MALTA
MEDICINES
AUTHORITY

Guidance for Notification for Modification of Performance Studies under the Regulation (EU) 2017/746

1. Introduction

The guidance described in this document is based on the principles outlined in the In Vitro Diagnostic Regulation (EU) 2017/746 (IVDR), concerning substantial modifications to clinical investigations in Article 71 and Annex XIV. This document is a guidance to the local form *MT-MDF18 Performance Study– Notification for Modification of Performance Study under the In Vitro Diagnostic Regulation (EU) 2017/746.* Reference should be made to *GL-MDF14 Guidance for Application/Notification for Performance Studies under Regulation (EU) 2017/746 on In-vitro Diagnostics and GL-MDF07 Guidance on fees in relation to Medical Device*, for guidance regarding submission of forms and fees related to performance studies to be carried out in Malta.

The authorisation for the conduct of a substantial modification to a performance study 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 performance study 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 study. 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 applicants when applying for a substantial modification to a performance study *(Refer to In Vitro Diagnostic Regulation (EU) 2017/746).*

The applicant is encouraged to refer to the International Standard ISO 20916:2019 - Clinical performance studies using specimens from human subjects – Good study practice.

3. Terms, Definitions and Abbreviations

Abbreviations:

EUDAMED	European Database on Medical Devices
GDPR	General Data Protection Regulation
IVDR	In-Vitro Diagnostic Regulation referring to Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic

medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU.

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.

PSP Performance Study Plan

Definitions:

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

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) 2017/746 Article 2(25)]

Authority
Authority in this SOP refers to the Malta Medicines Authority responsible for the regulation of medical devices.

Ethics Committee
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 this Regulation, taking into account the views of laypersons, in particular patients or patients' organisations. [Regulation (EU) 2017/745 Article 2(59)]

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

In Vitro Diagnostic Medical Device
Any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, piece of equipment, software or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information on one or more of the following:

(a) concerning a physiological or pathological process or state;
(b) concerning congenital physical or mental impairments;
(c) concerning the predisposition to a medical condition or a disease;
(d) to determine the safety and compatibility with potential recipients;

(e) to predict treatment response or reactions;
(f) to define or monitoring therapeutic measures.

Specimen receptacles shall also be deemed to be in vitro diagnostic medical devices. [Regulation (EU) 2017/746 Article 2(2)]

Legal representative
Where the sponsor of a performance study 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 this Regulation 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) 2017/746 Article 58(4)]

Manufacturer
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) 2017/746 Article 2(23)]

Performance Study
A study undertaken to establish or confirm the analytical or clinical performance of a device. [Regulation (EU) 2017/746 Article 2(42)]

Performance Study Plan
A document that describes the rationale, objectives, design methodology, monitoring, statistical considerations, organisation and conduct of a performance study. [Regulation (EU) 2017/746 Article 2(43)]

Sponsor
Any individual, company, institution or organisation which takes responsibility for the initiation, for the management and setting up of the financing of the performance study. [Regulation (EU) 2017/746 Article 2(57)]

4. Specific Guidance

4.1 Timeframe for applicants requesting the modification

Applicants requesting the substantial modification of a performance study 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, applicants should notify the Malta Medicines Authority by filling in the local form MT-MDF18 and the relevant European form and supporting documentation (MDCG 2022-20).

Until the EUDAMED is fully functional, applicants are requested to notify the Malta Medicines Authority of non-substantial modifications of performance studies.

4.2 Timeframe for the Malta Medicines Authority

As stipulated in Article 71 of the IVDR, 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	***IVDR Article No.***	***Process Stage***	***Timeframe***	***Extension of Timeframe***
Request for Substantial Modification to a performance study	Article 71	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-MDF18_Performance Study – Notification for Modification of performance study under the In Vitro Diagnostic Regulation (EU) 2017/746)* 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-MDF18 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 performance study 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 performance study 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 Performance Study

This section is divided into two parts:

4.4.5.1 Details on the performance study

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 performance study and date of the previous authorisation / notification.

4.4.5.2 Details of the Performance Study Plan (PSP)

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

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:

- Grade A to D- In Vitro Diagnostic Device as per Regulation (EU) 2017/746

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-MDF18 Performance Study – Modification of performance study under Regulation (EU) 2017/746 on in vitro diagnostic medical devices* by the applicant.

Reference should be made to MDCG 2022-20 guidance in the In Vitro Diagnostic medical device regulation 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 71 and Annex XIV of the IVDR. Refer to the MDCG 2022-20 guidance in the In Vitro Diagnostic medical devices (IVD) 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-MDF18, t*he applicant is requested to provide the Authority an acknowledged application request from the Ethics Committee/s in Malta. As stipulated in Article 71 (3b) of the In Vitro Diagnostic Regulation (EU) 2017/746, before the applicant can implement the modifications in question, a positive decision of the Ethics Committee/s in Malta 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 (2) years from the date of issue. Following this period, a new notification must be submitted.

4.7 Refusal of authorisation of the modification

The Authority can refuse the authorisation of the modification based on the grounds as stipulated in Article 71 (3b) of the In Vitro Diagnostic Regulation (EU) 2017/746.

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 20916 In vitro diagnostic medical devices — Clinical performance studies using specimens from human subjects — Good study practice

3. GL-MDF14 Guidance for Application / Notification for Performance Studies under Regulation (EU) 2017/746 on In-vitro Diagnostics and GL-MDF07 Guidance on fees in relation to Medical Device

4. MDCG 2022-20 Substantial modification of performance study under Regulation (EU) 2017/746

5. MDCG 2022-19 Performance study application/notification documents under Regulation (EU) 2017/746

6. MT-MDF18 Performance Study– Notification for Modification of Performance Study under the In Vitro Diagnostic Regulation (EU) 2017/746

Signatures on file

List of Appendices

N/A