

Adopted by the Danish Parliament on 10 May 2016

Danish Act on Clinical Trials of Medicinal Products¹

Title I

Clinical trials

Part I

Scope of the Act

1.-(1) This Act applies to the Danish Medicines Agency's and the medicinal research ethics committees' assessment and control of clinical trials of medicinal products in humans in accordance with the rules laid down in Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

(2) In addition, this Act applies to the Danish Medicines Agency's assessment and control of clinical trials of medicinal products in animals.

2. For the purpose of this Act, the following definitions apply:

- (i) Regulation means: Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
- (ii) Sponsor means: An individual, company, institution or organisation which takes responsibility for the initiation, for the management and for setting up the financing of the clinical trial.
- (iii) Investigator means: An individual responsible for the conduct of a clinical trial at a clinical trial site.
- (iv) Consent means: An informed consent which is a subject's free and voluntary expression of his or her willingness to participate in a particular clinical trial, after having been informed of all aspects of the clinical trial that are relevant to the subject's decision to participate or, in case of minors and of incapacitated subjects, an authorisation or proxy consent from their legally designated representative to include them in the clinical trial.
- (v) Legally designated representative means: A natural or legal person, authority or body which, according to the applicable law, is empowered to give informed consent on behalf of a subject (proxy consent) who is an incapacitated subject or a minor.

Title II

Clinical trials of medicines in humans

Part II

Consent to participate in a clinical trial

3.-(1) Proxy consent on behalf of a subject who is a minor must be given by the person who has custody of the minor, but see section 4(1).

(2) Proxy consent on behalf of a subject under guardianship, which comprises an authorisation to give consent to participate in health research projects, see section 5(1) of the Danish Guardianship Act, must be given by the guardian.

¹ The Act includes certain provisions from Regulation (EU) No. 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC, the Official Journal of the European Union 2014, no. L 158, page 1. According to article 288 of the Treaty on the Functioning of the European Union, regulations are directly applicable in all the member states. Any repetition of these provisions in this Act is only for practical reasons and does not affect the validity of the regulation in Denmark.

(3) Proxy consent on behalf of other incapacitated subjects must be given by the nearest relatives and the trial guardian. The trial guardian is a doctor, who is independent of the investigator's interests and has no interest in the clinical trial of medicinal products.

(4) The proxy consent must reflect the interests of the subject.

4.-(1) A clinical trial on a subject who has attained the age of 15 and is still a minor can only be conducted if the subject and the custodial parent consent to this.

(2) Children between 5 and 15 years of age should, to the extent possible, be consulted about their participation in a clinical trial.

(3) The Danish Minister for Health may lay down specific rules on the consultation, pursuant to subsection (2).

5.-(1) The requirement to provide a signature pursuant to article 29 of the regulation on informed consent can be met by using a technique that ensures unique identification of the person who is signing the document.

(2) The Danish Minister for Health may lay down specific rules on the contents of the subject information and any requirements for the form of the signature.

(3) The Danish Minister for Health may lay down specific rules on the qualifications of the person, who provides the oral information and receives the informed consent from the subject.

(4) The Danish Minister for Health may lay down specific rules on the consent and participation in trials for persons who may be under particular pressure to participate in a clinical trial of medicinal products.

Part III

Medicinal research ethics committees

6. The Danish Minister for Health establishes one or more medicinal research ethics committees.

7.-(1) A medicinal research ethics committee consists of 8 members who are appointed in the following way:

(i) The Danish Minister for Health appoints the chairman of the committee.

(ii) 5 members are appointed by the Danish Minister for Health on the basis of recommendations of the Regional Councils.

(iii) 2 members are appointed by the Danish Minister for Health on the basis of recommendations of organisations representing patients.

(2) The chairman must be actively engaged in health research.

(3) Pursuant to subsections (1) and (2), each region must recommend a layperson and a person who is actively engaged in health research. The recommendations of persons who are active within health research to the Danish Minister for Health must be based on recommendations from the relevant research forums to the individual Regional Councils.

(4) The committee must be composed of a chairman, 4 laypeople and 3 members who are actively engaged in health research.

(5) A committee appoints a deputy chairman.

(6) A committee can set up subcommittees which make decisions and handle other tasks of the committees.

(7) The medicinal research ethics committees prepare a common proposal for the rules of procedure, which the Danish Minister for Health must approve.

(8) The committee members are appointed for 4 year terms, corresponding to the election period of the Regional Councils. Members can be re-appointed twice. Alternates for the members can be appointed.

(9) The retiring committee will continue its activities until new members have been appointed and the new committee has appointed its chairman.

(10) The Danish Minister for Health may lay down specific rules on which forums are considered to be relevant research forums, see subsection (4).

(11) The Danish Minister for Health may lay down specific rules on the requirements for documentation that the members of the medicinal research ethics committee do not have conflicts of interest, and that they are independent of the sponsor, of the clinical trial site and the investigators involved and of persons financing the clinical trial, as well as free from any other undue influence.

8.-(1) If a medicinal research ethics committee or a subcommittee set up under section 7(6) cannot reach agreement on the assessment of an application or other matters pursuant to the regulation or this Act, the committee makes a decision by vote, but see subsections (2) and (3). The committee's decision will be based on

recommendations from a majority of the members of the competent committee. In the event of a tie, the chairman's vote, or in the chairman's absence, the deputy chairman's vote is decisive.

(2) The chairman, or in the chairman's absence, the deputy chairman must form part of the majority when the committee makes decisions in cases involving authorisation of a clinical trial.

(3) The chairman of a committee can, on behalf of the committee, make decisions in cases that do not give rise to doubt. Moreover, the chairman can make decisions when considered necessary for reasons of subject safety or to ensure that the timelines of the authorisation procedures set out in chapters II and III of the regulation are adhered to.

(4) If the chairman, or in the chairman's absence, the deputy chairman makes a decision, the other committee members are informed of the decision as soon as possible thereafter.

9.-(1) The medicinal research ethics committees follow the research development within clinical trials of medicinal products and promote the understanding of ethical issues that may arise as a result of the development in relation to the health service and health research environments.

(2) The committees must cooperate actively and coordinate the execution of tasks with relevant national and international authorities and organisations etc.

Part IV

Assessment of applications for and conduct of clinical trials

10.-(1) The Danish Medicines Agency and the medicinal research ethics committees coordinate the assessment of applications and the follow-up on authorised clinical trials. The Danish Medicines Agency and the medicinal research ethics committees must also cooperate on the execution of tasks pursuant to the regulation.

(2) The Danish Medicines Agency acts as national contact point, see article 83 of the regulation.

(3) When Denmark is the reporting member state, the Danish Medicines Agency handles all tasks imposed on Denmark as reporting member state pursuant to the regulation, unless otherwise expressly provided in this Act or provisions laid down in pursuance of this Act.

(4) The Danish Medicines Agency assesses whether a clinical trial or activities in connection with a trial are within the scope of this Act or the regulation.

11.-(1) The Danish Medicines Agency decides whether a clinical trial is authorised, whether it is authorised subject to certain conditions, or whether authorisation is refused, and gives notification in accordance with article 8(1) and article 14(3) of the regulation, but see subsection (6).

(2) The Danish Medicines Agency declares that Denmark disagrees with the reporting member state's conclusion, as regards part I of the assessment report, see article 8(2) of the regulation, when an application exclusively concerns aspects covered by part I of the assessment report, if either the Danish Medicines Agency or the medicinal research ethics committee disagrees with the conclusion in question.

(3) For each application, the medicinal research ethics committee decides whether a clinical trial is authorised, whether it is authorised subject to certain conditions, or whether authorisation is refused, see article 8(1), when an application exclusively concerns aspects covered by part II of the assessment report and if Denmark has not beforehand communicated its disagreement with the reporting member state's conclusion, as regards part I of the assessment report, see subsection (2).

(4) The Danish Medicines Agency assesses whether the health aspects of part I of the assessment report for an application for clinical trials on medicinal products for human use have been complied with, see article 6(1) of the regulation.

(5) The medicinal research ethics committee assesses whether the ethical aspects of part I of the assessment report are complied with, see article 6 (1) of the regulation, and whether the aspects covered by part II of the assessment report are complied with, see article 7(1) of the regulation.

(6) The Danish Medicines Agency cannot authorise a clinical trial or authorise a clinical trial subject to certain conditions, see subsection (1), if the medicinal research ethics committee disagrees with the reporting member state's conclusions, as regards part I of the assessment report, on any of the grounds mentioned in article 8(2) of the regulation or if the committee finds, on duly justified grounds, that the aspects addressed in part II of the assessment report are not complied with, see article 8(4) of the regulation.

12.-(1) The Danish Medicines Agency decides whether a substantial modification of a clinical trial is authorised, whether the modification is authorised subject to certain conditions or whether authorisation is refused, and communicates the decision in accordance with article 19(1) and article 23(1) of the regulation, but see subsection (3).

(2) The medicinal research ethics committee decides whether a substantial modification of a clinical trial is authorised, whether the modification is authorised subject to certain conditions or whether authorisation is refused, when the modification exclusively concerns an aspect covered by part II of the assessment report and communicates the decision in accordance with article 20(5) of the regulation.

(3) The Danish Medicines Agency cannot authorise a substantial modification of an aspect covered by part I of the assessment report, or authorise a substantial modification subject to certain conditions, see subsection (1), if the medicinal research ethics committee disagrees with the reporting member state's conclusions, as regards part I of the assessment report, on any of the grounds mentioned in article 19(2) of the regulation. Similarly, the Danish Medicines Agency cannot authorise substantial modifications of aspects covered by part I and part II of the assessment report, or authorise substantial modifications subject to certain conditions, if the medicinal research ethics committee disagrees with the reporting member state's conclusions, as regards part I of the assessment report, on any of the grounds mentioned in article 23(2) of the regulation or the committee finds that substantial aspects addressed in part II of the assessment report are not complied with.

13. The Danish Medicines Agency may decide to revoke the authorisation of a clinical trial or suspend the clinical trial, and the Danish Medicines Agency may require the sponsor to modify any aspect of the clinical trial, see article 77(1) of the regulation. The Danish Medicines Agency may involve the medicinal research ethics committee in the assessment of the basis for the decision. The medicinal research ethics committee can ask the Danish Medicines Agency to consider any corrective measures pursuant to the first sentence, if the committee finds that this is required.

14.-(1) The Danish Minister for Health lays down specific rules on the aspects of part I of the assessment report that also need to be assessed by the medicinal research ethics committee, including the clinical trial's potential risks for the subjects.

(2) The Danish Minister for Health lays down specific rules on the administrative cooperation, procedures and timelines for the Danish Medicines Agency's and the medicinal research ethics committee's assessment of applications for clinical trials and follow-up on authorised clinical trials.

(3) The Danish Minister for Health lays down rules on the language requirements for clinical trial applications.

Part V

Investigational medicinal products

15.-(1) The Danish Medicines Agency may grant an exemption from article 92 of the regulation, providing that subjects must generally receive, free of charge, investigational medicinal products, auxiliary medicinal products and any devices required for the treatment, if

- (i) the purpose of the trial cannot be fulfilled if the products are supplied free of charge, or
- (ii) they are used for an indication in the summary of product characteristics and the subject, regardless of the participation in the trial, is being treated with the medicinal product and pays for the medicinal product himself.

(2) In trials conducted at a hospital where the patient already receives the product etc. free of charge as part of the hospital treatment, the sponsor can make an agreement with the hospital, deciding that the hospital pays the expenses for the medicinal product etc. in connection with the trial.

16. The Danish Minister for Health lays down specific rules on language requirements for labels for investigational medicinal products and auxiliary medicinal products, see article 69 on the language of the information on labels.

Part VI

Monitoring, control and inspection

17. The Danish Medicines Agency supervises compliance with the obligations to notify about the start, interruption etc. of a clinical trial pursuant to articles 36 and 37 of the regulation.

18.-(1) The Danish Medicines Agency assesses reports of suspected unexpected serious adverse reactions according to article 42 of the regulation and the sponsor's annual report on the safety of an investigational medicinal product according to article 43 of the regulation. The Danish Medicines Agency involves the

medicinal research ethics committee if the Danish Medicines Agency, following a health assessment of the report, finds that there are grounds for taking corrective measures pursuant to article 77 of the regulation, see section 13.

(2) The Danish Medicines Agency and the medicinal research ethics committee assess serious breaches, unexpected events and urgent safety measures reported in accordance with articles 52, 53 and 54 of the regulation.

(3) The Danish Minister for Health may lay down specific rules on other obligations to report safety information under articles 41-44 of the regulation, which the Danish Medicines Agency and the medicinal research ethics committee must ensure compliance with.

19.-(1) The Danish Medicines Agency may before, during and after the conduct of a clinical trial of medicinal products in humans, including as part of the processing of a marketing authorisation application under the Danish Medicines Act and as follow-up on a granted marketing authorisation, inspect any company, hospital, clinic and other places that are or have been conducting a clinical trial in Denmark or have carried out activities in relation to a clinical trial conducted abroad. The Danish Medicines Agency may order the handing over of all information about the clinical trial, including written material, necessary for the inspection.

(2) On the basis of a request from a competent authority in another EU or EEA country or from the European Medicines Agency for assistance to inspect a clinical trial, the Danish Medicines Agency may inspect any company, any hospital, any clinic and other places that are or have been conducting a clinical trial of medicinal products or have carried out activities in relation to a clinical trial conducted abroad. The Danish Medicines Agency may order the handing over of all information about the clinical trial, including written material, necessary for the inspection.

(3) A medicinal research ethics committee may ask the Danish Medicines Agency to inspect a company, a hospital, a clinic and other places that are conducting a specific clinical trial if the committee finds that there is a need for such inspection. If the inspection concerns an authorisation of or follow-up on a clinical trial of medicinal products, the Danish Medicines Agency and the medicinal research ethics committee can decide that the committee participates in the inspection pursuant to subsections (1) and (2) and section 20(1). If the medicinal research ethics committee participates in the inspection, the committee representatives have the same rights as the Danish Medicines Agency according to subsections (1) and (2) and section 20(1) and (2).

(4) The Danish Minister for Health lays down specific rules on the collaboration between the Danish Medicines Agency and the medicinal research ethics committee in connection with the conduct of inspections of clinical trials.

(5) The Danish Minister for Health may lay down specific rules on the Danish Medicines Agency's conduct of inspections pursuant to subsections (1) to (3).

20.-(1) As part of the Danish Medicines Agency's inspection pursuant to section 19(1) and (2), the Agency's representatives must, upon the presentation of appropriate identification and without a court order, have access to companies, hospitals, clinics and other places involved in the conduct of the trial.

(2) The Danish Medicines Agency has direct access to collect information from patient records etc., including electronic records, to gain information about the health status of trial subjects that is required for the Danish Medicines Agency's inspection under section 19(1) and (2).

21.-(1) A consent given pursuant to chapter V of the regulation gives the sponsor and sponsor's representatives and the investigator direct access to collect information in patient records etc., including electronic records, to gain information about the health status of the trial subject that is required for self-inspection of the research project, including quality control and monitoring that they are obliged to conduct.

(2) A consent given pursuant to chapter V of the regulation gives foreign drug regulatory authorities direct access to collect information in patient records etc., including electronic records, to gain information about the health status of the trial subject that is required for the foreign drug regulatory authorities' quality control as part of an authorisation of the relevant medicinal product.

Title III

Clinical trials of medicinal products in animals

Part VII

Application for and monitoring and control of clinical trials

22. A clinical trial of medicinal products in animals can only be conducted if the Danish Medicines Agency has authorised the clinical trial in accordance with the provisions in this Act.

23.-(1) The sponsor must submit an application for authorisation of a clinical trial in animals to the Danish Medicines Agency.

(2) The Danish Minister for Health may lay down specific rules on timelines, on the information that should be included in applications for authorisation of clinical trials in animals and on the Danish Medicines Agency's processing of such applications.

24. The sponsor or sponsor's representative must have a permanent address in an EU or EEA country.

25.-(1) If the Danish Medicines Agency objects to a clinical trial in animals, the sponsor may amend the application once to allow for the objection. If the application is not amended according to the objection, the Agency will reject the application.

(2) The Danish Medicines Agency may set terms for the trial to the sponsor and investigator.

26. Once a clinical trial of medicinal products in animals has started, the sponsor can only amend the trial protocol and the documentation for the investigational medicinal product subject to approval from the Danish Medicines Agency.

27.-(1) The sponsor must

- (i) immediately inform the Danish Medicines Agency if suspected unexpected serious adverse reactions occur during the trial,
- (ii) inform the Danish Medicines Agency within 15 days if a trial needs to be interrupted earlier than planned and give the Agency a reason for the interruption,
- (iii) once a year throughout the entire trial period draw up a list of all suspected serious adverse reactions which have occurred during the trial period, and a report on the safety of the animals and submit the list and the report to the Danish Medicines Agency, and
- (iv) no later than 90 days after the end of the trial, inform the Danish Medicines Agency that the trial has been completed and as soon as possible and no later than one year after submit the result of the trial to the Agency.

(2) The Danish Minister for Health may lay down specific rules on the notifications mentioned in subsection (1).

(3) The Danish Minister for Health may lay down rules on the sponsor's obligation to inform others, including those responsible for clinical trials and the national authorities responsible for medicinal products in the other EU or EEA countries of the information submitted under subsection (1)(i).

28.-(1) If, during the trial, any deviations from the authorised trial protocol occur, the Danish Medicines Agency is entitled to demand from the sponsor and the investigator that the trial is amended or temporarily halted, or the Agency is entitled to prohibit the trial.

(2) The Danish Minister for Health may lay down specific rules on the conditions for the Danish Medicines Agency's corrective measures under subsection (1).

29.-(1) Medicinal products for clinical trials in animals must comply with the current standards for good manufacturing practice laid down in the Danish Medicines Act.

(2) The Danish Medicines Agency lays down specific rules on the requirements for the quality and safety of investigational medicinal products, including the manufacture of such products, and for the control thereof.

30. The Danish Minister for Health may lay down rules on the format requirements for applications and notifications under this Part, including that applications and notification must be made electronically.

31.-(1) The Danish Medicines Agency may before, during and after the conduct of a clinical trial of medicinal products in animals, including as part of the processing of a marketing authorisation application and as follow-up on a granted marketing authorisation, inspect any company, etc. that is or has been conducting a clinical trial. The Danish Medicines Agency may order the handing over of all information, including written material, necessary for the inspection.

(2) On the basis of a request from a competent authority in another EU or EEA country for assistance to control a clinical trial, the Danish Medicines Agency may control any company, etc. that is or has been

conducting a clinical trial of medicinal products. The Danish Medicines Agency may order the handing over of all information, including written material, necessary for the inspection.

(3) As part of the Danish Medicines Agency's control, the Agency's representatives must, upon the presentation of appropriate identification and without a court order, have access to companies, medical practices and other places involved in the conduct of the trial.

(4) The Danish Medicines Agency's access to control subject to subsections (1) to (3) also includes the Agency's compliance with requirements for investigational medicinal products under section 29(1).

Title IV

Final provisions

Part VIII

Complaints

32. No later than 30 days after receipt of a decision from the Danish Medicines Agency or the medicinal research ethics committee, the sponsor can appeal the decision to the Danish Ministry of Health, as regards legal aspects.

Part IX

Financing etc.

33. The Danish Minister for Health may lay down rules on the collection and payment of fees by the sponsor to cover the Danish Medicines Agency's and the medicinal research ethics committees' activities under this Act and rules issued thereunder or regulations issued by the European Union.

Part X

Compensation

34.-(1) The sponsor, or if the courts of Denmark do not have jurisdiction over the sponsor, the investigator must pay compensation of DKK 1,350 to persons who have participated in a project initiated in conflict with article 4 or articles 28-35 of the regulation.

(2) The amount of the compensation is adjusted annually at 1 January by 2.0% plus the adjustment percentage for the relevant fiscal year, see the Act on a Rate Adjustment Percentage. The resulting amounts will be rounded to the nearest DKK amount divisible by DKK 50. The adjustment takes place on the basis of the applicable amounts before rounding off at the time of the adjustment.

(3) The compensation under subsection (1) is fixed on the basis of the amounts applicable at the time when the subject participated in the clinical trial.

(4) A medicinal research ethics committee that becomes aware that a subject may be entitled to compensation under subsection (1) can order the sponsor, the sponsor's representative or, if the courts of Denmark do not have jurisdiction over the sponsor, the investigator to inform the affected persons. The committee can make requirements for the form and contents of the information. Moreover, the committee may impose a deadline on the submission of the information.

Part XI

Penalties

35. Unless the offence carries a more severe penalty under any other legislation, anyone who

- (i) initiates a clinical trial of medicinal products in conflict with article 4 or article 15 of the regulation or section 22 of this Act,
- (ii) fails to comply with the obligation to notify under article 12, article 36(1), (2) and (3), article 37(1)-(3), (5) and (6), article 38(1), article 52(1), article 53(1) and (2) or article 54 of the regulation or section 27(1) of this Act,
- (iii) fails to comply with the safety reporting under article 42(1), article 43(1) or article 46 of the regulation,
- (iv) does not comply with article 47 or article 48 of the regulation,
- (v) violates article 63 or article 65 of the regulation,

- (vi) fails to comply with an order under article 77(1) of the regulation,
- (vii) fails to comply with an order or a duty to inform under section 19(1) second sentence and (2) second sentence, section 20(2), section 21, section 31(1) second sentence and (2) second sentence or section 34(4), or
- (viii) denies access for representatives of the regulatory authority under section 20(1) or section 31(3), will be liable to a fine or imprisonment for up to four months.

Part XII

Entry into force etc.

36.-(1) The Danish Minister for Health lays down the date of commencement of the Act. The Minister can also determine that various parts of the Act enter into force at different times, but see subsection (2).

(2) Section 37(i), (vi) to (x), (xii), (xiii) and (xv), section 38(i) and (ii) and section 40 enter into force on 1 July 2016.

(3) The Act does not, for up to 3 years after commencement of the Act, apply to applications submitted before this Act entered into force or to applications which, for up to 1 year after commencement of the Act, are submitted under the previous rules, see article 98 of the regulation. The previous rules apply to such applications.