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World Courier

Delivering DtP trial success: Does central dispensing hold the key?

Five steps to deliver an effective central dispensing program to put your DtP trial on the right track

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Introduction

A decentralized trial (DCT) is an alternative approach to clinical trials that sees patients treated remotely — in their own homes, at their local clinics, or elsewhere in their own communities — instead of on a clinical research site.

They offer considerable benefits for both patients and trial sponsors compared with traditional trials by:

01 Reducing travel and inconvenience for patients, helping to boost enrollment and adherence

02 Expanding geographic and demographic reach for trial sponsors, giving more patients access to new medical treatments

03 Allowing continuous treatments and diagnostics, enhancing the quality and quantity of the data received

During the COVID-19 pandemic, DCTs became increasingly important as a way to continue or start clinical trials, mitigating against social distancing requirements and the reluctance of patients to risk visiting hospitals to allow clinical trial participation.

Direct-to-patient (DtP) and direct-from-patient (DfP) transport services are key to an effective DCT. DtP is the delivery of medication, including investigational medicinal products (IMP) and ancillaries, to a patient. Meanwhile, DfP is the collection of biological samples and unused IMP or supplies from the patient in clinical trials.

However, direct-to-and-from-patient (DxP) delivery does pose obstacles that must be addressed to minimize any negative impact on the success of a DCT. The DxP logistics model relies on multiple-site pharmacy-to-patient deliveries to get the drug product being trialed to patients and to get any patient samples back to trial sites or laboratories. This can be hindered by a lack of storage and outbound shipping capabilities at the clinical sites, as well as shortages of clinical trial materials which manufacturing is in the process of scaling up. There may also be lack of capacity at the clinical sites to organize the logistics in terms of shipment order management, temperature monitoring, and documentation. Furthermore, more advanced medicinal products are entering clinical research with special storage and temperature requirements which cannot be offered by a majority of clinical sites.

Introduction

Central dispensing from a regional pharmacy or depot has emerged as an answer to the questions asked of some DtP models.

Delivered via DtP pharmacy services, it has the potential to address existing DtP challenges, allowing central storage, dispensing, and transport of IMP/approved drugs to and from patient homes.

But how can this central dispensing be delivered effectively? What are the roadblocks to implementing an effective central dispensing model, and how can they be navigated?

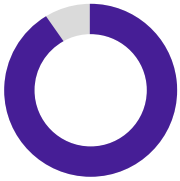
In this whitepaper, we will address these questions and explore the key steps to ensuring successful implementation of a central dispensing model.

We will explain what trial sponsors should look for in a logistics partner to ensure the success of their central dispensing supply chain.

We will explore:

- The role of DtP in maximizing the benefits of decentralized trial models
- The complexities of implementing DtP effectively through central dispensing
- Five steps to building an effective central dispensing model
- How expert logistics partners can help

Section 1: The role of DtP services in maximizing the benefits of decentralized trial models



94%

Recent studies suggest that 94 percent of patients do not have access to clinical trials, and one in four patients drop out before study completion[1].

The use of DCTs by product sponsors has been growing worldwide in recent years as a means of improving patient centricity, boosting enrollment, and retention in turn. At present, 37 percent of investigator sites under-enroll, while 15 percent fail to recruit a single subject, with negative consequences for the trial and the smooth passage of a new treatment on its development journey[2].

By moving trials into patients' homes or their local communities, often with the support of homecare professionals trained for the clinical trial, DCTs have the potential to address this issue and offer a host of other key benefits:

Faster than traditional approaches

On average, clinical trials (most of which use traditional models) over-run by 30 percent. Some 58 percent[3] of respondents to a recent study by the Medical Research Network (MRN) believe that, based on their own experiences, DCTs are faster than traditional designs, with trials completing between one and 12 months earlier than other models[4].

Better for patient recruitment

Some 71 percent of respondents to the MRN study feel they make it easier to find participants and expand the geographical reach of the trial, while 74 percent say they enhance retention rates[5]. Respondents say they would expect to recruit 36 percent more patients to a DCT compared with a traditional approach and retain 41 percent more patients[6].

Better for patients

80 percent of respondents to the MRN study say they save patients' time, minimizing disruption to their day[7]. Some 72 percent feel that the reduced travel requirements minimize the burden of the trial on participants and their caregivers[8].

Section 1: The role of DtP services in maximizing the benefits of decentralized trial models

To help facilitate DCTs, DtP and DfP logistics is crucial.

Nevertheless, given that the central benefit of a DCT is its ability to expand geographical reach for clinical trial sponsors and boost enrollment, such trial models require specialist logistics services. They require materials to be shipped to patients – either to their homes, to their doctors' surgeries, or to their local pharmacy or hospital.

In addition to being used for clinical trials, DxP services can transport commercial or early-access treatments to patients, and even in compassionate-use scenarios, such as with life-saving gene therapies.

A Vietnamese clinical trial patient living in a rural area with an urgent need for continuous treatment was unable to pick up their next dose from the clinical trial site in Hanoi.

The therapy required being maintained at a consistent temperature, however, there was no temperature-controlled packaging and data logger available at present in the country.

Harnessing our unique global network of local logistics and regulatory experts, World Courier provided a DtP service that successfully supported the sponsor to ensure the therapy was delivered to the patient on time and in good condition. To achieve this goal, we:

01 Sent a preconditioned shipper, including a logger, across borders from a World Courier office in a neighboring country to the clinical site in Hanoi within one day

02 Transported the therapy in a Global Thermal Container (GTC), chosen for its ability to keep the contents at a consistent temperature for up to 96 hours, whatever the external conditions

03 Included a data logger inside the container to provide monitoring of the temperature of the therapy throughout its journey

04 Collected the therapy at the clinical site in Hanoi and successfully delivered to the patient's home within the treatment window at the right temperature and documentation for the investigator and sponsor

05 Ensured the patient's continuous treatment and prevented drop-out from the clinical study

The value of DtP and DfP

Both DtP and DfP logistics services offer significant benefits across the entire supply chain, which contribute considerably to the success of any DCT:

- **Value for patients** - DxP services reduce the need for site visits, enhancing convenience and reducing travel and associated costs. They also enable patients with disabilities and other health issues to participate in trials. According to the International Society for Pharmaceutical Engineering, 78 percent of patients would find it helpful for treatments to be delivered to their home[9].
- **Value for clinical trial sponsors** - DxP services reduce the need to find and establish sites near each of their trial participants, as the medication is delivered either to the patient's home or to their nearest clinic or hospital. They also reduce the storage burden, enhancing convenience for sponsors.

Section 1: The role of DtP services in maximizing the benefits of decentralized trial models

The rise of DtP and DfP services

While DtP and DfP services have been available for some years now, demand from the pharmaceutical industry has significantly increased in recent years.

Among the principal drivers for these changes is the COVID-19 pandemic. Stay-at-home orders were issued in many countries around the world in a bid to limit infection rates by reducing social contact. This meant that many traditional clinical trials had to be put on hold, forcing product sponsors across the globe to rethink their clinical trial models. For many, the answer was the DCT approach, supported by DxP logistics, which enabled drug developers to continue clinical trials while participants were unable to visit investigator sites.

Pre-COVID-19, approximately five percent of product sponsors were using DtP services. By May 2020, World Courier saw a fivefold increase in volumes for shipments to support DCTs compared to pre-COVID levels, and by December 2020, volumes remained some three times higher than before the outbreak. A survey of trial sponsors found that 73 percent of industry respondents said COVID-19 had increased their use of decentralized trials[10].

Section 1: The role of DtP services in maximizing the benefits of decentralized trial models

It is unclear whether the current growth rate for DCTs is sustainable now that more and more countries are entering a "post-COVID-19" era, re-opening their economies. Nevertheless, the evident advantages mean that we can expect this approach to continue to draw clinical trial sponsors in the future.

As a consequence, we can expect ongoing demand for supporting DtP and DfP logistics into the future, as a crucial means of ensuring the success of any DCT.

85 percent of respondents to a Pharma Intelligence survey said they would increase their use of DtP in the next two years[11]. Research by World Courier into our own customers' thoughts found that, of the 46 percent of respondents that had begun using DtP services to support DCTs, 52 percent said they would continue with a DtP model until restrictions were lifted, and 24 percent said they would continue to use the approach afterwards[12].

Section 2: Overcoming DtP complexities with central dispensing

To implement an effective DtP and DfP service for a DCT, several factors must be taken into consideration by a product sponsor and its trial partners.

This is particularly the case when the trial is for a large international study, in an environment with a complex and evolving regulatory framework.

01 **Effective and transparent inventory management**

Any treatment inventory must be controlled effectively, and appropriate procedures need to be in place for temperature monitoring and reporting throughout the treatment's journey to the patient. Product sponsors require visibility across the supply chain so that they can be confident that there have been no meaningful temperature excursions or similar issues that could impact product quality. This can be a challenge for DtP logistics, due to the number of sites involved in the journey to and from the patient.

02 **Reconciling cost-efficiency and product integrity**

To be effective, a DxP service must be able to find cost–efficient ways to deliver treatments directly to patients, and to collect returns all while ensuring product integrity. This is complicated by the multiple site deliveries inherent to the DtP model. A lack of appropriate storage or outbound shipping capabilities can cause complications, particularly if the treatment requires consistent temperature control.

03 **Ensuring compliance**

Regulatory compliance is always paramount, regardless of the trial model or logistics service used. However, when undertaking an international DCT in particular, compliance can be more complex than with more traditional models. The treatment and returns may have to pass through multiple countries, each with unique customs and regulatory requirements. To be effective, a DtP service must be able to navigate multiple regimen with minimal delay or cost. A growing number of countries, in recognition of the increase in use of both DCT and DxP during the COVID-19 pandemic, are updating their regulatory requirements to accommodate both, with specific guidance available in many key markets. For example, the U.S. Food and Drug Administration (FDA) announced this year that it believes DCTs are here to stay and is working on guidance for clinical trial sponsors to ensure compliance in future[13]. A working group of the European Medicines Agency (EMA) published a guidance paper for DCTs in December 2022, which contains recommendations for DTP and DFP, including dispensing models with an overview of related regulations in each member state[14]. This overview shows clearly that some countries still do not regulate DtP or DfP services, with ramifications for the geographical reach of a DCT.

Section 2: Overcoming DtP complexities with central dispensing

04 Establishing effective global procedures

End-to-end patient-centric home logistics services require an effective and global standard operating procedure (SOP) to ensure compliance and consistency of setup and execution to maintain reliable quality at every stage for the clinical trial sponsor. These procedures need to include dedicated resourcing inclusive of local expertise, as well as highly-trained customer service, operations, and driver staff, in order to achieve a standardized, flexible, innovative, and continuously improving service. This can be difficult across a global transport network.

05 Ensuring patient confidentiality

Patient confidentiality is the cornerstone of ethical healthcare and is a requirement for compliance with good clinical practice (GCP), national privacy laws, such as the US Health Insurance Portability and Accountability Act (HIPAA) or the EU's General Data Protection Regulation (GDPR). Knowledge of all local patient privacy requirements and your partners' ability to suitably support their adherence are of paramount importance within DtP.

For those considering DtP, confidentiality is a very real and understandable concern. It is vital to ensure accurate collaboration between the dispensing site and logistics provider — respecting patient confidentiality while delivering the correct medication to the correct patient — using only the common metrics of anonymous patient ID numbers.

Section 2: Overcoming DtP complexities with central dispensing

Overcoming implementation issues with central dispensing.

It is clear that DtP and DfP services encounter issues that must be overcome in order to deliver an effective and cost-efficient logistics solution capable of supporting the success of a DCT.

One solution that is growing in popularity as a means of addressing the complexities of both DtP and DfP is known as "central dispensing".

Central dispensing simply entails transporting clinical trial materials to a central pharmacy or clinical trial depot in relatively close proximity to the home of trial participants, instead of the use of dedicated storage facilities at the clinical trial site. From the pharmacy or depot, doses can be shipped out to patients according to the dispensing schedule in the clinical trial protocol. Returns can be shipped to the pharmacy or depot for drug accountability and reconciliation instead of being transported back to the clinical trial site.

Depending on the size of the trial or the number of participants, there may be one central dispensing pharmacy or depot per country, or multiple to make it as easy as possible for treatments to reach patients.

There are multiple benefits to this approach:

- No or reduced need to identify or build specialist storage facilities in clinical trial sites
- Minimized IMP coverage per study by reducing storage places
- Reduction in time the treatment is stored outside of a good manufacturing practice (GMP) and good distribution practice (GDP) licensed facility
- Reduction of shipments and risk of temperature excursions or delays
- Existing local logistics management capability
- Well-established patient data privacy expertise

This approach, supported by specialist transport and IT infrastructure, can overcome many of the complexities posed by the DxP logistics model, helping to provide the efficient yet cost-effective transport network that is vital for the success of any DCT.

Section 3: Five steps to building an effective central dispensing model

An effective central dispensing model requires expert planning and preparation.

Here are the five key steps that we believe are vital to delivering a central dispensing model capable of supporting a large, international DCT:

01 **Where possible, establish depots in key countries**

Key to the success of any central dispensing model is the establishment of a central depot in the region of trial participants that treatments can be shipped to and from which they can then be easily transported directly to the patients or alternatively to patients' local pharmacies. These depots are specialized in storage, distribution, and returns of clinical trial materials with the respective GMP licenses and are familiar with GCP processes, clinical trial inventory, and randomization systems and documentation.

Depots can be complex to set up, not simply due to the need for specialist storage infrastructure, but due to the requirement for licenses in line with local clinical trial, medicinal product, and pharmacy regulations. For example, in some regions such as the U.S. or the UK, a depot can act as a central clinical site pharmacy when they have a pharmacist available with the required licenses. Logistics partners, like World Courier, have existing depot facilities and relevant licenses in major markets — working with them can help streamline the time taken to set up the required transport network for any trial. They also have the expertise to establish new depots in specific markets to support larger international trials and expand their licenses for DCT logistics when local regulations provide the right framework. World Courier has a central dispensing agreement with a U.S. pharmacy enabling direct-to-patient delivery and is applying for licenses in Australia to further expand its DxP and central dispensing services. Another member of Cencora's companies, Alcura UK, has recently received the license to dispense and ship clinical trial medication to patients in the UK in addition to their prescription drug home delivery services.

Section 3: Five steps to building an effective central dispensing model

02 Identify and set up partnerships with strategically located pharmacies

In addition to central depots, central dispensing models can depend on the use of pharmacies based in the same market as the patients receiving the treatment to provide clinical trial protocol-compliant storage and documentation ahead of final shipment to patients. Central pharmacies already have experience managing inventory, maintaining appropriate storage facilities, and completing the correct documentation. Working with them shifts the storage/distribution burden away from clinical trial sites so they can focus on patients.

World Courier is establishing partnerships with central dispensing pharmacies strategically located in the U.S. and Europe and is constantly working to build new relationships with those in other key markets. We have created a global network that allows us to provide consistent and reliable dispensing and transport of treatments to and from patient homes.

03 Seek the support of local regulatory experts

When transporting treatments across international borders, it is vital to ensure compliance with relevant local legislation, as well as customs requirements. It is also imperative to adhere to local data privacy laws to safeguard patient data. With large international trials, this can quickly become highly complex, as it is necessary to navigate multiple regimes simultaneously.

With this in mind, it is important to work with experts in the changing local regulatory environment to ensure a smooth transit for the treatment, and to maintain the highest standards of privacy for patients. The earlier a clinical trial sponsor begins building a team with regulatory expertise of all the key markets involved, the sooner it can embark on the DCT.

Section 3: Five steps to building an effective central dispensing model

Automation can be a vital means of minimizing risk during the transit of a treatment.

04 Harness solutions to automate processes

Not only can it help prevent temperature excursions, but it can also help optimize the accuracy of any customs forms or other documentation that needs to be completed to streamline the transport process. As such, it is important to seek out and harness any new technologies that have the potential to minimize manual intervention in the transport process.

World Courier is integrating interactive response technology (IRT) into its DtP services and partnering with DCT system providers as well. Our IRT system integration will be able to streamline several core processes, including:

- Ordering DtP and DfP shipments automatically by the IRT system instead of communication of the order by email, booking system, or phone call
- Transfer of all relevant information between IRT and transport management system systems
- Provision of confidential patient information through a validated, secure channel
- Availability of shipment data including temperature data after delivery
- Digital documentation of shipment data
- GCP compliant oversight of the investigator of all IMP dispensing activities

All of this can help minimize risk and inefficiency in the DtP process to deliver treatments faster and more securely than ever before.

05 Work with a single global logistics partner

It can be daunting for clinical trial sponsors to build their own network for central dispensing for the first time. However, they can streamline the process and help minimize the risk of unforeseen issues impacting the success of their DCT if they work with logistics partners to deliver the service on their behalf.

Logistics partners will have the infrastructure and local partnerships in place to ensure timely and controlled delivery of the treatment to the patient. Working with an experienced global partner that has expertise and presence in multiple markets across the world such as World Courier, process can be further streamlined. Working with a single team can minimize complexity, streamline documentation, and reduce duplication of effort, thus eliminating the risks associated with handing treatments and supporting documentation from one partner to another.

Conclusion: The right logistics partner can help

Early collaboration with a logistics partner is essential.

There are areas of complexity with central dispensing that must be addressed to ensure it can play its role in achieving the kind of effective DxP logistics model that is essential to the success of a DCT.

However, working with an expert logistics partner capable of fully integrating with your team can help successfully plan and deliver successful central dispensing solutions that help deliver a more patient-centric yet cost-effective DCT. A partner that has global reach and experience can also help ensure an international study has the international support it needs to achieve success.

Early collaboration with a logistics partner is essential. By contributing its transit expertise at the protocol development stage, a logistics provider can enhance efficiency, as well as identify and circumvent risk, helping to optimize the performance of the central dispensing model. It also gives the partner more time to devise and launch potential packaging or routing innovations to address product/trial-specific issues.

Even if a clinical trial sponsor does not wish to commit to full central dispensing for its trial, using the components of a successful model can deliver key advantages.

At World Courier, we have the global scale to meet any clinical trial sponsor's central dispensing needs, as well as being agile enough to respond quickly when change is required. We also have extensive experience providing DxP logistics and storage solutions for DCTs around the world. As a result, we have the capability to support any clinical trial sponsor in delivering a successful decentralized trial.

We provide the end-to-end support you need to deliver an effective and successful central dispensing model for your DtP trial. Contact us to find out more about how we can help you.

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