voluntary non-intervention PASS studies
- The study takes place in Denmark
- Date of PRAC approval (for studies with a condition in the marketing authorisation)
- PRAC's (Pharmacovigilance Risk Assessment Committee) assessment report for studies that are initiated on the basis of a condition in a European marketing authorization
- The trial protocol
- Updated trial protocols after substantial amendments
- The final trial report no later than 12 months after the end of the trial

Further details on what information must be forwarded to the Danish Medicines Agency regarding PASS studies appear in this **Guideline on good pharmacovigilance practices (GVP)**

The Norwegian Data Protection Authority/Data Regulation

1. Does participant information updated as a result of the data regulation (GDPR) have to be submitted to the Danish Medicines Agency?

No. Updated participant information must only be submitted to the Danish Medicines Agency if it has a significant impact on the safety of the subjects or the scientific purpose of the trial.

2. Do drug trials have to be reported to the Danish Data Protection Authority?

No, after the introduction of the data regulation, there is no longer a requirement to notify the Data Protection Authority. See more here: **https://www.datatilsynet.dk/emner/forskning-og-statistik/saerligt-om-sundhedsomraadet/**

3. How does 'revocation of consent' or 'the right to be forgotten' affect the use of the participant's information?

The use of the trial participant's information in clinical trials takes place on the basis of Article 9 of the Personal Data Regulation and not the trial participant's consent to participate in the trial. The trial participant's withdrawal of consent to participate in the trial thus does not affect the right to use already collected information about the trial participant. The trial participant thus does not have the right to have his data deleted during the trial either. Deletion of information about the trial participant could cast doubt on the results of the trial. A distortion could occur if data from, for example, trial participants who

experienced side effects and thereby withdrew from the trial upon withdrawal of consent were deleted.

4. Should it still appear from the participant information that the Danish Medicines Agency, as well as the sponsor, investigator and monitor have direct access to information in the patient record?

Yes. For all start-up attempts after 1 July 2016, the following applies:

- It must be clear from the participant information that the Danish Medicines Agency, as well as the sponsor, investigator and monitor can have direct access to obtain information in the patient record, including electronic records for the purpose of control and inspection. We refer to the Danish Medicines Agency **'s guidance on notification of clinical trials with medicinal products on humans, section 10** . It is also important that the Danish Medicines Agency is mentioned by name.
- On the basis of this legislation, the power of attorney is only required if relevant foreign health authorities are to have access to the patient records for the purposes of control and inspection both during and after the end of the trial.

Changes/Amendments

The experimental drug

Voluntary Harmonisation Procedure (VHP)

NOTE - The VHP procedure will be abolished upon transition to the regulation for clinical trials in 2022. The deadline for submitting applications for the VHP procedure is 15 October 2021. See more on our page regarding The VHP Procedure .

1. What is VHP?

The VHP (Voluntary Harmonization Procedure) is a procedure in which it is possible to obtain a coordinated scientific assessment of an application for authorization for a clinical trial that must take place in several European countries.

Read more: **Voluntary Harmonization Procedure (VHP), coordinated procedure for assessment before**

applying for authorization for a clinical trial .

2. What is VHP-plus?

The VHP procedure has been expanded with an option for ethics committees, in Denmark the National Science Ethics Committee (NVK), to participate in **VHP** , so-called **VHP-plus** . However, this only applies to trials with children and/or ATMP and phase I-II clinical cancer trials with drugs. However, NVK does not assess documents regarding the quality of medicines (IMDP). In the case of a national application, the trial must thus be approved by **NVK and not by a regional committee** .

3. Which documents must be submitted at the national VHP?

No later than three weeks after an application for a clinical trial has been approved in the VHP, the application must be submitted to the participating national authorities for approval. These must approve the trial within 10 days by means of a properly drawn up application.

The content of the application is the same as for an ordinary application for a clinical trial, therefore reference is made to appendix 10 in our guidance. It is important that it is the same documentation that is submitted with the national application that is approved in the VHP.

For the national application, in addition to the documents that have been approved in the VHP, special attention must be paid to submitting the following documentation:

- E-mail from which it appears that the application has been approved in VHP
- National EudraCT application form (PDF and XML file)
- **Invoicing information must be stated in the cover letter (if public institution EAN no.)**
- Example of labels
- Documentation that the manufacturer is aware of the trial
- Participant information and proxy statement

Side effects and safety monitoring

1. How often should I send a report incl. a list of serious side effects for the Danish Medicines Agency?

Once a year throughout the trial period, you must send a list of all seriously suspected side effects and a report on the safety of the subjects.

In the case of unmarketed medicinal products, the annual report and list of serious suspected side effects can be replaced by the Development Safety Update Report (DSUR, ICH E2F). **Read more about DSUR** .

DSUR is prepared per investigational medicinal product and can therefore cover several trials. Please list the EudraCT numbers for the trials taking place in Denmark in the cover letter to DSUR.

If marketed medicinal products are used in the trial, the **template on the GCP unit's website** can be used to prepare the annual safety report.

For further information, refer to " **Guidelines for applications for authorization for clinical trials with medicinal products on humans** ", section 12.4.

2. What is the Danish Medicines Agency's expectation for how frequently safety information must be exchanged from sponsor to investigator during drug trials on humans?

According to Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3'), the sponsor must ensure that all relevant information regarding SUSARs is reported to authorities and ethical committees as soon as possible and no later than 7 days for fatal and life-threatening SUSARs and 15 days for other SUSARs. Furthermore, the sponsor must also inform all investigators.

The purpose of informing the investigators is according to CT-3 to inform investigators about safety issues seen in the light of reported SUSARs. The information should be concise and practical and, if possible, in the form of aggregated periodic lists. The period is determined taking into account the protocol/project and the number of SUSARs generated. Along with the line listings, a concise summary of the development in the product's safety profile must follow.

Furthermore, it is stated in the ICH GCP guideline, point 5.16.2, that the sponsor must immediately inform all involved investigators of findings that may negatively affect the safety of the test subjects or have an influence on the conduct of the trial.

As a result of the above, the Danish Medicines Agency has no requirement for a specific number of days/weeks/months that must elapse at most before the investigators are informed of specific safety information. A procedure where all information is processed within the same deadline is generally not acceptable, as there may be a difference in how important the security information is.

The investigator must therefore have some information immediately, other information can possibly wait and be sent out as regular line listings,

where the period is set by the sponsor for the individual project/protocol. This will depend on an assessment in the specific case.

3. What does the Danish Medicines Agency require in relation to the sponsor's delivery of safety information to a site for the period from the time the Investigator's Brochure (IB) is final until the initiation of a site?

We would expect to find relevant safety information in the investigator's Trial Master File, which would typically be the most recent IB with subsequent SUSARs not yet included in an IB.

The information must be in the investigator's hands some time before an agreement is made about the trial and must be updated continuously depending on how important the information is.

4. What is a SUSAR?

A SUSAR is a Suspected Unexpected Serious Adverse Reaction, which translated means: unexpected and serious suspected side effect. SUSARs must be reported immediately to the Danish Medicines Agency.

A side effect is a SUSAR, and must be reported when the following criteria are met:

- serious, i.e. result in death, be life-threatening, lead to hospitalization or prolongation of hospital stay,
- result in significant or permanent disability or incapacity for work or
- lead to a congenital anomaly or malformation.
- The side effect must be related to the investigational drug. This means that there is supposed to be a causal connection between taking the medicine and the side effect that occurred. Both investigator and sponsor must assess causality. The sponsor must not reject the investigator's assessment, and reports where the sponsor does not agree with the investigator must be reported
- The side effect must be unexpected, i.e. a side effect whose nature or severity does not match the product information described in e.g. Investigators Brochure for an unapproved investigational medicinal product or the product summary if it is an approved medicinal product.

If it is a blinded trial, the assessment of the side effect must be carried out before unblinding, but data must be unblinded before reporting to the Danish Medicines Agency.

5. How should I send SUSARs to the Danish Medicines Agency?

SUSARs must be reported electronically, please see: **Reporting of Adverse Reactions in Clinical Trials** . The report must also be sent to EMA via E2B, as we do not forward the reports we receive from commercial sponsors via E2B.

Non-commercial sponsors can report via our e-form for non-commercial sponsors: **Reporting of suspected unexpected and serious adverse reactions (SUSAR) seen in clinical trials (e-form)** .

6. As a non-commercial sponsor, how can I report SUSARs when I do not have access to EudraVigilance?

If you do not have access to EudraVigilance, SUSARs can be reported to the Danish Medicines Agency via e-form.: Read more under **Reporting of suspected unexpected and serious side effects (SUSAR) seen in clinical trials (e-form.)**

The Danish Medicines Agency ensures that the submitted SUSAR is reported to EudraVigilance so that it is included in the overall European side effect data for the preparation.

7. Do I have to test reporting susars to the Danish Medicines Agency if I use EVWEB?

No, testing is not required if you use EVWEB, but in order for us to receive SUSARs, your Sender ID must be configured in our system. Please contact **Send an email** with information about the name and address of the Sponsor together with the relevant sender ID.

8. Do we have to test with the Danish Medicines Agency when we switch from being EVWEB users to using EMA's Eudravigilance gateway and Backend database?

Yes, contact **Send an email** to arrange a test.

9. Do we have to test with the Danish Medicines Agency if we update or change the Pharmacovigilance system?

Yes, contact **Send an email** to arrange a test.

10. Which ID should SUSARs be sent to?

SUSARs must be sent to DKMAEUDRA and to EVCTMPROD.

11. Which ID should we send to when we want to test?

Test SUSARs must be sent to TDKMAEUDRA.

12. Do we have to meet any special requirements to be able to test exchange with the Danish Medicines Agency?

Yes, you must have a profile in EMA's Eudravigilance test gateway and have completed testing with EMA.

13. Does the Danish Medicines Agency send confirmation (ACK) for received SUSARs?

And.

14. Do I have to resend a SUSAR if after two days I still haven't received an ACK?

No, you should never resubmit reports without being asked to do so by us. Contact **Send an email** . Please provide full XML file name and date of transmission. If the file name contains a reference to the case number, this is truncated with a number of Xs corresponding to the deleted one.

15. Do I need to state that I want to send a test SUSAR before I send it?

Yes, before you send a test file, you must contact us via **Send an email** . We are not able to process the file until your Sender ID has been configured in our system.

16. What happens when the testing phase is completed?

Once the test is complete, we will send an email confirming that the test is complete and that reporting SUSARs to our production environment is now available.

17. Can we stop submitting paper SUSARs during the testing phase?

No, during the testing phase Sponsor must continue to submit reports as usual (on paper).

18. When the testing phase is completed, will there be a period when reporting must be done both electronically and in paper form?

No, when files are exchanged in the production environment, you must stop sending reports on paper.

19. Is it the sponsor's responsibility to report SUSARs to EVCTM or does the Danish Medicines Agency send the cases to EVCTM?

Yes, Sponsor must report all Danish SUSARS electronically to EVCTMPROD and also to DKMAEUDRA. The Danish Medicines Agency does not forward SUSARs to EVCTMPROD.

20. Will the agency accept SUSARs from unblinded clinical trials?

No, all SUSARs must be blinded and sent to the agency within 7 days (life-threatening and fatal side effects) or 15 days (other serious side effects).

21. What should we do if our system is down and we want to send a SUSAR to the Danish Medicines Agency?

You can send it as CIOMS format via Eudralink to **Send an email** . Alternatively by fax to +45 44889599 ext. Section for Clinical Trials'

22. What should we do if the Eudravigilance database is down and we want to send a susar to the Danish Medicines Agency?

You can send it as CIOMS format via Eudralink to **Send an email** . Alternatively by fax to +45 44889599 ext. Section for Clinical Trials'

Virtual/Telemedicine trials

Virtual/Telemedicine trials

Today, there is an increasing focus on how to make it easier to recruit trial participants, how to increase the possibility of participation in clinical trials for people living far from hospitals, and how to make it easier to retain trial participants in, for example, long-term follow-up. As part of supporting this focus, we will continuously prepare questions and answers on regulatory challenges in connection with virtual/telemedicine trials.

We encourage you to contact us (**Send an email**) if you have regulatory challenges in connection with virtual trials. We will then assess whether it is a topic that can be added to our Q&A.

Q&A: IMP directly to trial participants

As a first step, we have prepared a series of questions and answers on how investigational drugs can be delivered directly to trial participants in clinical trials. The general rule for the use of such a procedure is that there must always be a justification/risk assessment for this.

1. Is it possible to deliver trial drugs directly to the trial participant's home?

Yes, it is possible for the investigator via pharmacy or courier etc. to send trial drugs to the trial participant after the doctor's prescription, as described in the protocol. However, there are certain conditions that must be met and a justification must be presented clearly in the application for the clinical trial (see also questions regarding documentation for the clinical trial). The procedure must also be clearly described in the participant information, which must be approved by the Scientific Ethics Committee.

- It must be described how it is ensured that given storage conditions for the investigational medicinal product are observed throughout the supply chain, i.e. right up to the subject.
- It is generally only acceptable to deliver directly to trial participants if there is a person who can acknowledge receipt of the trial drug. It must be clarified in the

application how it will be handled if the trial participant or relatives are not at home. As a rule, the investigational drug must be returned/taken back by e.g. the courier.

- It must be justified that it is justifiable to let the trial participant administer the medicine himself. The trial participant must be trained in the use/administration, and it must be considered whether additional guidance should be sent, in addition to the normal labeling of the trial medication.
- Alternatively, a trained, trained and qualified healthcare professional must handle the administration of the investigational drug. If the medicine is not brought by the health professional, but is sent separately, it must be clear to the trial participant that administration must await the visit of the health professional.
- If it is not personnel from the trial department who handle the investigational drug, but external health professionals are used, there must be a contract between the investigator and the company that has employed the health professional staff. See also **GCP Q&A on EMA's website** .
- There must be a clear line of communication to the investigator. This can be, for example, by a patient card with contact information, which is handed out to the trial participant.

2. Can the sponsor deliver directly to the trial participant's home?

No, it must be the investigator who is responsible for trial drugs being sent to the trial participant according to the procedure in question, as described in the application for permission for the clinical trial. Sponsor is overall responsible and can facilitate the preparation of contracts.

3. What must the sponsor state in the documentation for the clinical trial when it is desired to deliver the trial drug directly to the trial participant's home?

The procedure and the sponsor's justification must be clearly described in the application, which must be approved by us and the Scientific Ethics Committee. Furthermore, participant information must also clearly describe that the trial participants have the option of having the trial drugs sent to them. We suggest that you draw attention to the procedure for delivery of the investigational medicinal product in the cover letter, alternatively reference should be made to where in the application the description/justification can be found.

Furthermore, please confirm, if relevant, that there is a contract with a pharmacy/courier, etc., where health

professionals who, for example, must administer the trial drug, are employed.

4. Are there trials where the LMST will not accept the trial drugs being delivered directly to the trial participant's home?

The sponsor must always clearly justify why it makes sense to deliver trial drugs directly to the trial participant's home. This statement must contain a risk assessment. We do not expect the procedure to be relevant in early phase trials where observation of the trial participant is necessary. As a starting point, the procedure should only be used when the subject has gained some experience with the investigational drug, depending on the investigational drug's form of administration/route and safety profile.

5. Who can handle the task of delivering experimental drugs to the subjects' homes?

It may be a courier etc. or an educated and trained healthcare professional. However, there must be a contract between the sponsor and external health professionals or couriers, and these conditions must be described in the contract between the sponsor and the investigator. See also **GCP Q&A on EMA's website** .

The sponsor must ensure that the trial participant has received instructions on the conditions for storage and handling of the medicinal products, in connection with the delivery, and that the instructions are complied with. In addition, the contract with courier etc. take into account how the storage conditions are ensured during the entire transport, e.g. by temperature log (see also the first question).

The regulation

1. To which trials does the new legislation apply?

The new legislation applies to drug trials on humans.

2. Must trials that are *only* to take place in Denmark (Danish mononational trials, including trials from non-commercial sponsors) be submitted through the EU portal?

All drug trials must be submitted through the EU portal, however, see re. transition period the first year.

3. Must all submissions be made through the portal, e.g. annual safety reports?

All submissions during the lifetime of the trial including notifications, significant changes, annual safety reports, final report and results must be made through the portal. An exception, however, is SUSARS, which must be sent directly to the EudraVigilance database (however, we do not yet know the final solution).

4. When does the regulation come into force/apply?

The regulation will only come into force when the EU portal, which will support communication between the sponsor/applicant and the authorities, has been fully developed. Audit of the EU portal begins December 2020.

5. How should I submit my application after the regulation has entered into force?

You have to submit your application for permission for clinical trials to the EU portal, you no longer have to submit your application directly to the national authorities. This applies to both the application to the Danish Medicines Agency and the ethics committee. see also below regarding transitional arrangement the first year

6. How should ongoing national and VHP trials be handled - is there a transitional arrangement?

There is a transitional arrangement, which means that for up to one year after the regulation has come into force, you can still apply under the old legislation. If an ongoing trial has not been completed 3 years after the regulation came into force, you must transfer your trial to the regulation. **The EU Commission has prepared a guide on how (section 11)** .

7. Where can I see which documents need to be submitted?

Annex 1 of the regulation lists which documents must be submitted.

8. Will the Danish Medicines Agency inform about the concrete changes in relation to applying for permission for a clinical trial with medicines?

Yes, when we know more about what the EU portal will look like, we plan to hold orientation meetings, but also provide information on our website. If there is an opportunity to practice on the EU portal, we will of course also inform you about that.

9. Do I still have to send my application to the Danish Medicines Agency and the Scientific Ethics Committee System after the regulation comes into force?

The clinical trial application is processed by both us and the Scientific Ethics Committee System when submitted in the new EU portal. Therefore, applications must not be submitted directly to the Danish Medicines Agency or the ethics committee system. However, this only applies to drug trials.

10. How do I report SUSARs?

It is intended that SUSARs under the regulation must only be reported to EudraVigilance and thereby not simultaneously to the participating national member states. We don't know the final solution yet

Other things

1. Which types of contraception/prevention does the Danish Medicines Agency consider safe in clinical trials?

We recognize the following contraceptives as safe contraception/contraception in connection with drug trials: Spiral or hormonal contraception (birth control pills, implant, transdermal patch, vaginal ring or depot injection).

In certain cases, a sterile fixed partner or the use of a double barrier may be accepted. This presupposes a valid justification in special circumstances surrounding trial design, preparation characteristics and/or the patient population. Double barrier means a condom combined with a pessary and spermicidal cream.

Read more: **Guidance for applying for permission for clinical trials with medicinal products on humans** - 5.1. Contraception.

2. Does the Danish Medicines Agency accept deviations from the protocol (waivers)?

No, we do not accept waivers.

3. How can I get scientific guidance for the development of a product/medicine?

You can get guidance from the Danish Medicines Agency, so-called scientific advice.

Read more: **Advice on the development of medicines (scientific advice)** .

Changelog:

07 October 2022 - Corrected links regarding investigational medicinal products, added reference to GMP guidance and added text at the top regarding the new EU regulation for clinical trials.

Did you get answers to your questions?

Me	No

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