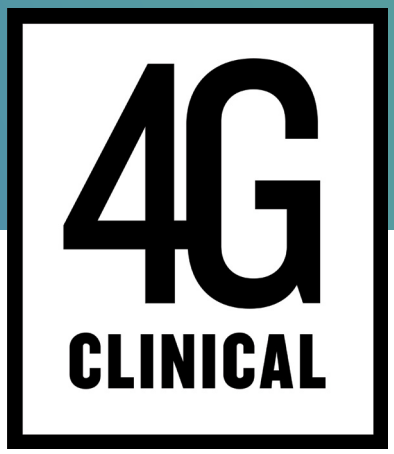

How Clinical Trial Complexity Impacts End Users

Knowledge Sharing Series

Redefining Complexity through the Lens of the End-user

Traditionally, complexity in clinical trials is translated into increased operational challenges due to the presence of several IMPs, populations, trial sites, multiple sponsors and/or manufacturers and contract research organisations (CROs).

Common examples of complex clinical trial designs are basket, umbrella, and platform trials. These designs are primarily used in Oncology, but they may be applied in other therapeutic areas if there is a good rationale and the design is appropriately justified. Basket trials investigate the safety/efficacy of an IMP or combination of IMPs across a variety of populations, while umbrella trials investigate the safety/efficacy of several IMPs in a single population. Whereas platform trials may test several IMPs in one or multiple populations in a highly dynamic design.

RTSM/IRT technologies that support these trials must be flexible enough to enable intricate designs while also protecting the blind, adhering to GDPR requirements and restrictions, managing frequent protocol amendments and more recently, aligning and setting up hybrid Decentralised Trials. As such, RTSM/IRT solutions can enable complex protocol designs by mitigating potential challenges inherent to the choice of complex design elements, features, methods in the protocol, etc.

This article examines clinical trial complexity through the lens of study investigators, site staff, CRAs, sponsor study and supply managers, and how the RTSM/IRT provides the ability to be as creative as needed within the design to meet trial endpoints. It does so by assessing the following 6 operational challenges.

1. **Amendments**
2. **Dose Finding Studies**
3. **Staffing and Resources**
4. **Decentralised Clinical Trials (DCT)**
5. **Study Operational Queries**
6. **Data Integrity**

Operational Challenges Addressed in the RTSM/IRT

Complex clinical trials require intensive peer-level interaction and agreement between clinicians (community of investigators, clinical researchers), methodology experts (statisticians, biometricians, modeling and simulation experts) and project teams (organisation, performance of trial) about the choices in scope (subjects and conditions to be included), main design features (medicinal products, arms, endpoints) and adaptations.

RTSM/IRT solutions can enable complex protocol designs by mitigating potential challenges inherent to the choice of complex design elements.

Below are 6 operational challenges that stem from complex clinical trial designs that are supported by the RTSM/IRT.

1. Amendments

Implementing new amendments due to protocol changes are very common during complex clinical trial conduct.

According to Tufts CSDD:

Less complex protocols—those containing fewer procedures and eligibility criteria—averaged two amendments; more complex protocols averaged 3.2 amendments.

These amendments delay studies and add incremental cost. Applying an amendment to an ongoing protocol may result in design changes, which can include dose modifications. The RTSM/IRT helps alleviate some of these challenges by enabling these changes as planned amendments within the system.

Operational Challenges Addressed in the RTSM/IRT

This can save time and cost for all involved. A structured training plan that instructs individual sites to apply the amendments and allows the RTSM/IRT to be updated and changed on a per site basis alleviates the possibility of amendment launch delays. For those amendments that cannot be planned, a quick turnaround, a good understanding of the protocol and a highly flexible system is required to support it.

So to summarise, to create a more stable process for amendments, sponsors should:

- Understand and address unknown variables within the protocol itself
- Build in as much flexibility into the RTSM system (advanced cohort management for example, backup arms, etc.)
- Plan for future study amendments (pre-validated test scripts)

2. Dose Finding Studies

Dose finding studies add burden on the site staff due to entering patient data and parameters into different systems, calculations and multi-check procedures. These procedures introduce the risk of misdosing patients. Those errors are not uncommon occurrences, **especially for IV therapy**.

Modern RTSM systems can be set up to make it more difficult to commit an error in the administration process. For example, if the site is allowed to enter raw data and the RTSM calculates dosage where the investigator is empowered to make decisions, some mistakes can be prevented and therefore increases patient safety. Adding more visibility of the drug and streamlining the process with the IRT are critical for patient safety and to prevent wrong drug errors.

3. Staffing and Resources

To manage a complex trial, experienced personnel on the site and the CRO are required. Within the current landscape, staff shortages and retention challenges in combination with a reduction in average years of experience is adding complexity to the management of clinical trials. Selecting sites with the needed expertise and working with CROs that have resources to support these trials is increasingly difficult.

Operational Challenges Addressed in the RTSM/IRT

4. Decentralised Clinical Trials (DCT)

Covid-19 has been a catalyst for the development of contingency plans globally and the running of DCT trials. There are several layers of complexity running a DCT trial. For sites, it means supporting two processes including traditional visits at sites and remote visits

In order to allow those processes, one of the main areas of focus today is how to handle the Patient Health Information (PHI) and be compliant with GDPR and HIPPA requirements. PHI handling is complex due to the differing regulatory status per country that is difficult to ascertain.

Sites struggle today with the burden it brings because they must collect the data from patients and must pass it to the right vendor each time, while complying with regulations and focusing on the patient's safety. There are many challenges along the way including technological issues and frequent communication to keep everything on track.

Using an RTSM/IRT to store this information centrally in an encrypted manner can meet local requirements and allow for more efficiencies by eliminating the need to enter the data per each shipment to the patient home and using manual forms that can be passed between key stakeholders. Instead, only the relevant people receive the data when needed.

5. Study Operational Queries

By speaking with CRAs and Sponsor site support teams, we've uncovered a high correlation between an increase in queries due to complexity, which eventually requires more Sponsor and CRA support for site users. Adding more training and guidelines during the process, and tracking who received training in the IRT can help determine gaps in real time, remove burden from sites and sponsors in managing that and documenting the training records and also meet current regulatory requirements.

6. Data Integrity

The amount of data collected throughout complex clinical trials is growing. As this happens, data integrity becomes even more crucial for the success of the trial. Challenges arise when determining the source of truth, viewing the trial holistically and defining the right integrations flow (CRF, RTSM, EDC, etc.). Alignment must be reached between data managers and the clinical staff to incorporate the site journey into those decisions. Using modern integration technology requires less time due to streamlining processes and less reliance on entering the same data into multiple systems.

Conclusion

Complex trials are here to stay, but they do not have to adversely impact trial operations and patient needs. Modern RTSM technology provides the opportunity to implement the most complex protocol designs, whilst mitigating the need for SOP updates and complex actions required by the end user. By allowing modern technology to automate error prone processes, end-users are able to focus on what matters most, the patient.

As such, these streamlined processes yield better data integrity, directly impacting efficacy assessments and timelines.

Biography

Get to know Neta.

About the Author

Neta Bendelac, 4G Clinical Senior Director of Strategy, has over 14 years of experience in Clinical Supply Chain Management. Her areas of expertise include identification of operational business needs and collaboration with leading players in the market to influence 4G's product future design and development. She headed the Clinical Supply Chain department at Teva Pharmaceuticals, where she established new and innovative approaches to managing IMPs in clinical trials, designing them with a highly acclaimed and unique patient perspective. Prior to Teva, Neta worked as an international Supply Chain consultant, providing simulations and optimisation tools to clients worldwide. Neta holds a BS in Industrial Engineering and a Master of Business Administration (MBA) from Tel Aviv University,

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