Bespoke RTSM Systems Empower Precision Medicine

Randomization & trial supply management (RTSM) are critical functions of interactive response technology (IRT) systems used for clinical trials.

Specifically, this system supports participant randomization as well as manage drug inventory, site resupply, and participant dispensation. Applying standard IRT design to the specific needs of personalized medicine trials has been challenging, as the design of these trials is non-standard.

Personalized medicine, also called precision medicine, refers to medication manufactured specifically for use by a single participant. Its key benefits typically include more successful outcomes for the participant: greater efficacy and a reduced likelihood of side effects.

Personalized medicine also can move more quickly through development phases and can fail more quickly if the therapy is not viable. However, the challenges of individualized medicine relevant to RTSM usage include:

- **Clinical trial supply chain** — accelerated manufacturing, manufacturing slot management, personalized shipments
- **Expiry management** — just-in-time (JiT) shipping, very short expiry, rapid time to treatment administration
- **Operational** — complex/innovative study designs, participant recruitment and scheduling, effective cross-team communication
- **Participant management** — participant-led supply chain, reserved medication, visit scheduling, brief time window from participant identification/consent to treatment

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Despite these difficulties, personalized medicines have accounted for about 25% of new drug approvals for each of the past nine years—versus accounting for less than 10% of new approvals a decade ago. In 2023, 20 personalized medicines were approved by the FDA, representing approximately 38% of all newly approved therapeutic molecular entities.

Of those approvals, 61% occurred in the rare disease space and 27% were intended for oncological therapies.[1] This increasing volume of personalized medicine trials is prompting drug developers to reconsider the associated clinical trial challenges as well as the capability of RTSM systems to help overcome those challenges.

1. "Personalized Medicine at FDA: The Scope & Significance of Progress in 2023." Personalized Medicine Coalition, 2024. https://www.personalizedmedicinecoalition.org/wp-content/uploads/2024/02/report-3.pdf

The Evolution of RTSM Clinical Supply Chain Management

In a typical study, bulk medication is released by a qualified person (QP), and it is not allocated to participants until dispensation.

A consignment/shipment generator in the RTSM system automatically selects appropriate stock from the depot supply and requests shipments to appropriate sites for use by any participant. However, in a participant-led supply chain, medication must be pre-allocated to a specific participant before being sent to a site (Fig. 1).

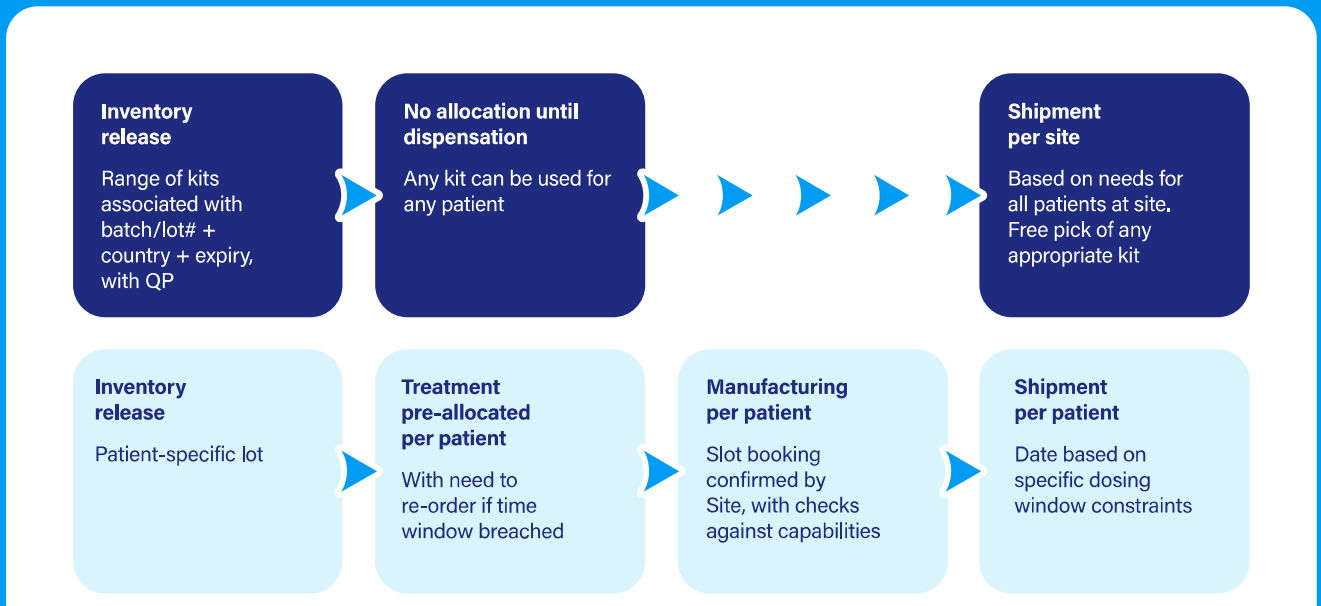

Fig. 1 — A typical (dark blue) versus a participant-led (light blue) clinical supply chain

RTSM design has evolved toward more configuration, with predefined, pre-validated design options to choose from. For at least a decade, RTSM systems have been able to capture proposed visit dates, enforce certain restrictions around those dates, and communicate those dates to the right people. However, customization is required to allow users to tailor solutions to overcome challenges associated with non-standard, novel requirements. Some modern IRT systems are now being used to track personalized stock from manufacturing to the depot and then on to the site.

For example, a recent Phase 1a/1b, open-label, multi-site cancer vaccine trial leveraged standard RTSM tools, such as recruitment target management and opening/ closing cohorts along the trial pathway (Fig. 2). Then, to handle personalized medicine, not only was a shipment raised specific to a participant, a chain of identity (COI) tracking number was also associated with both the medication and the participant. This may seem like a small addition to RTSM functionality, but it can be critical to managing a personalized study.

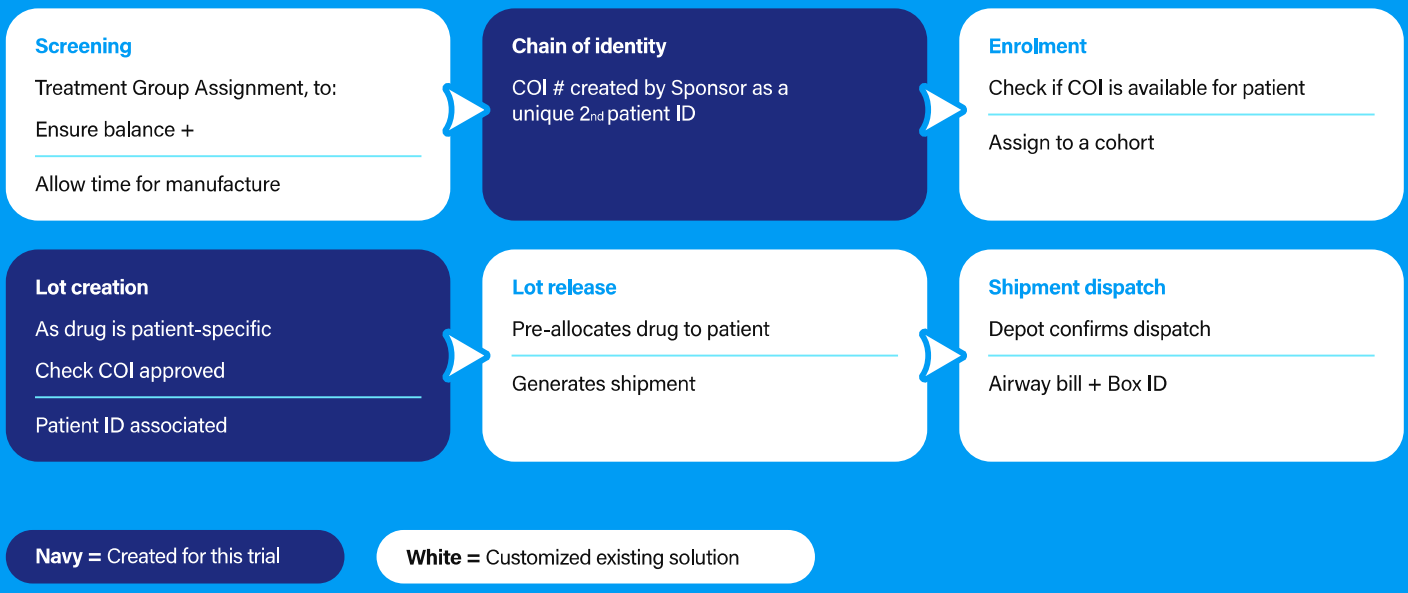

Fig. 2 — Supply chain progression of a Phase 1a/1b, open-label, multi-site cancer vaccine trial

Since personalized medicine is shipped just-in-time for use at specific visits, medication that arrives damaged/expired or encounters other issues during shipping must be accounted for. A typical study usually can overcome this problem through buffer stock, but in a personalized trial, it is more likely the medication will need to be reordered, remanufactured, and sent as a new shipment. Now, the visit schedule is out of step with medication administration and an additional visit must be scheduled to achieve the required number of treatments.

Additionally, when stock is dispensed for any visit, it is crucial to track whether blinded information exists in relation to that stock, as well as whether access to any elements of the personalized medication must be restricted to certain staff. For this purpose, an RTSM system must be able to appropriately tailor the information it shares with certain users or roles.

A second example of crucial RTSM system functionality involves a Phase 1, open-label, multi-site cancer biologics trial (Fig. 3). In this case, a Chain of Identify (COI) number specific to each participant and personalized medicine dose was not required by the sponsor; instead, a generic "dummy" number was used in the RTSM system to track quantities. The RTSM system provided the necessary alternative information to staff at the depot to raise a pre-assigned shipment to a particular location for a specific participant visit. More checks and approvals were required as part of this type of supply chain. As each participant planned their initial visit to the site, those visits had to be approved by the manufacturer to ensure production and shipping on that date could be accommodated.

Fig. 3 — Supply chain progression of a Phase 1, open-label, multi-site cancer biologics trial

Once that approval was granted, a medication order transaction opened in the RTSM critical pathway. The study team requested that ordering be a manual step, so the shipment generation system was used only when needed, rather than automatically as standard Every transaction was tailored to the study team's JiT needs; information was sent to the depot specific to the participant and the location, and the depot shared confirmation of the shipment being sent as well as an estimated time of arrival.

As this medication was a radiopharmaceutical the possibility of it decaying between the point of calibration and the point of dispensing had to also be considered as part of supply chain planning. While many RTSM systems enable built-in dose calculations, this trial took a different approach, calibrating exactly how much decay the medication would undergo, as well as that decay's impact on the volume required. So, the longer the period between calibration and dispensing, the more volume that was required. These calculations then were shared with sites to aid them in plotting out study steps.

Does Your RTSM Drive Effective Communication?

Timely sharing of the right information with the right people is key to supply management and manufacturing, particularly in circumstances where production or shipments must be tailored to an individual participant's schedule or dosing needs.

Accordingly, an RTSM system must provide an effective communication mechanism and support risk mitigation across numerous types of study design. Consider how Perceptive eClinical's customizable RTSM systems handle the following common scenarios:

If a participant needs to reschedule their visit

Perceptive eClinical's RTSM provides the ability to schedule individual visits on an event-by-event basis with configurable time window checks. So, users know how far in advance the manufacturing center would like the visit to be scheduled and understand the last point at which that event can change.

If the manufacturing center needs to change its capacity

Perceptive eClinical provides a mechanism for the manufacturing center or sponsor users to inform the system directly about the immediate impact of any updates to the capacity. This is typically accomplished through a slot booking system, wherein a user can look at the online calendar created for the trial to determine which days have available slots and when. Any updates to the slot booking system appear in real time.

If materials are delayed/damaged in transit, decay, or arrive out of temperature range

Perceptive eClinical's RTSM can communicate the information to relevant roles at the site or depot, as well as automatically reorder if that is what the study team prefers The system can accommodate updates as granular as the courier notifying the RTSM that it has been held up at a border or that traffic will delay delivery by two hours.

Adaptability is Vital to RTSM's Effectiveness

As noted above, an RTSM system's ability to adapt to visit and dosing schedules is imperative in personalized medicine; for example, in oncology, this flexibility helps manage the participants journey as the disease progresses. Consider that it may be necessary to manage and balance cohort assignments using a randomization technique that back-fills through the randomization list.

Similarly, in oncology, effective management of local versus central sourcing of medications that may be needed for Standard of Care treatment, scarce or unreliable, and the sponsor needs to switch to central sourcing, they need the ability to change the status of that medication type in a particular country or site and have the IRT manage the stock alongside any personalized medication, is vital. If a local stock becomes In addition, changing the sourcing information will automatically change both the site's supply strategy and medication checks performed by the RTSM at the start of dispensation transactions.

Personalized Medicine Demands a Personalized RTSM System

As the industry continues to embrace personalized medicine, both in terms of expanded research and increasing regulatory approvals, supply chain tailoring to support those initiatives will become even more important. Thus, the ability to implement an atypical supply chain to support personalized medicine clinical trials — as well as more traditional clinical trials with a personalized medicine element — is crucial.

Having supported clinical trials for more than 30 years, spanning more 4,700 trials, Perceptive eClinical is uniquely suited to support sponsors in this endeavor, whether the trial explores a cell or gene therapy, radiopharmaceuticals, or any other treatment option once thought to be complex for an RTSM system to accommodate. Whatever challenges your clinical trial presents, Perceptive eClinical's custom RTSM systems feature the functionality and flexibility to meet the needs of your study team and your manufacturing process critical path.

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