# It's All in the Details

**Direct-to-patient shipments of clinical trial drugs help ensure participants can conveniently take part in trials. There are, however, many considerations to take into account when designing a decentralised or hybrid trial with this dispensation model**

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The COVID-19 pandemic has changed our habits in countless ways, and it's interesting to surmise which new practices will catch on and remain with us and which ones will fade away in time. It seems likely that in the long term, some innovations – such as telemedicine visits – will become routine. Other modified behaviours – such as using hand sanitiser after touching any public surface – might turn out to be temporary concessions with no staying power. What then, do we think will become of sending study drugs directly to patients participating in clinical trials?

The practice did solve an urgent need to get treatments to trial participants who could not visit investigator sites and thus allowed many trials to continue without interruption. But will the innovation of direct-to-patient (DtP) drug shipments be worth continuing? Or will it be of limited value in a post-pandemic world? If we decide that it's worth continuing, are we really prepared to pull it off in a business-as-usual setting? Shipping drugs to patients may sound like a 'slam dunk', but there's more to it than meets the eye.


Figure 1: Unique complications that should be considered when designing a DtP shipping strategy for clinical trials

### Improving Patient Centricity

DtP drug shipments in particular, and decentralised clinical trials (DCTs) more broadly, have many potential advantages over more traditional site-based trials that require patients to make visits to sites to receive the study drug. When travel to a site is not required, a broader base of patients may be able to participate in research, increasing the diversity of the study population. If patients see DtP shipment of treatments as a convenience, the option could increase the speed with which patients can be recruited into trials and the rate at which they remain participants. It could also make it easier for investigators to serve more patients.

### Will Everyone Welcome DtP Shipments?

On the other hand, there are potential downsides to shipping study treatments directly to patients, which is a major factor in enabling trials to be decentralised. What was necessary – and what people were willing to do – during a health crisis may not be indicative of what should or could continue under more business-as-usual conditions.

If investigators are responsible for distributing the study drug routinely (as was generally the case in the early days of the pandemic), the additional burden of having a logistics operation within their practice may be too much for investigators on a regular basis. At the

same time, patients may not necessarily welcome a decentralised approach that minimises, or even eliminates study visits. A survey conducted by James Lind Care in the UK and Denmark revealed that 24% of the patients who responded are concerned about missing face-to-face visits with specialised medical staff in DCTs (1).

**Special Considerations**

There are unique complications to consider as well (see **Figure 1**). These include:

- ***Safeguarding personally identifiable information:*** If third parties (such as couriers) are involved in drug distribution, controls must be put in place around their having personally identifiable information (PII). Organisations that hold patient data must understand the responsibilities that go along with that, by country – there is no overarching data privacy rule, and what is permissible in the US may not be elsewhere in the world. Note: organisations that are compliant with GMP may not be set up to legally hold PII, while those that are compliant with GCP may well be.
- ***Including justification in the protocol:*** The clinical trial protocol should explain how DtP shipment supports the patient's safety and treatment.
- ***Gaining informed consent:*** The informed consent form (ICF) should be updated to include patient information and an agreement to send shipments to the patient's home. It should also include additional data protection clauses, explaining how the data transfer to external parties will safeguard patient information.
- ***Involving and informing investigators:*** From a regulatory perspective, investigators are responsible for dispensing drugs to patients. (This would seem to be an area where regulations are lagging behind technology and market dynamics.) How will investigators be kept apprised of shipments to patients if they're sent directly from a depot? Is informing them sufficient to satisfy regulators?
- ***Contracting with specialised couriers:*** Whether drugs are shipped to patients from sites or from depots, the transport will need to be handled by a courier that has dedicated processes for DtP shipments, trained drivers assuring handover to patients, and the ability to keep patient data confidential.
- ***Acknowledging drug receipt:*** In a traditional trial, the investigator site must acknowledge receipt of drug shipments and confirm that they arrive in good condition. How can this be ensured at the patient level, or will that no longer be a requirement?
- ***Arranging for kit return:*** All kits, used, damaged, and unused must be returned to the site responsible for the drug accountability process, so patients will need to be given instructions on how to handle returns.

**Technology Support**

It is unlikely that sponsors will be able to adopt DtP shipments with all patients, sites, and geographic regions in a given study either because of logistical considerations, regulatory restrictions, site willingness, or patient preferences. Indeed, if patient centricity is the main driver for shipping drugs directly to study participants, then it stands to reason that sponsors must be prepared to cater to individual patient preferences. If sponsors are not willing to do so, is this whole process really to the patient's benefit or is it really to the benefit of sponsors and those seeking a commercial opportunity?

In turn, the interactive response technology (IRT) system that is supporting the trial must be flexible enough to accommodate studies that take a hybrid approach to drug delivery, supporting the traditional process as well as DtP shipping. They must have the ability to take either approach, patient by patient. This clearly will affect the requirements gathering and the system build process, as it changes the dynamics of how orders are fulfilled. Will orders be sent to a depot and then to a site, to a depot and then to a patient, or to a depot to a site and then to a patient – or some as yet determined combination of the above? The IRT system has to be programmed to utilise the appropriate drug inventory based on the methodology to be used, and as discussed that could potentially be country, site, or even possibly patient specific.

**On-Site Drug Dispensing**

In traditional, site-based trials, investigators typically have a certain amount of buffer stock on hand, and the IRT uses algorithms to manage the investigational medicinal product (IMP). Based on the algorithm, the IRT generates an order to the depot, the depot distributes the IMP to investigator, and the investigator confirms receipt. The investigator then uses the IRT to assign or allocate the IMP to the patient, and if the patient is dosed in the clinic, the clinic manages the destruction/return process based on the sponsor agreement.

**Site-to-Patient Shipments**

The process is exactly the same in this scenario, up through the point at which the IRT system assigns/allocates the IMP to the patient. At that point, the investigator orchestrates with a third-party courier to deliver the IMP to the patient. In this scenario, there is a need for a second confirmation – that of the courier's delivery to the patient. Following treatment, the patient must return the IMP kit, creating the need for coordination and an entirely different pathway that we have not imagined here. This type of approach requires additional hand offs and the development of data pathways that are not standard in a typical model.

**Depot-to-Patient Shipments**

Depot-to-patient shipments are more complex to set up in a way that keeps the investigator in the loop.

This DtP process assumes that the site has very little buffer stock; it is reserved for true emergencies. The IRT generates the order to the depot for a particular patient at a particular visit, and the depot works with a third-party courier to arrange shipment to the patient. The courier confirms delivery of the shipment and that it is in good condition. The courier does this either through electronic means or by acting as a third-party user of the IRT system. Alternatively, the courier can inform the investigator who confirms the shipment in the IRT, or the patient could confirm receipt of the shipment through a patient-facing technology (not a current IRT construct), and those data are transferred to the IRT system. As in the above scenario, the patient must return the IMP.

**Asking the Right Questions**

Before embarking on a strategy of DtP drug shipments, and by extension some form of DCTs, sponsors should take the time to ask a number of key questions:

- Does this indication lend itself to this approach? Can the related evaluations be done without the patient going to the site?
- Are investigators in a position to support this?
- Will the target patient population welcome this?
- Is a hybrid solution necessary (by region, site, or even within a site)?
- Are we willing and able to adopt an approach that's customised by country, site, and patient?
- How would shipment failures be handled? (Think porch bandits)
- What is permissible in each geography?
- Do we need to enlist the help of a third-party provider, or can we do this ourselves? How must we change our contracts, master service agreements, etc.?

The pandemic has changed industry practices in many ways that may prove to be lasting and in others that may be only fleeting. It's too soon to tell if accommodating DtP shipments will become the former or the latter. But it's clear that sending drugs directly to patients as the usual course of business is not as simple as it may sound. Sponsors are well advised to undertake a formal evaluation process and to confer with other stakeholders before proceeding with the practice. They should carefully weigh the pros and cons on a study-by-study basis and review the IRT functionality that would be required to support a hybrid approach – down to the patient level.

*Reference*

1. *Visit: jameslindcare.com/wp-content/uploads/2021/04/The-Patients-Perspective-on-Decentralized-Trials-2.pdf*

**Craig Mooney**, Vice President, Scientific eTech-Enabled Services, at **Calyx** has nearly 30 years' experience in the clinical development industry, with concentrated focus on optimising IRT to improve clinical trial efficiencies. Craig brings a unique understanding of IRT from both a delivery and user perspective, having served as the Director of IRT at Bristol-Myers Squibb for most of the past decade and having held roles in clinical operations, IMP packaging, and labelling and logistics. He is considered an industry expert and has been a featured speaker at numerous IRT conferences, including positions as Conference Chairman.