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Direct-to-Patient Solutions: Technology to Help Improve Patient Recruitment and Retention

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Ongoing patient recruitment and retention challenges were intensified by the Covid-19 global pandemic. Adoption of alternative trial designs and technology solutions accelerated among clinical research professionals looking for ways to make it easier for patients to participate in clinical trials, regardless of their location. One alternative trial design is the Direct-to-Patient (DtP) strategy, where study drug is shipped directly to the patient, and technology solutions play a critical role in managing the supply chain and ensuring that, at the end of the lifecycle, there is full accountability.

What is a DtP trial design?

While a traditional clinical trial revolves around the patient traveling to the investigator site, DtP trials fit into a decentralized model. Decentralized trials are defined as trials "executed through telemedicine and mobile/local healthcare providers, using processes and technologies differing from the traditional clinical trial model." These decentralized trials may include investigational medicinal products (IMP) and clinical supplies shipped or delivered directly to the patient via couriers or mobile healthcare providers.

DtP shipping models include (see Figure 1):

1. Depot to patient, where the depot itself is recognized as and maintains a pharmacy license
2. Depot to central pharmacy to patient via a local or specialty courier
3. Depot to investigator site to patient via a local courier, specialty courier, or nurse (mobile healthcare provider)

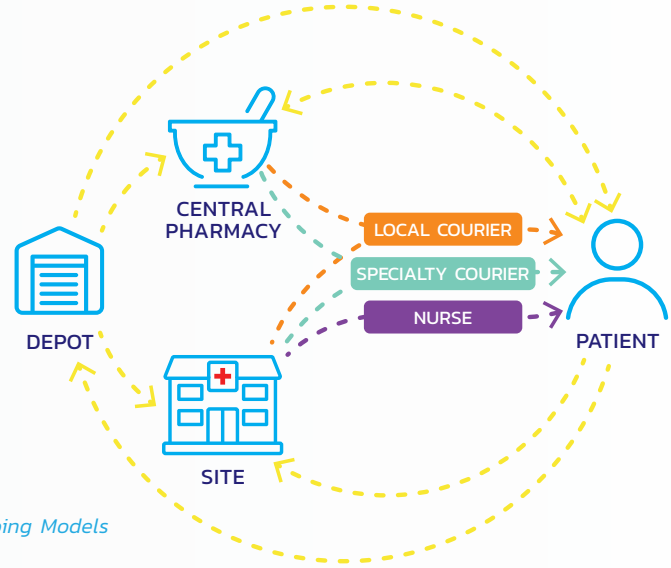

Figure 1:
DtP Shipping Models

Who benefits from a DtP trial?

A DtP trial makes participation easier for patients with geographic limitations, who do not live near major academic institutions or investigator sites, patients with work or care commitments, immobile or extremely sick patients, and those who simply cannot travel.

Sponsors benefit by reducing patient burden, thereby increasing access to a wider patient population, including rare disease and severely ill patient groups. Sponsors also benefit from improved patient retention, increases in operational efficiencies, reduction in wasted drug product, and faster completion times with more reliable results.

Complexities unique to DtP trials

IMP accountability and dispensing laws and regulations vary by region, countries, states, and according to the product's registration or legal status. During the height of the COVID-19 pandemic, the FDA, European Medicines Agency (EMA), and country-level regulatory agencies confirmed changes to the distribution of IMP (direct to patient) could be implemented if specific factors were considered to ensure accountability and product quality (i.e., that IMP storage conditions, as defined in the protocol, were maintained during shipping and that the IMP packaging was intact upon receipt). Regulatory agencies also provided recommendations for disposing of unused IMP in the absence of direct site involvement. Sponsors need to clearly outline in the protocol the procedures for shipping IMP to participants so that the process is clear to the investigator, any third-party providers, and applicable regulatory agencies.

Some therapeutic areas or indications may not be well suited for having IMP shipped to participants because of the route of administration (i.e., intravenously) or the drug has an unknown safety profile.

Not all drug products are well suited for DtP shipping—drugs that require special preparation like reconstitution of a lyophilized powder, thawing of an ultra-frozen drug product, or preparation of other concentrated drug product for weight-based dosing. In these examples, the drug may need to be prepared in a pharmacy setting before being administered to a patient.

Temperature management from sites to patients can pose challenges in some but not all instances. For example, if a patient receives drug product that has triggered a temperature excursion alarm, how can sponsors be sure that the patient did not use the drug in question, and how can a replacement shipment be sent in time? This can be solved with the introduction of a specialty courier whose staff are trained in the process for monitoring and reporting temperature excursions.

Reduced cost in wasted product may be offset by increased cost in specialty courier or in-home nursing.

DtP trials may involve managing more complex workflows and processes. If a site is shipping drug to a patient via local courier, the study team needs to consider if and how the status of the materials should be updated and tracked. Managing shipments DtP requires transferring and integrating data with depots, couriers, sites, pharmacies, and sponsors. Patient identifying information needs to be stored and used for shipping, so patient privacy must be maintained.

How can technology help manage the unique needs of DtP trials?

Interactive response technology (IRT) solutions must be flexible and robust enough to ensure that, at the end of the study, there is a clear history of when materials are moved from one status to another—allocated to the patient, returned (to site, pharmacy, or depot), ready for reconciliation, and reconciled. In addition, technology solutions must be able to support multiple direct-to-patient shipping models within a single study (see Figure 1).

A drug order management feature can allow the user to change the status of drug kits as the materials move through the workflow—from "Available at site" to "In transit to patient" or "Assigned to patient"—based on whether the drug was delivered via DtP or traditional methods. Other features to look for in an IRT technology solution:

- Dispense one time for multiple visits
- Ship to home health care
- Support hybrid remote and onsite visit schedules for individual patients
- Trigger shipments, either manually by sites or automatically, with the flexibility to do both within a study
- Provide electronic drug accountability when treatment is returned by the patient or marked lost
- Allow clinical research associate (CRA) to monitor and verify returns remotely or allow electronic verification without a CRA
- Allow any kit previously reconciled to be returned to the depot
- Provide a reconciliation reporting feature to make it easy to monitor compliance on a site level—automating a time-intensive process, eliminating the potential for manual data entry error
- Monitor lifecycle accountability to be always inspection ready

DtP clinical trials have made it easier for patients to participate in or continue to participate in clinical trials despite personal or global challenges. Patient randomization and IMP management in DtP trials can be complex and robust technology solutions can play a critical role in effectively managing accountability and product quality. Experienced technology solution providers have become experts at navigating the practical and logistical considerations related to alternative trial designs and implementing DtP trial strategies. Despite the challenges these types of trials may pose, working with the right vendor will help ensure the sponsor can derive the greatest benefits.

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[1] Clinical Trial Transformation Initiative (CTTI) Recommendations: Decentralized Clinical Trials, September2018, available at https://www.ctti-clinicaltrials.org/sites/www.ctti-clinicaltrials.org/files/dct_recommendations_final.pdf (accessed 28 April 2021)

[2] European Medicines Agency, Guidance on the Management of Clinical Trials During the COVID-19 (Coronavirus) Pandemic, 2 April 2021, https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf (accessed 28 April 2021).

[3] U.S. Food & Drug Administration, Guidance for Industry, Investigators, and Institutional Review Boards: Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency, March 2020, updated 27 Jan 2021, https://www.fda.gov/media/136238/download (accessed 28 April 2021)