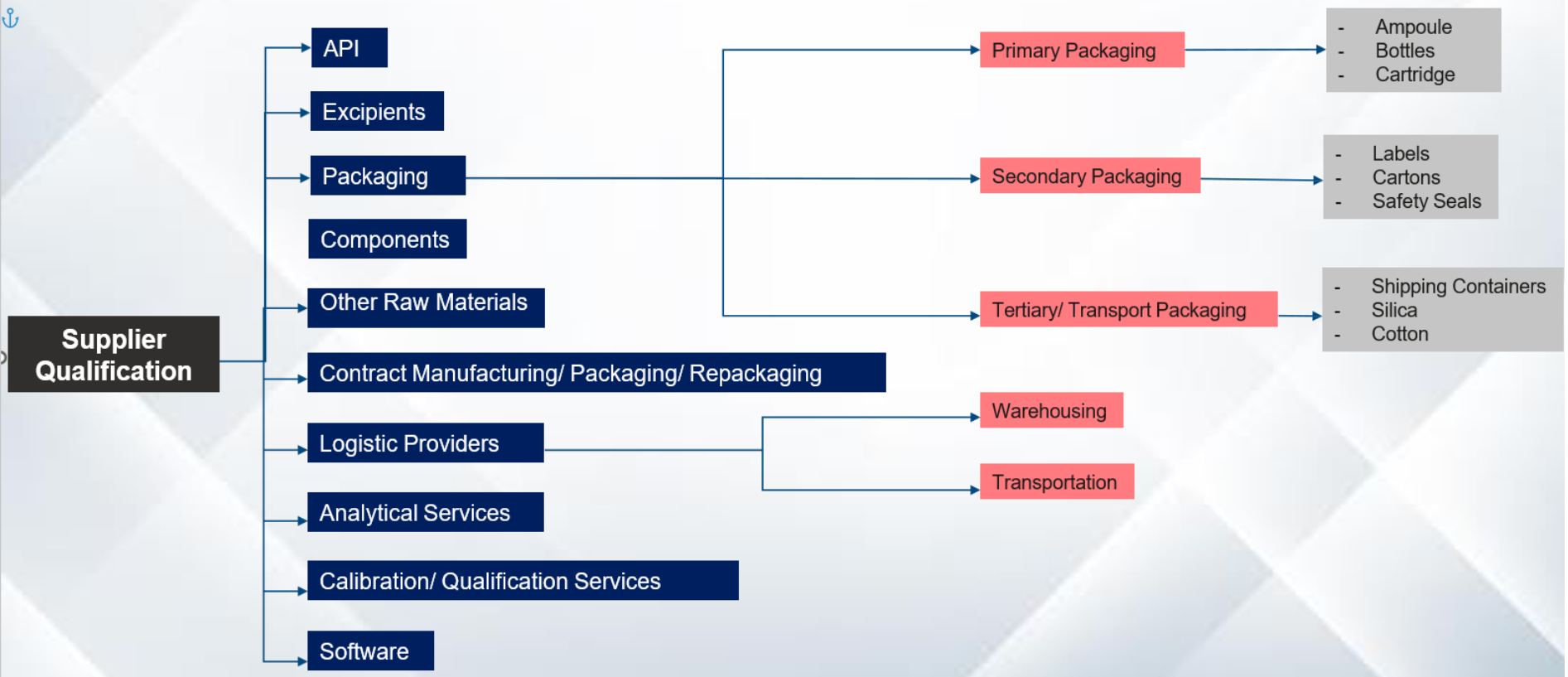
Qualification of the supplier of pharma packaging materials

Prof.dr Valentina Marinković
University of Belgrade
SERBIA

Content

* Risk management for the supply chain of packaging materials
* Regulatory requirements for the quality of packaging materials
* Implementation of standard ISO 15378- Why is it important?
* Suppler qualification lifecycle
* Case studies

Suppliers in the pharmaceutical industry



In USP: New General Chapter Supplier Qualification <1083>

Why certification of suppliers is required?

* Regulatory requirement
* It can help deliver high quality and safe medicines
* Prevent recalls
* Prevent deaths
* Prevent adverse events
* Prevent serious Illness

But In some cases, the standards expected were not maintained...

The main risks…

Primary packaging materials:

Contamination

Drug degradation

Secondary packaging materials:

Mix-up

Tertiary packaging materials:

Drug degradation

(cold boxes)

Regulatory requirements for manufacturers of packaging materials

GMP?

GDP?

ISO 9001?

ISO 15378?

An Overview on ISO 15378:2017 Documentation

Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2017, with reference to good manufacturing practice (GMP)

This standard was last reviewed and confirmed in 2023. Therefore this version remains current.

What is ISO 15378?

ISO 15378:2017 specifies requirements for a quality management system for manufacturers of medicinal product primary packaging materials.
These organisations need to demonstrate their ability to consistently meet customer requirements, including regulatory requirements and international standards applicable to primary packaging materials for such medicinal products.

ISO 15378 integrates the requirements of ISO 9001 as well as GMP.

The standard also helps to reduce the risks of safety hazards and product contamination, and ensure product efficacy and shelf life.

Benefits of ISO 15378:2017 Certification

- ✓ Helps organizations in the pharmaceutical and medicinal primary material packaging products manufacturing sector to minimize or eliminate instances of contamination, mix-ups, and manufacturing errors. Procedures Improves efficiency and cost effectiveness of business operations.
- ✓ Provides guidance on risk management and validation
- ✓ Ensures consistently meet customer requirements, including regulatory requirements.
- ✓ Additional assurance of quality products to the clients.
- ✓ Enhancement in processes.
- ✓ Evidence of adherence to legal requirements and contractual obligations.
- ✓ Clear statement of the organization's competence.
- ✓ Saves time and costs in day to day practice as per GMP guidelines.

Layout of the document

This document is an application standard for primary packaging materials, which contains the text of ISO 9001:2015.

The conventions for the layout of this document are the following:

— Those clauses, subclauses or annexes that are quoted directly and unchanged from ISO 9001:2015 and ISO 9000:2015 are in boxes.

— Additional GMP related requirements and recommendations as well as terms and definitions relevant to the manufacture of primary packaging materials are outside boxes.

Annexes

Annex A provides guidance on how to understand and implement the new structure, terminology, and concepts introduced in the updated standard, and it helps manufacturers to align their quality management system with the latest best practices in the industry.

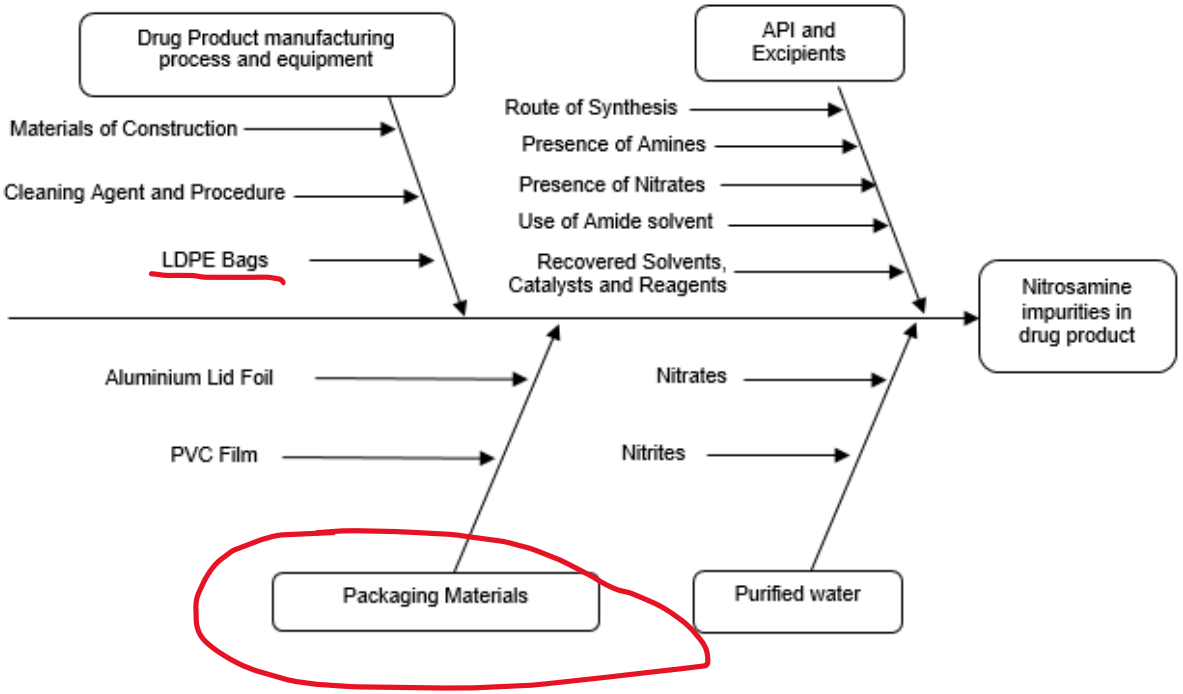
Annex B provides supporting information for organizations that apply this International Standard, and provides guidance for organizations that choose to progress beyond its requirements.

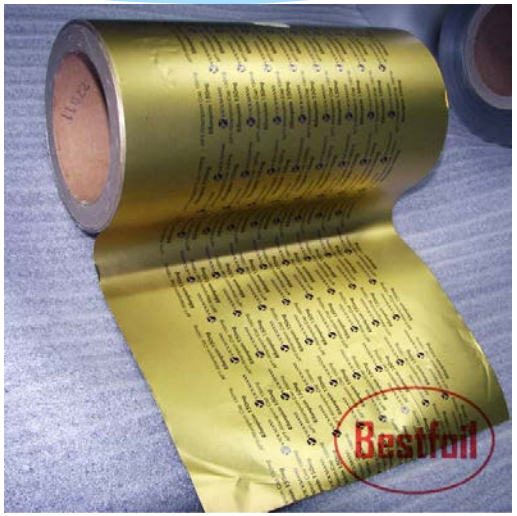
Annex C provides guidance on how to apply GMP requirements to the design, development, production, installation, and servicing of printed primary packaging materials for medicinal products. It helps manufacturers to ensure the quality and safety of these materials and to comply with regulatory requirements in this area.

Annex D provides guidance on how to ensure the quality and safety of primary packaging materials for medicinal products through verification, qualification, and validation processes. It emphasizes the importance of careful testing, documentation, and review to ensure that the packaging materials meet the intended use and performance requirements, and that they do not adversely affect the quality or efficacy of the medicinal product.

New risks?

Figure 1: Potential sources of nitrosamine impurities for a drug product

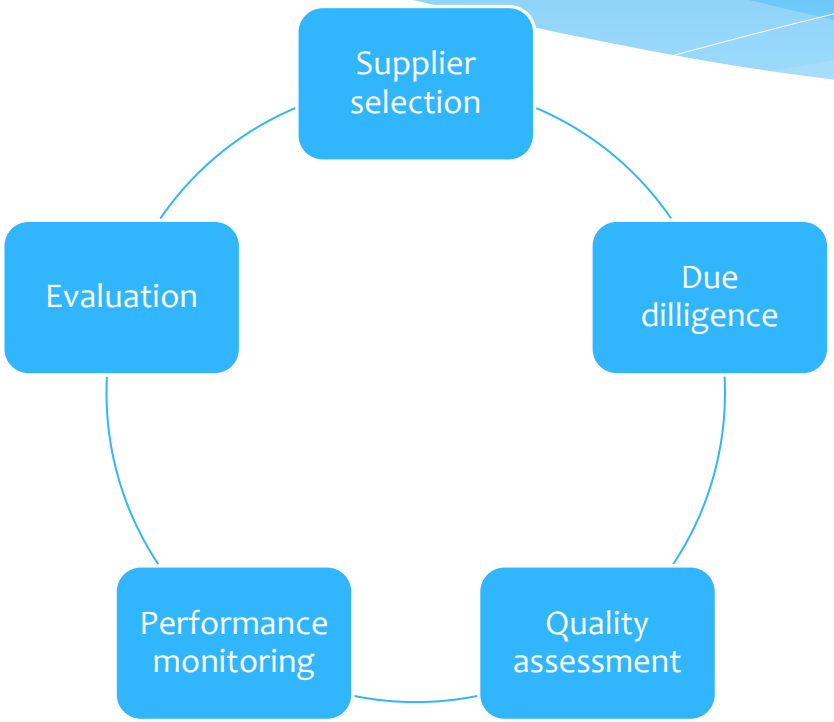




•**Primary packaging materials** such as blisters in which the nitrocellulosic lidding foil reacts with amines in the printing primer used to form nitrosamines, which would then be transferred to the product during the packaging process.

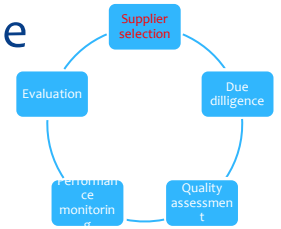
Imprinting inks based on nitrocellulose are the potential source of nitrites and azo pigments are another source of aromatic amines.

Supplier Qualification Life Cycle



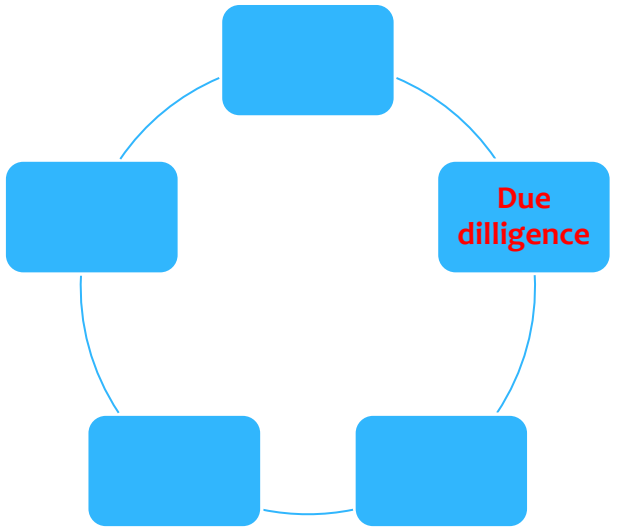
Supplier selection

- User requirement specifications should be provided for purchase based on which supplier will be selected.
- Information like
  - Manufacturing, Packaging, labeling details,
  -MSDS,
  -Analytical test methods to examine the sample against the specified criteria are to be requested from the supplier.
  -lead time to produce,
  -delivery time,
  -quality system certificate,
- The material supplied by the supplier should comply with the specification



Due dilligence

- Identify potential suppliers
- Sign confidentiality/ nondisclosure agreements
- Make a risk assessment (financial, legal, quality...)



Points to be considered when assessing and controlling risks

Risk Category	Points to Consider
Material-related risks	• Use in patient and/ or business critical products (irrespective of material cost) • Degree of use across product lines (irrespective of material cost) • Available inventory (internally and/ or externally) irrespective of material cost • Consider supplier's reject/ discard rate • Consider variability in process capability impacting the final product • Material performance based on information supplied by supply chain intelligence • Financial impact: cost of material and/ or service, cost and time of the alternate source • Product sensitivity ○ Sterility, temperature sensitivity, light sensitivity, etc. • Impact of primary and secondary packaging on material integrity

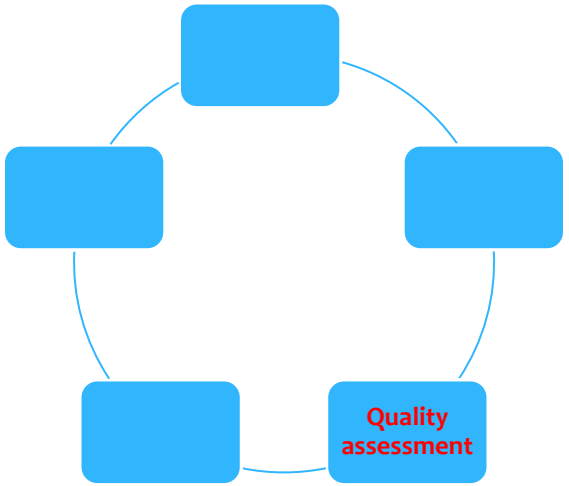
Capability	• Manufacturing
	  ○ Pharmaceutical: biologic, vaccine, sterile, nonsterile, etc.
	  ○ Device: Class III, Class II, Class I, etc.
	• Service
	  ○ Familiarity with changing regulations in all countries of service
	  ○ Upgrade capabilities
	  ○ Package, delivery, and route qualification and traceability

Stock-out risk to patients	• New product • Orphan product • Availability of alternatives
Financial risk to the business	• High cost of discards, loss of market share, impact to share-holders, etc.
Location/ Supply chain complexity	• Physical distance • Political boundaries and regulations

Quality assessment

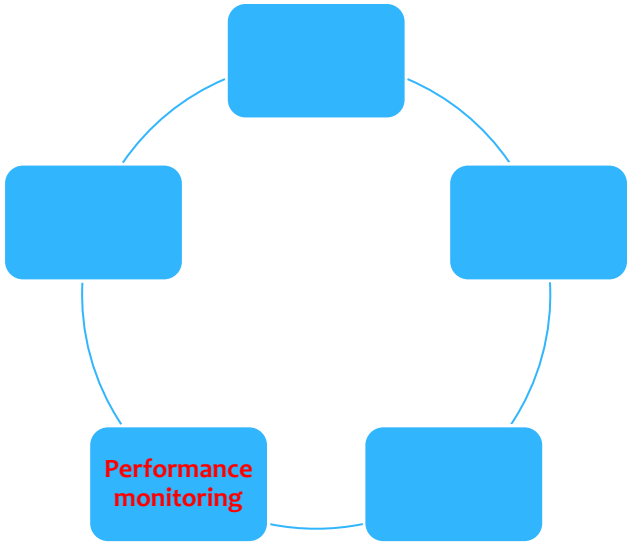
* Perform evaluation based on risk assessment through the following:
- desk audit- documentation review-QMS quaestionnaire
- on site audit
- sample request for analysis

Build the supplier qualification database



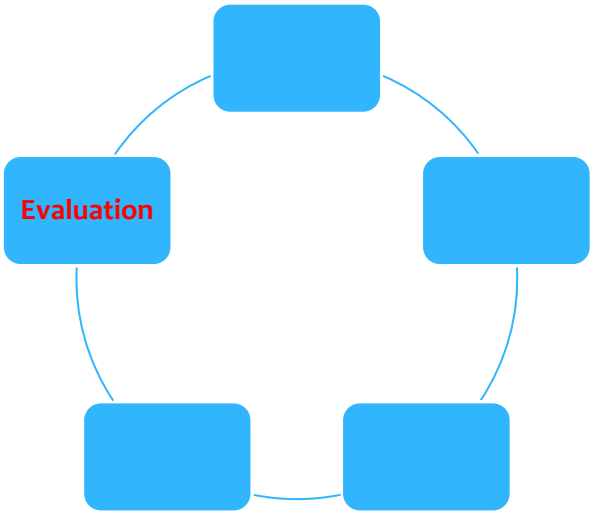
Performance evaluation

* Establish and agree on key performance indicatiors (KPIs) and monitor the supplier performance against the contract and QTA
* Evaluate the supplier performance at regular intervals
* Make decisions based on the evaluation, e.g., ask for correction action and preventive action (CAPA), quality agreement review, contract termination



Evaluation

* Explanation and measures to mitigate the risk
* Disqualification - document the circumstances
* Update the supplier database

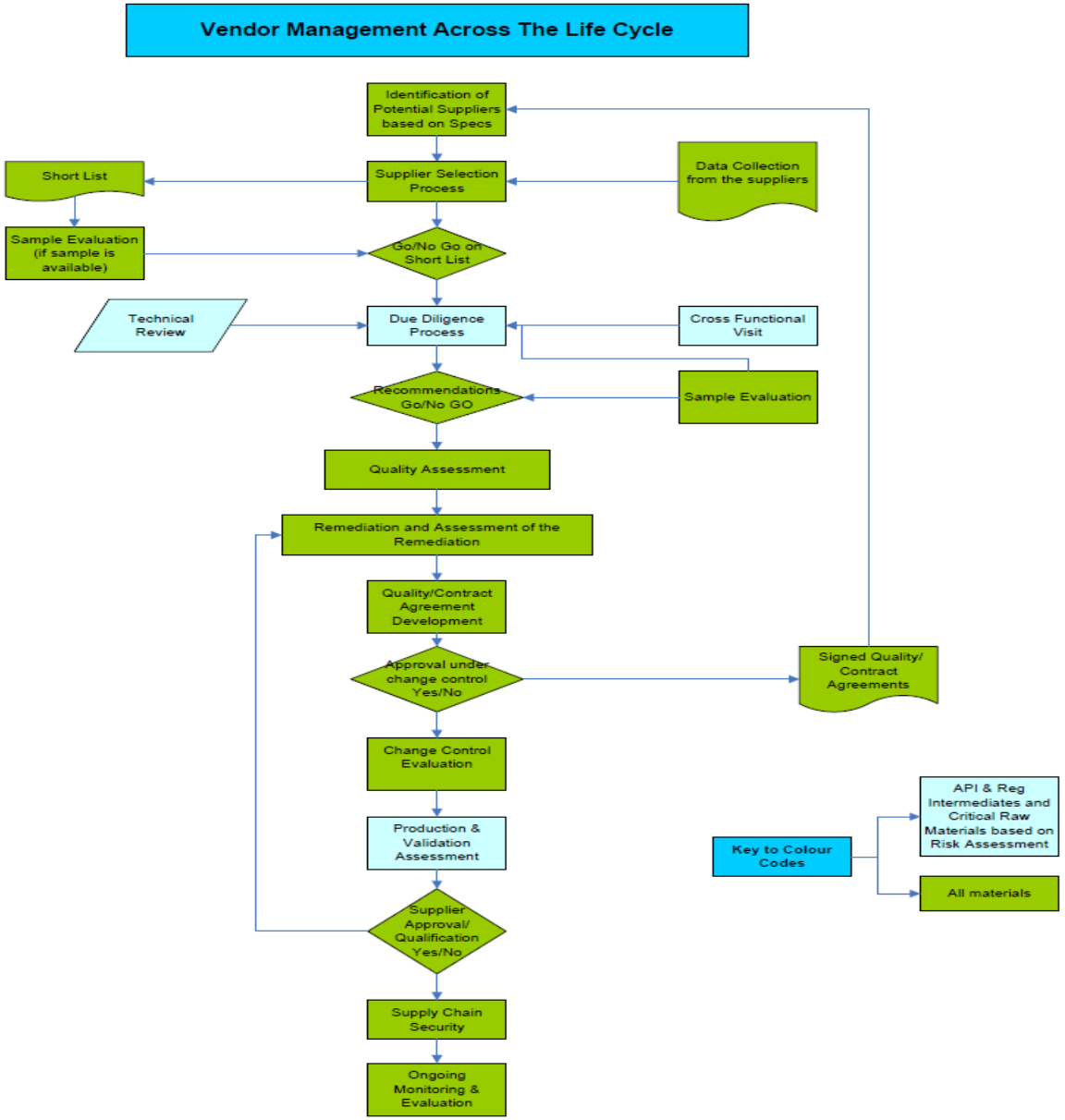


Supply chain security

- The entire supply chain from the manufacturer to the customer should be assessed and qualified from a quality perspective.

  Changes on the original container should be avoided e.g. while repackaging, relabeling. It can cause risk of alteration or contamination.

  * Packaging Requirements
- * Assessment of the CoA against an authentic manufacturer CoA


Vendor Management Across The Life Cycle
Identification of Potential Suppliers based on Specs
Supplier Selection Process
Short List
Data Collection from the suppliers
Sample Evaluation (if sample is available)
Go/No Go on Short List
Technical Review
Due Diligence Process
Cross Functional Visit
Recommendations Go/No GO
Sample Evaluation
Quality Assessment
Remediation and Assessment of the Remediation
Quality/Contract Agreement Development
Approval under change control Yes/No
Signed Quality/ Contract Agreements
Change Control Evaluation
Production & Validation Assessment
Key to Colour Codes
API & Reg Intermediates and Critical Raw Materials based on Risk Assessment
All materials
Supplier Approval/ Qualification Yes/No
Supply Chain Security
Ongoing Monitoring & Evaluation

Case studies

Which standard is applicable for quality assessment for?

* *Manufacturer of the glass bottle for Hydrogen peroxide as disinfectant agent for cleaning room*
* *And manufacturing of the glass bottle for Hydrogen peroxide as medical device?*
* *Manufacturer of the isothermal containers with high insulative material* (transportation of the products in the cold chain regime)

THANK YOU!

Valentina.marinkovic@pharmacy.bg.ac.rs