Practical considerations for clinical investigations with medical devices in Spain

Memorandum of July 2025 on Collaboration CEIm-AEMPS for the evaluation of clinical investigations with medical devices

The Spanish regulatory framework for clinical investigations involving medical devices and performance studies involving in vitro diagnostic medical devices (IVDs) is complex.

Clinical investigations with medical devices are governed by Regulation (EU) 2017/745 (MDR), Royal Decree 192/2023 and Royal Decree 1090/2015. Performance studies with IVDs are governed by Regulation (EU) 2017/746 (IVDR) and Royal Decree 1662/2000, until the new Royal Decree currently under preparation is approved.

As happened previously with Regulation (EU) 536/2014 and Royal Decree 1090/2015 on clinical trials with medicinal products, the Spanish Medicines Agency (AEMPS) published a memorandum in July to clarify the applicable regulatory framework for clinical investigations involving medical devices.

In particular, the memorandum explains the roles of AEMPS and the Research Ethics Committees for Medicines (CEIm), and sets out the obligations and responsibilities of sponsors across the different types of clinical investigations with medical devices and IVD performance studies. Based on the experience gained over the past few months, we highlight below the aspects we consider most relevant.

Pathways depending on the type of study

If the investigation involves a medical device without CE marking, or a CE-marked device used outside its intended purpose as described by the manufacturer in the instructions for use, AEMPS authorisation is required.

By contrast, if the investigation requires participants to undergo additional procedures beyond those used under normal conditions of use, and these are invasive or burdensome, the study must be notified to AEMPS, but authorisation is not required.

Finally, where the medical device is CE-marked, is used in line with its intended purpose and instructions for use, does not involve invasive or burdensome procedures, and the purpose of the study is not to assess device conformity, neither authorisation nor notification to AEMPS is required.

In all cases, it is mandatory to obtain a favourable opinion from an accredited CEIm, which will be single and binding for all participating sites. In addition, approval from the management of each site is required, usually formalised through the relevant agreement.

For IVD performance studies, the pathways are similar. For studies involving companion diagnostics, AEMPS clarifies that where only leftover samples are used and no therapeutic decisions or patient selection decisions are made, it is sufficient to notify the competent authority. In Spain, in the absence of Eudamed, this is processed through the NEOPS database.

Compensation and insurance

Clinical investigations intended to assess the conformity of non-CE-marked medical devices (or CE-marked devices used outside their intended

purpose within the conformity assessment process) require insurance coverage.

By contrast, insurance is not required for investigations involving CE-marked medical devices used within their intended purpose.

For IVD performance studies, insurance is required where the investigational device does not have CE marking, or where it does have CE marking but is used outside its intended purpose.

Combined trials

Combined trials are studies where an investigational medicinal product is assessed at the same time with a non-CE-marked medical device, or a CE-marked device used outside its intended purpose.

In these cases, the relevant authorisations must be requested in parallel. Documentation for the medicinal product trial must be submitted through CTIS(Clinical Trial Information System), while documentation for the device investigation must be submitted—until the European database Eudamed becomes operational—via the AEMPS General Registry, addressed to the Medical Devices Department.

The same CEIm will assess both parts of the study. The sponsor must submit a single patient information sheet for review.

Informed consent

The AEMPS memorandum also specifies the format, maximum length, and the mandatory content that must be included in the patient information sheet and informed consent form for participants in medical device investigations, which must in all cases be approved by the CEIm.

These requirements are very similar to those set out in Annex VIIIA (Guidance for the correct preparation of a patient information sheet and informed consent form + Appendix on personal data protection) and Annex VIIIB (Text to be included in informed consent for the collection and use of biological samples in clinical trials), previously published by AEMPS as part of its instructions for conducting clinical trials with medicinal products in Spain.

As a new requirement, AEMPS states that for investigations involving medical devices with artificial intelligence systems, participants must be informed about the use of this technology. Specifically, the consent document must indicate whether the output will be used for clinical decision-making, diagnosis, prognosis, or medical care, or whether the results are exploratory or preliminary.

Participants must also be informed of the risks associated with the use of artificial intelligence, such as system errors (i.e. incorrect outputs), the risk of discrimination, and the potential existence of bias.

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