



Compliance Auditing: Diving into Common Critical Findings.

Compliance auditing is a crucial process in the healthcare industry, helping to ensure that therapeutic and diagnostic products are safe, effective, and of high quality. Compliance auditing incorporates a systematic approach that evaluates whether a firm is following regulatory requirements, industry standards, and has appropriate internal policies and procedures.

The importance of compliance auditing cannot be overstated, it plays a vital role in protecting public health and safety. In this article, we will delve into frequent Critical audit findings that Health Authorities routinely find as well as what ProPharma's GxP Compliance Auditors are observing in the audits that we conduct.

A Reflection on the Importance of 3rd Party Auditing

Being heavily regulated by various government agencies, like the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom, and the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan, global clinical development and research, manufacturing, testing, and storage/distribution companies of healthcare products must follow strict requirements.

There is no room for error, industry is expected to provide safe and effective products to consumers 100% of the time. Regulatory agencies specify that a contracting organization is ultimately responsible for the quality of contracted services and that the contract facilities are considered and extension of the sponsor. Auditing helps confirm that companies adhere to these requirements and expectations. This includes verifying that clinical study protocols are followed, device design records are maintained, manufacturing processes are performed correctly, and that the product is labeled correctly. Failure to comply with these

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regulations can result in severe consequences, including patient, participant, or consumer injury, legal action, fines, and damage to the company's reputation and the list goes on.

Auditing can also help propel companies by identifying potential issues and mitigate risks before they become significant problems, reducing the risk of product recalls, and preventing damage to the company's reputation and even find efficiencies such as process optimization, reduce redundant costs, and increase productivity.

In summary, auditing is essential for the healthcare industry. Auditing helps to ensure that products are safe, effective, and of high quality. Auditing helps to identify potential issues before they happen and implement corrective actions before they escalate, protecting public/patient health and product safety. Therefore, healthcare companies must make compliance auditing a priority to ensure the success and sustainability of their business.

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Ensuring Patient Safety & Business Sustainability

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The Daunting Task of Global Health Authorities

Global Health Authorities are faced with a daunting task of monitoring and enforcing safety, efficacy, and quality of food, drugs, medical devices / diagnostics. Conducting inspections of regulated firms is one way they facilitate this oversight against regulations. During these inspections the Health Authorities identify various findings, or non-conformances, against expectation and regulatory requirements. Ranging from minor issues to serious "Critical" violations that can lead to enforcement actions, including product recalls or even shutdowns of studies or facilities.

Staying aware of common issues identified by health authority during industry Inspections is a productive way of introspectively evaluating your own systems to watch for similar problems and ensure that your Quality Management System is robust and functioning optimally.

Defining "Critical"

Findings, also known as observations, are Violations from regulation or SOP that if not followed can pose a significant risk to the safety (participant, patient, consumer), quality, integrity or efficacy of products or materials. Most audit programs rank findings based on severity based on the level of "risk" is associated with the violation. Critical issues can result in the termination of a study or product recall, injury, or loss of life. Below are some of the most common findings cited.

Exploring Common Critical Findings by Health Authorities:

Inadequate Documentation

One of the most frequent findings during FDA, EMA, and MHRA inspections is inadequate recordkeeping. This means that the firm does not maintain complete, accurate, and/or up-to-date records that document various aspects of their operations, including study conduct, manufacturing, quality control, and distribution. Such that activities cannot be reviewed and verified as to have been conducted correctly.

Inadequate Quality Control

Another common finding during agency inspections is inadequate quality control. This means that the facility does not have adequate procedures in place to ensure that products are manufactured consistently and meet established quality standards. Quality control includes a range of activities, such as testing, inspection, and documentation, that are designed to identify and address potential quality issues before they can impact clinical trial conduct, product safety or efficacy.

Failure to Conduct Thorough Investigations

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Failure to Obtain Informed Consent

In the clinical trial space, Informed consent is a critical component of ensuring a study participant understands potential risks and implications of unapproved drugs, devices, and therapies. Documenting that participants are aware and agree to risks is a regulatory requirement.



Inadequate Personnel Training

Globally it is often found that facility personnel are not adequately trained to perform their jobs. This can include insufficient training on trial management, manufacturing processes, quality control procedures, and regulatory requirements. Proper and robust training is essential for ensuring that personnel have the knowledge and skills they need to perform their jobs effectively and comply with applicable regulations.

Inadequate Change Control

Changes to equipment, processes, protocols, and methods can impact adjacent, downstream, or approved quality and safety of healthcare products. Robust procedures evaluate potential risks of change before changes are made effective in their decision/approval process.

Contamination or Cross-Contaminations

Contamination control is a top system evaluated during inspections. Failures in contamination control can occur when products are not manufactured, stored, handled, or transported in a way that preserves the integrity of the product. Not having or following sufficient procedures to protect from microorganisms, chemicals, or other sources serve as a frontline for potential harm and are viewed as a significant risk to public health.

Data Integrity

Losing the ability to "trust" the authenticity of data erases the ability for inspectors to confirm that quality, safety, and efficacy was maintained. Intentional scientific misconduct and fraud are not the only thing that can lead to Data Integrity findings, incomplete or incorrect data can lead to this too.

Clinical Protocol Deviations

Another common finding is the deviation from the study protocol. A protocol is a detailed plan that outlines the study's objectives, methods, and design. Deviating from the protocol can impact the integrity of the study data.

Inadequate Clinical Study Documentation

Inspectors may find that documentation is incomplete or missing altogether. Documentation is critical in clinical trials, and insufficient documentation can make it challenging to assess the trial's validity.

Failure to Report Adverse Events

Adverse events are unexpected or harmful drug/device safety events that occur during a clinical trial or general use. Monitoring for possible drug/device events that cause risk can be an early indicator of potential related harm and must be reviewed quickly to help prevent potentially widespread harm.

Noncompliance to Regulations

General failure to comply with GxPs is cited frequently and can result in the production of unsafe or ineffective products, which can pose a significant risk to public health or failure to follow regulatory requirements for the conduct of clinical trials.

Inadequate Validation

Validation is the process of ensuring that equipment, processes, and methods can produce consistent and reliable results. Inspectors commonly find inadequate validation practices, including incomplete or inadequate validation protocols, inadequate testing, testing parameter failure, and insufficient documentation.

ProPharma's Global Audit Program Results

As Global GxP Auditing is one of our core service offerings, like most companies, we provide standard categorizations of audit findings to assist with the prioritization of action based on level of risk. Our standard categorization definitions are:

CRITICAL

Significant violations from regulation or procedure posing a significant risk to the safety, quality or efficacy of study, device, distributed or held products or materials. Requires immediate attention and should be addressed prior to performing process, task, or activity again. An accumulation of multiple similar "Major" findings can be categorized as a critical systemic issue.

We anticipate that Critical findings if left unchecked would lead to possible injury or costly regulatory actions.



MAJOR

Violations from regulation or procedure posing a potential risk to the safety, quality or efficacy of study, device, distributed or held products or materials. The finding may be indicative of a system failure. CAPA should address promptly. An accumulation of multiple similar "Minor" findings can be categorized as a potential systemic issue.

MINOR

Slight departures from regulations or SOP, not necessarily indicative of a systemic problem but should be addressed to improve compliance. CAPA should address in a timely manner..

RECOMMENDATION

Provided as recommendations not necessarily associated with a specific observation. Recommendations are generally provided for quality improvement but may be considered as a potential for deficiency if the system involved is not evaluated.

1000 Audits Later: Are Our Audits Echoing Global Trends?

Looking at our recent audits, we compiled and trended our "Critical" audit finding data from the last 1000 audits. We were interested in determining if our data shows similar results to what global Health Authorities are identifying.

Only 9% of GxP Audits Show 'NO FINDINGS'

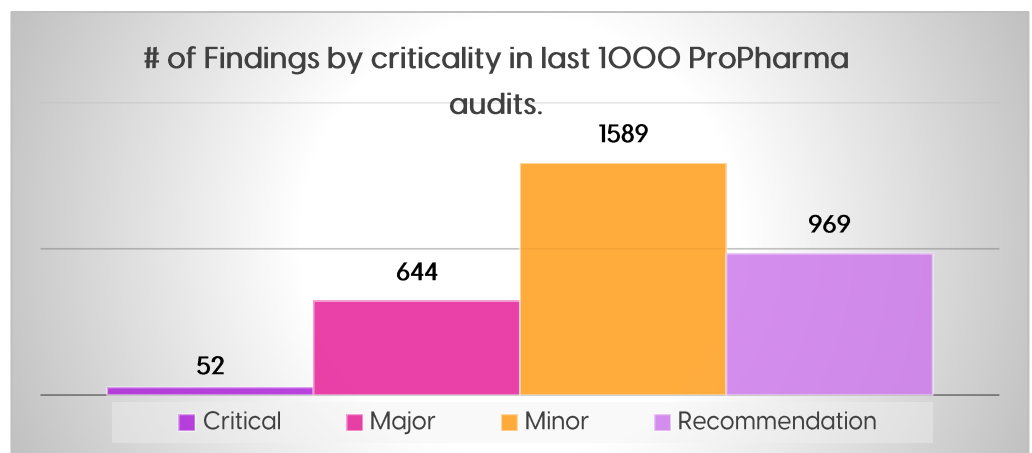
Severity Category	Avg. / Audit
Critical	5%
Major	64%
Minor	159%
Recommendation	97%

In the past 1000 GxP audits, our Compliance Auditors cited over 3000 compliance related observations and recommendations for improvements:

Nearly 70% of the time, we identified Critical and Major findings at sites and service providers, these are issues that if left uncorrected could result in injury or costly regulatory actions. Only 9% of audits result in no findings.

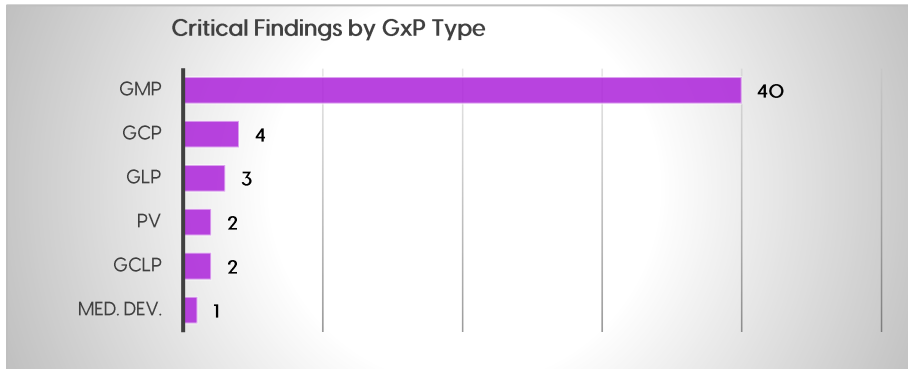
The chart to the left outlines all observations.

Each of these findings and every recommendation represents an opportunity for improvement of a quality system / process that if left unchecked could have adverse impact ramifications or injury.





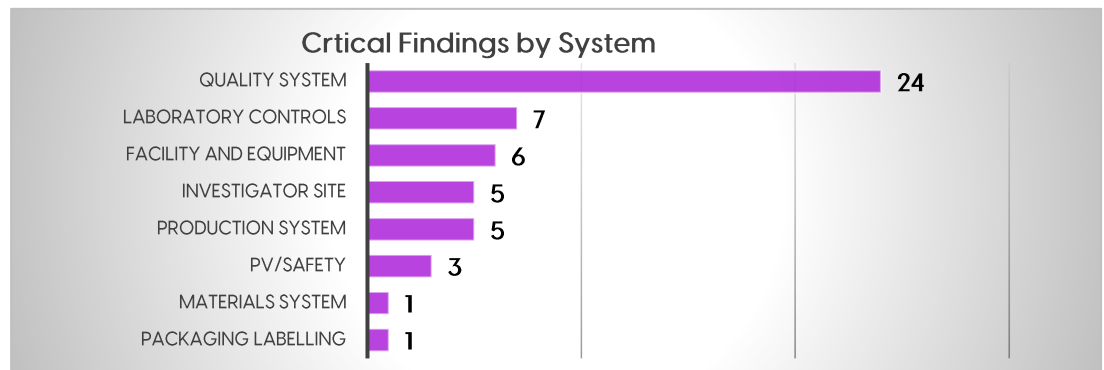
Good Manufacturing Practices Bear the Brunt of Critical Audit Findings



Critical findings in the segment of Good Manufacturing Practices (GMP) were most prevalent, this is not too surprising as this segment represents highly stringent requirements and can quickly impact a large patient/consumer population and typically involves widespread throughput of products and materials under complex systems that all must work in concert with each other.

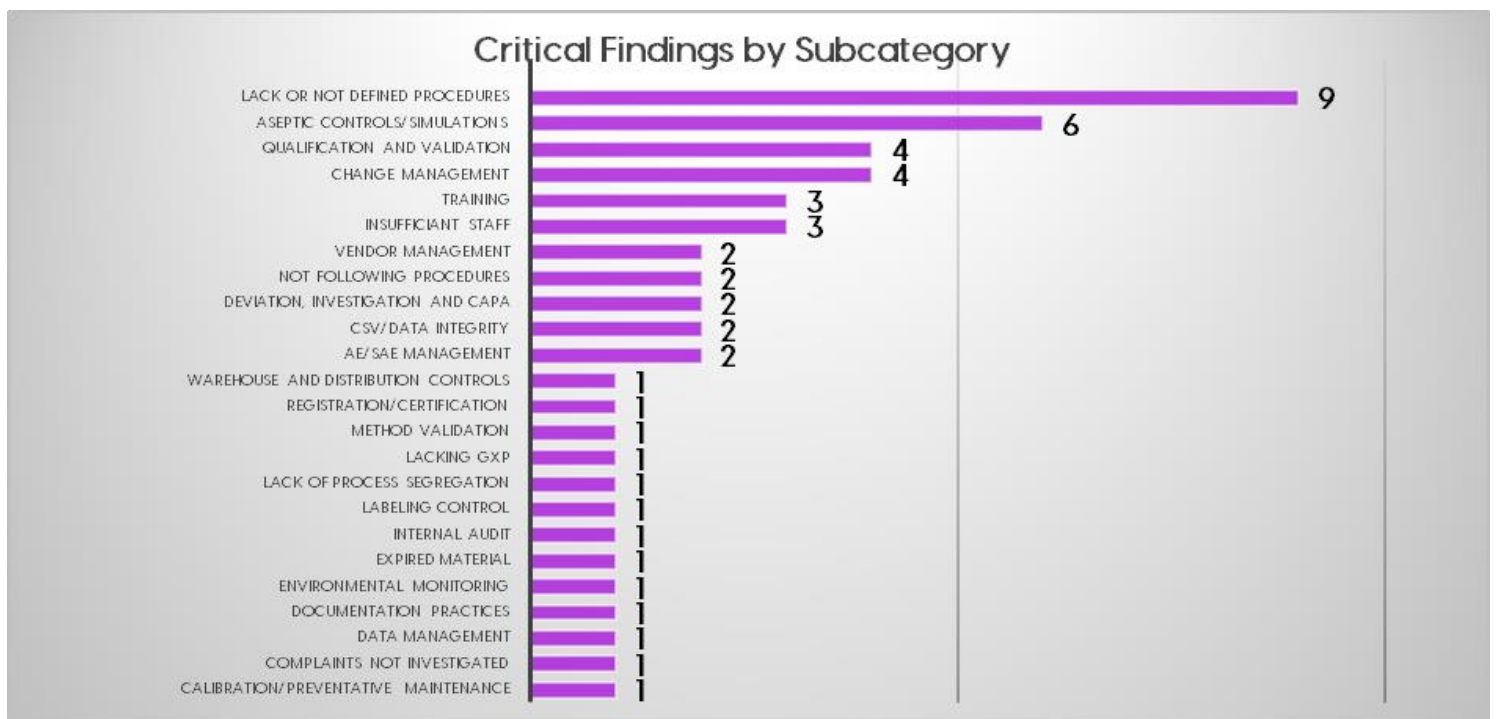
Neglecting Quality Systems Spells Trouble

Violations against the Quality Systems ratchet quickly to "Critical" status, as this system involves core elements for defining and controlling all aspects of quality. Deficiencies here can directly lead to negative impact on study conduct, strength, safety, and efficacy.



Our Audits Find Critical Observations in 12 out of 13 Categories

Pairing Critical findings down even more, our Compliance Auditors cited observations in twelve of the thirteen common Health Authority finding categories during audits that we conducted, leaving out "Informed Consent" we did not cite any recent Critical observations falling under that category.





Critical Audit Findings Put Procedures, Aseptic Controls, and Qualification Validation in Spotlight

From our evaluation of past Critical findings, we can see that the importance of auditing is ever prevalent. Our auditors are finding the same compliance struggles with companies as health authorities are.

Leading the List of Observations is Lack of or Not Defined Procedures.

Quality system documents, SOPs, Work Instructions, Protocols, Policies, etc. are specifically designed to establish a consistent and safe manner of conducting compliant pre-clinical, clinical, or commercial activities. These set the foundation for consistent and safe actions and if they are not existent or do not accurately describe the tasks, compliance cannot be defended.

Deficiencies in Aseptic Controls Next Most Prevalent.

Contamination and cross-contamination are leading direct causes of SAE and injury, the importance of maintaining sterility and having proper sterile controls and monitoring is vital in maintaining public/subject health.

Third Highest Frequent Finding was Qualification and Validation.

Whether it is a sphygmomanometer used for collecting clinical data during a trial's home patient visit, or a large processing reactor, not being able to demonstrate the fit for purpose functionality and integrity of data produced may leave you a difficult situation when asked to defend the results.

Uncovering Compliance Risks and Empowering Quality Management in the GxP Landscape

Despite the wealth of awareness campaigns and publications from Health Authorities, our auditors are still uncovering compliance risks. These risks can pose a significant threat to data acceptance and potentially jeopardize the safety of patients and consumers.

Our analysis indicates the best starting point for identifying potential risks is the governing Quality Management System (QMS). This system's deficiencies or adherence levels are the leading cause of Critical findings. This comes as little surprise given that a firm's QMS is the foundational bedrock upon which compliance is built.

Understanding where common problems often "hide" in GxP Quality Systems is a great place to begin looking for compliance strains and potential areas for improvement at your own site and of your service partners. ProPharma can help identify these before they become out of control. In addition to Auditing, our Compliance Quality consultants have extensive auditing, technical writing, and operational experience to support your organization's clinical and commercial quality needs. Additionally, our wide array of regulatory and compliance services includes vendor qualification audits, mock regulatory inspections, gap analyses, quality management system (QMS) development and optimization, and interim quality management.