Guidelines to facilitate the conduct of decentralised clinical trials of medicinal products in the European Union

European Commission, EMA and HMA recommendations on decentralised elements in clinical trials of 13 December 2022

Decentralised clinical trials are those that are conducted largely outside the physical facilities of a healthcare centre, taking advantage of the use of technology. The increasing use of digital tools, and in particular the Covid-19 pandemic, has led to certain elements of clinical trials being conducted in a decentralised manner (e.g. informed consent management, investigational medicinal product (IMPs) delivery, trial monitoring).

At European level, some regulations have been adopted in this regard. In the case of Spain, the Spanish Agency for Medicinal Products and Medical Devices (AEMPS) has modified the document of instructions for conducting clinical trials in our country on several occasions to include some measures in this regard. Initially, it was expected that these measures would be maintained until the World Health Organisation declared the end of the pandemic. However, given the positive experience gained, especially for patients, it was considered appropriate to facilitate the use of these decentralised elements in clinical trials, beyond the existence of a health crisis. To this end, the European Commission, the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) have issued the Recommendation Paper, which we will analyse below.

Equivalent guarantees

The Recommendation Paper provides a set of guidelines on how and under what conditions it is acceptable for certain elements of clinical trials to be conducted in a decentralised manner. All these guidelines, which should be taken into account by sponsors when designing and conducting such trials, revolve around one basic principle: in decentralised clinical trials, the safety and rights of trial participants and the reliability of data should be ensured to at least the same extent as in a "traditional" clinical trial, i.e., one that is conducted entirely within a healthcare centre facility. For the same reason, it is also advisable that, when the sponsor prepares his trial with decentralised elements, the investigators and other healthcare professionals involved in the care of the patients participating in the trial should also be consulted.

"Enhanced" obligations of the sponsor

For decentralised trials, the sponsor should adequately identify all decentralised elements in the trial documents, particularly the protocol, so that they can be properly assessed by the regulatory authorities. It is also the sponsor's responsibility to assess the specific risks associated with the decentralised processes it intends to implement, and the measures it intends to take to mitigate those risks.

In addition, it is very common for decentralised trials to involve other service providers, such as nurses who can perform certain actions in the patient's home, or IT service providers responsible for the telematic management of the trial data. It is therefore crucial that the roles and responsibilities of the sponsor, investigators,

and other stakeholders are well defined, and that any delegation of tasks is contractually agreed.

Informed consent

In the process of obtaining informed consent, face-to-face communication between the potential trial participant and the investigator is considered essential. Therefore, if such communication is conducted remotely, it is recommended that this takes place in real time, where both can see and communicate with each other, with audio and video, and also check their identities. With regard to signature, informed consent can be signed either by handwriting or by digital signature, provided that the signing process, including the validity of the signatures, can be reconstructed and its security and confidentiality can be guaranteed.

On the other hand, the greater number of parties involved in decentralised trials and the apparent delocalisation of the activities carried out make it necessary to pay special attention to compliance with the rules on the protection of personal data.

Home interventions

Where home delivery and/or home administration of the IMP is planned, the sponsor's risk assessment of the appropriateness of these measures should consider, among other things, the safety profile of the product, the route of administration/preparation requirements, the trial population, and the logistics of delivery and storage conditions. In any case, the sponsor retains overall responsibility for the supply process and the arrangements to be made with the parties involved in the supply process. It is recommended that a healthcare professional should always be involved in the home administration of the product in the case of complex administrations, where special preparation or handling is required, or where the safety profile of the product so requires. In all cases, procedures will be established to verify patient compliance and to manage product returns.

If any other trial-related procedure (e.g., collection of biological samples) is to be performed at the patient's home, it may be performed if it does not pose an additional risk to the patient or to the reliability of the data, and in any case if the person performing the task is qualified and/or trained to do so. Any harm to the patient as a result of a procedure performed at home must also be covered by the appropriate insurance policy or equivalent guarantee.

"Living" reference document

Given the rapid advances in the field of decentralised clinical trials, it is expected that this recently published Reference Paper will evolve over time as new "real-life" data from experience in this area become available. For the time being, this paper can be a good reference to confirm that a clinical trial with decentralised elements is ethically and legally acceptable, both for sponsors wishing to conduct such trials and for the ethics committees and regulatory authorities that have to approve them.

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