Sundhedsstyrelsen
Danish Health and Medicines Authority

Amendments to clinical trial application (CTA)

Approval by the Danish Health and Medicines Authority

The sponsor must apply for authorisation[1] to make amendments in so far as the changes may affect:

- the safety of the trial subjects
- the interpretation of the scientific documentation
- the completion or management of the trial
- the quality or safety of the investigational medicinal products
- any other substantial amendments

The Danish Health and Medicines Authority considers changes made to the below as substantial:

- **Trial design**
- **Trial objective**
- Changes affecting the **safety** of the trial subjects
- **Change of the total number of trial subjects**
- **Change in age range of trial subjects**
- **Inclusion/exclusion criteria**
- **Safety monitoring**
- **Change of the reference document (RSI – reference safety information)**
  RSI should remain unchanged in the annual safety report's reporting period, and it is not recommended to change RSI. If a decision to change RSI is made anyway, submission of a substantial amendment is required.
- Substantial changes to **participant information sheet and informed consent form – in relation to safety, efficacy and investigational medicinal product**
- **Changes to the power of attorney**
- **Measures of efficacy,** new measurement for primary endpoints
- **Addition or deletion of tests or measures**
- **Duration of exposure to the investigational medicinal products**
- **Change of dose of the investigational medicinal product(s)**
- **Change of comparator**
- **Substantial change of statistical analysis**
- **Withdrawal of Safety Monitoring Committee/Data Monitoring Committee**
- **Changes in the definition of the end of the trial**

[1] Section 4 of Danish executive order no. 295 of 26 April 2004 (Danish title: Bekendtgørelse nr. 295 af 26. april 2004 om kliniske forsøg).

- Changes to the investigational medicinal product, please see the CHMP guideline: http://ec.europa.eu/health/files/eudralex/vol-10/18540104en_en.pdf and for biological investigational medicinal products: http://ec.europa.eu/health/files/eudralex/vol-10/2012-05_quality_for_biological.pdf
- Changes to Investigator's Brochure: Only if changes have an impact on the safety of the trial subjects.
- Other changes considered substantial by the sponsor

Please use this application form: http://ec.europa.eu/health/files/eudralex/vol-10/substantial_amendment_notification_form_.doc

A fee is charged for applications to amend a clinical trial. Please follow this link to the e-form for notification of invoice details concerning clinical trials: http://laegemiddelstyrelsen.dk/en/topics/side-effects-and-trials/clinical-trials/fees/form-for-notification-of-invoice-details--als-e-form

Notification to the Danish Health and Medicines Authority

The Danish Health and Medicines Authority is to be **notified** of the following:

- Extension of trial period relative to the date approved on the Danish authorisation.
- New trial sites/change of trial sites (including updated XML file).
- Change of principal/coordinating investigator (including updated XML file).
- Changes in CRO/applicant (incl. updated XML file if changed)
- When the trial ends in Denmark

The above changes are not to be approved by the Danish Health and Medicines Authority.

Please do not notify the following changes to the Danish Health and Medicines Authority:

- Number of trial subjects per trial site
- Changes to the principal investigator’s research team, e.g. sub-investigator
- Changes in **funding arrangement**
- Changes to **recruitment material** for trial subjects
- Changes in **insurance or indemnity arrangements** related to the study
- Change/addition of **sub-investigator**
- Correction of **typographical errors** in the trial protocol or other study documentation
- Annual update of Investigator's Brochure if no influence on the safety of trial subjects
- Updates made to the participant information sheet and informed consent form which have no bearing on safety, efficacy or the investigational medicinal product