PATIENT COMPLIANCE
THE ELEPHANT IN THE ROOM

If Hippocrates[1] knew that patients are noncompliant with their treatment and nearly every clinician since would agree, why does the ***"elephant in the room"*** continue to be ignored?

A clinical trial is simply an exercise in optimizing a ***signal-to-noise ratio.*** The signal is the desired clinical effect; the noise everything else that obscures the signal. Poor patient compliance is a major source of noise that can now be measured and controlled to increase the accuracy of a trial.

> Drugs don't work in patients who don't take them.
>
> *C. Everett Koop, Surgeon-General*

Why are trials not all monitoring compliance, as suggested by Bradley Efron in 1998? The short answer is that trial planners focus on the initial cost of electronic compliance monitors (ECMs) such as IMC's Med-ic® and Proteus' Discover® and overlook the tremendous ROI they provide by accelerating trial fulfillment.

> At some point, perhaps not in the far future, it will seem as wrong to run a clinical trial without compliance measurement as without randomization.
>
> *B. Efron, Statistics In Medicine, 1998(17), 250.*

Compliance data are even more important for adaptive trials due to the increased number of decision points increasing the probability of a Type I error, and the smaller signals' vulnerability to being obscured by noncompliance (and other) sources of noise.

> Pray, Mister Babbage, if you put the wrong figures into the machine, will the right answers come out?
>
> *Charles Babbage, Polymath, 1864*

In addition to providing more accurate data, ECM is a powerful tool for monitoring subjects' medication-taking behaviour during a clinical trial and providing data to increase the power of the design. This results in cost savings due to the ability of smaller sample sizes to show statistical significance (drug effectiveness) giving earlier regulatory approval with longer time on patent protection. With a well-designed blister package equipped with an electronic compliance monitor and good subject education, poor patient compliance can be changed from a liability to an asset with enormous return on investment.

[1] *Hippocrates of Cos, Decorum, XIV*

Compliance data are used in a number of ways:

1

To screen patients for compliance characteristics prior to enrolling them in a trial.

2

To motivate subjects to be more compliant as they progress through a trial. It can be shown that increasing compliance by x% allows for a reduction of the trial's N by 2x% without changing the study's power. Fewer subjects means faster regulatory approval and longer patent protection. Hence the large ROI.

3

To assess subjects' compliance post hoc, Data mining can throw light on many aspects of subject behaviour and can be tailored to the interests of the sponsor, In one trial it was found that 40 percent of subjects deblistered their medication, something that would have otherwise gone undetected. The problem was solved by developing a more user-friendly packge format.

Another trial showed no significant difference between treatment groups by the primary outcome analyses. However, when the subjects were stratified into tertiles according to their compliance, the drug was highly effective for the compliant group.

4

ECM can serve as a REMS (Risk Estimation and Mitigation Strategy) for trials where noncompliance can have more serious consequences than 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. ECM detects the deblistering that might suggest such activities and allows the investigator to intervene.

5

ECM can detect subtle medication -related bias effects that can lead to erroneous conclusions about drug efficacy, which would otherwise go undetected.

Engineered by:
imc | INFORMATION MEDIARY CORP.

For details about why Pharma finds value in ECM, please refer to our ROI calculator at
http://www.informationmediary.com/roi/roi-calculator