



# The Solution to More Effective Clinical Trials: Adherence Packaging

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Patient adherence is critical in a clinical trial setting -- it has a direct impact on the validity of clinical trial data, an issue of utmost importance to pharmaceutical manufacturers, as well as the scientific and regulatory community. While adherence is influenced by a variety of factors, packaging has proven to play an important role in improving compliance rates. MWV Healthcare has performed extensive research to determine the key drivers of non-adherence and concluded that integrated blister and paperboard "calendarized" packaging eliminates some of the key barriers to medication adherence by patients in general, and those participating in clinical trials.

MWV's conclusions are also supported by previous clinical and academic research. A 2005 study conducted by K. Holroy found that 25 to 50 percent of participants at clinical trials do not adhere to the prescribed drug regimens. Non-adherence or partial adherence of research participants can result in inconsistent or altered study results that misrepresent the effectiveness of a drug and the impact it might have on the patient.

Non-adherence or poor adherence constitutes one of, or a combination of the following:

- Taking more medicine than prescribed
- Taking less medicine than prescribed
- Taking medication at a time of day or time intervals other than prescribed
- Taking medication in conditions other than prescribed (with or without meals, etc.)

Tainted trial results could lead to the rejection of a drug that could be effective in the market or, conversely, to the approval of a drug that would not be effective under recommended use. Ultimately, non-adherence could also lead to inaccurate dosage or ineffective treatment of the disease. Inaccurate dosing, for example, can be quite costly in the marketplace, as launching a drug in a higher dose than required can result in price erosion if a lower dose proves effective in a non-clinical setting. Twenty-two percent of the drugs entering the U.S. market between 1980 and 1999 required significant post-launch dose adjustments, due to poor dosing during clinical trials. And, occasionally, drugs are pulled from the market altogether when unexpected effects are seen among a large-scale group.

Therefore, poor trials due to problems with adherence can result in lost revenues for pharmaceutical companies, higher costs for payers and potentially increased health complications for patients.

## Patient Adherence Influencers

A patient's decision to take a drug is driven by a range of factors, influenced by emotional and functional needs. Emotional needs include the motivation to take the drug, the desire to maintain control over one's life, and the belief in the benefit of the drug. A trial patient may assume (correctly or incorrectly) that the medication is not working, come to the conclusion that there is no personal benefit for continuing the treatment, and decide to stop taking the scheduled dose.

Functional needs encompass a patient's ability to integrate the drug into his lifestyle, understanding of the drug and the necessity to adhere to the regimen, and the ability to remember and understand the regimen schedule. Many patients simply forget to take a scheduled dose, or they don't follow specific dosing instructions such as time of day or whether a prescription should be taken with food.

## Blister Packaging Improves Patient Adherence

Packaging can play an important role in addressing and mitigating a variety of emotional and functional barriers that patients experience during clinical trials. While traditional pharmaceutical packaging – standard bottles and amber vials – do not provide any support for patients in following their treatment regimen, a combined blister and paperboard, unit dose package provides a variety of benefits that encourage prescription compliance and ease of access for patients. Clearly printed symbols and directions for use (i.e. suns for morning and moons for evening BID

regimens) are employed with blister packaging, while senior-friendly, child-resistance features (a regulatory requirement for US trials in the home but respected worldwide) discourage child access. Some clinical researchers claim that project lead times are shortened with bottles, but lead times for calendarized blister packaging can be reduced with effective clinical supply planning.

Clinical adherence blister packaging solutions, which consist of a foil-backed blister card housed in a paperboard carton and/or wallet “sandwich,” are compact, patient-friendly and portable. The convenient unit-dose dispensing system prompts patients to take medication correctly and on time, leveraging printable areas and attached or printed directions for use. Additionally, the outer case or carton provides protection, room for patient education, prescription information, clinical labels and barcodes or RFID tags. Effective clinical trial supply packaging should be appropriately matched to the clinical suite or clinical supply company’s packaging equipment, and most clinical manufacturers have blister and wallet equipment.

### **Improving Convenience and Lifestyle**

Easy-to-use, unit dose packaging encourages patients to be more diligent in taking their medication. Multiple studies show that patients prefer blister packaging to the traditional vials and bottles because blisters are portable, convenient and easy to dispense. With blisters, multiple drugs can be placed in the same pack (for multi-medication therapy or titration), while multiple bottle solutions can be expensive and cumbersome to the patient. Push-through blisters can easily be opened and dispensed by adults and seniors, but also provides for extra security through child-resistant features. Cognitive opening features (requiring reasoning rather than dexterity or strength), such as that employed on MWV’s Dosepak® blister system, are preferred over traditional child-resistant methodologies, which can be inconvenient for patients. Calendarized blisters enhance product integrity and identity, leveraging an outer carton or case on which identifying visuals, barcodes and text are printed.

### **Calendarizing on the Prescription Package**

One of the problems with clinical trials is patients’ inability to keep track of when they last took the medication. As such, many study participants are accustomed to – and prefer using – pill organizers boxes for their prescription medications. In some studies, these patients manually remove the pills from the supplied bottle (sometimes even if it’s electronically monitored with an e-cap) and transfer them to the calendar organizer to keep track of dosing. Manually transferring pills carries the risk of mixing up medications contained in the boxes, contamination and spilling.

Blister packs, on the other hand, seal in the medication to protect its integrity and prevent inadvertent spills, resulting in fewer lost doses. As they can be imprinted with dates and times that the medications should be taken, the package serves as a visual aid, encouraging patients to take their medication during the prescribed times, making the drug regimen easier to remember and giving the patient the ability recognize whether or not they have taken the scheduled dose. Use of different colors and graphics on the inner blister wallet or pack can further support the importance of following the regimen.

A variety of studies have proven that unit-dose medications packaged in blister packs provide a more systematic dosing schedule that helps patients remember to take medication. A recent Ohio State University study showed that unit-dose calendar packaging improved continued prescription adherence in elderly patients taking medication to treat hypertension. After 100 days, prescription adherence among patients using the calendar pack was double that of patients using the standard pack (about 50 percent compared to 25 percent, respectively). While prescription adherence among patients using the standard pack dropped off to below 20 percent after a year, the adherence rate for those using the calendar pack stayed well above 40 percent. More importantly, blood pressure dropped more significantly with the calendarized pack, as compared with the standard bottle pack.

### **Education at the Patient’s Fingertips**

We’ve found that attaching the prescription information and educational materials as part of the medication’s packaging can improve patients’ understanding of the medication and its effects, as well as remind and guide the patient toward following the prescribed regimen. In addition to an instructional area on the blister pack itself, the outer carton of the package contains space for dosing instructions, reminders and branding in large, readable fonts. The space can also be used to motivate and inspire patients by reinforcing why full participation in the trial is important and impactful. A large, fold-out panel displays all the relevant information and ensures that detailed instructions stay with the package, even during transportation.

A more detailed instructional insert/leaflet or booklet can also be included in a fold-out panel. Including this type of detailed information has proved successful with oral contraceptives, and it was recommended by a recent study on Drug Regimen Compliance that all chronic-use medications adopt this type of informational addition to the packaging in order to mitigate non-adherence.

### **Conclusion**

Patient adherence is critical to the outcome of clinical trials in determining the drug's efficacy, receiving approval to put the drug on the market and establishing dosing guidelines. Using a calendarized blister pack is a meaningful way to improve patient adherence in clinical studies, which, in the long term, will result in better care and outcomes for patients and improved efficiency for pharmaceutical companies.

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