

Benefits of smart blister packaging in clinical trials

Undocumented dosing non-adherence in drug development results in poor-quality data or even the failure of the trial. Ward Smith, director of marketing at **Keystone Folding Box Company**, explains how smart packaging can provide real-time information for accurate data capture.

Smart packaging is more than just a high-tech package, it is a vehicle in which valuable data is captured; data previously unattainable to a reasonable degree of accuracy. The average per-patient cost in a phase II trial is just over \$19,300 per patient. The cost per-patient in phase III studies exceeds \$26,000. If a subject fails to take medication to protocol and doesn't disclose this information, the study sponsor has spent time and money collecting poor-quality data, which can distort efficacy analysis.

Electronic monitoring methods reveal that over 30% of patients omit many prescribed doses, irrespective of disease, prognosis or symptoms. Ideally, smart packaging monitors and records when each individual dose is expressed from the blister package. Thus real-time data relating to patient dosing compliance or adherence is accurately captured.

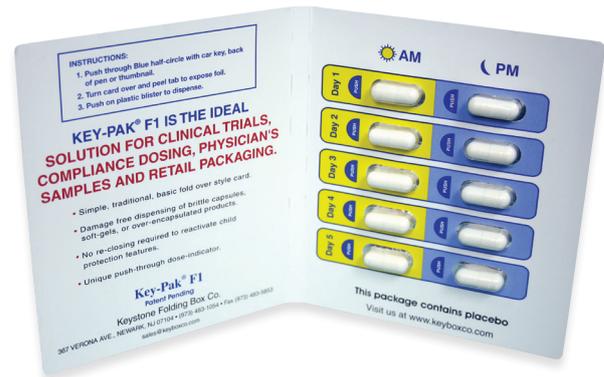
Human error

Clinical trials often rely on patient-reported adherence data which is collected in diaries. A study in 2002 published in the *British Journal of Medicine* showed that only 20% of patients made diary entries within the 90-minute window of dosing time. Many patients do not fill in information until they complete a week or more of dosing, and then rely on memory to recall dosing times. Some completely fill out the diary before ever taking the first dose. In another, it was revealed that patients failed to write the truth in their diaries, over-reporting usage more than 50% of the time.

Patients who over-report the use of drugs often maintain an appearance of being compliant. A study at the University of Texas Southwestern Medical Center illustrates how this can happen, stating: "Using electronic monitoring methods, the study showed that clinician assessments dramatically underestimated antipsychotic medication non-adherence. This finding questions the ability of clinicians to detect clinically meaningful antipsychotic non-adherence, even in patients with nearly complete non-adherence."

Understanding efficacy in patients who adhere relatively well to a prescribed dosing regimen is critical to selecting the correct optimal dose. Equally important is understanding when little or no efficacy correlates to clinically significant non-adherence.

According to Carl Peck MD, FDA director of CDER (retired), "it is now well established that there is a systematic flaw in dose finding during drug development that has resulted in strong evidence; about one in five products will undergo a 50% dose reduction post market. Suboptimal adherence is a serious



Smart packaging monitors and records when each individual dose is expressed from the blister package.

problem when the analysis of the trial uses the intent-to-treat approach, which is required by the agency. If there have been significant missed doses or insufficient adherence during the trial, it can lead to the failure of the trial diluting the effect size or the results by having patients that were not exposed to enough drug dose."

The cost of non-adherence

According to a recent report by The Tufts Center for the Study of Drug Development, the average cost to develop a new prescription drug today exceeds \$800 million. If a drug has an estimated revenue of \$1 billion dollars and it runs a one in five risk of an over 50% post-market dose reduction, there is a 20% chance that the revenue potential could be affected.

The introduction of smart packaging technology into clinical trials will improve data quality and reduce the risk of post market dose reduction. Cost per patient to include this technology ranges from \$300–800. Some clinicians feel that, depending on the study design, using smart blister packaging will allow for a reduction in the number of patients needed in a study, thereby reducing the overall cost and time needed to conduct a clinical trial. With this in mind, can you afford to avoid smart blister packaging in your clinical trials? ■

References are available upon request.

Further information

Keystone Folding Box Company
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