



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

Malta

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

The Maltese legislation concerning interventional clinical trials on investigational medicinal products (CTIMPs) consists of the *Clinical Trial Regulations, 2004* (LN490), *Good Manufacturing Practice in Respect of Medicinal and Investigational Medicinal Products for Human Use Regulations, 2004* (LN485) and *Good Clinical Practice and Requirements for Manufacturing or Import Authorisation of Investigational Medicinal Products (Human Use) Regulations, 2006* (LN119). The respective legal framework for these regulations is set out in the European Clinical Trials Directive 2001/20/EC, the GMP Directive 2003/94/EC and Directive 2005/28/EC.

The above Regulations cover interventional drug trials. Under these Regulations, 'ethics committee' means an independent body, consisting of healthcare professionals and non-medical members, whose responsibility is to protect the rights, safety and wellbeing of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to recruit and inform trial subjects and obtain their informed consent.

The Medical Devices Regulations, 2003 (LN 47) as amended by LN 27 of 2004 and LN 113 of 2007, cover trials involving medical devices. The legal framework for these regulations is set out in Directive 93/42/EEC. The Maltese government is also considering legislation on biotechnology.

Furthermore, there is also The Active Implantable Medical Devices Regulations, 2001 (LN 66). The legal infrastructure for these regulations is set out in Directive 90/385/EEC.

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 establishment of the Health Ethics Committee (HEC) is under the remit of the Ministry of Health. The Ministry also appoints a Bioethics Consultative Committee, which is an advisory committee but which is not involved in the assessment of clinical trials. However, there are also other ethics committees, including the Research Ethics Committee of the University of Malta (appointed by the Senate of the University) concerned with research involving human subjects being done by university members/students, the Ethics Subcommittee of the Faculty of Medicine and Surgery concerned mainly with audit studies on patients in the public healthcare system and the Ethics Committee of the Institute of Healthcare. All clinical trials are nevertheless the sole responsibility of the HEC as established in the Clinical Trials Regulations, 2004 (see 1 above).

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

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

(NB: For Malta these two questions are most appropriately answered together.)

In order to conduct a clinical trial in Malta the application must be submitted to the Medicines Authority and a separate application must also be submitted to the HEC (clarifications may be sought by the sponsor before an application is formally submitted). Following successful validation, each body generally has a 60 day period to assess the application (excluding clock-stops). A clinical trial may start if both the Health Ethics Committee and the Medicines Authority have separately issued an authorisation.

The Regulations can be accessed on <http://www.doi.gov.mt>.

The website of the Maltese Medicines Authority is at <http://www.medicinesauthority.gov.mt>.

The website of the Health Ethics Committee is at <http://www.sahha.gov.mt/pages.aspx?page=134>.

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.

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

The website of the Health Ethics Committee is at
<http://www.sahha.gov.mt/pages.aspx?page=134>.

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

There is good communication between the two bodies since a representative of the Medicines Authority may be invited to meetings of the HEC which necessitate feedback from the Medicines Authority. In order to avoid any conflict of interest, when the representative attends meetings of the HEC, he has no voting rights on clinical trials which are currently being assessed by the Medicines Authority.

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

Either in parallel or sequentially, either way. However, most sponsors opt for parallel submission.

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

Only one that has the power of approval (the HEC), but other advisory ethics committees are also established at the University of Malta, at the Medical School of Malta and at the Institute of Health Care.

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

The HEC is self-funding and fees charged for the review of clinical trials are used for administrative purposes. For example, office supplies, subscription to medical journals and the cost of obtaining the opinion of external experts during the assessment of clinical trials are paid for in this way. Members of the HEC receive no remuneration. Academic research without financial support from industry and clinical trials on orphan drugs may apply for reduced fees. Other clinical trials may also apply for reduced fees and will be evaluated on a case by case basis.

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 the principal/coordinating investigator.

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

There is only one HEC in Malta.

13. How many members serve on an EC?

There are nine members (one is non-voting and one replacement is not yet appointed).

14. How many members constitute a quorum?

50% + 1 (= 5)

15. How are EC members appointed?

The Ministry of Health, following a review of their respective competence, appoints them. There is no call for applications to serve on the HEC.

16. How is the independence of members ensured?

The Ministry of Health and the Chairman of the HEC, following an evaluation of the declaration of conflicts of interest, ensure this.

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

By declaring any conflicting interests. In most cases the members are personally known to the Ministry of Health and the Chariman of the HEC.

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

The HEC includes clinicians, a statistician, a pharmacist, an ethicist (who is also a Catholic priest) and a lay person.

19. How do ECs obtain specialist expertise?

By referring to suitable local experts usually in government and/or university employment who are also independent of the trial study.

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

Each HEC member is individually briefed on, and supplied with, the applicable legislation and guidance notes. However all members have now acquired experience concerning the review of ethics concerning clinical trials.

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

None.

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

The HEC operates according to the Regulations and generally has a maximum of 60 days, plus one clock-stop to request supplementary information, from the receipt of a valid application.

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

The Regulations apply and the HEC has a maximum of 35 days from the receipt of a valid application to issue an opinion.

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

Documentation submitted for review to the HEC includes facilities for the trial, CV of investigators and information about supporting staff in each site. Investigators are personally known to the members of the HEC. Investigators and applicants may also attend meetings of the HEC at their request or are invited, when their clinical trial application is being discussed.

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?

An indication of the contractual/financial arrangements in clinical trials for investigators/hospitals is sought. Financial arrangements are normally disclosed.

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

The amount and procedure for compensation of study subjects is evaluated on a case by case basis. This includes a description of the amount paid for participation in the trial such as travel costs, loss of earnings and discomfort.

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

No.

28. Is there an appeal mechanism?

No.

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

A member of the HEC is appointed as rapporteur and s/he delivers an overview of the documentation that s/he has reviewed to the rest of the committee during a meeting. If there are any concerns the sponsor is contacted. The information is retained in a local database.

30. How are 'substantial amendments' defined?

According to the European Commission's guidelines, substantial amendments may arise from changes to the protocol or from new information relating to the scientific documents in support of the trial. Substantial amendments include changes which can have a significant impact on

- the safety or physical or mental integrity of the subjects;
- the scientific value of the trial;
- the conduct or management of the trial;
- or the quality or safety of any IMP used in the trial.

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

Sponsors are requested to provide their own indemnity measures to safeguard the subjects and to protect the investigators.

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

Liability of the HEC members is covered by the Ministry of Health.

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

The HEC follows Directive 2001/20/EC, ICH Guideline on Good Clinical Practice and any other relevant guidance documents published by the European Commission.

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

This is mainly assessed through the periodic safety reports (including the Annual Safety report) and other documentation. However if there are any concerns, the sponsor is contacted.

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?

The HEC was only established in March 2005. However, each clinical trial is tracked.

Validated February 2008

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