

Audits and Quality Agreements

Key aspects of the Supplier Quality Process

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Outline

- Auditing – what and why
- Business benefits and regulatory expectations
- Standards and tools available
- Summary
- Quality Agreements
- Summary
- Questions

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Audit definition

An audit may be broadly defined as

'A systematic, planned, independent and documented examination'

ISO 9000:2005 – "A systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which audit criteria are fulfilled."

- **audit evidence** - records, statements of fact or other information which are relevant to the audit criteria and verifiable
- **audit criteria** - set of policies, procedures or requirements.

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Why do we audit?

Final Quality level of medicinal products results from the sum of many activities

End product testing alone is not sufficient to ensure product quality

- **An overall quality system is required that builds in the quality**
- **This includes the entire supply chain**

Audits assess the effectiveness of the quality system and help to ensure the requirements of GMP are being met for the finished product.

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Why audit?

- Regulations require us to have Approved suppliers
- Well conducted audits serve both to meet regulatory requirements and to benefit the business
- Auditing is often the most appropriate way to gain the knowledge required to assess and approve our suppliers.

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Why apply GMP to supplied materials?

- Protect (assure) public health
- To ensure consistent standards of manufacture and control are applied
- For OINDP medicinal products, the components are a critical and integral part of the overall product.
Process improvement and understanding
 - e.g., there is no MDI product without a functioning valve.
 - The complexity of components, with multiple sub-components and N-2 and N-3 suppliers, increases the risk for the wheels to fall off
 - ┌ Multiple suppliers = more locations/operations in which GMP and changes must be adequately controlled (or indeed can vary!!!)
 - Component defects may not be evident until too late, e.g., until the defect causes a batch of finished OINDP to fail.

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Business benefits of auditing

- Audits can be a valuable business improvement tool
- A good audit looks at systems against current and anticipated future needs – from both a regulatory and business perspective.
- Audits are an important part of the partnership building process and can benefit both suppliers and customers
 - Process improvement and understanding
 - Ensure customer requirements are understood and met
 - Enable reduced activity – e.g. reduced quality control testing
 - Reduce the risk of costs associated with failure.

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US and EU Regulatory Expectations for Auditing

- Limited detail on actual requirements
 - No explicit requirements within the USA Code of Federal Regulations
 - EU GMP Directives only have a clear requirement for self inspections (internal audits)
- However the need for audit is implicit to comply with other requirements
 - 'Each manufacturer shall evaluate suppliers...on basis of ability to meet specified requirements, including quality requirements. (CFR part 820.50)
 - 'Starting materials should only be purchased from approved suppliers' (EU GMP).

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Non Governmental Organization Regulatory Expectations for Auditing

WHO GMP guide notes that:

- 'Before suppliers are approved, they should be evaluated.
- The evaluation should take into account a supplier's history and the nature of the materials to be supplied.
- If an audit is required, it should determine the supplier's ability to conform with GMP standards'.

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Regulatory Expectations for Auditing: Take-Home Point

Regardless of specific GMP guidance there is a **clear expectation from regulatory authorities worldwide that audits are performed** – both internally and externally.

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Supplier's view of OINDP industry?

A view of the OINDP industry could be that

- companies have inconsistent views on quality expectations
- Don't understand suppliers and therefore have unrealistic expectations
- Apply pharma standards where not necessary.

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Why?

A supplier could be audited by companies using any of the following...

- ISO 9000:2001
- 21 CFR 210 & 211
- EU GMP
- Company internal standards
- Others...
- PQG PS 9000:2001
- WHO GMP
- ISO 13485
- ISO 15378



None of these Guidelines speaks specifically to OINDP

- No guide for suppliers as to expectations of customers specific to OINDP components
- Difficult to prepare for OINDP customer audits.

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Use of Standards

Standards or tools (or combination) are available for assessing appropriate quality standards and/or GMP standards in OINDP suppliers

Standards can be used

- Either through an audit of a supplier by a customer; or
- For suppliers to perform internal audits in readiness for customer audit; or
- For continuous improvement.

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Use of Standards: Role of IPAC-RS GMP Guideline

The IPAC-RS guideline is a harmonised quality standard

- Incorporates PS 9000:2001, which includes ISO 9000 requirements (which many companies are familiar with)
- Includes additional GMP considerations important for OINDP
- Has been compared against ISO 15378 and is in alignment with it
- Aim is to minimise the impact/number of differing customer requirements or auditing approaches.



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Use of IPAC Guideline – Auditor (OINDP manufacturer)

- Clarity of requirements, as follows ISO 9001:2000 with specific GMP clauses
 - Aids audit preparation.
 - Lead auditor needs to be knowledgeable in GMP and specific requirements
 - May need to be accompanied by a technical expert familiar with specific requirements for OINDP
- The IPAC-RS guide gives a common basis against which to discuss appropriate standards with auditee at supplier.

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Use of IPAC Guideline – Auditor (OINDP manufacturer)

- Able to assess all OINDP suppliers against a common standard
 - Initial evaluation and ongoing monitoring
- Increases 'value added' from audits if the basis is appropriate Quality and continuous improvement
 - Reduces the potential for frustration from both parties and helps to build partnership
 - Gives suppliers more guidance regarding your expectations
- Training and internal education
 - Helpful to get buy-in and support from QA leadership on use of Guideline
 - Critical to train your auditors on the use of the Guideline and specific concerns for OINDP.

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OINDP Manufacturers

Please use the guide as often as possible with suppliers

- as a basis for consistent auditing using a harmonised standard
- to drive continuous improvement
- to clarify requirements with suppliers

Please make it available to all auditors of OINDP suppliers.

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Use of IPAC Guideline – Auditee (OINDP Supplier/ N-1)

Clarity as to the expectations from the customer

- Gap analysis and audit preparation
- Common language during audit and subsequent follow up

Improve own business and better meet the needs of the customer – Proactive approach

- Attracting new business & retaining current customers
- Reduce frequency of audits
- Demonstrate appropriate control.

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Use of IPAC Guideline – Auditee (OINDP Supplier/ N-1)

Use to build requirements into own quality systems, and use as a basis for internal audit and continuous improvement

- Understand operations/ what is critical
- Design and improve processes
- Constantly seek better ways of doing business

Tool for OINDP supplier to increase the understanding of requirements with n-2, n-3 suppliers and in preparation for auditing these suppliers

- Context of increasing pharmaceutical standards

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OINDP Suppliers (N-1)

Please use the guide for internal audit/ self inspection

- Gap analysis for process design and improvement

Use in preparation for audits by OINDP customers

Use for improving the communication and dialogue for quality improvement both internally, with your own suppliers (n-2) and with your customers.

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Summary

- **Pharmaceutical manufacturers need to audit for business benefit and as a regulatory expectation**
- **The IPAC-RS guide provides a harmonised standard for GMP for OINDP suppliers.**
- **The guide can be used for auditing suppliers to improve quality standards and help promote continuous improvement**
- **The guide can be used by OINDP suppliers for internal audit, audit preparation and to demonstrate commitment to meeting required quality standards.**

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Quality Agreements

- **These agreements define a contract, which states the manufacturing, quality control and regulatory provisions and any specific GMP provisions required to provide material, product or service in adherence to relevant Quality requirements**
- **A contract established between the contract giver and the contract receiver to outline their respective responsibilities**

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Why have Quality Agreements?

- A common definition of 'quality'
- Quality expectations understood on both sides
 - Regulatory
 - Company
 - Industry
- To give guidance on handling quality issues
- Defines confidentiality and is a starting point for long term processes.

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Who is responsible

- Coordination of Quality agreement process can vary company to company
- Typically involves quality, supply chain, technical personnel
- A common agreed template will often speed up the approach where multiple agreements required.
- Quality needs to keep a list of Q Agreements in place and define which suppliers need to have a Q agreement.

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Plan ahead

- Quality agreement completion can take time
- Negotiation to and from is often required. Have a face to face if possible to soften the 'ping pong'
- Explain and justify your reasons for the items in question. It is important for your supplier to understand your needs
- Listen to their advice and act on it where possible
- Know what is mandatory and optional in your template a little flexibility can buy you points.

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Approval and maintenance

- Once approved, perform periodic reviews of Q agreements
- Is the information still current?
- Are responsibilities defined clearly?
- Have we expanded the business with them beyond the Q agreement?
- Keep a log of what Q agreements you have and what you have not

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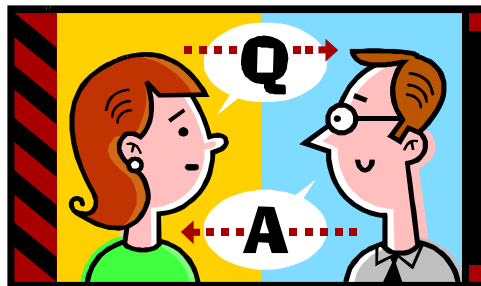
Summary

- It's a up front process that can be long winded.
- But it sets out definitions for a way forward.
- Once in place, maintenance becomes easy.
- It's a good demonstration of control in the evaluation of suppliers.

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Thank you for your attention

- Any Questions?



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