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FDA DRAFT GUIDANCE IMPACT ON THE E-PRO INDUSTRY

As some treatment effects are only known to the subject enrolled in a study, patient-reported outcome (PRO) measures have become a common metric in determining treatment efficacy and safety in clinical trials. Advances in PRO technologies, such as electronic patient diaries (e-diaries) and interactive voice response (IVR), have grown exponentially. To address these shifts in the industry, the FDA released in February its draft guidance Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. One topic addressed in the guidance is the electronic collection of patient-reported outcome (ePRO), spurred additional interest in this issue. (Editor's Note: The complete draft guidance is available at www.fda.gov/cber/gdlns/prolbl.htm.)

Many different methods for capturing PRO data are discussed within the guidance, including the use of technology-based tools. In addition, the FDA's draft guidance encourages sponsors to review their options in selecting a data-collection method for capturing PRO data. Although the guidance is still being revised, the anticipation is that the FDA's recognition and encouragement of PRO data (both electronic and nonelectronic) will drive pharmaceutical, biotech, medical-device, and CRO companies to incorporate more PRO into their trials.

It is expected that the final guidance will help the clinical-trial industry determine how PRO methodologies are documented and validated in the future, including, for the first time, special attention to electronic means of assembling, securing, and validating patient data.

EPRO TECHNOLOGY

As expected, the FDA recommends that when using PRO instruments "... sponsors should plan carefully to ensure that FDA regulatory requirements are met for sponsor and investigator record keeping, maintenance, and access." This not only includes record keeping, audit trails, and full access to appropriate information, but also in using accepted PRO testing questions and methods.

All of the implications of the guidance — including the evaluation, development, and modification of instruments — are applicable to both ePRO and paper methods. This includes the FDA's evaluation of electronic data-collection methods that must be thoroughly documented and validated. In addition, sponsors should be involved in the product development, including identifying specific endpoint measurement goals and planning a timeline that considers the development of the ePRO device. But there is still a question of whether the FDA's evaluation of the PRO tools will happen before or after the guidance is complete.

To further ensure the efficacy of an ePRO solution, sponsors should make sure that the best tool — paper, IVR, or e-diaries — is used to capture patient-reported outcomes.

The guidance also addresses the PRO provider's ability to "maintain source documentation" or in other words, keep a continuous record of the original, unadulterated patient data. With technology, the ability for electronic means to verify these data is even stronger and more reliable than paper, which often poses difficulties in maintaining data accuracy. Most ePRO providers incorporate continuous audit trails into their technology, which helps maintain data integrity.

The audit trail tracks each and every interaction that the patient has with the device. This allows sponsors and the FDA to examine data at any point during or after the study and recreate the flow of data. In addition, new technologies, such as biometric authentication, are being examined and implemented in the clinical space to serve as another means to track the access and modification of data.

DATA INTEGRITY AND QUALITY

The FDA addresses security concerns by encouraging sponsors to "establish appropriate system and security controls, as well as cyber security and system maintenance plans that address how to ensure data integrity." Part of this stability comes from the adaptability of the ePRO software. Many sponsors have turned to Windows-based technology to support a wide-variety of devices, including tablet PCs and other handheld electronic devices.

Beyond stability, the FDA also gives special attention in the draft guidance to the need to identify the intended population of the study, specifically with respect to patient age, sex, ethnic identity, and cognitive ability. This is of special interest to the providers of ePRO tools, particularly in terms of understanding the technology and the size and flexibility of the tools. It is imperative that ePRO vendors design tools that allow for full adaptation of fonts, formatting, etc.

This also leads to questions regarding the subject's understanding of the electronic tools used, trainer understanding of the technology, and the validation of certain assessments within some studies. As the patient population becomes more familiar with the technology, there will be faster implementation with a higher demand for ePRO solutions.

The FDA's draft guidance analyzing PRO helps to demonstrate the importance of evaluating PRO instruments fully, whether electronic or paper. Of course, this guidance is not yet final and ready for implementation, but it does provide the industry with a look into the future of PRO. As with any guidance, there are a number of points that still need to be finalized and decided upon. Input from the industry, including CROs, ePRO providers, and biotechnology and pharmaceutical companies is currently being considered before the draft is finalized.

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