Understanding the Finer Points OF THE ELECTRONIC SOURCE DOCUMENTATION DRAFT GUIDANCE

Contributed by

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For those involved with collecting data generated by clinical trials, the recent draft guidance on electronic source documentation released by the FDA deserves your scrutiny. The impact of this guidance for sites is significant and the implications for CRAs, data managers, and technology vendors could be potential show stoppers. Since the draft guidance may not be considered light reading by some, I've summarized the major points the guidance (as indicated in the document) was intended to address:

- To eliminate unnecessary duplication of data
- To reduce the opportunity for transcription errors
- To promote the real-time entry of electronic source data during subject visits
- To ensure the accuracy and completeness of data (e.g. through the use of electronic prompts for missing or inconsistent data)

For the record, I agree that all of these targets are laudable, but I suggest the guidance needs some adjustments in several key areas.

The Mother of All eCRFs

One of the central points of this draft guidance concerns the role of a redefined eCRF. The guidance promotes the eCRF from its humble origin as the digitized form of a paper CRF to the nexus of all clinical data (electronic and paper-based) associated with a protocol. This is certainly a vision shared by many sponsors and technology vendors (though maybe via a system and not a form), but the reality is that the current standards, embedded technologies, and siloed purchasing habits will not support this goal for many years to come. Directly related to this expanded role of the eCRF is new language describing precisely how investigators should handle the processes surrounding the data flow.

More Work for Overburdened Sites

The data elements that make up the eCRF are the subject of both further definition and added girth. For example: when data elements are transcribed by an individual from a source clinical trial document into an eCRF, the recommendation is that they carry a data element identifier reflecting the originator responsible for entering the transcribed data element. This is just one example of the level of detail contained in this guidance.

Switching to a higher level view, when electronic source is used, the draft guidance indicates the following procedures and practices that add significant overhead for involvement in clinical trials:

- Principal Investigators (PIs) should generate their own write-protected copy of the eCRF (the newly defined uber-integrated-eCRF) for the study
- PIs must maintain control of these copies
- A copy of the eCRF should be write-protected (read-only) at the time of PI sign-off
- The PI must review and sign the eCRF before any data are made available to IRBs or sponsors
- Procedures for selecting appropriate data elements out of an electronic health record for use in the eCRF must be in place
- A list of prospectively determined originators (persons, devices and instruments) must be maintained, on-site

Are there safety issues if unreviewed data are unavailable to sponsors and IRB's? Does this mean a return to on-site servers and replicated databases or simply gold copy CDs on site?

The current recommendation would appear to require the programming of interfaces to electronic medical records and clinical systems at each site. This is beyond even the largest sponsors' abilities today. Apart, each of these guidelines could add procedural and administrative overhead at sites for the conduct of trials, together, they might well convince many investigators that it's not worth the trouble.

Related to the added site overhead, the job of the CRA just got a lot more technical. CRAs will require a thorough understanding of database design and audit trails as well as becoming expert with the technologies used at the site.

It's a Small World, Right?

It's a fact that most Phase III clinical trials are now multinational. Changes as substantial as the ones proposed in this guidance must be synchronized with the other regulatory agencies worldwide to be either effective or practical.

What about electronic health records (EHRs)? Meaningful integration with EHR systems will probably require an international mandate to standardize those systems, too.

This draft represents a curious mix of recommendations. Some appear to go backwards and ignore the capabilities of current systems and others leap so far ahead that they border on wishful thinking.

There are huge, relatively near-term potential benefits associated with some aspects of this guidance, such as the remote monitoring of electronic clinical trial data. A clear definition of what is acceptable could result in worthy savings and operational gains for sponsors. I urge the FDA to clarify guidance supporting near-term efficiencies that can help the industry thrive on the way to the electronic nirvana.

Editor's Note: Mr. Andrus led the SCDM's task force on submitting comments to the FDA on this draft guidance. PV

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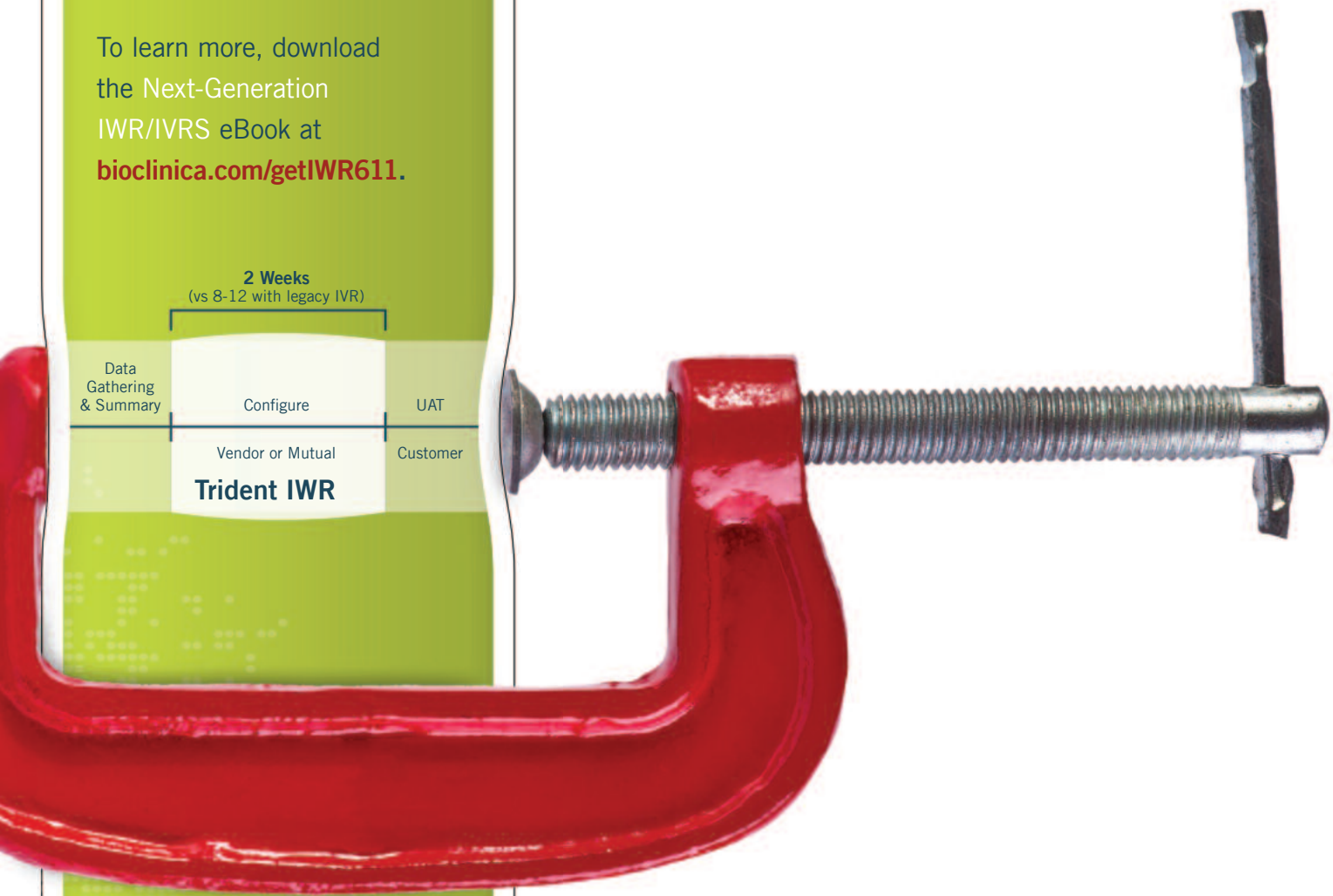

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