White paper on how to best manage Compliance Auditing	Page: 1 / 2

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Recent legislation in both the EU and the USA has made the auditing of suppliers compulsory. This audit is understood to be a full audit of the quality systems, the amount of effort required is considerable on both the auditor (travel time plus at least one full day by one person, often 2 days for 2 auditors, but this depends on the extent of the scope and the size of the site), and the audited site (an audit is transversal to all the activities of the company that have GMP elements: warehouse, production, labs, engineering, HR training files, etc..).

Trends on falsification of medicines and the escalating growth of illegal APIs that find their way into the legal supply chain explain the need for a concern over its authenticity and Regulators' expectations are that more audits take place.

An API producing site that sells $50-$100m of an average basket of off-patent APIs to an average international clientele is very likely to have an audit going on every week of the year if all clients decide to perform an audit to each of their API suppliers at least once every 3 years, if no sharing of audit takes place. This is an unacceptable burden on both sides for reason of costs, resources and common sense. Indeed no activity is more repetitive than a general quality systems audit. The new legislation has in effect mandated that shared audits performed by 3rd parties are to become the norm, rather than the unusual.

This white paper has been written with a view to generate reflection as to how can the Pharma supply chain best manage this matter to ensure a high level of compliance as well as efficiency and cost reduction.

A compliance audit is a must-have tool in every vendor qualification program, it is used to assess the supplier's Quality Management System and its compliance with applicable regulations. We believe that the resources put currently into audits need to be re-thought and rationalized for better returns.
Hovione will continue to encourage Clients to visit the Hovione Sites. We want to ensure that face-to-face meetings continue to take place with as much frequency if not more than in the past, however the typical routine quality system audit needs to reduce in frequency by becoming shared.

Hovione recognizes the following audit categories:

a) Qualification audit
With the purpose to qualify a supplier. This type of audit evaluates the supplier quality system to conclude if it is acceptable for client project requirements.
In some cases a 3rd party audit may be adequate, in others the audit should be performed by in-house auditors or specially contracted.

b) Routine audit
Audit performed on a periodic basis for supplier requalification purposes. This type of audit re-evaluates the quality system and goes through product specific related activities. Industry practice has defined as reasonable a periodic frequency for such audits of 3 years.
These audits should increasingly be a 3rd party audit and should be shared.
In the event a customer desires to conduct routine audits with shorter frequencies than every three years, the customer may be charged (cost based on audit hour/auditor), depending on what was defined in the quality agreement.

c) Technical audit
This is an audit on a specific product issue. It usually focuses on a plant area, specific equipment and documents related to a matter that was flagged for specific attention. The audit time is spent on the specific matter and no general quality system, or a walkthrough of all GMP areas of the plant is covered.

d) For cause audit
Audit performed after a major non-compliance has been identified, such as product out-of-specification, product recall or other critical occurrence related with any product manufactured and delivered by the supplier, with the objective of understanding the root causes and defining the corrective/preventive actions, with the collaboration of the client. This will not be a shared 3rd party audit.

e) Pre - PAI Inspection audit ("MOCK audits")
Audits performed by the client ahead of an FDA inspection that is due as part of the FDA review of either the client's NDA or a pre-approvable supplement referencing a supplier facility. By definition such audits are product specific though GMP procedure may also be covered. This will not be a shared 3rd party audit.

The resulting report and CAPAs of all audit categories are always a valuable element of a supplier file in a vendor qualification program. It evidences an effort to develop client/supplier intimacy which is a necessary condition for GMP compliance.

Savings from the reduction in the number of routine audits (achieved through audit sharing) should release resources to increase technical audits. Overall this should increase compliance, communication and product quality at an overall lower cost.

Risk Assessment
Much of the decision-making around audits (frequency, length and depth, whether performed by in-house auditors or contracted, shared or otherwise) is driven primarily by a risk-assessment process. Critically relevant to such decisions are: the importance of the API to the Pharma company's business, the nature of the API itself, past experience, etc… nobody else but the API user's quality unit or QP can make that determination.

Audit findings:
Irrespective of the type of audit, Hovione commitment is to correct any clear non-conformities with the regulations/guidelines detected during the audit, as such, all the non-conformities reported in the audit report must be referenced to the respective regulation/guideline. Agreed-to corrections shall be implemented within an agreed time-frame.

Anything else that is clearly described as not being a non-conformity (i.e. improvement suggestion or specific customer request) will be subjected to an evaluation prior to implementation.
The decision on whether to implement the additional requirement will be based on the added value that it may bring to the Hovione's Quality System and product Quality versus the effort, cost and resources it requires. It hurts efficiency, and is a source of noncompliance risk, if one client imposes a special system for its own product that is different from the standard practice in the plant for the rest of the products.
Both sides must be committed to a high standard of compliance but must remain focused on efficiency and productivity.

3rd Party audits, shared audits
The quality systems of both Hovione and the client need to contemplate and accept the use of a 3rd party auditing company and the sharing of audit reports.
Legal mechanisms must be in place between the several parties to ensure that both confidentiality and competition law is respected. The process itself must be, and be seen to be, free of any risk of conflict of interests. If the audited company is paying for the audit, a 3rd party must stand between the auditing company and Hovione to ensure absence of conflict of interests and the impossibility of a bias.
Companies must set up KPIs to reduce the number of routine audits and promote the use of sharing audit reports.
Once a company has opted to benefit from the efficiencies of a 3rd party audit process where the audit report is shared, it is important to continue with such practice as Clients will arrange their annual audit plan on such a basis.