HOW IS MED-IC® USED IN CLINICAL TRIALS?

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Electronic adherence monitoring adds up-front cost to a clinical trial but offers enormous net return on the investment (ROI). This is why progressive clinical trials are using Med-ic®.

A clinical trial is simply an exercise in optimizing a signal-to-noise ratio. The signal is the desired therapeutic effect; the noise everything else that obscures the signal. Poor patient adherence with medication has long been known to be a large source of noise – noise that can now be measured by Med-ic®.

Adherence information is used in a number of ways.

- To screen patients for adherence characteristics prior to enrolling them in an intent to treat (ITT) trial. A short placebo pre-trial identifies those who are non-adherent. They are either removed from consideration or targeted education is used to train them to be more adherent before they are enrolled in the ITT trial.

- As insurance against "just missing" a primary endpoint. Confident as a sponsor may be that the IND will show a significant treatment effect, the fact is that 8.5 percent of INDs obtain regulatory approval and failed trials are often reported as "just missing" their endpoints. Med-ic® can serve as low cost insurance against "just missing" on an enormously expensive trial, turning p =.057 into p <. 05, for example, by powering up the design.

- The best use of adherence data is to give feedback to participants about their adherence as they move through a clinical trial. At follow-up visits, packages are scanned, adherence data reviewed with the subjects, and targeted motivational counseling used to improve adherence during the remainder of the trial. If all treatment groups participate in the process, this simply reduces the error variance and increases the power of the study. This means fewer subjects are required to detect a statistically significant treatment effect, reducing the cost and duration of the trial. Quicker regulatory approval translates into longer patent protection, and generates ROI.

- Many Med-ic®-enabled trials have used adherence data to assess subjects' adherence *post hoc* (on completion of the trial). This data mining can throw light on many aspects of the subjects' behavior and can be tailored to the interests of the sponsor. For example, in a recent trial it was found that 40 percent of subjects deblistered their medication on at least one occasion, something that would have otherwise gone undetected. This implicated poor package design (too large) and resulted in the sponsor using user-friendlier packaging for subsequent trials. This reduced deblistering to a more typical 3 - 4 percent.

- A Phase II trial showed no difference between treatment groups according to the primary outcome analyses.The subjects were stratified *post hoc* according to their adherence and the IND showed a highly significant treatment effect for the patients who actually took the drug as prescribed. The drug was subject to further assessment.

- Med-ic®can serve as part of a FDA REMS (Risk Estimation and Mitigation Strategy) for trials where non-adherence can have serious consequences beyond those associated with simple data inaccuracy. Opioids, for example, can result in fatal overdose when taken to excess, and these drugs are often diverted for sale on the street. Med-ic®can detect the deblistering suggestive of such activities, allowing the investigator to initiate a timely intervention.

- Using Med-ic®may in itself improve subject adherence although this has not been demonstrated due to the ethics of monitoring adherence without informing the subject.

- Med-ic®can detect subtle medication-related biases that might lead to erroneous conclusions about drug efficacy. For example, subjects in a treatment group might experience subtle positive (e.g. mild euphoria) or negative (mildly unpleasant) side effects that control subjects do not. Such subtle effects would typically go unreported by the subjects and might bias the results and confound standard tests of significance. Differential adherence rates between treatment groups can flag treatment-related bias.

- Med-ic®is important for adaptive trials due to the increased number of decision points and the consequent inflation of the probability of making an erroneous decision (compounding type I errors).

In summary, Med-ic®is a powerful tool for monitoring patient medication-taking behaviour during a clinical trial and using the non-adherence data to increase the statistical power of the design. This results in cost savings due to the ability of smaller sample sizes to show statistical significance (drug effectiveness) and earlier regulatory approval with longer time on patent protection. With a well-designed blister package equipped with an electronic adherence monitor and good subject education, patient adherence can be changed from a liability to an asset with enormous ROI.

Our customers find Med-ic® to be an invaluable tool for their clinical trials, as evidenced by the fact that much of our work is with repeat sponsors. For details about why Pharma finds value in Med-ic®, please refer to our ROI Calculator.