WHITE PAPER

Direct to Patient Models

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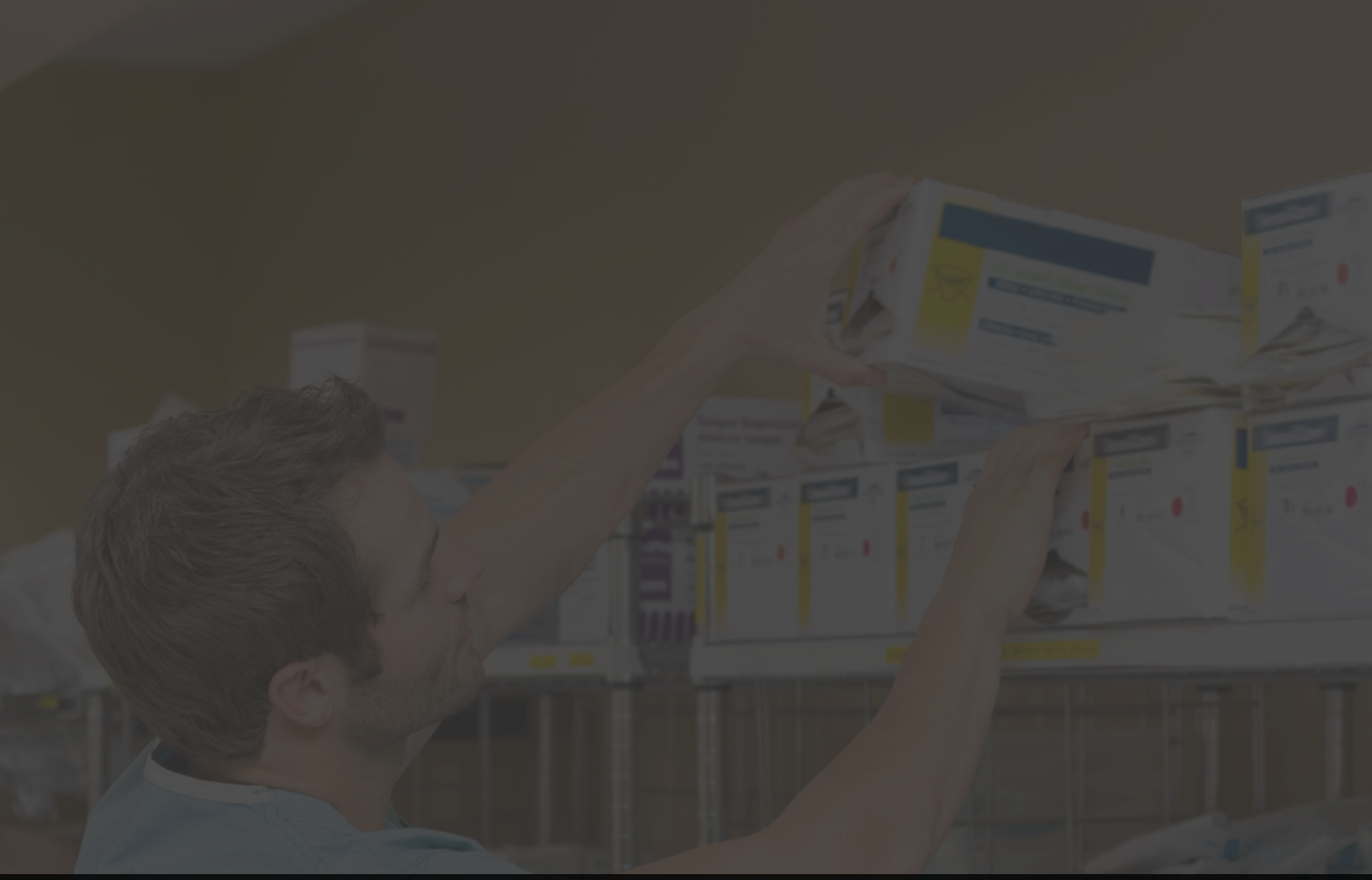

INTRODUCTION

Since the advent of centralized randomization and trial supply systems in the late 1990's, IRT has been at the heart of clinical supply management across countless trials in all regions of the globe. Clinical Research is continuously pushing boundaries and pioneering new models to better provide hope for patients everywhere who are volunteering their time, bodies, and health to advance medical science. The introduction of decentralized trial design, with a "Direct to Patient" DTP component, for the first time ever, brings supply chain directly into the realm of patient experience.

Traditionally, the clinical supply chain's goal has been to ensure that supplies are available for use at clinical trial sites and buffered with levels that account for normal trial variances. However, modern trial designs are changing the requirements for clinical supply chains. The goal of this whitepaper is to explain direct-to-patient models and how to assess pro's and con's for each.

APPLICATION OF THESE CONCEPTS IS SUPPORTED BY A REVIEW OF A DTP STUDY LAUNCHED BY SIGNANT HEALTH IN PARTNERSHIP WITH A STRATEGIC PARTNER IN MID-2020.

DIRECT TO PATIENT MODELS

In a hybrid trial design, where some visits are done in clinic and some at home, there are two general models that can be applied. These are as Depot to Site to Patient, or Depot to Patient

1 DEPOT TO SITE TO PATIENT

- In this instance, traditional IRT algorithms are largely unaffected by this design. However, extended expiry windows must be considered to account for logistical lead times ahead of patients physically receiving the medication.
- Patients are allocated the investigational product directly from site inventory. This is normally done with a standard "study visit" or similar transactions in IRT.
- Finally, last mile delivery logistics are handled by the site or local pharmacy. This may include local courier services, home health services or direct site personnel facilitating delivery.

2 DEPOT TO PATIENT

- Depot to patient models facilitate direct delivery to a patient of medication from a central (non-site based) warehouse. This may be the same depot which supplies sites, or in many cases, a specialized central pharmacy which is able to handle the logistics of patient delivery, as specified by the IRT.
- For hybrid trial designs, care must be taken to adjust traditional predictive algorithms to ensure that sites do not become overstocked with inventory. This is because only a subset of overall inventory demand will pull from local site inventories.
- A benefit of concentrating inventory into a centralized depot is increased visibility and control of supplies. Less buffer will be sitting as sites, reducing overall wastage.
- Companies must adhere to local regulations in this model. In addition, there is generally a level of prescriptive authority that must be provided from a study physician before material can be shipped directly to a trial participant.

DESIGN CONSIDERATIONS: WHICH MODEL IS RIGHT FOR YOUR TRIAL?

Unfortunately, there is no one size fits all solution to support a Direct to Patient model. Instead, there are a number of variables to be considered, and with the right technology backbone, the solution can be tailored to fit the specific needs of the study.

SOME VARIABLES:

- Will patients be fully remote, or will visits be a combination of in-clinic / remote?
    - Will this occur on a fixed schedule or at the investigators discretion?
- What is the administration route for study medication?
    - Is specialized training required to be able to safely handle/administer medication?
- Will there be home healthcare services involved to support patients? How often will they visit?
- What is the stability profile of the product? Can it be safely stored outside of pharmacy?
- Do certain temperature profiles need to be adhered to for the product?
- Are there patient technologies involved that can assist with training or adherence monitoring, enabling remote compliance monitoring?
- How will accountability and reconciliation occur?

HOW SIGNANT IRT CAN SUPPORT DIRECT TO PATIENT

With Direct to Patient models, not every IRT provider is capable of applying the level of flexibility required. This is because DTP design elements were not traditionally included in standard IRT models. Signant Health offers a configurable and customizable IRT platform with industry leading delivery processes and extensive integration capabilities which enables it to pivot and support a wide variety of DTP models:

- Advanced Inventory Management Capabilities for All Supplies and Packaging Models
- Innovative Resupply Algorithms
- Extensive Integration Capabilities with Distribution Networks
- Flexible Roles
- Advanced Returns Management Solutions

BACKGROUND ON THE DTP CASE STUDY

In the case study outlined below, the Sponsor was actively recruiting into a phase 2 study which required daily dosing of a temperature controlled, IV administered investigational product. As the patient population was home based and not hospitalized, the study design placed a substantial burden on these patients to commit to daily dosing in clinic. The sponsor approached Signant Health to assist in designing, in partnership with third party courier and home healthcare nursing services, a solution to enable home visits over the course of the trial to reduce patient burden. The frequency of at home versus in clinic visits remained at the discretion of the Investigator, in conjunction with patient preferences.

CASE STUDY: SIGNANT HEALTH EXECUTES A MID-TRIAL SWITCH TO A CENTRAL PHARMACY DTP MODEL

1. In the original study design, all patients were traveling to clinic for all visits. However, as this proved burdensome for patients, an optional transaction was added to IRT to enable patients to transition to at home visits after enrollment. This was only available to patients in specific regions within the study.

2. One of the challenges with a transition to at home visits in a trial with daily administration is that there needs to be a transition period to allow for the logistics of at home delivery to occur, while the patient is still actively visiting the clinic. Thus, the IRT solution was adapted in such a way to enable an approval flow to specify which upcoming visits would be at home while continuing to enable for current visits to be recorded.

    - For example, if a patient was in clinic for day 10, and was approved to begin at home visits, the site will mark them as eligible to start for a future visit, ex: day 15
        - Because of the logistical requirements of preparing and delivering drug to the patient's home, the day 15 visit will be recorded several days in advance of the intended dose.
    - IRT is then configured to enable visits to be recorded "out of order", allocating inventory to a patient as appropriate at each visit from the site and/or the central pharmacy.

3. Site inventory levels were adapted such that they could managed via a specialized algorithm which accurately accounts for which upcoming visits are scheduled for in clinic, and which are at home. This ensures that sites have proper buffer levels, as well as drug on site for planned visits, without overstocking the site for visits that are setup for at home dosing.

4. A central pharmacy model is used for all at home visits. This means that all home visits are recorded against inventory in a single pharmacy location, as opposed to the site that the patient was previously associated with. The central pharmacy prepares and ships IV bags directly to the patients' homes.

5. Due to the administration method of the supply, patient's receive a daily visit from an at home health care provider. Once a home healthcare nurse arrives for the patient's visit, they inspect the shipment, ensuring the contents are intact and stayed within the appropriate temperature range. Finally, the nurse administers the study drug and documents the visit appropriately. Following administration, standard drug accountability processes are followed in IRT.

6. Lastly, specialized reporting is enabled to ensure site and home health staff only have visibility to what they needed to complete their responsibilities. Essentially, site staff retain full visibility to all activity for their patients, regardless of if visits were in clinic or at home. However, home health providers only have visibility to reports related to home visits.

SUMMARY

Direct to patient models have become more prevalent in the industry with the rise of remote trials and hybrid trials. Recently, the COVID-19 pandemic has caused sponsors to re-evaluate the methods in which they can best provide study drug and supplies to patients. Direct to patient methods offer sponsors viable alternatives in getting study drug to patients in accordance with trial protocol, and can be effectively transitioned to mid-study if needed. Doing so requires a complete understanding of the trial, it's protocol, the patient population, as well as making key decisions around administration and roles.

SIGNANT HEALTH IS THE INDUSTRY'S PREMIER IRT PROVIDER, AND CAN SUPPORT VARIOUS FLAVORS OF DIRECT TO PATIENT MODEL, OR TRADITIONAL IRT MODEL FOR YOUR STUDY. TO LEARN MORE, VISIT – SIGNANTHEALTH.COM

WHO IS SIGNANT HEALTH?

The best technology succeeds in the background. Signant Health provides solutions that simplify every step of the patient journey to make it easier for people to participate in, and for sites and study teams to run, clinical trials. Signant unites eCOA, eConsent, Patient Engagement, IRT, Clinical Supplies and Endpoint Quality into the industry's most comprehensive patient-centric suite – an evolution built on more than 20 years of proven clinical research technology. Our intense focus on the patient experience, deep therapeutic area expertise and global operational scale enable hundreds of sponsors and CROs (including all Top 20 pharma) to extend the reach of drug development, expand patient opportunities and improve data quality – helping them bring life-changing therapies to our families and communities around the world. Take a significant step toward patient-centricity at signanthealth.com.

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