Performance studies of *in vitro* diagnostic medical devices

The new Regulation (UE) 2017/746 on in vitro diagnostic medical devices (IVDR) came into force in May 2017, with application from 26 May 2022. This regulation introduces significant changes for manufacturers, distributors and users of in vitro diagnostic devices (IVDs), with a strong focus on the safety, quality and performance of devices. Here you will find the requirements relating to performance studies and the submission of a conformity dossier under the IVDR in Luxembourg.

Performance studies and clinical evidence

Performance evaluation, as defined by Article 2 of Regulation (UE) 2017/746 (IVDR), is the process through which a manufacturer demonstrates that their device meets performance criteria in terms of safety and effectiveness. This evaluation includes three essential components:

1. **Analytical performance** – Art. 2(40): the ability of a device to correctly detect or measure a particular analyte.
2. **Clinical performance** – Art. 2 (41): the ability of a device to yield results that are correlated with a particular clinical condition or a physiological or pathological process or state in accordance with the target population and intended user.
3. **Scientific validity of an analyte** – Art. 2 (38): the association of an analyte with a clinical condition or a physiological state

To ensure an appropriate level of clinical evidence, all performance evaluation documentation is planned, generated, and documented by the manufacturer in accordance with Article 56 and Part A of Annex XIII of Regulation (UE) 2017/746. This evaluation must be objective, thorough, proportionate, and appropriate to the device's characteristics.

In Luxembourg, any request for a performance study involving human subjects or a substantial modification of a performance study is also subject to prior authorisation by the Minister, based on the scientific and ethical opinions of the Health Directorate and the National Research Ethics Committee (**Article 27 of the Law of March 8, 2018, relating to hospital establishments and hospital planning**).

Additional guidance on definitions, IVDR requirements, regulatory pathways, submission documents, documentation of reports and studies, transition periods, etc., is available in MDCG (Medical Devices Coordination Group) documents, including **MDCG 2025-5 - Questions & Answers regarding performance studies of in vitro diagnostic medical devices under Regulation (EU) 2017/746 (June 2025)**.

Submission of an application for performance studies

Pending the entry into force of the European Database on Medical Devices (EUDAMED), the performance study request must be submitted using the form available in Annex I of the MDCG_2022-19 document to the Ministry of Health via the following email addresses: recherchebiomedicale@ms.etat.lu and meddevices@ms.etat.lu. The list of documents to be attached to the request can also be found in the annex of the document MDCG_2022-19_e-appendix.

If additional devices, comparators, or sites are added to the performance studies, specific forms as well as a checklist of general safety and performance requirements, standards, common specifications, and scientific opinions are also available.

The application file can be written in one or more of the following languages: German, French, Luxembourgish, or English.

The information provided to the participant, or their legal representative must enable them to understand the nature and objectives of the study, the rights and protections concerning their safety, the conditions and duration of the study, as well as any potential alternative treatments and follow-up measures. In this regard, it is important to provide both French and German versions of all documents intended for participants (informed consent forms, questionnaires, recruitment materials, etc.) to meet the linguistic expectations of the Luxembourgish population.

Proof of insurance is mandatory and must specify the project, the number of participants covered, and the coverage for the entire duration of the study.

Application for a substantial modification of a performance study

During any performance study, so-called substantial modifications may occur. These are changes that could impact, for instance, the safety, health, or rights of participants, or the robustness or reliability of the data obtained from the study.

Within one week, the applicant must:

- Inform the relevant authorities of the reasons and nature of the modification.
- Submit their request using the application form available in the Annex of the **MDCG_2022-20** document to the Ministry of Health and Social Security via the email addresses: recherchebiomedicale@ms.etat.lu & meddevices@ms.etat.lu;
- Attach an updated version of the relevant documentation referred to in Annex XIV of Regulation (EU) 2017/746, with any modifications clearly visible in this documentation. For a non-exhaustive list of substantial modifications, please refer to Annex II of document MDCG 2025-5 - Questions & Answers regarding performance studies of in vitro diagnostic medical devices under regulation (EU) 2017/746 (June 2025).

Notification of the end or the halt of a performance study

Information related to the end, temporary halt or early termination of a study must be notified to the Ministry of Health and the Social Security via the following e-mails addresses: **recherchebiomedicale@ms.etat.lu** &**meddevices@ms.etat.lu**, in accordance with the instructions in the table below:

Notification type	**Motive**	**Deadline for notification**	**Deadline for submission of the report** (Annex XV, Chapter I, Section 2.8 and Chapter III, Section 7) **accompanied by the summary**
Temporary halt or Early termination	for security reasons	24h	3 months
	for any other reason	15d	
End	/	15d	Within the year

The summary and the performance study report should be submitted to the Ministry of Health and Social Security within one year of the end of the performance study or within three months of the early termination or temporary halt, using recommendations of MDCG 2022-2.

Notification of events occurring during a performance study

What is an adverse event?
Any untoward medical occurrence, inappropriate patient management decision, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a performance study, whether or not related to the device for performance study.

What is a serious adverse event?
Any adverse event that led to any of the following:

a) a patient management decision resulting in death or an imminent life-threatening situation for the individual being tested, or in the death of the individual's offspring.
b) death.
c) serious deterioration in the health of the individual being tested or the recipient of tested donations or materials, that resulted in any of the following:
   - life-threatening illness or injury.
   - permanent impairment of a body structure or a body function.
   - hospitalisation or prolongation of patient hospitalisation.
   - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
   - chronic disease.
d) foetal distress, foetal death or a congenital physical or mental impairment or birth defect.

What is a device deficiency?
Any inadequacy in the identity, quality, durability, reliability, safety or performance of a device for performance study, including malfunction, use errors or inadequacy in information supplied by the manufacturer.

For additional guidance, the documents **MDCG 2024-4**, **MDCG 2024-4 Appendix** et **MDCG 2022-9 Rev.1** can be consulted.

What events to report and within what period?

For any event linked to a performance study carried out in Luxembourg, the sponsor notifies without delay using the form available in the document **MDCG 2020-10/2 Rev. 1** to the address **meddevices.vigilance@ms.etat.lu.** The period for reporting shall take account of the severity of the event. Where necessary to ensure timely reporting, the sponsor may submit an initial report that is incomplete followed up by a complete report.

Event type	Deadline
1) any serious adverse event that has a causal relationship with the device, the comparator or the study procedure or where such causal relationship is reasonably possible;	**Immediately,** but no later than 7 calendar days following the date the sponsor becomes aware of the new event, or any added information related to an event already reported
2) any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate. **3) any new findings** in relation to any event referred to in points 1) et 2).	**Immediately,** but no later than 7 calendar days following the date the sponsor becomes aware of it, or any added information related to an event already reported

Notification of events related to performance studies with CE-marked in vitro diagnostic medical devices.

f the event is related to a CE-marked device used within the limits of its intended purpose, the notification process described above applies and must be sent to **meddevices.vigilance@ms.etat.lu**, using the most recent version of the MIR (Manufacturer's Incident Report) form available on the European Commission website.

Retrospective studies on in vitro diagnostic medical devices or studies involving the use of leftover samples

Retrospective studies, involving, for example, the collection of retrospective data or leftover samples, must be notified to the Ministry of Health and Social Security via the email addresses recherchebiomedicale@ms.etat.lu and meddevices@ms.etat.lu, using:

- for the companion diagnostics: application form **MDCG-2022-19**
- for 'non-companion' in vitro diagnostic devices: the information defined in Annex VIII §2 of the RGD of 24 July 2001 relating to in vitro diagnostic medical devices.

Approval from the National Research Ethics Committee (CNER) is also required for these studies.

FOR MORE INFORMATION

External links

- **Legilux**
- **MDCG guidelines**
- **CNER**
- **MIR application form**