HOW VALID ARE YOUR CLINICAL TRIALS DATA?

Allan Wilson MD PhD

It is widely accepted that patients participating in clinical trials are less than perfectly adherent with their medication regimens. The extent to which non-adherence affects the results of clinical trials is unknown. Several factors interfere with the assessment of this phenomenon, principal of which is the lack of a methodology to monitor patient adherence in a non-invasive (i.e. unbiased) way.

Adherence with medication is thought to decrease with duration of therapy, the number of times a day the medication is to be taken, side effects, and break-through of clinical signs and symptoms. It is also over selected in certain populations such as elderly and psychiatric patients.

Clinical research depends largely on pill counts and self-report medication diaries. Participating patients are interviewed at intervals and their remaining pills counted. However, patients are known to be poorly forthcoming about non-adherence, generally from embarrassment or a desire to please the researcher. They are also known to fill out medication diaries retrospectively just before their interviews, often with less-than-perfect recollection.

Even patients who have positive interviews and correct pill counts may be non-adherent. With most medication trials the aim is to keep plasma levels within a therapeutic window. Not taking medication on time, taking extra medication, missing one dose and doubling up on the next can all result in plasma levels dropping below or exceeding the therapeutic window. The result may be ineffectiveness of the therapy due to inadequate plasma levels, or side effects due to elevated levels. Both have serious implications for the clinical trials decision-making process.

Until recently, mechanical devices used to assess non-adherence were flawed for a variety of reasons. They tended to interfere with the process of medication-taking by requiring the patient to behave differently when using them, and by their bulk and resultant inconvenience. They also increased the cost of the clinical trial. For these reasons, they were not very useful in clarifying the adherence issue.

The newer generation of Electronic Compliance Monitor (ECM©)such as the Med-ic® Smart Blister Package, eCap™ and Med-ic® Syringe Pack monitor adherence without additional patient input or inconvenience. They integrate seamlessly with the manufacturing and dispensing processes, are reasonably priced and can generate significant positive return on investment.

As the ultimate goal of a clinical trial is to demonstrate efficacy and safety, this should clearly not be left to data of questionable accuracy. Accurate measurement of patient adherence is the key to more accurate clinical trial results.