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Decentralized Trials: EU Study Explores Different Models For Directly Shipping Drugs To Patients

by Vibha Sharma

Researchers working on behalf of the EU's public-private Trials@Home project offer insight into practices for direct-to-participant supply of investigational medicinal products in clinical trials.

The EU lacks harmonized regulatory requirements on how investigational medicinal products (IMPs) can be shipped directly to study participants instead of being dispensed at clinical trial sites, but this has not deterred trial sponsors from experimenting with different approaches on this front.

The most commonly deployed model is one with the least regulatory barriers in which the IMP is shipped from the investigative site or the site's pharmacy to the participant's home or other address. Other models have involved delivering IMPs from local and central pharmacies.

These are the finding of a *study* conducted by researchers on behalf of Europe's Trials@Home Consortium, which examined how direct-to-participant (DtP) IMP supply has been used in clinical trials in Europe.

As noted by the study authors, DtP supply of IMPs can enable the decentralization of drug trials – decentralized clinical trials (DCTs) are trials in which activities are conducted in participants' homes and local settings, rather than at investigative sites, potentially improving accessibility and reducing the burden on participants.

However, they said that while EU laws do not prohibit at-home dispensing or administration of IMPs, previous research had found that national provisions on DtP IMP supply are often lacking and unharmonized, necessitating case-by-case decisions by national competent authorities and

ethics committees.

The authors believe that their findings could support the development of harmonized regulatory guidance and the implementation of DtP IMP supply approaches.

Discussions With Regulators & Ethics Committees

The latest study, published last month in the *British Journal of Clinical Pharmacology*, was conducted by researchers from Utrecht University, in the Netherlands.

It involved conducting interviews with staff at investigative sites and representatives from pharmaceutical companies and courier services between May and November 2021. The interviewees were asked about their experience with, or plans to implement, DtP IMP supply in the EU/European Economic Area before or during the COVID-19 pandemic.

Notably, the need to use DtP IMP supply approaches during the pandemic became necessary to keep the clinical trials running in face of social distancing and travel-related related restrictions.

"This research has shown that it is feasible to employ DtP IMP supply models in Europe," the researchers said, adding that their findings could be used by trial sponsors when "discussing these supply models with regulatory bodies and ethics committees." The models and associated definitions described in the study can also be used to identify best practices regarding DtP IMP supply.

Pros & Cons Of Different Models

The study identified three main DtP IMP supply models that were being used in Europe, all of which were associated with advantages and disadvantages (see table 1 below). The models all involved supplying trial participants with IMPs through one or more delivery modes, ie via courier, post, a health care professional or via collection at a local pharmacy.

For example, in a Phase II and III trial that investigated monoclonal antibody infusions in oncology patients in several European and North American countries, the IMP was shipped from the investigative sites to the patient's home via couriers, and patients were administered intravenous infusions at home by nurses. "For a patient residing near the site, the home nurse was given the possibility to collect the IMP before visiting the patient," the authors said.

While the investigative site-to-participant supply model was dubbed as "relatively easy to implement," it was linked with potentially increased burden for sites due to the logistics associated with shipping IMPs. The model may be facilitated with "easy-to-use interfaces and processes," according to the study.

As for shipment of IMPs from central locations, this was considered "most efficient" because

under this method only interactive response technology (IRT)-ordered IMP is dispensed (provided this can be accommodated by the central location) and no excess IMP is dispensed due to inflexibility in quantity contents. However, regulatory barriers related to maintaining participants' privacy and investigator oversight were identified for this model.

The use of local pharmacies was identified as "particularly suitable" for trials involving drugs with a marketing authorization. This is because under the new EU Clinical Trials Regulation low intervention trials investigating authorized IMPs following the terms of the marketing authorization are subject to less stringent rules regarding the labeling and traceability of the IMP. However, the need to train local pharmacists in good clinical practice was identified as a challenge for this model.

The study did not identify any instances of a sponsor-to-participant model (in which the IMP is shipped from a private company sponsor or distributor depot) in Europe, although some respondents during the interview talked about having implemented this model in trials conducted outside Europe. Challenges associated with this model involve privacy issues (ie, shielding personally identifiable data from trial sponsors) and the need for pharmacy controls required in the dispensing of the IMPs.

Model	Definition	Potential Pros	Potential Cons
Investigative site-to-participant	The IMP is shipped from the investigative site or site's pharmacy to the participant's home or other address.	Few regulatory barriers.	Increased burden for site staff.
Central pharmacy/pharmacy depot-to-participant	The IMP is shipped from a central (or remote) pharmacy depot with distribution facilities under the control of a pharmacist, and not the investigative site's pharmacy. In a multicenter clinical trial, one site's pharmacy could act as a	Reduced costs and IMP spillage. Enables direct-to-participant delivery of IMP with stringent stability requirements	Increased distance between site study staff/pharmacist and the participant. Not accepted by regulators in all EU countries.

	central pharmacy, shipping the IMP to the trial participants. This can also include cross-border shipments.		
Local pharmacy-to-participant	The IMP is picked up by the participant or legal authorized representative at, or shipped from, a local pharmacy. A local pharmacy is a community or hospital pharmacy that is not the investigative site's pharmacy.	Enabling low-intervention trials with authorized IMP.	Increased burden for local pharmacists (eg, training).
Sponsor-to-participant	The IMP is shipped from a private company sponsor depot, or a contracted manufacturing site, wholesaler depot or distributor location without the involvement of a pharmacist, to the participant.	No experience with this model in the EU.	No experience with this model in the EU.

Source: Trials@Home

The findings of the study are consistent with the December 2022 EU recommendation paper on DCTs, which includes an annex on the acceptability of various decentralized elements, including DtP IMP delivery, by EU member states. (Also see "*EU Aims To Drive Uptake In Decentralized Clinical Trials With Harmonized Guide*" - Pink Sheet, 15 Dec, 2022.)

According to this national overview, most EU countries allow for IMP delivery from the investigative site or pharmacy associated with the investigative site, the researchers said. "Several EU countries further allow for IMP delivery from any delegated pharmacy or dispensing by a local pharmacy, and only a few countries allow for delivery directly from the manufacturer or sponsor or are currently developing their respective regulatory framework."

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