In this digital age, many life sciences companies still do not use electronic solutions to collect patient-reported outcomes (PROs) from clinical trial participants. Although digital solutions have been accepted in small pockets of the industry, they are used roughly 35% of the time when sponsors ask patients to report their health status via electronic methods only about 35% of the time.

Electronic reporting solutions—which include voice, Web, specialized handheld devices, and smartphones—offer advantages over paper-based instruments. This article will examine the use of electronic Clinical Outcomes Assessments (eCOA, previously referred to as ePRO) tools, including the potential use of bring-your-own-device (BYOD) solutions that work on patients’ smartphones or tablets.

THE ROLE OF PATIENT-REPORTED OUTCOMES

Information collected directly from patients is increasingly important to the success of Phase II-III studies as a means of proving a product’s efficacy and safety. Indeed, regulators recognize that the patient experience “…complements the use of clinician evaluations, objective statistics such as survival rates, and other indicators of clinical efficacy and safety.”

There is also a growing demand for patient-reported data collected during post-marketing studies. When payers require evidence demonstrating a product’s health economic value in order to make their coverage decisions, capturing data on patient experiences will be integral to manufacturers’ gaining and sustaining market access for their products. To that end, larger patient populations will be required to capture that quantitative data to support Health Economics and Outcomes Research (HEOR) claims. When that’s the case, e-solutions will come into their own.

The U.S. Food and Drug Administration (FDA) issued guidance for the industry in 2009 on the use of PRO, which quite clearly allowed for digital instruments, stating: “Data collection methods can include paper-based, computer assisted, and telephone-based assessments.” The section of the guidance relating to eCOA deals most specifically with the need for recordkeeping, maintenance, access, and security.

As part of Good Clinical Practice (GCP), any method used to collect patient-reported outcomes must minimize the burden on patients and at the same time provide feedback that it is correct, dependable, and repeatable. Yet, the process will always be limited by the following facts, no matter how much scientific rigor is applied:

• Patient compliance will be a perpetual challenge; patients will report as directed—or not—based on their own internal motivation and regardless of the survey modality used.
• Two sources of potential bias exist, independent of the survey modality:
  1) patients want to get better and so often say whatever they think will support the drug’s approval and

Will e-Solutions End the CLINICAL PAPER CHASE?

*e-Solutions offer advantages in collecting patient-reported trial outcomes*

Mark Wade
Director, Patient Focused Solutions, Almac
2) patients tend to want to please the Principal Investigator (PI) and so often say what they think the PI wants to hear. The awe or trepidation that some patients feel when in the presence of a physician is referred to as the “white coat syndrome” and can shape responses to questions. For example, it is well known that blood pressure (BP) taken in a clinic can be artificially higher than the patient’s regular test.

• The validity of results diminishes the longer patients wait to report, and patients do tend to put off their reporting. This tendency has been dubbed the “parking lot syndrome,” because so many patients complete weeks’ worth of diaries just before entering the principal investigator’s office for a study visit. The FDA clearly states that “PRO instruments that call for patients to rely on memory…are likely to undermine content validity.”

THE GREAT MISCONCEPTION ABOUT PAPER

Paper-based survey tools, which have been in use for 50 years, have successfully supported thousands of label claims. Paper is ubiquitous, familiar, and proven. Indeed, paper-based instruments are held up as the standard against which all other modalities are compared. Despite this history, paper cannot compare to e-solutions in speed or data cleanliness. Unlike digital tools, paper-based surveys have no mechanism to prevent patients from skipping questions, writing in margins, or providing out-of-range or ambiguous data. And there is no way to tell if a patient completed the diary from memory recall. Errors can also be introduced in interpreting patients’ handwriting and in keying their responses into a database. Each of these issues is addressed by electronic solutions (Box, P. 60).

“One operations director with a large biopharma company noted, “We spend $14.7 million per year on paper for clinical trials, yet this is not a line item in our trial costs.”

Interactive Voice Response (IVR) Systems

Interactive Voice Response systems are the oldest electronic solution, but are not, by any means, outdated. They may, in fact, just be coming into their own, given the ubiquity of cell phones even in emerging markets. According to Pew Research, “…the rapid rise in cell phone ownership is quite breathtaking and might be due to the fact that many nations, unlike the U.S., have skipped landline technology and moved straight to mobile.”

Through IVR systems, patients are given a toll-free number and can dial in (using either a landline or a mobile phone) to report their information following voice prompts. Voice response is ideal for short instruments (10 questions or less) and can accommodate all types of survey questions. And one of their biggest benefits is that they are extremely cost effective; there is no need to provision hardware. Plus, the phone requires no learning curve—even children know how to use it.

Web Portals

This modality is similar to IVRS in that it is widely available to patients and very inexpensive for sponsors. Patients simply log on to a computer and access a portal to complete their survey. Another advantage is that it is easy to render questions
on a website to appear just as they do on paper, which makes equivalence testing quite easy. And, where patients have smartphones or tablets, this solution becomes, in essence, one of the BYOD modalities discussed below.

**Proprietary Handheld Devices**

Approximately 20 years ago, some clinical trials service providers created specialized data collection software to run on personal data assistants (PDAs). The idea behind this method—allowing patients to report via a mobile device—was groundbreaking at the time and is now mirrored in the BYOD approach today.

Today, of course, giving patients a separate device to carry (along with their cell phone or tablet) is as costly as it is inconvenient for the patient. Proprietary devices must be leased, programmed, shipped, and re-provisioned if lost. It is difficult to envision any scenario in which using these outdated devices would be preferable to today’s other eCOA solutions.

**Tablets**

Capitalizing on the world’s love affair with tablet technology, some companies have provided patients with tablets installed with a data-collection application. The format of surveys presented on tablets is faithful to paper versions (similar to the Web solution). Unfortunately, the hardware itself is still very expensive. If a tablet were lost or misplaced, a replacement would need to be swiftly furnished, which has both time and cost implications. Hardware must also be shipped to study countries and clear customs. The investment might, however, be justified if used for by clinicians to collect patient data (ClinRO).

**Patients’ Smartphones and Tablets (or BYOD Solutions)**

There are two ways that sponsors can arrange for patients to provide data via their existing smartphones: either through a dedicated application that patients download or through WAP/WEP accessing a Web portal (Figure 2). By leveraging assets that the patient already has, these solutions reduce patient burden and are especially cost effective for the sponsor.

These options are so appealing because companies wouldn’t have to provision devices to patients all over the world. And the devices wouldn’t have to be pre-loaded with instruments.

Currently, due to the complexities of having to adjust to different device platforms (and validate each version), the BYOD application version is challenging. The use of smartphones and tablets to enter data on a Web page has some

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**THE BENEFITS OF ELECTRONIC SOLUTIONS**

Vendors have been extolling the virtues of cleaner, date-stamped, verifiable data for more than 10 years. Studies have consistently shown that patient compliance for completion of PROs and data quality is significantly higher when PRO assessments are administered electronically. eCOA solutions successfully:

- Eliminate the data entry errors in transferring paper results into a database
- Provides immediate access to data in real-time reports
- Increase patients’ willingness to report sensitive information

In thus improving the quality of the data collected, e-solutions actually reduce the number of cohorts needed to achieve the desired statistical power in a study. This is no small feat and could reduce the cost significantly.

The typical break-even point for paper vs. eCOA is at 40,000 pages of incoming data. If a patient is completing two diaries per day over a trial lifetime, the number of pages can be three times that amount, but there is no added expense when the diary is electronic. The costs remain constant because hardware and software have already been provisioned. If hardware costs are removed, all that would be needed is software. But if one did not have to purchase software, but simply provide a stipend to cover patient data costs, the potential savings become clear.
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tangible advantages; it is essentially the same solution as the Web portal modality that has been in place for years, simply made portable on mobile devices and more useable with larger screen sizes.

In general, there is no solution that is best in every situation. The most applicable modality depends on a number of factors, including:

- The actual assessment to be used
- The disease state measured
- The length and complexity of the instrument
- The infrastructure for cellular signals and Internet connectivity in target trial markets
- The size of the patient population to be surveyed

That said, paper solutions may give way to digital ones when:

- Decision makers become attuned to the true cost of using paper solutions.
- HEOR professionals begin driving patient-reported research. They will need a ubiquitous modality that is inexpensive enough to use with larger volumes of patients and that will deliver quantitative data. The two existing modalities that fit best are IVR systems and BYOD. In all probability, the use of both will explode in the next few years through HEOR’s interest in using them for Phase IV studies. Meanwhile, bespoke handhelds will become a costly proposition.
- A body of evidence is formed as proof that these modalities have been successful in meeting regulatory requirements. Currently, sponsors are reluctant to share their success stories in using electronic modalities, but all could benefit by pooling information on their experiences—perhaps through a neutral party that serves as a clearinghouse for the information.

Of course, when the subject is technology, changes are always ahead. New technologies are on the horizon, such as wearable health tracking devices, for instance, which could conceivably become the latest new way to collect patient data. In the short term, however, eCOA solutions such as IVRS, Web Portals, tablets and BYOD offer benefits compared with traditional paper-based systems, and can improve efficiency and accuracy in clinical trials. CP

References