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Water Cooler Chat

Switching to Direct-to-Patient Rapidly in the EU

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YOUR BRIDGE BETWEEN LIFE-CHANGING THERAPIES AND PATIENTS

PCI Clinical Trial Services hosts a weekly virtual ***Water Cooler Chat*** series, where our subject matter experts host informal discussions around a number of clinical supply hot topics.

Switching to Direct-to-Patient Rapidly in the EU

Gavin Morgan, PCI's Senior Manager of Global Logistics discusses logistical risk management factors to consider when deciding to switch to direct-to-patient shipments in the EU.

In response to COVID-19, clinical trial sponsors are looking to site-to-patient transfers as a viable method to deliver medicines to patients and keep their trials on track. In April 2020, the European Medicines Agency (EMA) published guidelines allowing sponsor companies to use site-to-patient transfers as an alternate supply delivery method, without having to get an approval for this deviation from the original clinical protocol. This article will explore the logistical considerations of this including:

- Maintenance of patient confidentiality in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and General Data Protection Regulation (GDPR) in the United States and Europe respectively
- Temperature deviation management
- Execution of contactless deliveries
- Trans-border / International site-to-patient deliveries

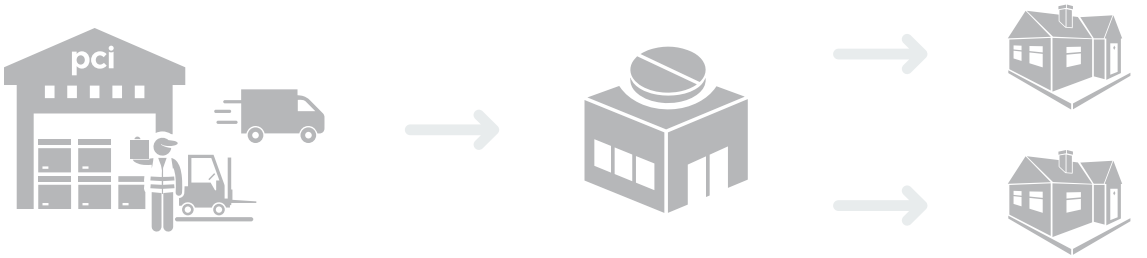
What is the difference between a full Direct-to-Patient (DTP) protocol versus the site-to-patient transfers?

From a logistical and regulatory perspective, there is a clear difference between a full DTP protocol and a site-to-patient transfer. A full DTP protocol already has the regulatory submissions in place, the entire protocol is designed to bypass the standard investigator site and utilize a central pharmacy to dispense the medication directly to a patient's home. A site-to-patient transfer occurs when a clinical trial protocol is initially set up for the investigator site to handle the dispensing but requires a temporary change to site-to-patient transfer due to unforeseen circumstances. This includes where an enrolled patient is unable to visit the investigator site as expected (such as during the COVID-19 pandemic).

In such extenuating circumstances, implementing site-to patient transfer does not require a protocol design alteration, and a substantial amendment is not currently required.

PLEASE NOTE: As guidelines do change, please do check with your local regulatory authority group to confirm before implementing any change to your protocol.

DIRECT-TO-PATIENT PROTOCOL



CMO | Depot / Central Pharmacy | Patient Homes

SITE-TO-PATIENT TRANSFER

CMO | Investigator Sites | Patient Homes

Is it possible to bypass an investigator site altogether and deliver directly to a patient from a CMO or in-country depot?

Typically, this would not be possible because the CMO or in-country depot is not licensed as a dispensing site. However, during the height of the pandemic in April 2020, the European Medicines Agency (EMA) released guidance regarding the distribution of Investigational Medicinal Product (IMP), outlining that in-country depots can ship directly to the patient's home, as long as the following are in place[1]:

- A completed risk assessment, including whether the IMP is appropriate for self-administration, how the products stability will be maintained in transit and how the safe custody of product will be maintained
- A robust process is defined to ensure all GDPR requirements are met and adhered to.

1 *Please have your regulatory group confirm this before proceeding with Direct-To-Patient shipments as an alternate protocol to your clinical trial.*

FOLLOW GDPR

Regardless of how you have material delivered directly to your patient's homes, it is imperative to have a strict patient confidentiality process in place with all parties involved in the supply chain.

How is patient confidentiality maintained throughout the site-to-patient transfer process?

To maintain confidentiality throughout the process, the courier is the only party with access to the patient's information, this is given to them directly by the investigator site. Further, the use of a specific "DTP" account with the courier will also ensure the "Proof of delivery" remains blinded.

How is temperature control handled and what happens if a temperature excursion occurs?

It is the sponsor's responsibility to conduct a risk assessment to determine whether or not a DTP delivery will require temperature controlled shipping and monitoring. If the patient is only 30 minutes away and the product has great stability data, the sponsor may decide to send the material temperature controlled, but without a temperature monitor. For DTP shipments containing a temperature monitor, the courier will review the temperature data before leaving the package for the patient. If a temperature excursion has occurred, the courier will report it, along with the full downloaded data, to the investigator site and the clinical services provider. However, it is important to have project specific instructions in place to instruct the courier to return the shipment to the investigator site and not leave with the patient while the product disposition is determined. Further, it is vital that the initial risk assessment and process mapping includes clear instructions for the patient to await authorisation before taking the medication.

False temperature excursions are possible due to how the material was packed – for material packed by the investigator site or pharmacy, the temperature monitor is started by the courier prior to the site/pharmacy obtaining the preconditioned shipping system. Regardless of the cause of the temperature excursion, the material disposition will need to be determined by the sponsor company as the courier will not authorize the patient to administer the medication. As mentioned above, building this into the process through a communication plan is recommended to ensure everybody involved is aware of what the roles and responsibilities are and who is going to be given what information.

CONTACTLESS DELIVERIES

Ensure the courier responsible for delivering your DTP transfers have a robust contactless delivery process in place to follow the current social distancing requirements.

How do contactless deliveries work?

Due to the COVID-19 pandemic, DTP transfers are increasingly complex, with the addition of social distancing and the need for contactless deliveries. Most couriers have robust systems in place for contactless deliveries, involving the following:

- Not entering the patient's home
- Arriving at the patient's home at the agreed time
- Letting the person know they have arrived and leaving the shipping system on the doorstep
- Stepping back to ensure they are 2 meters away
- Not requiring the delivery note to be signed for proof of delivery, just asking for the name of the person accepting the shipment

Will the courier go into the investigator sites to collect a specific kit number?

No, the courier will not be requesting a specific kit number. It is the investigator site who will dispense the medication just as they would if the patient went to the site for their visit. The courier will arrive at the investigator site with a preconditioned shipping system, where the investigator or

pharmacy staff will package the medication into the shipping system.

What if the patient is not located within the country where the actual clinical trial is taking place, how can you ensure the medication reaches them?

There are a couple of solutions that can be employed to effectively deliver medication to a patient who may have moved out of the country where the clinical trial is taking place.

1. Hand Carry – The courier collects the material from the investigator site and takes it on a flight, as their hand luggage, to the destination to deliver it to the patient. In this case, a customs invoice is not required because it is not going through cargo, but you would require the following documents to accompany the shipment:

- The doctor's prescription from the investigator
- A document from the Medical Board of the investigator site's country
- A document from the Ministry of Health from the patient's country authorizing the courier to carry the product through customs.

NOTE: Temperature control is not possible where a hand carry option is utilised.

2. Ship by air – At the time of clearance, once the material arrives at the destination country, a CRO or 3rd party depot can assist with the customs clearance and the courier will then deliver directly to the patient. In this case, you would need the following to accompany the shipment:

- Customs paperwork (Proforma Invoice)
- Documents from the dispensing doctor
- A letter from the sponsor detailing why it is being shipped to this country

How are site-to-patient returns handled?

In order to ensure used and unused IMP is reconciled as per the study design, all supplies must be returned from the patient to the investigator site prior to destruction or being returned to a clinical services provider for receipt and destruction.

To ensure none of the confidentiality agreements are breeched, the investigator site should liaise directly with the courier when arranging the drug collection.

What are the cost implications of DTP transfers?

The cost of a DTP protocol is higher because you are utilizing specialist couriers to make individual patient deliveries. During the COVID-19 pandemic, the potential cost increase is higher as you could be conducting 20+ DTP shipments. To mitigate the increase in cost, you could evaluate the following:

- How many times will DTP be needed?
- How many times will it require temperature control?
- Can you utilize one driver to do multiple deliveries?
- Will there be a temperature monitor download needed?

About Gavin Morgan, Senior Manager, Global Logistics - Clinical Services, PCI Pharma Services

Since 2009, Gavin has been leading the clinical distribution team at PCI's Bridgend facility. His main responsibilities include the overseeing of all activities associated with UK imports along with supporting the full supply chain of clinical trial supplies including the selection and management of 3rd party couriers and depots. Gavin has over 20 years of experience within the clinical trial industry, with a focus on the distribution of clinical materials globally.

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