Integrating the Rx-360 Joint Audit Program into an Existing Supplier Quality Management Process

Introduction

It is becoming increasingly hard for manufacturers to keep up with the expectation of supplier management. With supply chain management expectations increasing in global regulatory agencies, manufacturers are resource challenged to audit their suppliers to ensure supplier quality. Suppliers are also feeling the strain as more of their customers (manufacturers) require time on site to perform their audits.

This paper will discuss the situation and a potential solution for the pharmaceutical manufacturers worldwide.

Assumptions

- Manufacturers are responsible for all materials used in their production.
- Manufacturers have suppliers and service providers that require management.
- Suppliers to the pharmaceutical industry also have suppliers and service providers that their customers expect to be managed in a similar fashion.
- Both manufacturers and suppliers have discretion in determining which of their suppliers they will audit, however, these decisions need to be based on firm principles, taking into account regulatory expectations and potential risks.
- For critical suppliers, there is an expectation that an audit has been performed on-site, at least to initially qualify the supplier, prior to procuring the material for production.
- Many suppliers manufacturing locations are located in regions that are a great distance from their customers (India, China, etc.), thereby decreasing the chance that the manufacturer will have actually audited the supplier's facilities and systems.

Increased Expectations

Regulators expect that manufacturers manage their suppliers to ensure that the materials used to produce therapeutics are of the quality and consistency required to produce safe and effective therapeutics. As an example, in March 2015 The EMA Eurdralex revised the API manufacturers requirements to manage their suppliers. The change requires API manufacturers to audit their suppliers on, at minimum, a three year rolling schedule. The new rule also allowed the manufacturers to employ third-party auditors to conduct these audits on the manufacturer's behalf.

By allowing third-party auditors to be used, API manufacturers have been offered a solution of sorts, to manage the increased workload. But for Suppliers, there is no solution offered, and they must manage the increasing numbers of requests to host customer audits.

In the US we have seen regulatory agencies request more evidence of supplier management, beyond the typical manufacturer's yearly audit schedule and progress towards completion. And regulatory agencies continue to audit suppliers who provide materials to the pharmaceutical industry.

The Audit Burden: Manufacturers and Suppliers

Manufacturers have, on average, 528 suppliers and service providers[1] that fall under their supply chain. Not all of these suppliers and service providers require on-site audits, as some present verifiable lower risks to the manufacturer and patient.

However, a diligent manufacturer will ensure that they have taken the steps to ensure that they have a full understanding of the supplier's processes, management systems, release testing, and premises (this is especially true for their "critical" suppliers). This, however, often presents issues for the manufacturer, for multiple reasons:

- They have so many suppliers that they cannot audit all of them.
- Their suppliers are located in different regions of the world.
- The expense of sending staff to audit is prohibitive.
- They do not have the number of personnel required to accomplish these audits.
- Their suppliers are overloaded with audit requests, and cannot accommodate all customers (which can lead to audit refusals, or requests for audit fees).

Options are limited for manufacturers when it comes to ensuring compliance, and especially patient safety. The result of having an insufficient supplier management program can range from quality and supply issues, to regulatory actions, and ultimately, and most regrettably, lack of therapeutics for patients worldwide who require these treatments to improve their quality of life, or even save their lives.

Rx-360 Joint Audit Program

Rx-360 has worked closely with pharmaceutical manufacturers and their suppliers in understanding and avoiding supply chain risk. As a non-profit consortium, Rx-360 is made of up industry volunteers, who, working together, and share their expertise and enthusiasm for safe, complaint supply chains. This is accomplished through the identification and communication of supply chain threats, the production of white papers on related industry topics, and a solutions-based audit program.

The Rx-360 Joint Audit Program was developed to help alleviate some of the pressure that has been placed on manufacturers and suppliers. The Joint Audit program allows multiple member companies to sponsor single audits of their shared suppliers.

Key Points:

- Audits are conducted on behalf of members using third party auditing service providers
- Audit costs are equally divided amongst audit sponsors
- Prior to conducting an audit suppliers can exclude specific companies (i.e., competitors) from viewing the audit reports
- Audits may be requested by both manufacturers and suppliers

Rx-360 has developed a proprietary database, AuditsPLUS, which allows manufacturers and suppliers to indicate which suppliers and locations they require to be audited. By combining multiple manufacturer's audits onto a single audit, multiple benefits are produced:

- The required audit is completed;
- The supplier sees a reduction in the number of audits they host each year;
- And hard-to deliver audits, due to distance, supplier refusal, etc. are performed, allowing greater compliance and management on behalf of the Rx-360 sponsors.

The program respects the member's confidentiality, and with Rx-360's processes and database, provides the security of information its members require.

Rx-360 has developed documented practices, templates and forms to ensure consistency in all audits conducted.

Implementing the Rx-360 Joint Audit Program

The Joint audit program was designed to be flexible, to allow it to fit the needs of Rx-360's members. As manufacturers and suppliers, Rx-360 members already have their own Supplier Management Programs, and the Joint Audit program enhances their current systems.

Through a "Voice of the Customer" process, the Rx-360 Audits Operations Group (AOG) determined what was important to their members in an audit program. The program was built to ensure quality of the reports, be economical, and meet regulatory requirements. All of this was designed to alleviate the stress of the increased audit burden placed on manufacturers and suppliers.

Manufacturers and suppliers do not need a system to replace their Supplier Management Programs. We have seen members use the program to buttress aspects of their own programs. Members use Rx-360 to audit their lower risk suppliers. Others use Rx-360 to audit their overseas suppliers. And still others find benefit in Rx-360's reduced audit cost.

Observations generated in Rx-360 audits are categorized into two classifications:

- **Potentially Critical**: A deficiency that indicates a critical system failure that may pose an immediate risk to patient safety or health, or may result in adverse impact to the safety, identity, strength or purity of a product.

- **Other**: A deficiency against the Rx-360 audit standards, guidelines, checklists, but that are not potentially critical.

Because manufacturers may use the same audited material in drastically different ways, Rx-360 determined that using these two types of classifications allowed the sponsors and licensees to determine the importance of the audit findings within their own system, and classify them internally based upon their needs.

Sponsors are allowed to make special requirements in terms of the areas covered in the audits they sponsor. If there is a particular issue that they have had with a supplier, they can request that that area be highlighted. They can also focus the audit on particular materials.

The program is "plug and play". The member determines how the program would best work for them, and that is how they use it.

Benefits of the Joint Audit Process

Because the AOG is made up of industry professionals, the joint Audit Program was built by experts to meet the needs of the industry.

Key Benefits:

- Reduce the number of audits at a supplier site while increasing the effectiveness of the audits performed
- Utilize a standardized audit approach and report template
- Improve transparency of audits and improve 'collective' assessment of supplier QMSs
- The report can then be licensed (with supplier approval) in lieu of conducting an on-site audit

Licensing

Completed reports and managed by Rx-360, and are kept confidentially in the AuditsPLUS database. Members are provided access to the reports and corresponding materials through auditsPLUS.
Audit reports originating from the Joint Audit Program may be licensed to both members and non-members for a fee through the Rx-360 Secretariat.
A list of reports available for licensing can be found on the Rx-360 website using the following link Rx-360 Reports for Licensing.

An important feature is that suppliers are in control: audited suppliers can determine which organizations may license an audit report through an addendum to the original CDA.

CAPAs

The Joint Audit Program manages CAPAs to closure.

When observations have been issued in an audit, the supplier provides a CAPA plan to address these issues. The auditor reviews the proposed CAPAs and determines if they address the observation. The

CAPAs are posted in auditsPLUS, andRx-360 works with the auditee to ensure that the CPAs are closed and that evidence is presented upon closure. All of this information is supplied to the sponsors and licensees.

Auditors

Rx-360 has developed audit criteria that all auditors must meet before they are allowed to audit on behalf of Rx-360. Auditors must have industry experience within the areas that Rx-360 audits:

- API and Registered Intermediates
- Excipients
- Basic Chemicals/Raw Materials (including Chromatography Resins Index)
- Packaging/Printed Materials
- GDP

All sponsors are provided with auditor CVs and qualifications forms for review prior to the audit.

Rx-360 has partnered with BSI as the primary audit provider for the program. BSI operates under the direction and oversight of the Rx-360 AOG.

Regulatory Reception

Rx-360 audit reports have been used in regulatory inspections with no issues. Rx-360 works closely with regulatory agencies to ensure that the program is seen as a partner to industry. Regulatory leaders have presented at Rx-360 conferences in the United States and Europe.

Ease of Implementation

Rx-360 has staff willing and able to work with you so assist in the implementation of the Joint Audit program within your organization.

Members participating in the Joint Audit Program are allowed access to the auditsPLUS database, and each member can designate select members of their staff to have log-on privileges, thereby making the monitoring of requested audits easy and transparent.

Because all Rx-360 members share a common concern around Supply Chain safety and efficacy, the consortium has a vested interest in reducing the burden that auditing places on both suppliers and manufacturers, worldwide.

About Rx-360

Rx-360 mission:

> **Protect patient safety by sharing information and developing processes related to the integrity of the healthcare supply chain and the quality of materials within the supply chain.**

Management of the pharmaceutical supply chain has become one of the top public health concerns with respect to consumer safety. The globalization of distribution for both drug components and finished products has introduced many complications that to date have yet to be resolved. Unethical players and noncompliant companies along the supply chain can introduce counterfeited, adulterated and contaminated materials, often with tragic consequences. Naturally, such incidents lead to a loud and swift reaction from the public, the health authorities and the policy makers.
As regulators, pharmaceutical executives, supplier executives and members of professional organizations, our ultimate mission is to serve patients. Millions of people around the world are treated everyday with the vital medicines that we collectively provide. That is what we do. However, the threats to the supply chain have not only prevented us from treating patients, but have caused the deaths of hundreds if not thousands of the individuals we are trying to serve.

In order to achieve this mission, we require secure and reliable supply chains that deliver the right materials at the right quality so that these vital medicines can be trusted by health care practitioners and patients.

Legislators, regulators, and other organizations around the world are developing and implementing local measures to curtail these activities or mitigate their impact. A global consortium will complement these efforts and deliver a level of consistency and scope world-wide, that local measures cannot achieve.

In support of its mission to develop and implement enhanced global quality systems and processes to help members ensure product quality and authenticity throughout their supply chains, the Consortium may undertake the following activities:

(i) development of voluntary standards for the quality and authenticity of supplies and suppliers;
(ii) development and implementation of audit standards and auditor training and certification regarding the quality and authenticity of supplies and suppliers;
(iii) joint development of technologies to enhance the quality and authenticity of supplies;
(iv) development and implementation of a method for exchanging among members public information regarding the quality and authenticity of supplies and suppliers and non-public information regarding the quality and authenticity of supplies and suppliers that could adversely impact patient health or welfare; and
(v) Adoption of a seal for use by members that meet the Consortium's standards.

[1] Number derived from the Rx-360 member manufacturer supplier lists.