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# Getting IRT Right – Part 1: Randomization

This is the first of two articles on the consequences that could arise if an interactive response technology (IRT) system isn't designed and/or implemented correctly and how a trial could quickly go off track based on risks related to randomization, drug allocation, and trial supply.

The randomization of participants is one of two primary functions of an interactive response technology (IRT) system. It provides the capability to deploy sophisticated stratifications as well as dynamic randomization algorithms. No one would imagine conducting a clinical trial without a biostatistician. The same is true about implementing randomization in IRT.

If randomization is implemented incorrectly, the scientific integrity of the entire study could be called into question. But, effective and reliable randomization requires more than simply loading the randomization schedule into the IRT system. It involves determining how the list will be implemented, for example:

- Should blocks be assigned by a site when the site is activated?
- Should they be assigned dynamically to a site as needed?
- How will mis-randomizations or 'randomized in error' be handled?

Not employing expertise in this area can have negative impacts on the study, as outlined below.

## Randomized in Error

"This participant was randomized in error; can you please just remove them from the list?" This might seem like a reasonable request until you consider the implications.

By removing a participant, you disturb the intent-to-treat analysis. You create a situation where you could call the action into question. Were they removed because the Investigator was dissatisfied with the allocated treatment? Were they removed because the sponsor felt they would contribute negatively to the study? Are you trying to game the system? Optics matter.

Additionally, every subsequent participant will be impacted by this decision and random assignment becomes less random even if only by very little. There is a high likelihood that every study will have at least one participant randomized in error. As such it should be considered in the design and participant population calculations.

## Mis-stratification

Fortunately, we have evolved to a point where it is a generally accepted practice that mis-stratified participants will remain in the randomization slot consumed. Nonetheless, there are still those in the industry who would consider moving a participant after randomization.

The same consequence applies here in that moving a mis-stratified participant post-randomization would call into question the integrity of the randomization process.

Randomization is a "moment in time." It is not a visit; it is a discrete action. And as such the data used in the transaction has a material impact on the randomization record chosen. This is true even if the data was not materially correct. Any action that tries to "correct" this process is damaging to its integrity. Even if we accept the premise that nothing can be done about the mis-stratification as it relates to the randomization schedule, we often scramble to make sure that the answers to the stratification questions are made to be accurate in the patient dataset.

## Randomization Date

Another request that may seem reasonable, but in fact is not, is "Can you please change the randomization

date? We ran randomization in the system the night before so we could prepare for the next day."

As previously mentioned, IRT randomization is a discrete action. It is an almost instantaneous process based on data (stratification) to determine what treatment a participant will be allocated to. This is an immutable truth in the IRT system. What it is not is an office visit.

A fundamental challenge is the lack of understanding between a transaction and a visit. Dates in IRT are the dates of the transaction, they are not the dates when the participant was present at the clinic. Trying to make them the same thing dilutes both. While it may be annoying for transactions such as allocation of study drug, it is seriously problematic for randomization. It can cause regulators to question the integrity of the randomization process and by association, the entire study. Imagine a randomization table where dates of randomization are not sequential and jump all over the place. The process would not seem under control. You would need to go to the audit trail to see the true date/time. Again, optics matter.

Getting randomization right requires more than just technology. It requires insight that can only be gleaned from having implemented RTSM extensively and successfully across trials of all shapes, sizes, and complexities. The same holds true for drug allocation and supply management, which we'll cover in Part 2.

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And they remain involved in your study until its closure, addressing the inevitable issues you'll face, from recruitment delays to drug shortages to protocol amendments – all of which drive your trial's success.

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