

# The 7<sup>th</sup> System: Integrating Clinical Systems into a Comprehensive Quality Audit Program

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## Abstract

Clinical quality systems are often managed independently of manufacturing and laboratory operations. This can result in a fractured view of each compliance area (GCP, GMP and GLP) and a failure to provide adequate oversight of an organization's overall compliance. Using FDA's six-system inspection model as a starting point, this article will discuss how to integrate the requirements of clinical quality systems with a GMP compliant quality program to provide a system for comprehensive quality oversight.

**Keywords:** GCP; GMP; GLP; Standard operating procedures; FDA

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The goals of a quality audit program are: to provide an accurate view of compliance across the organization, including suppliers and vendors; to identify and prevent or correct compliance issues; and to inform management of the compliance status of the organization. However, differences in the implementation of GMP (Good Manufacturing Practice) and GCP (Good Clinical Practice) compliance programs may occur due to the different focus of each program. The GMP audit program is concerned with ensuring the identity, strength, safety, purity and effectiveness of the product or device, whereas the GCP program is focused on subject rights and safety, protocol conduct and data integrity.

Communication between the manufacturing and clinical disciplines may be obstructed in part by the use of different terminology, or by not using terms in the same manner to appropriately compare audit observations. For example, use of the audit observation type "Validation" may describe an issue related to methods, equipment, packaging, or computer systems. Without an appropriate description, this audit observation type is too ambiguous to be useful in assessing, preventing or correcting compliance issues. "Investigational Product" is a common audit observation type used by clinical auditors, but this term is not sufficiently descriptive when relayed to manufacturing personnel as it does not describe whether the issue is related to the use, storage, labeling, or quality of an investigational product.

The use of different audit observation terminology and separate reporting systems may also obstruct an accurate assessment of the impact of systemic compliance issues and weaker compliance signals may be lost because they are maintained and reported separately. The accurate assessment of compliance with Standard Operating Procedures (SOPs), personnel training, vendor management, and complaints requires the ability to view issues across the organization, and the use of separate terms and reporting may make it difficult to accurately quantify the total compliance risk of these activities or identify cross-functional issues that can impact investigational product integrity and/or subject safety. Information from inspections of raw materials, production activities, packaging, labeling, warehouse and

distribution, and clinical use may not be communicated effectively if issues are reported and communicated separately.

A shared quality system, using integrated audit observation categories, terminology and reporting can help to improve communication across functions and better meet the objectives of the quality audit program. It should be noted that integrating the GMP and GCP quality audit programs does not necessitate a particular organization of the Quality Unit, rather than the same system for assessing, reporting and resolving audit observations should be shared across the organization.

The Six-System Inspection Model [1] defined by the U.S. Food and Drug Administration (FDA) provides an excellent foundation upon which to define the categories of a quality audit program. The model defines the following six systems:

- Quality System
- Facilities and Equipment System
- Materials System
- Production System
- Packaging and Labeling System
- Laboratory Control System

Most of the systems defined in the six-system model are readily transferable to audit observation categories useful for the inspection of both manufacturing and clinical activities. Many clinical requirements can be integrated into the six-system model. Within the *Quality System*, observation types such as *audit program*, *complaints*, *deviations*, *personnel training and qualification*, *Standard Operating Procedures*, and *vendor qualification* may be appropriate to both GMP and GCP activities. Audit observation types related to the *Facilities and Equipment System*, such as *calibration/preventive maintenance*,

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**Received** December 21, 2012; **Accepted** January 25, 2013; **Published** January 27, 2013

**Citation:** Vengroff B (2013) The 7<sup>th</sup> System: Integrating Clinical Systems into a Comprehensive Quality Audit Program. J Clin Trials 3: 126. doi:[10.4172/2167-0870.1000126](https://doi.org/10.4172/2167-0870.1000126)

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equipment management, facility security, cleaning, and sanitation may be appropriate to both GMP and GCP functions. However, audit observation types related to contamination controls, environmental monitoring, HVAC systems and water systems may be used primarily for manufacturing rather than clinical activities.

Although the six-system model provides an excellent starting point, not all clinical audit observations fit well into the six-system model. The addition of a seventh *Clinical System* can accommodate the addition of clinical audit observation types within an integrated inspection model. Examples of audit observation types within the *Clinical System* may include: adverse events, case report forms/source documents, ethics committee, informed consent, monitoring, protocol compliance, regulatory approval, serious adverse events, trial management and oversight, and trial master file. Although it may be appropriate to create additional systems or categories (e.g., to distinguish safety from other trial management activities) for the purpose of this discussion we will create only one additional category for *Clinical Systems* (Figure 1).

With the integration of clinical requirements into FDA's inspection model, and the addition of a *Clinical System* to accommodate additional GCP observation types, the seven-system inspection model provides an integrated structure of audit observation categories to help achieve the

goals of the quality audit program. The use of audit observation terms in the same manner to define, report and compare audit observations promotes improved transparency and communication between GMP and GCP functions, and a more accurate view of compliance across the organization to effectively assess, communicate and resolve compliance issues identified by the quality audit program.

#### References

1. Guidance for Industry, Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations (2006).



Figure 1: Clinical Systems.