ARTICLES

The 'Business' of Quality Assurance

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Summary

This article will address how a quality assurance function (QA) can and should be a value to the business. QA represents a Management control; it is, or should be, the business instrument by which management is advised as to the status of regulatory compliance. And regulatory compliance is a business issue – make no mistake about it. But QA does not always discharge its responsibilities or perform its activities in a manner that truly serves the business purposes. The article examines some of the common scenarios in the industry, which are 'sin-dromes' because they can result in increased business expenses and reduced profitability, and thus they are business 'sins'.

Key Words

Quality assurance; quality control; common sense; profitability; management control

Introduction

"Good quality is cheap; it's poor quality that is expensive." This 1998 quote from *Money Magazine* provides the article's premise, which is that the Quality Assurance (QA) function should be of value to the business. Value will be provided if QA effectively supports the objective of obtaining approvals for drugs with minimal problems or delays, at the least possible expense, and with maximum profitability. So, what exactly is a QA function and how should it support this objective? This article will address these questions, and in the process, illustrate how ineffective QA can increase expense and help to minimize profitability.

The QA Function

Using the US Code of Federal Regulations (CFR) as a guide, the requirement to have a Quality Assurance Unit (QAU) is not consistent across the regulatory landscape. Good Laboratory Practices (GLPs) – 21 CFR Part 58.35 – mandates that a testing facility '... have a quality assurance unit which shall be responsible for monitoring each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with the regulations.' There is no such requirement in Good Clinical Practice (GCP) regulations (21 CFR Parts 50, 54, 56, 312) or Good Manufacturing Practices (21 CFR Parts 210 and 211).

However, every testing facility, sponsor, Contract Research Organization (CRO) and manufacturing facility I have worked with has a QA function. This group is normally responsible for performing independent audits and assessments regarding compliance with regulations and internal policies and procedures. It is also often the case that the QA group is responsible for activities such as, but not necessarily limited to:

- Maintaining standard operating procedures (SOPs);
- Overseeing that employee training is performed according to policies;
- Reviewing protocols for regulatory compliance;

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- Inspecting data for completeness and accuracy;
- Interfacing with Food and Drug Administration (FDA) during inspections;
- Consulting on regulatory issues;
- Preparing corporate compliance policies, procedures, guidelines and checklists.

Additionally, in the GMP environment, the QA group may also be actively involved in managing activities such as, but not necessarily limited to:

- Manufacturing/packaging batch review, approval and product release;
- Consumer product quality complaint investigation;
- Discrepancy/deviation and failure investigation;
- Reprocessing/rework;
- Process/cleaning/test method/test method transfer validation;
- Change control;
- Product recall.

The QA Function as a Management Control

In evaluating the scope of the QA group's responsibilities and activities, one can see that QA represents a Management control; it is, or should be, the business instrument by which management is advised as to the status of regulatory compliance. And regulatory compliance is a business issue – make no mistake about it. While an isolated compliance deficiency can be considered 'expected' (no company can be perfect 100% of the time), numerous and/or significant deficiencies can result in cataclysmic business results.

What might the result be if a submission is rejected or delayed for lack of regulatory compliance? Lost research and development costs and lost revenue. What can happen if you are shut down for a time for lack of regulatory compliance? No production and lost revenue. What is a likely consequence if chronic regulatory noncompliance becomes known in the industry? Loss of current customers and no new customers, which equates ultimately to lost revenue. What is the common denominator here? Risk to business continuity and success, the business issue above all business issues.

So exactly how does QA serve as a management control? I am talking about a continuous feedback loop between company management's responsibilities and QA's responsibilities therein. An effective QA group performs the activities described above in a timely manner, with requisite skill and common sense. Its advice and recommendations are timely and practical. This allows company management to enhance existing controls, strengthen enforcement of existing controls, institute additional controls, and spot and act upon trends, in an appropriate and opportune manner. QA then assimilates the new control environment in its scope of responsibilities and activities and continues providing practical and timely advice and recommendations. This provides management the control environment needed to support profitability and competitiveness in today's business environment.

A Fly in the Soup

There is a fly in the soup, however. QA does not always discharge its responsibilities or perform its activities in a manner that truly serves the business purposes. Let us take a look at some of the common scenarios in the industry. I call them 'sin-dromes', a play on the medical term, because these situations can result in increased business expenses and reduced profitability, and thus they are business 'sins'.

The incomplete scope sin-drome

While most if not all large pharmaceutical/biotech companies and contract research organizations have a QA function, a large number of these QA groups do not look at business processes that involve computer systems or supporting functions. A look at the Master Audit Schedule will indicate that processes like system development, validation, physical/logical security, backup and recovery, disaster recovery, etc., are not part of the scope. The main reason for this situation is

that the QA staff does not understand this aspect of the business and/or does not understand its significance.

This is a business problem because these 'technical' processes are as much part of the business environment as are processes associated with study setup/conduct, manufacturing, etc. In fact, most companies rely heavily on computerized systems to maximize infrastructure elements such as processing efficiencies, knowledge-sharing capabilities, file storage capacity, and speed. Companies employ such technology to reduce operational time and costs, to gain a market advantage, or to become 'first in class'. If QA does not look at these operations, it cannot advise management if they are being performed in an acceptable manner. If data generated through these processes is rejected because of regulatory issues, the result will be that market advantage or 'first in class' status may not be obtained, not to mention the specter of increased costs and potentially lost revenue.

The bottleneck sin-drome

A number of QA groups do not have sufficient staff to support their organization. Some fairly large organizations have a QA group of one or two people. This results in a limitation on what QA can get involved with, the consequences of which are similar to those addressed in the 'incomplete scope sin-drome'. There is another consequence, however. QA normally reviews documents (e.g. study protocols, SOPs, various analyses) for regulatory compliance. Inadequate staffing can mean that these reviews are delayed. Delays will mean that issues are not identified and brought to management's attention or otherwise resolved in a timely manner.

An example: two independent groups validated a large document management system, and the publishing system with which it is supposed to interface. QA oversaw both validation efforts. The documentation management system was validated first, and the system owner removed the requirement to test the interface with the publishing system since the publishing system was not yet available to test with.

However, the requirement to test the interface was never meant to be included in the validation of the publishing system, and was not. Because QA did not review the validation documentation of the document management system for over a year, it did not know that the user removed the requirement to test the interface with the publishing system. Reviewing the publishing system documentation in a timely fashion did not help: the requirement for interface testing in this package was not to be included in the first place.

The result? After a year delay, QA noted that the interface testing was not included in either effort. The impact? Two large validation efforts, costing several hundred thousand dollars, have resulted in two large but unusable systems: an operational document management system that cannot send documents to be published for submission, and an operational publishing system with no documents to publish. You can not make this stuff up.

The quality control sin-drome

The only commonality between Quality Control (QC) and QA is the word 'quality'. In the GMP environment, a QC unit is usually responsible for performing testing to ensure adherence to proper specifications and limits. As stated in 21 CFR Part 211.22 (a), the QC unit '... shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated [and] ... shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company.' By contrast, QA is a function independent of any process and is tasked with reviewing and evaluating the respective activities and advising management if regulatory issues exist.

I have had extensive experience with QA groups, staffed with people who have extensive QC experience, that bring the QC mindset to the QA function. This is what happens. It is typical

that, in the document review process, QA gives as much weight to errors in spelling and punctuation as to issues such as missing approvals, steps being done improperly, etc. In one instance, QA would not approve a protocol because the page number in the footer was slightly off from the SOP specification. While this rigidity is necessary in a manufacturing setting (nobody wants adulterated product going out the door), the fact is that nobody ever died because of a misplaced page number or modifier.

The results of this rigidity are (1) that reviews are delayed and (2) the credibility of QA is negatively affected. As we have seen, delays can have a direct affect on a given business process. The impact of QA credibility being negatively impacted is in some ways more severe; management will be less likely to take QA's advice and recommendations seriously. Additionally, other departments will not have faith in QA's judgment, thus making compliance difficult.

The lack-of-common-sense sin-drome

QA advice and recommendations have to be practical. They have to exhibit some basic common sense, lest the 'cure become worse than the disease'.

An example: QA has gone through hoops assuring that stability data is sufficient to extend the expiry date of the bulk drug to *x* months. Unfortunately, the expiry date of the packaged drug product is only *X* plus a couple of months. Distributors do not want to accept any packaged drug product with the expiry date of less than a year left. Under the current scenario, every lot of the packaged product would become unsellable in just a couple of months.

Another example: In order to establish a 'use by date' for the clinical drug products manufactured by the company's other location, QA has created a general rule for the 'use by date' assignment based on their understanding of the issue and limited historical data that they have in house. But the manufacturer had its own process in place for this, unbeknownst to QA. The impact? Every lot of the same drug product ended up with two different 'use by dates' assigned to it. Clever.

Taking Care of Business

Building a QA group that is an effective management control is not a regulatory issue. It is a business issue and it starts at the top. The common denominator of the scenarios presented above is a lack of understanding of the potential value of an effective QA function. You can undoubtedly identify more 'sin-dromes' from your experiences. It is company management's responsibility to manage the business and to hire an adequate number of QA professionals who have an understanding of business principles, practical experience and a working understanding of the relationship between regulatory requirements and the company's business needs.

QA management and staff also have a responsibility. They need to understand the nature of business, and they also must be thoroughly familiar with the regulatory environment in which we all operate. Finally, they must be thoroughly familiar with the company's processes – be they automated, manufacturing, clinical, whatever – to be able to audit and inspect effectively, provide appropriate support and render practical advice.

Final Words

My final words take the form of one more 'sin-drome', the 'Disease-of-Conceit' Sin-Drome. The symptoms are pretty simple; the QA professional thinks the business starts and stops with QA. There is nothing more for them to learn and they can do no wrong. In the words of the Bob Dylan song Disease of Conceit, 'Then they bury you from your head to your feet from the disease of conceit'. And so might go the business.