



**The EFGCP Report on
The Procedure for the Ethical Review of Protocols
for Clinical Research Projects in Europe
(Update: March 2008)**

Portugal

1. What laws or regulations apply to an application for conducting a clinical trial in Portugal?

The Law 46/2004 of 19 August 2004 (Clinical Trials on Medicinal Products for Human Use) which incorporates the principles of the Clinical Trials Directive 2001/20/EC. This also includes the establishment of the Comissão de Ética para a Investigação Clínica (the Ethics Committee for Clinical Research (CEIC)).

Other laws include:

The ratified convention on biomedicine

The national laws on medicinal products

The national law and privacy of personal data

The law on medical devices

There is no legislation covering observational studies

All these documents can be found on the website of the Instituto Nacional de Farmácia e do Medicamento (INFARMED) which is the Portuguese Regulatory Agency, at <http://www.infarmed.pt>.

2. Which government, legal or authoritative body or bodies is or are responsible for the establishment and/or accreditation of (research) ethics committees for reviewing clinical trials for investigational medicinal products, their supervision and quality? Are there different (research) ethics committees reviewing other projects?

The review of Clinical Trials on Medicinal Products for Human Use is responsibility of the Ethical Committee for Clinical Research (CEIC), which is a national ethics committee and the competent one as defined in the law 46/2004 of 19 August 2004.

CEIC can delegate the evaluation of a protocol in some cases to a local health institution ethics committee. The requirements of these ethics committees are defined by CEIC.

For all other clinical studies, the local health institution ethics committee should be consulted.

3. What is the process for achieving clinical trial authorisation from the competent authority in Portugal?

The sponsor must apply for a clinical trial authorisation to the Medicines Evaluation Agency (INFARMED).

4. What is the process for obtaining ethical review of a clinical trial protocol by a competent (research) ethics committee in Portugal?

The sponsor requests a favourable opinion from the National Research Ethics Committee – CEIC according to the guideline available on the website http://www.infarmed.pt/portal/page/portal/INFARMED/MEDICAMENTOS_USO_HUMANO/CEIC.

5. Is there a single organisation to which to apply for ethical review of a clinical trial for an investigational medicinal product, regardless of whether this is for a single site or multiple sites?

Yes, the National Research Ethics Committee (CEIC).

6. What is the website for the organisation that issues guidelines on the ethical review of a clinical trial for an investigational medicinal product?

http://www.infarmed.pt/portal/page/portal/INFARMED/MEDICAMENTOS_USO_HUMANO/CEIC.

7. Is there a procedural interaction between the national or local competent authority and the (research) ethics committee during the approval process?

No.

8. Does the application to the EC and to the competent authority have to be submitted in parallel, or, if not, in which order?

The applications may be made either sequentially (in either order) or in parallel.

9. How many (research) ethics committees are there in Portugal?

There is only one (the CEIC) that is responsible for assessing CTIMP applications, though it may delegate to a research ethics committee established by a local health institution. By law all health care institutions must have an institutional ethics committee.

10. How are ECs funded in Portugal? Do they charge fees? If yes what is their scale of fees?

No fee is directly charged by CEIC. The National Ethics Committee for Clinical Research which is otherwise independent is funded by the National Medicines Agency (INFARMED). INFARMED charge sponsors according to a scale of fees. Local committees are financed by local health institutions and do not charge fees.

11. Who is responsible for submitting the request for ethical review to the competent ethics committee for single-site and for multi-site clinical trials?

The sponsor or its representative is responsible for both.

12. How is a "single opinion" achieved for multi-site studies?

The National Research Ethics Committee (CEIC) is responsible for a single opinion.

13. How many members serve on an EC?

By law institutional research ethics committees have seven members. The CEIC has 35 members: a president, a vice-president, seven executive committee members and 28 other members.

14. How many members constitute a quorum?

CEICs meetings may only occur when the majority of its members are present. If a quorum is not reached at the 1st call for the meeting, a new one must be called and then a quorum is constituted as long as one third of the voting members are present.

Deliberations are taken with the qualified majority of two thirds of the present members.

15. How are EC members appointed?

Members of the CEIC are appointed by the Health Minister. Members of the local institutional ethics committees are appointed by the clinical director of each institution.

16. How is the independence of members ensured?

The law has established that the National Research Ethics Committee (CEIC) is independent and multidisciplinary and that all the members must declare publicly their conflicts of interest.

17. How are conflicts of interest of EC members avoided?

The internal regulations of the ethics committee and the law ask for a permanent declaration for the conflict of interests. At the beginning of each meeting every member must declare any conflict of interests on any topic of the scheduled programme.

18. What backgrounds and/or qualifications of members are actively sought?

Members of the CEIC have recognized qualifications on medical sciences (clinical specialities, clinical pharmacology), ethics, teology, pharmaceutical sciences, epidemiology and pharmacoepidemiology.

19. How do ECs obtain specialist expertise?

It is recognized that there may sometimes be the need for external expertise. Any independent external expert may be requested to give advice to the CEIC.

20. What are the training requirements for members of ECs?

As far as the National Research Ethics Committee (CEIC) is concerned members are appointed by the Health Minister and different expertises are granted (see 18 above).

Local institutional ethics committee members have, so far, been chosen by the clinical director of each healthcare institution with no known specific training requirements.

The new legal frame attributes to the National Research Ethics Committee (CEIC) the accreditation of local committees based on a specific formation program to be implemented soon.

21. What training programmes are available for EC members in Portugal?

Academic training on clinical ethics, bioethics, pharmacology and epidemiology is available in the Universities of Lisbon, Oporto and Coimbra.

Yet to be developed is an annual training programme for CEIC members. –However, before each plenary, training sessions are provided to the Committee members (these training sessions will be publicly available when the specific internet site of CEIC is implemented).

22. What are the timelines for the assessment of single- and multi-site studies?

The timelines are in line with what is defined in the national law (Lei 46/2004 de 19 de Agosto) and the 2001 EC directive.

23. How are substantial amendments submitted during the review process dealt with?

The evaluation is made on a case by case basis. If the amendment has an impact in the patient's recruitment process, the time frame for evaluation is a further 60 days. If this is not the case the amendment is evaluated within 35 days.

When an unfavourable opinion is given to the clinical trial protocol the amendment consequently obtains the same decision.

24. How does an EC assess the suitability of investigators and of sites?

For the time being the suitability of investigators is decided by the analysis of CVs. Investigational sites are considered suitable if the clinical director of the medical centre declares so, explicitly reporting the human and material resources disposable in their site.

25. How are the requirements for (research) ethics committees to review the contractual or financial arrangements in clinical trials for both investigators and hospitals handled?

The national law requires that all financial arrangements (financial contracts between sponsors and health institutions) that are conducted with the board of each participating healthcare institution must be presented and approved by CEIC.

26. How are the requirements for ethics committees to review the compensation arrangements for study subjects handled?

These are required to be fully detailed in the clinical trials application and are evaluated in the review process.

27. Is there an ongoing quality assurance process (e.g. audits, inspections, internal SOP) for (research) ethics committees in Portugal?

No. However, it is intended that all committees will be prepared for external audit in the near future.

28. Is there an appeal mechanism?

Yes, by administrative law it is possible to appeal to the ministry of health.

29. How do ECs deal with SUSAR reports and Annual Safety Reports?

The guideline: "Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use" should be followed.

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National SUSARs should be reported by e-mail to the following address: ceic@infarmed.pt. Annual safety reports and quarterly line-listings should be sent by mail to the CEICs address using paper or a CD-ROM..

The EC procedures are currently being developed.

30. How are 'substantial amendments' defined?

Substantial amendments are defined according the Law 46/2004 of 19 August 2004 and the directive 2001/20/CE.

31. What are the indemnity insurance requirements for research projects?

The ethics committee must be provided that insurance and indemnity arrangements are in line with what is proposed to do in the clinical protocol and in the national law.

32. What are the indemnity insurance requirements for ethics committee members themselves?

There are no specific arrangements.

33. How is informed consent obtained from vulnerable subjects who are potentially to be involved in a clinical trial?

There is special guidance issued by the ethics committee concerned. In general, this is given by the legal representative.

34. How do ECs assess the progress and outcome of research projects that they have approved?

By reviewing the annual report for each clinical trial.

35. How does the EC ensure reception of the Annual Safety Report and the Summary of the Final Report of a research project that it has approved?

These are required by law and by the European guidance.

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