Avoiding the CAPA Trap:

Process Optimization & GCP

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CAPAs in GCP

It is no secret that the development and implementation of effective, streamlined Corrective and Preventive Action (CAPA) processes for addressing noncompliance is a critical aspect of maintaining compliance within Pharmaceutical GMP operations. Navigating the nuances of developing effective CAPAs for GCP operations, however, can prove to be difficult for pharmaceutical companies of all sizes. While the processes and procedures involved in GMP tend to be easily defined and measureable, GCP procedures are often more nebulous and difficult to pin down with reliable metrics. Following the Food & Drug Administration's (FDA) increased emphasis on clinical CAPA processes (which can be traced back to the FDA's 2009 adoption of ICH Q10: "Pharmaceutical Quality System"), hundreds of Form FDA 483 observations and subsequent warning letters citing CAPA deficiencies within the GCP space have been issued to companies throughout the industry. This increased emphasis on clinical CAPA processes warrants increased diligence within the industry with respect to developing, executing, and reporting the outcome of CAPAs within clinical operations in order to avoid increased vulnerability to warning letters and repeat findings.

Within the clinical space, it is well-accepted that CAPAs are necessary when patient safety, data quality, and/or data integrity are impacted by an issue or insufficient process. According to ICH 10, effective CAPAs include a thorough root cause analysis. Additional criteria used to determine the CAPA include severity of the issue, temporal considerations (urgent or non-urgent), frequency (single instance issue or recurring), error type (systematic or isolated), etc. A Clear SOP or set of SOPs outlining the different paths for determining the CAPA for issues within GCP are an important aspect of formulating effective CAPAs. Additionally, CAPA SOPs should designate distinct paths for Corrective (addresses existing issues) vs. Preventive (address potential issues) Action Plans.

Putting the P back in CAPA

Like all clinical operations procedures, CAPA procedures should be scalable and include a clear outline of metrics from which the effectiveness of the CAPA can be reliably determined. Within GCP, a common problem is the tendency to treat CAPAs as point solutions, placing too much emphasis on *Corrective* processes as opposed to the proper formation and use of Preventive action plans. In its most basic form, Preventive action plans are essentially a form of process improvement. Preventive action plans work to change processes that could potentially negatively impact patient safety, data integrity, and/or data quality before the process results in any tangible issues or problems. Increased emphasis on Preventive action plans in the GCP realm could potentially lead to the initiation of fewer Corrective action plans and, subsequently, reduced risk for CAPA-centric FDA 483s or warning letters.

Process optimization and preventive action plans

In the GMP space, the case for development of preventive action plans is usually a bottom-up process whereby end-users of a product or participants in a given process make suggestions for changes to process based on their experiences with the product or processes. Due to the nature of process in the GCP context, this bottom-up development of preventive action plans may not be the best method, as it is typically difficult to identify potential problems related to clinical processes before they become a tangible issue. Compared to the GMP environment, GCP processes are often more cross-functional in nature and have multiple parallel handoffs between functions.

Process optimization may be the best way to develop effective preventive action plans in the GCP space as process optimization inherently includes many of the steps and tools necessary to generate an effective preventive action plan process. The top-down, cross-functional view of process afforded by process optimization techniques makes potential problematic aspects of process in the GCP space more salient. Process optimization tactics also allow for a clearer understanding of how the preventive action plan will interact with other clinical processes and functions, allowing for a more seamless integration of the preventive plan within the framework of the overarching clinical procedures. Constructing preventive action plans in parallel with clinical process optimization allows for the sharing of useful tools that work well in both circumstances including the development of performance metrics, placement of proper monitoring and controls, and development of tools (RACIs, task matrices, dashboards, etc.).

Case example

It is somewhat difficult to understand exactly how process optimization accommodates the development of effective preventive action plans when speaking about the concept in abstract terms. A good example of the successful use of process optimization as a compliance increasing tool is seen in the recent preventive action plan formed at a mid-sized pharmaceutical company experiencing typical growing pains within the GCP space. This particular company has seen more FDA 483s since the rapid expansion of its clinical program as its operations and procedures strain under the weight of increased load. Seeing the need for increased scalability, the company decides to undertake end-to-end clinical trial process optimization, focusing first on study start up. High level process mapping of the as-is process shows the gaps and inefficiencies/deficiencies of the current process. Subject matter experts and business analysts worked together to redefine the study start up processes and construct new process maps that reflect the new, streamlined procedures. During the cross-functional review and critique of the new procedures, which will ultimately be reflected in new and revised SOPs, the clinical quality management group notices a potential gap in the new procedure for the reporting of protocol deviations. Using the information, tools, and cross-functional communication plan already in place due to process optimization, the clinical quality management team works to develop a preventive action plan related to protocol deviation reporting to avoid potential errors in executing the protocol deviation reporting process and associated increased compliance risks.

Due to the ever changing regulatory and drug development environment, process optimization seems to be an ever present necessity of clinical programs at Pharma companies of all sizes. Leveraging process optimization tools to improve CAPA procedures is an efficient means to mitigate compliance risks in the GCP space while also increasing operational efficiency.

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