SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

The Signal

Best Practices: RTSM Strategies to Avoid Partially Unblinding Clinical Trials

Randomization and Trial Supply Management (RTSM) solutions are routinely used in today's clinical trials to manage randomization, enable emergency code break to be conducted efficiently and traceably, and to enable clinical studies to operate with reduced medication overage and wastage due to efficient demand-driven supply chain management.

However, if not implemented correctly, this technology may bring with it the possibility to inadvertently unblind parts of a study, undermining the integrity of the clinical trial. At Signant Health, the expertise we have developed over 20+ years' experience of deploying RTSM solutions provides robust protection against these potential sources of unblinding.

Unblinding and partial unblinding

First, what is meant by "unblinding" and "partial unblinding"? Unblinding occurs when one or more people become aware of the treatment allocation of one or more trial participant. Partial unblinding occurs when someone can infer something about the treatment allocated to one or more participants, without knowing the actual treatment. For example, if I am able to deduce that two participants must be in the same treatment groups, this is partial unblinding.

Common pitfalls to avoid that may cause partial unblinding

Dispensing order unblinding

Site personnel will be able to identify participants in the same treatment group if 1) medication packs of one treatment type are used at a different rate to others (e.g., higher withdrawal rate on one treatment), and 2) packs are shipped to sites in pack number order where over time the numbers on packs within each treatment group can begin to separate.

Mitigation:
To ensure a random selection of packs at the site, it is possible to use a double-randomized pack list where there is no association between the pack number and its position in the packaging list.

Single pack shipments

There is a risk of unblinding if consignments to site are sent that only contain medication for one participant. For example, if one pack is dispensed to participant A, and a second pack then re-supplied is given to participant B, I can reasonably deduce that A and B are in the same treatment group.

Mitigations:
Adding a random number of packs from other treatment groups to avoid single pack shipments. However, this can introduce wastage.

Failed randomization

In the case of short supply medication, there is the possibility that no medication of the required treatment group is available at the point of randomization. Putting this randomization on hold while medication resupply is awaited, and yet randomizing a subsequent participant would partially unblind: in this case, it is clear that the two participants must belong to different treatment groups.

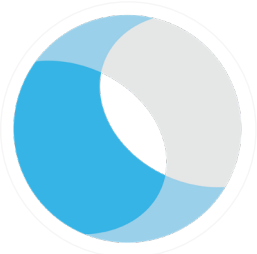
Mitigations:
One approach to mitigate this is to prevent the randomization of all new participants (independent of the treatment group they would be allocated to) while the site has no stock for any treatment group. However, this approach can be disruptive to the continuation of the trial and retention of participants. Other approaches are possible and our experienced team of experts can discuss the pros and cons of each to ensure the right solution for each study.

Titration trials

For blinded titration studies it is important to ensure that the same rules apply to subjects on all treatment arms. For example, a placebo group participant should have the same titration rules applied as one on active treatment but receive placebo with every titration.

The best way to avoid these and other pitfalls that lead to partial or complete unblinding is to identify risk factors from the outset and build safeguards into the design. At Signant Health, our experienced teams design RTSM solutions to protect against issues like partial unblinding by thoroughly labelling very data point as blind or unblind and performing verifications through user-accepted testing before going into production.

Learn more about Signant's RTSM solution and contact us to speak to our experts.



Signant Health

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