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On Site: Icon Steps Up for Patient-Reported Outcome Measure Endpoint Validation

The FDA has chosen Icon to create industry-standard patient-reported outcome (PRO) measures and to validate those endpoints for antibacterial drug trials. The Biomarkers Consortium and the Foundation of the National Institutes of Health (FNIH) are partnering on the initiative with Icon. The Infectious Diseases Society of America and the National Institute of Allergy and Infectious Diseases are also involved.

The academic research community and pharmaceutical and biotech companies are coming together to identify new methods for assessing the success factors for antibiotics. The research will be applied in clinical trials for three endpoints — hospital-acquired bacterial pneumonia (HABP), acute bacterial skin and skin structure infections (ABSSSI), and community-acquired bacterial pneumonia (CABP).

The FDA awarded Icon the contract following a period of review after the company responded to the FDA Broad Agency Announcement for solicitation of research to advance regulatory science.

The FDA is interested in these PRO instruments because they directly measure how a patient feels or functions in clinical trials of new drugs for CABP, HABP and ABSSSI. Studies conducted by Icon under the contract will address the refinement of clinical endpoints for trials in patients with these serious infections. HABP is a leading cause of death in intensive care units and one of the most common hospital-acquired infections. CABP and ABSSSI also result in high rates of morbidity worldwide. PROs are important because they are a measurement based on a report that comes from the patient about the status of the patient's health condition without amendment or interpretation of the patient's report by a clinician or any other healthcare representative.

"Despite the high mortality and morbidity of these conditions, sponsors engaged in this clinical research do not currently have a consistent methodology to assess primary endpoints, which can slow development and ultimately delay the delivery of medicines to patients," said Brittany Erana, senior director, Clinical & Scientific Research, Icon Commercialization and Outcomes. "The PROs currently in development could be used to define endpoints that can provide direct evidence of treatment benefit on how patients feel or function. When developed appropriately, they can increase the efficiency and clinical relevance of clinical trials."

The PRO project is a critical component of the work that Icon, together with the FNIH and the Biomarkers Consortium, has been carrying out for the FDA to support the development of safe and effective antibacterial treatments in areas of unmet need in infectious disease. The relationship dates back to 2012, with the FNIH-funded development of PRO measures for use with patients diagnosed with CABP and ABSSSI. In 2014, the FDA funded the development of the third PRO measure for patients diagnosed with HABP. All three instruments have been designed to accurately and comprehensively assess the symptoms of each disease area at various time points over the course of the infection. Icon's Clinical Outcomes Assessment (COA) scientific research team has shown content validity for all three instruments through the analysis of qualitative data collected through interviews with patients and clinical experts.

Icon's COA team will design and execute a psychometric validation study for the three PRO instruments in accordance with the FDA guidance for PRO measures used to support

labeling claims. The project will be performed in line with the Drug Development Tool (DDT) Qualification Program.

As part of the project scope, these measures will be adapted for administration via electronic Clinical Outcomes Assessment technology (eCOA). This technology will allow patients to answer the questionnaire on a handheld device at specified time points over the course of the infection in order to measure the effects of antibacterial drugs.

Once the measures are psychometrically validated, it is intended that each measure will be used as a standard tool to gather key endpoint data on future clinical research in each of the respective indications. Icon will also be conducting a formal translatability assessment of the measures to minimize risk in the future translation and linguistic validation process. The process will help to ensure the content is written in so it can be easily translated and linguistically validated in additional languages. "As the PROs are available on the eCOA system where data is transmitting instantly upon patient completion, the data will be available for assessment in real time," said Erana.

The PRO instruments are in the final stages of development. Icon's eCOA system is being developed in parallel. "We are actively recruiting sites and patients to participate in the psychometric validation research stage," said Erana. "Once the eCOA system has gone through all phases of the software development lifecycle, including design, testing and user acceptance testing, the handheld device and web portal will be available for use in the research study."

— Jeremy Zucker

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