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White Paper

The secrets of a successful supply strategy: How to ensure your IRT will support your clinical trial needs





In clinical trials, the Interactive Response Technology (IRT) system is vital to ensuring that the right drug gets to the right patient at the right time. Many study managers may not realise just how that feat is accomplished – i.e., exactly how the IRT executes a drug supply strategy that's optimised to protect patients, reduce wastage, and streamline the supply chain.

If we were to look under the metaphorical "hood" of the IRT, we would see a sophisticated algorithm that serves as the engine driving initial supply orders, drug assignments, and supply reorders and returns. The smooth operation of the trial thus depends on the logic and comprehensiveness of that algorithm.

Study managers need not understand the algorithm *per se*, but they should be familiar with the assumptions and variables that feed into it, since these factors will impact the volume and frequency of supply orders.

Here we uncover what study managers should be prepared to discuss with their IRT partner to ensure that the IRT system addresses the trial's needs with precision.

The drug-ordering algorithm

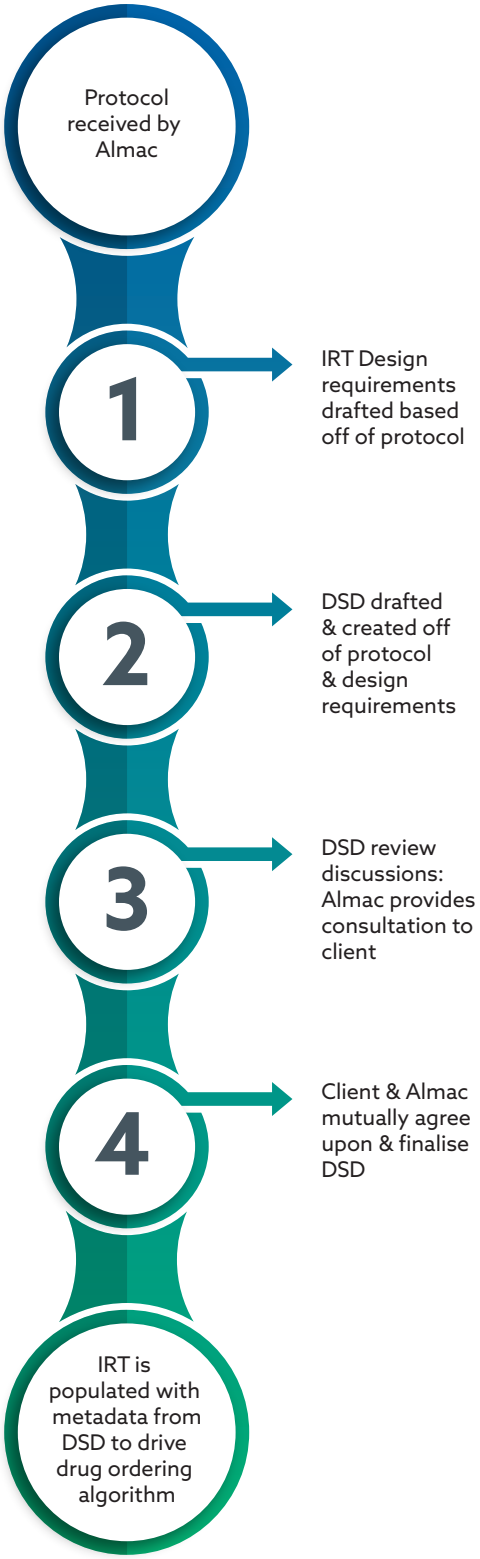
In computing, an algorithm is an ordered set of computer-implementable instructions for solving a problem. In an IRT system, the drug-ordering algorithm controls how the system executes the drug supply strategy to order supplies for trial sites. It uses a well-conceived set of assumptions about product demand and business rules related to supply practices.

An iterative process

The goal of the drug supply program is, of course, to ensure there is always enough supply at site to treat subjects. This must be done by striking a delicate balance between over- and under-supplying the investigational or comparator products to trial sites; ensuring minimal wastage from non-use. Fortunately, best-in-class IRT systems are very flexible and can accommodate a variety of factors that influence demand and supply. The challenge is in knowing which ones to take into account.

Almac Clinical Technologies has devised a carefully constructed and long-proven process to ensure that the right questions are asked as the system is being set up to capture all the variables and reflect all the contingencies required to maintain the drug supply. This best-practice approach begins with the Sponsor sharing the protocol. Almac's inventory management group refers to this in proposing the IRT algorithm settings and design. The Almac team consults with the Sponsor on the proposed plan; covering any unanswered questions, ensuring that all contingencies have been addressed, and, together, to finalise the details. The drug supply algorithm is then ready to be put into action.

It is important to understand that creating the algorithm that will execute the strategy is not a "one and done" activity. The initial algorithm is based on a set of assumptions about how the trial will progress, and those assumptions must in time be replaced with actual details on enrolment rates, drug availability, drug stability, etc. that may well differ from the original assumptions. Because demand is fluid, supply must also be fluid, and the algorithm needs to be refreshed during the course of a trial.



Commonly overlooked variables that impact the supply strategy

Study teams naturally understand how enrolment rates can affect the demand for kits, but there are several other factors that should be taken into consideration:

- **Sites' storage capacity.** General supply strategies may not be suitable for all sites, depending upon their ability to store kits. This is especially true for IP that must be stored in a controlled ambient temperature setting or that must be refrigerated or frozen. Sites that have limited storage space but high enrolment will obviously need to be supplied more often than sites with large capacity and/or slow enrolment, which means that supply strategies may need to be developed to tailor to these types of individual site needs.

- **Country-specific needs.** There may be variation in IP, doses, or kit configurations being used by participating countries. Thus, the drug ordering system needs to reflect these specific restrictions and ensure only the proper types of supplies are sent to sites and the supplying depots.

- **Study phases and kit type variability.** Study designs may dictate that different kit types are used at various points within the patient's schedule. A subject may be assigned run in medication prior to enrolment / randomisation; double blind supply at and after randomisation. There may be a point during the visit schedule that the kit types being assigned change at a certain visit to reflect visit duration (for example: 1 month kit packaging vs. 3 month kit packaging). Studies may have a cross-over treatment point, an open label phase or run out phase where kit type changes need to be accounted for. The system algorithm must account for this timing so that the system doesn't prompt an order of types of kits until they are needed.

- **Product stability.** When stock is approaching the expiry (use-by date), the goal will be to maximise its use while also managing timely stock replacement. The IRT algorithm settings aim to prevent shipping any product to sites that will expire before it can be dispensed. The IRT is also set up to account for timing of when to send replacement supplies to ensure they arrive before expiring stock would cause any shortage. The visit projection window (future outlook period) for resupply orders must work in concert with the product stability duration and any changes during the course of the trial should be considered.

- **Variable subject need.** The amount of supply assigned to subjects will certainly differ based on treatment arm assignment, but there may be other patient specific factors that will be accounted for by the inventory algorithm. For example, a study using weight based dosing will need to account for different subject weights as well as the potential for subject weight fluctuation during the trial. The resupply needs must account for these unknowns and have the right settings applied to ensure the proper inventory levels. If the exact dose required for a patient is not available in a kit, the system could be set up to construct a dose out of a combination of existing kits. For example, if there are only 150 mg and 300 mg kits available, but the patients' dose should be 600 mg, the system could draw from a number of different kit combinations to get to the proper dose.



> There are times where the patient's discontinuation is not registered in real time which can result in additional inventory being supplied that isn't truly needed.

- **Alternative kit configurations.** This is important to consider for the setup of both the drug assignment functionality and the drug ordering algorithm. The drug ordering algorithm may be set to provide the site enough drug based on the current patient population and the ideal kit configurations to achieve their dose. However, the drug assignment methodology may allow greater flexibility to assign the kit configurations based on the site's available inventory.

- **Temperature excursions.** Sometimes, despite the best efforts of everyone along the supply chain, a product is exposed to temperatures outside of its required range. The product is then quarantined, and may, after review, be deemed usable or damaged. The IRT will need to know how to account for quarantined drugs during the review period. Immediate replacement of the quarantined supply can be made via a replacement drug order. Alternatively, the system can be set to not decrement this inventory until the final review and decision is logged, resulting in no immediate replacement.

- **Visit windows.** If a patient's visit is not registered in the IRT in the expected visit window, how long should that patient be included in the resupply calculation? There are times where the patient's discontinuation is not registered in real time which can result in additional inventory being supplied that isn't truly needed. The IRT includes settings to account for these instances to prevent including subjects who haven't returned for visits after a certain amount of days.

Inventory-related concepts

Sponsors will need to work with supply management experts to review all of the variables that can come into play in ensuring that the drug-ordering algorithm works as desired to supply sites. They should be prepared to make decisions that account for the protocol design and any supply specific constraints. These include:

- **Do not ship to site and depot.** This function calculates the last day product is eligible to ship to a site or depot. The site and depot will each have their own respective values where the setting represents the number of days prior to expiry. The value to set should account for shipment transit time, the amount of time the stock will sit on shelf prior to patient assignment (when at site) or sit in inventory at the depot (when at depot).
- **Do not count at site.** This setting is used to calculate time for replacing supplies that will soon be expiring. Similar to the prior setting, it represents the number of days prior to expiry. Once this date is met, the IRT will no longer count that supply as available at the site for purposes of supply ordering only. This will result in replacement drug orders being raised based on current site projected need.
- **Initial.** This setting determines the number of kits of each medication type that will be sent in the initial order to sites.
- **Trigger.** Once the amount of medication at a site reaches or drops below this specified level, the system will prompt a new order.
- **Order all.** This function ensures that the system considers all item types when one kit type hits the trigger threshold.
- **Resupply.** This dictates the amount of medication required to bring medication levels back up at a site.
- **Visit projection trigger.** Based on the existing patients at a site, the system will look at the future supply needs for a specified number of days. When there isn't enough drug at a site to meet this demand, an order will be triggered.
- **Visit projection resupply.** This calculates in the same way as the visit projection trigger. However, this tells the system how many kits need to be ordered once the trigger is met. This number of days can be set to a higher value than the trigger projection to reduce the number of shipments to a site and consolidate shipments.

"When there isn't enough drug at a site to meet this demand, an order will be triggered."



Working with your IRT partner

The engine driving the IRT is, admittedly, esoteric and complex. Therefore, Sponsors need to select an IRT partner whom they can trust to ask the right questions, consider all the details, and provide for the necessary contingencies in developing the drug supply strategy and the technology that will support it.

Study managers, for their part, should be intimately familiar with the study protocol, and as much as possible, be prepared to answer the system designer's questions and to make decisions on how the system's algorithm should function to support the trial needs. They should also alert the IRT vendor of any protocol amendments or upcoming scenarios that will logically affect demand or supply in a timely fashion. It may be necessary to update the IRT drug supply algorithm accordingly, and the more notice that the vendor has, the better.

Sponsors also need to remember that the drug supply algorithm will initially be based on assumptions that may or may not bear out in actuality. The algorithm will likely need to be adjusted to reflect actual product demand and the different study phases of enrolment, supplying known subjects and close out.

Conclusion

Study managers need not become computing experts to ensure that their trial's IRT system functions as it should to manage supplies for optimal results. They should, however, understand the basic variables that can affect demand and that will need to be factored in to an effective supply strategy. By working with a trusted IRT vendor they can uncover and consider the factors that should be reflected in the IRT's drug-ordering algorithm.

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