BEST PRACTICES IN IRT IMPLEMENTATION: A PRIMER FOR APAC

ARTICLE

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Pharmaceutical sponsors conducting clinical trials in the Asia Pacific (APAC) region have a rare opportunity at hand: by adopting Interactive Response Technology (IRT), they can automate one of the last bastions of manual record-keeping in clinical trials and realize a significant uptick in productivity and data integrity.

Software platforms that integrate the processes and information related to randomization and delivering drugs to clinical trial participants have been in use in major drug development countries for well over a decade. They have, however, not yet been widely adopted in APAC where study managers, investigators, and supply chain managers often continue to manage randomization, track patients, and monitor inventory manually.

In 2013, 16% of clinical trials were conducted in APAC, and that percentage is destined to climb. It only makes sense for study teams in the region to avail themselves of the same automation and efficiencies that their counterparts in other regions enjoy. Fortunately, users in APAC can “stand on the shoulders” of those in other regions and automatically reap the benefits of functions and features that have been developed over the years and across thousands of trials.

**IRTs: ANIMAL, VEGETABLE, OR MINERAL?**

So, what exactly is an IRT system, and what can it do? IRT systems, which were first introduced about 20 years ago, deliver a wide range of applications for managing patient interactions and drug supplies throughout the trial lifecycle. In serving sponsors, drug depots, and sites, they automate:

- **PATIENT RANDOMIZATION**, replacing physical envelopes or scratch-off cards. The system is pre-programmed to assign patients to treatment arms in a way that preserves blinding and allows for complex stratifications and randomization designs, with enhanced balance among treatment arms

- **PRODUCT INVENTORY MANAGEMENT**, allowing supply chain managers to have a real-time view of drug supply levels, locations, expiration dates, and storage conditions so as to forecast accurately and reduce wastage. Automatic re-supply shipments can be triggered, expired or damaged products can be removed from the system, forecasts can be updated based on enrollment rates, shipments can be adjusted based on storage conditions and the product’s requirements, and drugs with or without individual kit numbers can be tracked

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1 Clinicaltrials.gov
- **PATIENT TRACKING**, so that study managers can monitor the trial’s progress and make adjustments to visit projections that ultimately impact supplies.

- **STUDY REPORTING**, as data on drugs and patients are collected efficiently from sites and depots. Those with approved access can get real-time updates of study metrics as well as alerts when pre-defined thresholds are reached.

- **DRUG ACCOUNTABILITY AND RECONCILIATION**, capturing records on drug shipments, receipt, returns, and destruction.

Basically, through functions designed for sites, study administrators, and supply chain managers, an IRT supports all of the activities and decisions involved in ensuring that sites have the supplies they need to successfully treat patients. (See Figure 1.)

**FIGURE 1: A CLOSED-LOOP TECHNOLOGY SOLUTION**

Interactive Response Technology creates a virtuous cycle of information for coordinating all of the complex activities involved in distributing products to trial sites and the associated mitigating risks.
A well-designed technology platform will deliver efficiencies and performance insights, allowing sponsors to complete studies smoothly, on time, and on budget. IRTs commonly offer the following benefits to sponsors:

- **ENHANCED REGULATORY COMPLIANCE**, IRT systems improve blinding, data integrity, product handling, and accountability. They also provide regulators with documentation that a trial has adhered to Standard Operating Procedures.

- **IMPROVED PATIENT SAFETY AND TRIAL PERFORMANCE**, IRTs ensure that subjects are randomized correctly and receive the right medication. By helping to ensure that the right product is on hand at sites, IRTs can minimize treatment delays that jeopardize a patient’s therapy and ongoing participation in the study.

- **SPEED AND EFFICIENCY**, in automating data collection, analysis, and reporting, IRT systems save time in what would otherwise be very manual data entry and manipulation steps. Because data collection is automated, there is no need for sponsors to enlist personnel to enter it – or worse, clean it due to human error.

- **IMPROVED DATA INTEGRITY**, because information is captured and tracked electronically, there is less opportunity for human error. Plus, the system can be configured with automatic alerts and checkpoints to aid decision making.

- **REDUCED PRODUCT WASTAGE**, visibility to the entire supply chain allows supply managers to accurately forecast product demand, manage against impending product expirations, and prevent stock outs.

**DESIGNING A FIT-FOR-PURPOSE SYSTEM**

IRT systems can support virtually every type of clinical study, from the simplest to the most complex. The key is to follow a well-thoughtout design based on input from all stakeholders within the sponsor company and its supply services partner. A fundamental goal should be to design the simplest system that can accommodate the study protocol and support the functional needs of the study team.

Companies that have not had any prior experience with an IRT system may want to consider beginning with a pilot, adopting a system for a relatively uncomplicated study before committing to using the technology more extensively.
The following steps serve as a best-practice approach to developing an IRT in the APAC region, where familiarity with the technology is still limited. When system development proceeds in this fashion, the resulting tool will suit the study, and development time and costs will be minimized.

1. Assemble the project design team. On the sponsor side, this group typically includes the clinical team, the drug supply team, biostatisticians, and data managers. The vendor would normally involve developers, testers, and quality assurance specialists, led by a business analyst. To ensure efficient and clear communication, designate a project leader to funnel information from the stakeholders to the vendor.

2. Hold a workshop to introduce the project design team to what an IRT system can do prior to kicking off the project. Walk through the system capabilities and show team members a demo of a sample system. This step ensures that all parties have the same understanding of what is possible before they embark on the challenge of determining what is needed.

3. Gather the specifications for the IRT using a systematic process. Working through a User Requirements Specification (URS) sheet can direct the process of defining the project scope and the particulars of what will be needed. To properly configure the system, the developers will need input on a host of study elements, including:

   - **THE SCOPE OF THE STUDY**, this usually includes the trial design, number of sites and countries, recruitment plan and number of patients, duration of treatment, number of scheduled visits, and phases of drug use
   - **THE RANDOMIZATION DESIGN AND KIT LISTS**, what is the randomization design strategy that will be used for the study (i.e. centralized, stratified)? Will adaptive randomization or cohorts be required?
   - **THE DRUG FORMULATION AND KIT MAKE-UP**, will the product be delivered in tablet form, vials, or a device? What will constitute one kit? How will kits be labeled?
• **MEDICATION SHIPPING AND TRACKING REQUIREMENTS**, what import/export regulations will be involved? How many depots will be used? What shipping and storage conditions will be required?

• **DATA LOAD REQUIREMENTS**, what format will be used for the randomization and kit list? Which user groups will have access to what data?

• **DATA INTEGRATION AND TRANSFER NEEDS**, will the IRT need to communicate with the Electronic Data Capture (EDC) system and/or Clinical Trial Management System (CTMS)? How will blinded data be handled vs. unblinded data?

• **LANGUAGE TRANSLATIONS REQUIREMENT**, will the system need to be translated into local languages for participating countries?

• **CLINICAL AND PATIENT DATA TO BE CAPTURED**, what patient demographic information will be collected by site users?

• **REPORTING NEEDS**, what metrics will be monitored? Standard report formats and dashboard graphics will serve most companies’ needs a majority of the time.

• **SYSTEM CONFIGURATION REQUIREMENTS**, will sites be able to override validation checks, such as registering a visit outside of a visit window? Will medications be tracked at the kit or dose level?

An experienced development team can ensure that the recommended approach is compliant with all applicable regulatory mandates, such as the U.S. Food and Drug Administration’s Title 21, Code of Federal Regulations, Part 11.

4. Develop the system, using templates for standard functionality and customizing only those elements that are unique to the study. When standard functionality will suffice and the system can be built using established templates, the development time can be slashed significantly.

5. Perform User Acceptance Testing (UAT) of the system. This is usually a multi-step process, with the vendor performing an initial UAT, followed by a sponsor UAT. The sponsor is provided with a Test Plan containing specific test cases and instructions on how to execute the UAT.

6. Launch the system. All site users should be invited to an Investigator Meeting where they receive training appropriate to their role. Ideally, they should all be provided with a quick reference guide bearing step-by-step directions on how to access and use the system.

The ultimate performance and usefulness of an IRT system can be assured through rigorous quality checks at four stages in the startup phase: when requirements are finalized, once the code is programmed, after testing is completed, and during the implementation process when the system is ready to go live.
COMPANIES OPERATING IN APAC CAN LOOK FORWARD TO A GREAT LEAP IN EFFICIENCY BY ADOPTING AN IRT SOLUTION.

AVOIDING COMMON PITFALLS

Following the advice of others on “lessons learned” is a good way to avoid the pitfalls that can make adopting any new technology challenging. The following tips reflect the advice of specialists who’ve been involved in hundreds of IRT builds and implementations around the world. In general, newcomers to IRT should try to avoid:

- **GLOBAL FOOTPRINT**, whether the trial is local, or part of a global program, the system configuration can take advantage of lessons learned across thousands of trials, provided that the developer has global experience. This ability—to draw on best practices and guide sponsors—is particularly critical for sponsors who are newcomers to the technology and who may not know what is and isn’t possible. Such breadth will also help in ensuring that the system conforms to the expectations of regulatory agencies in other regions—an important factor if the study drug is intended for the international market.

- **LOCAL PRESENCE**, on one level, this is a matter of convenience. Vendors with staff on the ground in the region can offer project management and technical support to system users in their own time zone and languages.

- **INTEGRATION WITH CLINICAL SUPPLY TEAMS**, when these services are offered by the same company, sponsors enjoy seamless communication and coordination both in the development and execution phases.

- **VALIDATION PROCESS**, the system should be validated as complying with all relevant regulatory guidelines such as HIPAA, CFR 21, Part 11, and Guidelines for Good Clinical Practices.

- **ESTABLISHED PROCEDURES AND INFRASTRUCTURE**, designing IRT systems requires considerable operations experience in all phases of supply management.

Companies operating in APAC can look forward to a great leap in efficiency by adopting an IRT solution. Fortunately, the technology is well tested and has been applied successfully for years. Provided that sponsors work with a vendor experienced in supporting trials globally, their first experience with IRT systems is destined to be smooth, productive, and rewarding.