

## ***Expanding GCP Quality Systems for Inspection Readiness***

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*“Inadequate monitoring resulted in deficiencies in recordkeeping with respect to case histories and drug accountability by clinical investigators”; “study monitors failed to identify that on multiple occasions, study coordinators documented administration of study drug to two different subjects at the same time”; “one hundred percent source documentation verification was completed by study monitors for Subject A, according to monitoring reports; however, study monitors failed to identify that no physical examination, wound assessment, or overall clinical assessment was documented in study source documents or on the Case Report Form (CRF) for this subject’s Day-8 visit, as required by the protocol”; and “study monitors failed to identify that subjects who did not meet eligibility criteria were enrolled”.*

These are quotes from a recent FDA Warning Letter to a sponsor company that failed in many basic GCP areas of clinical trial conduct. Basic, because most GCP requirements call for common sense tasks designed to make a clinical trial safe for those involved. While these reports suggest complex operational issues in the clinical trial process for the sponsor in question, they also clearly indicate this sponsor was not ‘inspection ready’ when the FDA inspected its clinical investigator site and reviewed its site monitoring practices. So, if these requirements are basic and should be well known by everyone in the industry, why is the FDA finding such errors in the way clinical trials are being run and monitored?

At CIS we have the opportunity to observe clinical processes at many sponsor companies; what we see is that these clinical R&D organizations are often not operating in an ‘inspection ready’ state. GCP ‘inspection readiness’ means taking a quality systems approach to clinical trial processes and patient data: defining clear performance standards; communicating those standards effectively to those doing the work of clinical trial conduct; determining areas of clinical conduct that may not be in compliance with policies, procedures, or regulations; putting plans into action to prevent future non-compliance in identified areas; and continuing to monitor processes and patient data to ensure that both are meeting compliance targets. These quality assurance steps are routinely taken at pharmaceutical manufacturing sites, but recent FDA 483s and Warning Letters suggest these steps also apply to the increasingly complex and vendor-driven clinical trials process. Instead of the feelings of dread and panic that generally ensue right before a pre-approval inspection, there are clinical quality assurance measures that can be taken in a broad organizational way that can allow a company to be ‘inspection ready’ at all times.

Knowing the state of your organization at any given time is really the key to being ready for an inspection that could feasibly occur at any given time. Collecting data in specific areas in which regulatory authorities might be interested could lead to an understanding of where non-compliance might exist within an organization. Extensive data collection, however, doesn't guarantee successful inspection readiness. Data must be collected appropriately, assessed against acceptable targets, and shared with staff to implement interventions to improve performance and outcomes.

In order to know the state of your organization, you must first assess the current systems that you have in place, taking into consideration recent industry warning letters, agency growth and trends, as well as your own compliance history. This might include reviewing GCP controlled documentation against regulations and current practice and conducting interviews with those closest to the clinical trial processes. This will allow you

to identify regulated areas for which there is inadequate or no existing compliance mechanism. Once you know your current state of clinical compliance, you can begin to work toward a cohesive inspection readiness state.

You may begin by considering a range of solutions to address the identified areas of non-compliance. These could be as simple as updating policies and standard operating procedures that would impact the day-to-day clinical tasks being conducted; making adjustments to your internal audit and monitoring strategies; or it might include designing and implementing a clinical metrics program that would keep management informed on an ongoing basis about data-driven areas that should be operating within compliance targets at all times. You also may choose to use detailed 'inspection readiness checklists' that would aid an investigator, sponsor or CRO when a pre-approval inspection is imminent. These checklists can be reviewed at intervals to ensure that the information required for inspections is accessible and organized from the beginning throughout the duration of a trial.

Once you have addressed those areas of non-compliance and they are operating within your compliance targets, you can put controls in place to ensure that those targets continue to be met monthly, quarterly or annually. 'Inspection readiness' does not have to be a scary entity. It can be a state of compliance that your company can achieve in an ongoing fashion so that when agencies do come knocking, you are confidently ready.

#### References:

FDA Compliance Program Guidance Manual, Chapter 48: Bioresearch Monitoring; Sponsors, CROs and Monitors, February 21, 2001

EU Guidance for the Conduct of Good Clinical Practice Inspections: Annex IV, Sponsor and CRO, parts 2.1 – 2.3

[http://carl1anderson.files.wordpress.com/2010/02/investigator\\_final\\_reports\\_tool\\_fda\\_inspection.pdf](http://carl1anderson.files.wordpress.com/2010/02/investigator_final_reports_tool_fda_inspection.pdf)

<http://www.ctndisseminationslibrary.org/webinars/QAsitemonitoring2009slidesaudit.pdf>

[http://depts.washington.edu/clinres/clinicaltrials/handbook/10FDAinspections.html# PrepareFDA](http://depts.washington.edu/clinres/clinicaltrials/handbook/10FDAinspections.html#PrepareFDA)

<http://www.fda.gov/NewsEvents/Newroom/PressAnnouncements/ucm174983.htm>

<http://www.fda.gov/NewsEvents/Newroom/PressAnnouncements/ucm176040.htm>

<http://www.outsourcing-pharma.com/Clinical-Development/Warning-letters-increase-as-DSI-rejigs-operations>

#### About the Author:

Beth Kline is a consultant for Compliance Implementation Services (CIS) a consulting firm specializing in compliance strategies for pharmaceutical companies, from Global Clinical Research & Development through U.S. Commercial Compliance and Government Programs. Over the last 12 years, Beth has provided sponsor management of clinical trial sites, implemented new safety systems, conducted training needs assessments and developed compliance training materials. In addition, Beth has effectively managed cross-functional project teams and clients.

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