

# Managing the medication supply chain process using Interactive Voice Response systems

**C**linical trials face increasing challenges as a result of the drive to bring new drugs to market faster. During clinical drug development, manufacture of bulk active ingredients and production of the clinical trials formulation is performed in parallel with the clinical trials program. Careful planning is required to ensure that sufficient medication is available and forecasted in the supply chain to meet the needs of ongoing and future studies. The acceleration of clinical research often means that studies must start with shorter lead times and with less raw material and therefore fewer supplies available.

This represents a significant challenge for pharmaceutical company clinical trial supply groups, many of which are adopting new processes and techniques to ensure sufficient stock is in place to meet the needs of each site treating patients in each study. Technologies such as Electronic Point Of Sales (EPOS) systems assist this process in the retail sector whereby automated re-ordering of stock is triggered by the volume of sales and projected stock levels at each retail outlet. In clinical trials, Interactive Voice Response (IVR) systems provide a sophisticated method of tracking medication packs throughout the supply chain, and optimising the re-stocking of sites.

## Interactive voice response (IVR) systems

An IVR system uses the telephone as a means of inputting data. Pre-recorded prompts are played listing the various options available to the user or requesting responses to particular questions. Data are entered using the telephone touch-tone keypad, and are written to the underlying databases. For example, if dispensing medication to a patient, the IVR system may be configured to request the patient identification number and date of birth. After referring to the study database, the IVR system would then return the blinded medication pack number to be issued to that patient.

Using an IVR system brings many advantages to the management of the medication supply chain, but also requires a change in the way medication is packed and labelled.

## Conventional medication packing

Traditionally, medication has been packed for clinical trials in patient-numbered packs, each pack containing the complete supply that may be required by the patient

for the duration of the clinical trial. Patient numbers are randomised so that the required proportion of patients receiving each study treatment is achieved. This approach has the benefit of simplicity, but also requires significant pre-loading of sites with medication before the recruitment performance of each study site is known. Centres with low recruitment will be left with a significant quantity of study medication, which cannot be transferred to another site. High recruiting centres may run out of medication before further supplies can be ordered and delivered.

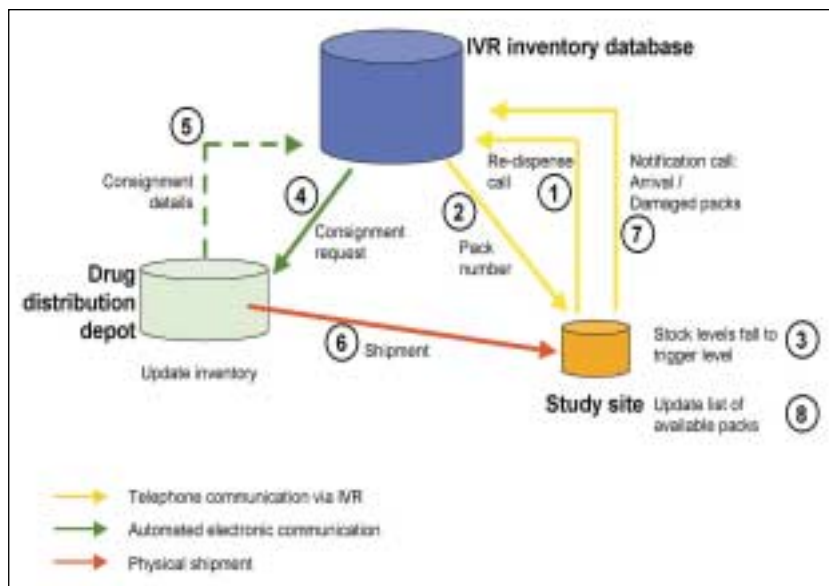
## IVR approach

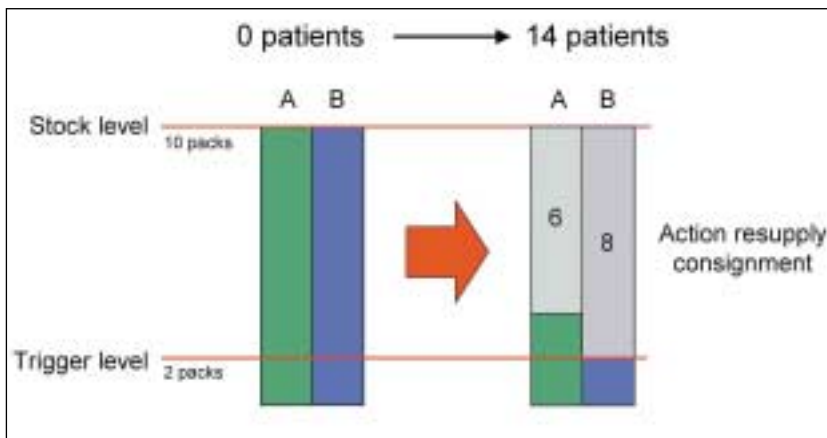
The objective of the IVR approach is to ensure that sufficient medication is available to supply new patients and re-supply existing patients whilst keeping wastage to a minimum. In addition to wastage of drug due to pre-loading of sites, the conventional approach is potentially very wasteful in terms of unused medication from withdrawal patients. For example, consider a trial with duration of 12 months of treatment. A conventional medication pack for each patient would contain 12 months of treatment, perhaps in one-month blocks. If a patient withdraws from the study during the second month, the remaining 10 months of medication labelled up for that particular patient will be wasted.



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**Figure 1. Medication dispensing and automated site inventory control using an IVR system.**





**Figure 2. Controlling site stock levels using the trigger and re-supply process.**

IVR offers a solution to minimising this wastage in addition to reducing that due to pre-loading of study sites.

When using IVR, drug supplies are packed not in subject numbered blocks, but each dispensing unit of medication is given a unique numerical code. The study database can relate each unit's code to the actual treatment being dispensed. By doing this it is possible to dispense any pack of medication to any patient, so long as it is of the appropriate treatment. Take the example of the trial with a 12-month duration of treatment. If the dispensing units represented one month of medication, then if a patient withdraws in the second month, the remaining 10 months of treatment (10 undispensed dispensing units) can be assigned to a different patient at that centre on that treatment.

As with an EPOS system, the IVR system will send stock only where stock is required by the study. Sites recruiting many patients will automatically receive replacement supplies; inactive or low recruiting sites will not be re-supplied as frequently. In this way, the IVR system channels the study supplies only to the sites that require them, minimising the wastage of medication by over-stocking inactive sites. Using IVR has been shown to reduce the need for supplies from the often-packed 75% overage to 25% overage, provided it has been designed into the planning of the study. This results in direct cost-savings, but importantly also enables studies to be started when fewer supplies are available.

## Dispensing medication and maintaining stock at site

Figure 1 illustrates how an IVR system is used to dispense medication packs to patients, and in a simple way, how to maintain appropriate stock levels at site.

In Figure 1, the three main interaction locations are depicted: the IVR inventory database, the drug distribution depot (usually either a pharmaceutical company or an external packing/distribution agency) and a study site enrolling and treating patients in the study. When a patient arrives at site to be (re-) dispensed with medication [1], the investigator or site coordinator makes a toll-free call into the IVR system. During the IVR call, they indicate their wish to dispense medication, and the patient requiring medication is identified. The system then reports back the medication pack number that should be dispensed to that patient, with reference to the known inventory of stock held at that site [2]. This information is normally confirmed by an automated fax or email. At this point, the involvement of the site staff is completed. However, let's say for example that in dispensing the medication pack, the IVR system now identifies that the stock at site for that treatment has now fallen to a pre-defined minimum level (trigger level) [3]. The IVR system will then automatically send an electronic request to the drug

distribution depot for a consignment of further supplies to be sent to the site [4]. This request will detail the number of packs of each treatment that should comprise the consignment. In some circumstances, the IVR system will dictate the pack numbers that should be sent; in others [5] the drug distribution depot will report back electronically which pack numbers were issued in the consignment. The choice of method depends on which fits best with the working practices of the depot. Following the consignment request, the medication is shipped to site [6]. On arrival, the site coordinator or pharmacist makes an additional call into the IVR system to register the consignment as having arrived [7]. During this call, missing or damaged packs can be identified which may trigger a further consignment. Following the medication arrival call, the IVR database updates the study site inventory to include the new packs, which are then available for dispensing to patients in future [8].

This simple example illustrates both how the IVR system can be used to control dispensing of medication, and how site inventories can be managed using a simple trigger and re-supply process. By inference, it is clear that only sites using medication by enrolling patients will meet their trigger levels and be re-supplied with additional study supplies – thus the trial medication is targeted only to where it is required by the study. In addition to the simple trigger and re-supply method, a more sophisticated predictive method is also employed by some IVR systems to control medication inventories but reduce costs by optimising the number of shipments. Both methods are described briefly below.

## Method 1: Trigger and Resupply

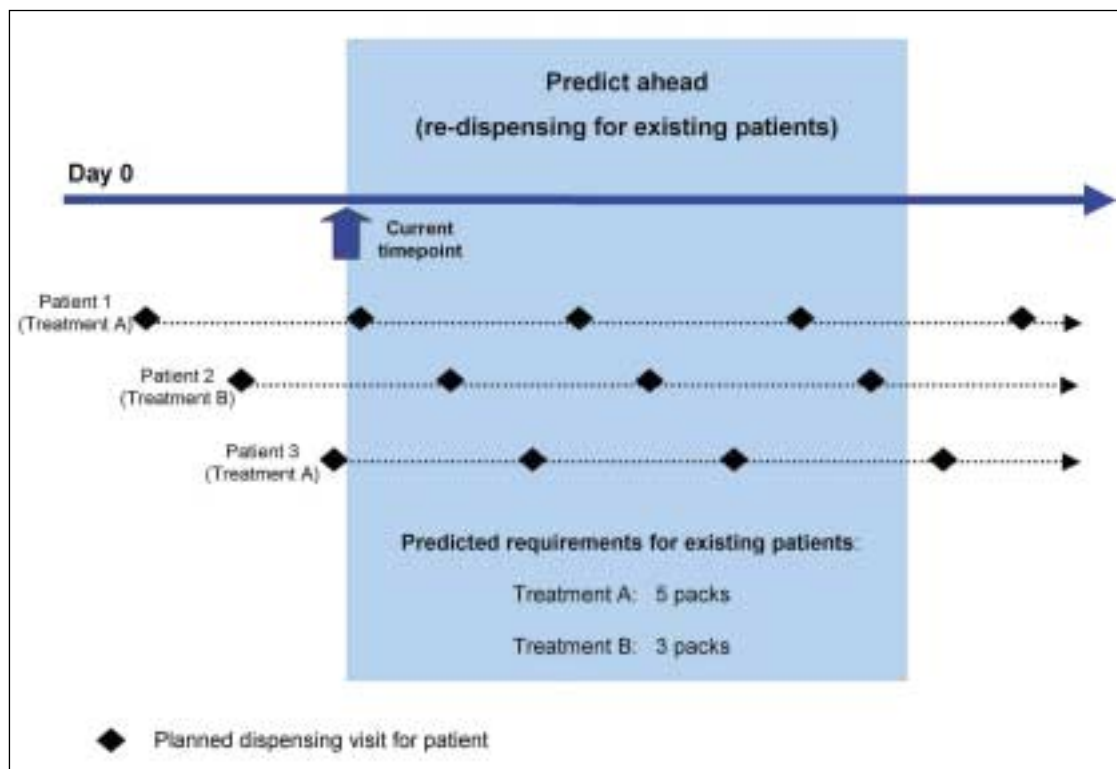
In this approach each site has a unique supply strategy defining the minimum stock level for each treatment group (which triggers re-supply once reached) and a maximum re-supply level (up to which that drug is restocked whenever re-supply takes place (see Figure 2). The trigger levels are normally estimated depending upon the re-supply rate (or recruitment rate) of the individual sites, and the time it takes to deliver new supplies to site. IVR systems should be flexible to enable trigger and stock levels to be adjusted throughout a study, as the performance of individual sites can be quite different to the pre-study assumptions. To maintain treatment blinding, whenever a re-supply consignment is triggered by any treatment group, all treatment groups are re-supplied up to their corresponding re-supply level at the same time. This has the additional benefit of minimising the number of shipments required, an important cost consideration.

The downside of this method is that it maintains adequate levels by purely monitoring supply usage and does not take account of known repeat dispensing requirements of individual subjects. Trigger and re-supply works best where only a single dispensation of study medication at randomisation is required. For studies where subjects are returning for regular determined re-dispensing visits, a more sophisticated algorithm can be used to account for the future requirements of returning subjects. This is termed Predictive Re-supply.

## Method 2: Predictive Resupply

In many longer-term trials, there is a protocol-defined schedule defining the time-points at which additional medication packs will be dispensed to the patient. In this event, it is possible to predict when subjects will be returning for their next visit and what pack type they will require. In this way, unless a patient has withdrawn from the study, the future supply requirements for existing patients can be forecasted.

In this approach the system looks ahead over a predictive "window" of time and identifies how many subjects should be returning for repeat dispensing visits, and how many such visits will occur. In this way, the system can calculate the total number of packs required, assuming these patients do not withdraw. By comparing the forecasted requirements to that available at site, the system can determine if there is a supply need and request material accordingly (see Figure 3). However, using this approach it is still important to maintain a buffer stock of supplies at the site to account for any new subjects or allow for medication allocated to the subject that requires replacement due to loss or damage.



### Managing the entire supply chain

In large multinational clinical trials, the logistics of supplying individual study sites are simplified by the use of local depots that serve the study sites in each country. This is particularly important when importation regulations may slow delivery of medication direct from the main distribution depot.

In this case, the IVR system can be configured to manage inventory levels at both site and local depots by activating shipments from main depot to local depot and from local depot to site (see Figure 4). Other issues are important for consideration at this stage, such as the language of the labelling applied to individual medication packs. Techniques such as multi-lingual labelling using multi-panel or booklet labels maintain the flexibility of study supplies when a number of countries are involved.

### Supply chain forecasting

By using an Interactive Voice Response system to manage medication supply, supplies groups have access to real-time information regarding where each pack of medication is at any point in the study, and also (un-blinded) information on the number of packs of each treatment still available for dispensing to patients. This is important when studies start without supplies formulated and packed to meet the requirements of the complete clinical trial. In many cases, medication may be packed in stages throughout the study to meet the ongoing needs.

In long-term studies, the amount of medication available to patients on each treatment may be disproportionate even when the randomisation schedule requires a 1:1 treatment ratio. For example, if one of the blinded treatments is placebo, more patients may withdraw early without completing the full treatment period due to lack of efficacy. This would result in more packs of placebo treatment being available for future placebo-treated patients and hence a reduced requirement to formulate and pack placebo in a future production run. Conversely, in active-controlled studies, side effects may limit the completion of patients on one particular treatment leading to a reduced requirement

for further production of medication packs of that treatment.

This kind of real-time information can be valuable in planning both the timing and content of future production runs, optimising the availability of study medication and reducing the wastage in medication produced.

### Summary

Interactive Voice Response (IVR) systems offer a valuable technology in the optimisation and management of the clinical trial supply chain. Working practice changes are required to enable the full benefits of IVR to be realised. This includes modifying the way medication is packed and considering the optimal dispensing unit of medication to provide the best flexibility and savings in drug supplies. Real-time inventory data could be valuable in the planning of timing and content of production runs to meet the ongoing requirements of a clinical trial.

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Optimising the control of site inventories by considering the future medication demands of enrolled patients - the predictive re-supply method.

Figure 4. Managing stock distribution and inventories between global depot, local depot and study site.

