SIDLEY

New Europe Medicines Agency Guidance on Use of Software Tools in Clinical Trials

Zina Chatzidimitriadou

On April 7, 2020, the EMA published a "Notice to sponsors on validation and qualification of computerized systems used in clinical trials" (Notice) and accordingly updated the Good Clinical Practice (GCP) Q&As, Questions 8 and 9. This is a timely guidance given the increasing use of software tools in every stage of the clinical development of medicinal products. Use of tools such as wearables for patient monitoring, electronic consent and data collection and analysis and collection of safety information have become part of the new clinical trial landscape, where remote operation of parts of a clinical trial is becoming the norm. To ensure that the generated data is robust, reliable and accurate, the software must be validated accordingly so that it does not adversely influence the conduct and integrity of the trial data.

The Notice was jointly produced by EMA's GCP Inspectors Working Group (IWG) and the Committee for Medicinal Products for Human Use (CHMP). Given that these software tools are often not developed by the pharmaceutical company using them in their clinical trials, it is key to ensure that all operators are aware of the regulatory obligations and their role in complying with them. Although ultimate responsibility for the conduct of a clinical trial falls on the sponsor, third-party providers must facilitate compliance and ensure the software tool is fit for use in a clinical trial.

The guidance provides that in accordance with International Harmonized Guidance ICH E6(R2), computerized trial data systems should be validated. This consists of demonstrating that the software design, use and analysis of data is accurate and reproducible in accordance with a specification that is key to the reliability, robustness and integrity of the data. Failure to document the validation state of a computerized system may jeopardise the ability to use the generated data, and recent inspections have revealed a lack of adequate documentation supporting the qualification of the software tool. Of course those electronic systems that qualify as medical devices should independently comply with all the obligations set out under the medical device legislation.

Sponsors should be sure to maintain an audit trail for data entry and any subsequent changes, maintain a security system to protect against unauthorized access, maintain the blinding of a trial and account for the individuals with access to the data.

The dichotomy between the trial sponsor and the technology/software vendor can often be a reason for missed checks and uncommunicated information. One way of remedying this is by way of sound contractual arrangements, apportioning detailed responsibilities and subjecting the technology vendor to strict data collection and monitoring obligations, to support a marketing authorization application. The GCP Q&A contains relevant guidance notes. The vendors should be made aware that the contractual assumption of relevant

sponsor duties in the context of a marketing authorization application opens them to potential regulatory inspections.

For Swiss sponsors, the Notice is of course relevant for all their clinical trials performed on the territory of EU Member States. And although similar guidance from Swissmedic is currently missing, sponsors performing clinical trials in Switzerland may assume that Swissmedic would request that the sponsor take similar precautions to the ones described in the Notice.

Alongside data integrity, the use of software tools is still faced with a plethora of issues, including reimbursement methods, patient confidence and data privacy considerations. Many of these issues can be addressed through a combination of national decision-making and collaboration across regulators, and it is hoped that these matters will start being addressed in due course.