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Have a pet peeve about quality ?

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DQRI Submits 21CFR11 Feedback

Over the past years, the FDA has become aware of the extreme burden that 21 CFR Part 11 has placed on those conducting clinical trials for regulatory submission. The absence of clarity on validation has generally resulting in a very conservative interpretation by industry. This has resulted in an enormous financial outlay with little assurance of improved quality. On 8 July 2004, in response to a call for public input from the FDA, DQRI submitted a commentary on 21 CFR Part 11. This document, based on work performed by the DQRI Software Validation group, followed the agency's lead and outlined a risk-based approach to software validation. On 29 September 2004, the FDA issued a draft revision to the guidance titled *Draft Guidance for Industry: Computerized Systems Used in Clinical Trials*. DQRI's commentary is in line with the new guidance document.

There is no simple answer to the question of how to assess risk in the many types of clinical trials software, nor is there a clear rationale for what level of validation is appropriate for what software. The efforts of the DQRI working group over the past year resulted in an outline of an approach that would allow software developers to categorize their products based on function, risk of failure and likelihood of failure, and determine the appropriate level of validation to apply.

The team will wrap up the current project by writing a white paper that outlines their approach, and will then establish new working groups to address the parts of the model that still remain to be detailed.

DQRI is very grateful to the members of the working group, and wishes to recognize the team facili-

tator, Sue Carroll from SAS, as well as the team members for their dedication. Team members include Don Hopkins from Ursa Logic; Anthony Costello from Nextrials; Bob Lyons from Nextrials; Christopher Costello from the University of California at Santa Barbara; Dave Christiansen, an independent consultant and member of DQRI's Board of Directors; and Kaye Fendt, founder of DQRI.

Address Change

DQRI's ground mail has changed to:
P. O. Box 9124
Chapel Hill, NC 27515

Next Quality Project

DQRI is very pleased to announce that the next quality project has been launched. Facilitated by Alec Vardy from CV Therapeutics, it will address the question of what value, if any, does the practice of database audits provide in assuring clinical trials data quality. A database audit is the process by which a sample of data is selected from a database, and that sample is compared to source data. There is currently no standard methodology for determining how to select the sample, its

size, how to define what constitutes an error, how to calculate an error rate, the applicability of the procedure to EDC studies, or indeed even what question is being asked by this practice. The team that will address these issues has been drawn from industry and academia, and will have a liaison to the FDA. It expects to produce a draft recommendation by April 2005 that will be issued for public commentary. A final result is anticipated by September of 2005.

Many Thanks to



for their generous support of DQRI

Reducing the Burden of Quality

In past years, industry and the FDA have often been at loggerheads, with the FDA looking for 'gotchas' and industry overcompensating in its desire to avoid them. This history colors some companies' views of the idea of partnering with the agency in engaging in research into clinical data quality. They fear that new, more onerous processes will be devised requiring yet more effort, time and money in preparing drug submissions.

These days, little could be further from the truth. The agency is facing enormous pressure from Congress and the public to speed patients' access to new therapies while still guaranteeing safety at affordable costs. Recently the FDA issued its 'Critical Path' report that identified a lack of innovation in drug development, possibly resulting from a number of factors beyond industry control, stating that the reason that fewer therapies are being approved is that fewer are being submitted¹.

Industry faces similar pressures, not only from Congress and the public but also from health care agencies and insurance companies, to reduce costs, speed development, and improve safety. While part of the issue is certainly that the 'easy' therapies have been developed already, part of it is also a reaction to the historically-based concerns for the 'gotchas' that result in enormous expenditures up front in order to try to forestall any possible agency concerns. Both sides are beginning to recognize that this paradigm does not work. Instead, the agency has proposed adoption of risk-based models for many aspects of drug development, and is eager to work with industry to develop practical approaches for the implementation of such models. Indeed, the Critical Path report seeks to create a number of tools to help industry and the agency work together to increase drug development flow. Many in industry are responding to the call, and there is reason to

believe that progress can be made. DQRI's goal to establish standards for defining and assessing quality in clinical data is intended to mesh with those efforts. DQRI recognizes that in the current environment, recommendations that address quality at the expense of timeliness and/or cost are not feasible. The institute's desire to partner with the agency in their projects stems from the idea that if all stakeholders are at the table at the beginning, the design can accommodate all needs and the end result will be useful for all. Far from increasing the bureaucratic burden on industry, it is DQRI's fervent hope that the results of the research projects will make the process more efficient and less costly, while increasing the quality of the outcome.

That is being true to "Advancing the Quality of Clinical Data".

¹*Innovation or Stagnation? - Challenge and Opportunity on the Critical Path to New Medical Products*, March 2004

**"In 1992 ...
[Kaye's] vision of
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People Profiles

This column will profile the people involved with DQRI. It is written by Quality Matters staff. -Ed.

In 1992, Kaye H. Fendt received her MSPH at the University of North Carolina in their seminal data management program funded by the US Public Health Service. During this time she came to realize that there was no coherent body of knowledge about clinical data quality, and her vision of clinical data quality management as a robust research-based discipline was born. In 1995 she joined the FDA, and was selected to be a Fellow at the Council for Excellence in Government, working to improve quality processes in the US federal government. This was when she began to put the data quality building blocks into place.

There were many hurdles to overcome before her vision could come to pass. Soon after joining the agency, she became a founding director of the Clinical Data Standards Interchange Consortium, (CDISC), which defines how to store and transmit clinical data in a consistent manner. She then turned her attention to helping to transform the profession of clinical data management into a recognized and respected field by throwing her efforts into the newly formed Society for Clinical Data Management. While there, she and a team of others initiated the development of the Good Clinical Data Management Practices document, which defines what good data management looks like. Along the way, she held positions in industry

and academia, rounding out her expertise.

Now the time has come to complete the vision with the establishment of a research institute to facilitate the creation of the body of knowledge that will define clinical data quality. She took this step in January of 2004, founding the Data Quality Research Institute as a 501(c)3 non-profit organization. Kaye's mix of regulatory, industry and academic experience, along with her ability to inspire others with her vision, creates a potent combination to energize the institute. As it's Scientific Director, and the chair of the Board of Directors of DQRI, she is uniquely qualified to lead it in its mission to use clinical data quality to improve medical decision-making.

“You can’t control what isn’t named.”*



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Advancing the Quality of Clinical Data.

The **Data Quality Research Institute (DQRI)** is a non-profit organization that provides an international scientific forum for academia, healthcare providers, industry, government, and other stakeholders to research and develop the science of quality as it applies to clinical research data.

DQRI is run through an Operating Board drawn from industry, academia, regulatory agencies and support services. The Institute also has been assigned an FDA liaison, Steve Wilson.



DQRI at Meetings

DQRI is committed to the notion of open and transparent development of quality standards, with full participation of all stakeholder communities. One way of doing this is to ensure that DQRI has a presence at appropriate meetings and presents on topics related either to institute projects or quality generally.

Representatives of DQRI have given presentations at a number of meetings in the past quarter. In September 2004, Kay Obenshain presented a “The Case for Clinical Data Quality” to SPIN, the Software Process Improvement Network in RTP, North Carolina. In early October, the Society for Clinical Data Management (SCDM) held their Fall Conference in Toronto. Anthony Costello presented an updated version of the

model developed by the software validation working group, and Kit Howard presented a paper on myths of standardization and standards in support of quality. In late October, Kaye Fendt presented “Advancing Clinical Data Quality in the 21st Century” at the DIA West Coast Drug Development Forum in San Francisco, California. Copies of most of these presentations will be made available



on the DQRI website, accessible by clicking on the “Papers and Presentations” button on the home page.

In the coming months, DQRI expects to give papers at the American Society for Quality annual meeting in Seattle, WA, in May, the ENAR meeting of the American Statistical Association in North Carolina in March, the SCDM Spring Forum in Atlanta in March, the DIA Annual Clinical Data Management meeting in Arlington VA in April, and the Society for Clinical Trials meeting in Portland OR in May. DQRI representatives may also be attending other meetings, so if you are interested in seeing DQRI at a particular meeting, or have an idea for an event at a meeting, please contact us at info@dqri.org.

*Eugene J. Wittry, *Managing Information Systems: An Integrated Approach*, 1987.