



## ISO Updates Medical Device GCP

On October 22, 2009, the International Standards Organization (ISO) issued the final draft of ISO 14155.2, "Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice." ISO's member organizations are voting on it and, if approved, it will be final some time after December 22<sup>nd</sup>. This revision combines two prior documents (ISO 14155-1:2003 and ISO 14155-2:2003) covering general research requirements and clinical investigation plans, respectively.

The revisions bring the standard further into alignment with ICH E6 "Consolidated GCPs" and add references to recent "hot topics." Although E6 was not explicitly written for drug development, it does not contain specific guidelines needed for device development, and that is the role the ISO standard plays. **This article summarizes the changes from the old to the new versions of the ISO standard.**

*(Continued on page 2)*

## Cutting Edge Education

Registration is now open for Kestrel's greatly expanded suite of educational webinars. Below are descriptions of some of the available courses. Unless otherwise noted, your instructor is Kit Howard, MS, CCDM, CRCP. All webinars are held from 11:30 am - 1:00 pm, Eastern time. For more information and to register, please visit [www.kestrelconsulting.com](http://www.kestrelconsulting.com).

### Track: Standards in Clinical Trials

#### Best Practices in Designing Clinical Data, Parts 1 & 2

This two part webinar looks at different ways of designing data, and when design matters. Topics include: why and when to use horizontal, vertical, and tree dataset structures; modeling questionnaires horizontally vs. vertically and when it matters; pros and cons of three options for capturing serious AE data, and many more. Offered twice: January 11/February 8, and April 12/April 21, 2010.

#### Data Lifecycle Plans®: Maximize the Power of Your Standards (Free!)

A Data Lifecycle Plan® is a document that describes the standard structure and process for handling clinical trial data from protocol definition through clinical study report. DLPs support cross-functional collaboration, and facilitate robust CDISC standards implementation. This non-technical webinar describes the structure, content, and benefits of DLPs. May 5, 2010

### Track: Quality in Clinical Data

#### A Collaborative Approach to Improving Data Quality

Some believe that the more queries there are in a study, the worse the data quality. This really measures



*(Continued on page 3)*

### Free Webinar!

**Coming in January  
Mark your calendar!**

#### An Overview of Current Standards and How They Can Help You

Description: Examines definitions of "standards"

Reviews numerous standards relevant to clinical research, including

- NIH initiatives
- Joint Initiative Council
- Relevant ISO standards
- Electronic health records
- CDISC's contributions
- Therapy area standards

Discusses how each can benefit clinical research

Duration: 75 minutes of presentation, plus 15 minutes of Q&A

Price: Free

Date: 6 January 2010, 11:30 am - 1:00 pm EST.

Registration: Prior registration not required. Join us at [this link](#) & log in with your email address. For questions, call 734-576-3031 or email [inquiries@KestrelConsultants.com](mailto:inquiries@KestrelConsultants.com).

### ISO Updates Medical Device GCP

(Continued from page 1)

The main new themes in the revised standard are:

- A strong emphasis on the need for training and documentation of training of all investigative personnel on key documents and procedures, including the clinical investigation plan (CIP, or protocol in the drug world), the Investigator’s Brochure, administering informed consent, CRF completion, and device accountability or tracking procedures.
- Recommending the use of corrective and preventative action (CAPA) and other quality system approaches in the clinical setting
- Ensuring and verifying the qualifications of all personnel conducting or working on the study
- Distinguishing non-medical complaints from adverse device effects and treating them separately
- Even greater attention to subject rights (e.g., ensuring that informed consent is re-administered when new information arises, and including in the informed consent an explanation of the comparator groups in the study and the mechanism and likelihood of the subject being in a given group)
- Including in the protocol the procedures for data review, database cleaning, issuing and resolving queries, and verifying, validating and securing electronic data systems where applicable
- The expectations when tasks or functions are outsourced
- The use of Data Monitoring Committees



While not exhaustive, the table below highlights the more significant changes from the old versions. It does not distinguish between the two parts of the old version.

Section	Change
Definition: Adverse Device Effect	<ul style="list-style-type: none"> <li>• Slightly expands &amp; clarifies definitions to include implantation, installation, operation or malfunction of the device, as well as any result of intentional misuse</li> </ul>
Definition: Adverse Event	<ul style="list-style-type: none"> <li>• Slightly expands definitions to include “unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the investigational device”.</li> <li>• It specifies that it includes events related to the device or to the comparator</li> <li>• For persons other than the subject, it is restricted to events related to the device. Note: this appears to contradict the decision tree provided in Annex F for identifying the kind of event.</li> </ul>
Definition: Serious Adverse Event	<ul style="list-style-type: none"> <li>• Original definition included “resulted in medical or surgical intervention to prevent permanent impairment to body structure or body function”</li> <li>• New definition adds “life threatening illness or injury”</li> <li>• Planned hospitalization for a preexisting condition, or a procedure required by the CIP is not an SAE unless there are serious consequences or outcomes.</li> </ul>
Definition: Serious Adverse Device Effect	<ul style="list-style-type: none"> <li>• Original definition included “or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune”</li> <li>• New definition removes this from SADE to the definition of “complaint”</li> </ul>
Definition: Unanticipated Serious Adverse Device Effect	<p>New definition: “Serious adverse effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.”</p>
Definition: Complaint	<ul style="list-style-type: none"> <li>• New definition “Written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability reliability, safety or performance of an investigation device. NOTE 1: For the purpose of this standard, complaints involving a medical occurrence are handled under the adverse event system. NOTE2 : These can include complaints that might have led to a medical occurrence if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate.”</li> <li>• All such complaints shall be captured on CRFs, tracked and reported. Non-medical complaints are to be handled through the sponsor’s quality management system</li> <li>• As complaints are reported, the sponsor is to assess the relatedness to the device and document this, along with the investigator’s opinion. This is expanded in a later section.</li> </ul>

(Continued on page 4)

### Cutting Edge Education

(Continued from page 1)

how well the investigative site followed the sponsor's data quality rules, but sites rarely know or understand those rules. In fact, few sponsors or CROs agree internally on what "data quality" means. This webinar explores these ideas and presents a practical method for defining and improving quality. February 22, 2010



#### Using Aggregate Data Checks to Look for Bias and Fraud

While current data cleaning may reduce data variability, it is not designed to detect bias and fraud, which may significantly distort trial conclusions. Aimed at non-statisticians, this webinar presents methods for using aggregated data to identify suspect patterns in data, and discusses how to interpret them and what to do about them. May 3, 2010

#### Applying Risk Assessment in Cleaning Clinical Data, Part 1: Understanding the Concepts

Delivering "perfect" data is neither cost-effective nor feasible, but the risks of imperfect data must be managed. This pair of webinars examines the concept of "risk" in data quality, describes a two-tiered approach to risk management in data quality that includes a decision model for classifying errors into low, medium or high risk, and presents a mechanism for applying those decisions systematically and objectively to specific data points. March 22, 2010



#### Database Audits Today

Database audits have been long been used to measure data quality but are of questionable value, especially for EDC studies. Based on work done by the Data Quality Research Institute, this webinar demonstrates a better way of designing these audits. March 8, 2010.

(Continued on page 5)

# Establishing an eClinical Vendor Management Program

**Kestrel is pleased to welcome Jonathan Andrus, M.S, CQA, CCDM, as an instructor with our educational programs.**

**Webinar Title:** Establishing an eClinical Vendor Management Program

**Presenter:** Jonathan Andrus, M.S., CQA, CCDM. VP Data and Study Operations, BioClinica, Inc.

**Description:** This course describes how to establish a vendor management program for effective qualification and management of eClinical vendors. Case studies and exercises bring the course materials to life and allow the participant to apply information covered during the course.

**When:** Monday, January 25, 2010, 11:30 am - 1:00 pm EST

**Registration:** Please visit [www.KestrelConsulting.com](http://www.KestrelConsulting.com) to register.



**Don't See a Topic?**  
If you don't find the specific standards, quality or CDM training you need, please contact us.  
We have many additional courses, or can develop one for you.

## ISO Updates Medical Device GCP

(Continued from page 2)

Section	Change
Investigator's Brochure	Expected content is greatly expanded and is included as Annex B
Informed Consent Process	<ul style="list-style-type: none"> <li>• Adds ensuring that the consent is administered by the PI or authorized designee, and that the document contain all the aspects of the trial relevant to the subject's decision</li> <li>• Specifies that the subject should both sign <i>and date</i> the informed consent.</li> <li>• Any important new information that emerges during the trial should be <i>provided to the subject in writing and consent should be re-administered.</i></li> </ul>
Special Circumstances for Informed Consent	New section detailing the process for obtaining informed consent when the subject is unable to provide it. And the conditions must be met for this to be allowable
Informed Consent Content	<p>Adds that the informed consent should specify</p> <ul style="list-style-type: none"> <li>• What parts of the study are experimental</li> <li>• If there are comparator groups and how subjects are assigned to a group</li> <li>• The expected number of participants</li> <li>• That there may be risks to others if applicable (e.g., foetus)</li> <li>• That unanticipated risks may occur</li> <li>• That subject records will be kept confidential to the extent allowed by law</li> <li>• Any anticipated expenses the subject may have to cover</li> <li>• The role of the sponsor's representative in the study (e.g., monitor, auditor)</li> </ul>
Suspension, Termination and Close-Out of the Clinical Investigation	Consolidates and greatly expands upon the reasons for considering early termination or suspension of the trial and the processes to be followed for both suspension and resumption
Document and Data Control	<p>Greatly expands the section, including specifying</p> <ul style="list-style-type: none"> <li>• That only qualified individuals should capture and record data</li> <li>• The expectations for CRF completion</li> <li>• The acceptability of electronic data capture systems</li> <li>• The requirements for "validation" of electronic systems; these are essentially of synopsis of 21 CFR Part 11</li> </ul>
Accounting for Devices	New section added that specifies what data are expected for device accountability
Auditing	Section greatly expanded to include the purpose, plan and characteristics of audits
Routine Close-Out	New section providing expected processes and documentation
Essential Documents	Annex E lists the essential documents that should be generated and maintained at the sponsor and the site.
Sponsor Responsibilities: Clinical Quality Assurance & Quality Control	New section outlining expected processes for quality assurance & quality control
Monitoring Responsibilities: Routine On-Site Monitoring Visits	<p>Expands requirements to include insuring that:</p> <ul style="list-style-type: none"> <li>• Only qualified individuals are conducting trial</li> <li>• Only eligible subjects are enrolled</li> <li>• Source documents are accurate, complete, up to date, &amp; stored and maintained appropriately</li> <li>• CRF corrections &amp; additions made properly</li> <li>• All serious AEs and serious adverse device effects immediately reported to sponsor</li> <li>• Subject non-compliance with requirements in the informed consent are documented and discussed with the principal investigator or designee</li> <li>• Site personnel all aware of relevant updates to docs</li> </ul> <p>Monitoring reports will be <i>in writing</i> and submitted to sponsor</p>

(Continued on page 5)

ISO Updates Medical Device GCP

(Continued from page 4)

Section	Change
Safety evaluation & Reporting	Sponsor will review all AEs & non-medical complaints and determine and document their view of the relatedness to device. Any disagreements with the investigator will be documented & both opinions communicated
Clinical Investigation Close-Outs	New section describing expectations for closing a trial
Outsourcing of Duties & Functions	New section documenting expectations with duties and/or functions are contracted out to individuals or companies
Annex A in Old Version, Suggested Procedure for Literature Review	Removed
Annex C in New Version, Case Report Forms	<ul style="list-style-type: none"> <li>Provides expected content for identifiers, and list of suggested CRFs.</li> <li>Except for identifiers, it lists CRF modules rather than the specific data items, as the old version did.</li> <li>It specifies that there should be a way to correlate the versions of CRF with versions of CIP</li> </ul>
Subjects	<ul style="list-style-type: none"> <li>Point of enrollment should be clearly defined</li> <li>Should include what, if any, medical care subjects will receive after the study</li> </ul>
Clinical Investigation Plan Deviations	Adds expectations of definition of corrective & preventative actions and <i>PI disqualification criteria</i>

**Different Time Zone?**

Are EST/EDT times difficult for you? Contact us and we can arrange a special session for your company.



**Need More?**

Bring our webinars to your site. We add in-depth material and exercises for a robust learning experience.

**Cutting Edge Education**

(Continued from page 3)

**Standards Management 101**

Good standards management requires a unique and specialized body of knowledge. This pioneering webinar series teaches the range of skills needed for ongoing development, management, maintenance, tracking and retirement of standards. Please visit [www.KestrelConsulting.com](http://www.KestrelConsulting.com) for more information and to register.

Part 1, An Introduction to Standards: Wednesday, 13 January 2010, 11:30 am - 1:00 pm EST

Part 2, Standards Development: Wednesday, 27 January 2010, 11:30 am - 1:00 pm EST

Part 3, Standardization and Flexibility: Wednesday, 10 February 2010, 11:30 am - 1:00 pm EST

Part 4, Governance: Wednesday, 24 February 2010, 11:30 am - 1:00 pm EST

Part 5, Managing Standards: Wednesday, 10 March 2010, 11:30 am - 1:00 pm EST

Part 6, Standards in Contracted Clinical Development: Wednesday, 24 March 2010, 11:30 am - 1:00 pm EDT (note the change from EST to EDT)

Part 7, When Standards Conflict: Wednesday, 14 April 2010, 11:30 am - 1:00 pm EDT