MALTA
MEDICINES
AUTHORITY

Guidance for Notification for Modification of Clinical Investigations under the Regulation (EU) 2017/745

1. Introduction

The guidance described in this document is based on the principles outlined in the Medical Device Regulation (EU) 2017/745 (MDR), concerning substantial modifications to clinical investigations in Article 75 and Chapter II of Annex XV. This document is a guidance to the local form *MT-MDF17 Clinical Investigation – Notification for Modification of Clinical Investigation under the Medical Device Regulation (EU) 2017/745.* Reference should be made to *GL-MDF13 Guidance for Application/Notification for Clinical Investigations under Regulation (EU) 2017/745 on Medical Devices and GL-MDF07 Guidance on fees in relation to Medical Device,* for guidance regarding submission of forms and related fees related to clinical investigations to be carried out in Malta.

The authorisation for the conduct of a substantial modification to a clinical investigation is granted by Malta Medicines Authority, upon request by the sponsor or legal representative. The substantial modification request can only be considered after the decision on the clinical investigation has been taken. Such modifications are likely to have a substantial impact on the safety, health, or rights of the subjects or on the robustness or reliability of the clinical data generated by the investigation. The notification should be accompanied by the request to the relevant Ethics Committee/s in Malta.

The mandatory use of the European databank platform as a registration system will start when the entire EUDAMED modules have been declared fully functional, in accordance with Article 73 of the Medical Device Regulation.

Any further clarification on this guidance document may be obtained from the Malta Medicines Authority, by sending an email to mdforms.medicinesauthority@gov.mt.

2. Scope

The purpose of this guidance document is to outline the requirements for sponsors when applying for a substantial modification to a clinical investigation *(Refer to Article 75 of the Medical Devices Regulation (EU) 2017/745).*

The sponsor is encouraged to refer to the International Standard ISO 14155:2020 – Clinical investigation of medical devices for human subjects.

3. Terms, Definitions and Abbreviations

Abbreviations:

EUDAMED	European Database on Medical Devices
MDCG	Medical Device Coordination Group
MDR	Medical Device Regulation referring to Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on Medical Devices,

	Amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and Repealing Council Directives 90/385/EEC and 93/42/EEC.
GDPR	General Data Protection Regulation

Definitions:

Authorised Representative
Authorised representative means any natural or legal person established within the Union who has received and accepted a written mandate from a manufacturer, located outside the Union, to act on the manufacturer's behalf in relation to specified tasks with regard to the latter's obligations under this Regulation. [Regulation (EU) 2017/745 Article 2]

Applicant
Applicant in this guidance document refers to either sponsor or legal representative.

Clinical Investigation
A clinical investigation is defined as any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device. [Regulation (EU) 2017/745 Article 2]

Ethics Committee
Ethics committee means an independent body established in a Member State in accordance with the law of that Member State and empowered to give opinions for the purposes of the Medical Devices Regulation, taking into account the views of laypersons, in particular patients or patients' organisations. [Regulation (EU) 2017/745 Article 2]

Ethics Committee/s in Malta
Health Ethics Committee; Research Ethics Committee.

Legal Representative
Where the sponsor of a clinical investigation is not established in the Union, that sponsor shall ensure that a natural or legal person is established in the Union as its legal representative. Such legal representative shall be responsible for ensuring compliance with the sponsor's obligations pursuant to the MDR and shall be the addressee for all communications with the sponsor provided for in this Regulation. Any communication with that legal representative shall be deemed to be a communication with the sponsor. [Regulation (EU) 2017/745 Article 2]

Manufacturer
Manufacturer means a natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under its name or trademark. [Regulation (EU) 2017/745 Article 2]

Medical Device
Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

diagnosis, prevention, monitoring, treatment or alleviation of disease,
diagnosis, monitoring, treatment, alleviation or compensation for an injury or handicap,
investigation, replacement or modification of the anatomy or of a physiological process,
control of conception,
and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means. [Regulation (EU) 2017/745 Article 62]

Sponsor
Sponsor means any individual, company, institution or organisation which takes responsibility for the initiation, for the management and setting up of the financing of the clinical investigation. [Regulation (EU) 2017/745 Article 2]

4. Specific Guidance

4.1 Timeframe for sponsors requesting the modification

Applicants requesting the substantial modification of a clinical investigation should notify the Malta Medicines Authority within one (1) week by means of the European Database on Medical Devices (EUDAMED) system. In the absence of EUDAMED, sponsors should notify the Malta Medicines Authority by filling in the local form (MT-MDF17) and the relevant European form and supporting documentation (MDCG 2021-28).

Applicants are advised to refer to Annex II of MDCG 2021-06 Questions & Answers regarding clinical investigation for a non-exhaustive list of modifications to determine whether the modification is substantial or not.

Until the EUDAMED is fully functional, sponsors are requested to notify the Malta Medicines Authority of non-substantial modifications of clinical investigations.

4.2 Timeframe for the Malta Medicines Authority

As stipulated in Article 75 of the MDR, the Authority is responsible to review and assess within thirty-eight (38) days the notification for substantial modification whereby such period can be extended by a further period of seven (7) days, if experts are to be consulted (Table 1).

Request	***MDR Article No.***	***Process Stage***	***Timeframe***	***Extension of Timeframe***
Request for Substantial Modification to a Clinical Investigation	Article 75	Review and assessment of the notification	Within thirty-eight (38) days of the notification.	Can be extended by a further period of seven (7) days if experts need to be consulted.

Table 1: Timeframe for the review and assessment of a notification for a substantial modification notification.

The clock is stopped when the applicant is requested to send additional information or comments and restarted upon receipt of responses and review resumes. If further queries arise or responses are not satisfactory, the applicant is informed and clock stops/starts accordingly, with the cycle repeating itself.

4.3 General Details related to Applying

4.3.1 Notification Form Title

The notification form related to this guidance document is *MT-MDF17 Clinical Investigation – Notification for Modification of Clinical Investigation under the Medical Device Regulation (EU) 2017/745*) which may be accessed from the Malta Medicines Authority website https://medicinesauthority.gov.mt, under the section for medical devices.

4.3.2 Notification Format

MT-MDF17 Notification Form is in a fillable pdf format. Form should be filled in electronically using the shaded areas. Handwritten forms may not be accepted if writing is considered illegible. Forms should be signed and submitted as a scanned copy or as a signed pdf file.

4.3.3 Official Languages

The official languages in Malta are Maltese and English. Notification forms and supporting documentation for a modification of clinical investigation must be completed in either Maltese or English.

4.4 Filling in the Notification Form

For the notification to be considered, all sections must be filled in completely and accurately as per this guidance document. Sections not applicable to your organisation must be filled in with N/A.

The notification form is divided as follows:

- Section A – Notification Introduction & Applicant Details
- Section B – Sponsor Contact Details
- Section C – Legal Representative Contact Details
- Section D – Investigator Contact Details
- Section E – Identification of the Clinical Investigation
- Section F – Information on the Device
- Section G – Notification Form (EU)
- Section H – Data Protection Consent Statement
- Malta Medicines Authority Declaration for Form Submission

4.4.1 Section A: Notification Introduction & Applicant Details

Section A is divided into two sections:

4.4.1.1 Date of notification and applicant details

The date of notification for the modification of clinical investigations will be completed automatically. The individual completing the notification shall provide their name, surname, email address and contact number. The applicant refers to sponsor or legal representatives.

4.4.1.2 Applicant

The applicant making the request, whether the sponsor or the legal representative, must be selected.

4.4.2 Section B: Sponsor Contact Details

The details of the sponsor should be included in this section if applicable. It is the responsibility of the sponsor to update the Authority of any changes in these contact details.

4.4.3 Section C: Legal Representative Contact Details

The details of the legal representative should be included here, if applicable. It is the responsibility of the legal representative to update the Authority of any changes in these contact details.

4.4.4 Section D: Investigator Contact Details

The details of the investigator should be included here. It is the responsibility of the legal representative to update the Authority of any changes in these contact details.

4.4.5 Section E: Identification of the clinical investigation

This section is divided into two parts:

4.4.5.1 Details on the clinical investigation

The information in this section will appear on the Letter of Authorisation from the Authority. This section includes the reference number given by the Authority, identification number and title of the clinical investigation and date of the previous authorisation/notification.

4.4.5.2 Details of the Clinical Investigation Plan (CIP)

This section includes the code, version no and date of the CIP.

4.4.6 Section F: Information on the device

4.4.6.1 Name of the Device

This indicates the name of the device and will be included in the Letter of Authorisation.

4.4.6.2 Model of Device

This includes the model of the device and will be included in the Letter of Authorisation.

4.4.6.3 Classification of Medical Device

This indicates what type of device will be included in the Letter of Authorisation. Only one type may be selected per application:

- Class I to IV - Medical Device as per Regulation (EU) 2017/745

4.4.6.4 Description of device including its intended purpose

This section must include brief description for each device including its intended purpose. The description of the device should ideally be kept to one line of text.

4.4.6.5 Changes to device since the previous application/notification

If applicable, this section must include a rationale and description of these changes.

4.4.7 Section G: Notification form (EU)

This section includes the relevant EU forms and supporting documentation that is required to be filled in and attached to the local notification form *MT-MDF17 Clinical Investigation– Modification of clinical investigation under Regulation (EU) 2017/745 on medical devices* by the applicant.

Reference should be made to the MDCG 2021-28 guidance in the Clinical Investigation and Evaluation section.

4.4.8 Section H: Data Protection Consent Statement

Applicant shall confirm consent, by ticking the box in this section, to the processing of personal data by the Malta Medicines Authority and understands that this data shall be processed in accordance with the General Data Protection Regulation (GDPR).

4.4.9 Malta Medicines Authority Declaration for Form Submission

Applicant shall sign the Malta Medicines Authority declaration that all the information submitted within this notification form is correct and complete.

4.5 Documents Required

The applicant is responsible to complete and submit all requested forms and supporting documentation to the Malta Medicines Authority, in accordance with Article 75 and Chapter II of Annex XV of the MDR. Refer to the MDCG 2021-28 guidance in the Clinical Investigation and Evaluation section for the relevant EU form and supporting documentation.

Ethics committee approval is not mandatory before the notification for modification is submitted to the Malta Medicines Authority. As part of the documentation submitted with *MT-MDF17, t*he applicant is requested to provide the Authority an acknowledged application request from the Ethics Committee/s in Malta. As stipulated in Article 75 (3b) of the Medical Device Regulation (EU) 2017/745, before the sponsor can implement the modifications in question, a positive decision of the Ethics Committee/s should be provided to the Malta Medicines Authority.

4.6 Letter of authorisation validity

The letter of authorisation is valid for a period of two years from the date of issue. Following this period, a new notification must be submitted.

4.8 Refusal of authorisation of the modification

The Authority can refuse the authorisation of the modification based on the grounds as stipulated in Article 75 (3b) of the Medical Device Regulation (EU) 2017/745.

5. References

1. EU legislations- Medical Devices and In-Vitro Diagnostic Medical Devices https://health.ec.europa.eu/medical-devices-sector/new-regulations_en
2. ISO Standard 14155:2020 Clinical investigation of medical devices for human subjects — Good clinical practice
3. MT-MDF17 Clinical Investigation – Notification for Modification of Clinical Investigation under the Medical Device Regulation (EU) 2017/745
4. GL-MDF13 Guidance for Application / Notification for Clinical Investigations under Regulation (EU) 2017/745 on Medical Devices
5. GL-MDF07 Guidance on fees in relation to Medical Device
6. MDCG 2021-08 Clinical investigation application/notification documents
7. MDCG 2021-06 Regulation (EU) 2017/745 – Questions & Answers regarding clinical investigation
8. MDCG 2021-28 - Substantial modification of clinical investigation under Medical Device Regulation

Signatures on file

List of Appendices

N/A