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Incorporating Global Supplier Quality Regulations for Effective GMP Auditing

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Editor's Note: The following was adapted from Janeen Santarosa's presentation given at IVT's Supplier Quality conference.

US Food and Drug Administration's goals in participating in supplier quality international harmonization include:

- To safeguard US public health
- To assure that consumer protection standards and requirements are met
- To facilitate the availability of safe and effective products
- To develop and utilize product standards and other requirements more effectively
- To minimize or eliminate inconsistent standards internationally.

Ultimately, we are ultimately responsible for assuring the quality and compliance of our products. Thus, by aligning international supplier quality goals, we can reach high levels of performance without excessive costs or redundant and conflicting requirements. Avoiding the risk of service/product failures and ensuring specification match supplier capabilities are further benefits of a harmonized and integrated approach to supplier quality. A thorough grasp of global regulations will also benefit the supplier through increased knowledge and better understanding of customer expectations.

Systems for managing and controlling supplier include qualification, assessments, agreements (quality/change), and monitoring. A comparison of global requirements for supplier qualification, assessments, and quality/change management agreements are outlined in Tables I¬–III; assessments as a continuous monitoring tool are shown in the Figure.

Table I: Supplier Qualification Comparison Chart.

Australian Government - TGA Guidance	Starting materials should only be purchased from approved suppliers named in the relevant specification and, where possible, directly from the producer.
EU Volume 4 Part II	Manufacturers of intermediates and/or API's should have a system for evaluating the suppliers of critical materials. Materials should be purchased against an agreed specification from supplier or suppliers approved by the quality units.
FDA 21 CFR 820	21 CFR 820.50, Purchasing Controls, requires in part: "Evaluate and select potential suppliers, contractors, and consultants on the basis of their ability to meet specified requirements, including quality requirements. The evaluation shall be documented."
FDA 21 CFR 211	211.84, d (2) Each component shall be tested for conformity with all appropriate written specifications for purity, strength, and quality. In lieu of such testing by the manufacturer, a report of analysis may be accepted from the supplier of a component, provided that at least one specific identity test is conducted on such component by the manufacturer, and provided that the manufacturer establishes the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.
GHTF/SG3/N17R9:2008	As part of the planning activities, the manufacturer should identify the risks associated with the product or services to be obtained. When selecting potential suppliers the manufacturer should investigate their business and operational capability. The manufacturer should select potential suppliers according to predefined criteria and the results of capability investigations.

Health Canada GMP Guidelines (GUI-001)	Testing other than identity testing: The testing is performed on a sample taken after receipt of the raw material on the premises of the person who formulates the raw material into dosage form, unless the vendor is certified. A raw material vendor certification program, if employed, is documented in a standard operating procedure.
ICH Q7A 7.1	Manufacturers of intermediates and/or APIs should have a system for evaluating the suppliers of critical materials. Materials should be purchased against an agreed specification from supplier or suppliers approved by the quality units. If the supplier of a critical material is not the manufacturer of that material, the name and address of that manufacturer should be known by the intermediate and/or API manufacturer.
ISO 13485	Purchasing process: The organisation shall evaluate and select suppliers based on their ability to supply product in accordance with organisation's requirements.

Table II: Supplier Assessments—Comparison Chart.

Australian Government-TGA Guidance	Period Review: As part of the qualification process a program for Periodic Review should be established. This program should include a mechanism for removing the qualified status of a packaging or starting material supplier and should prevent the use of reduced sampling and reduced testing until identified critical issues are satisfactorily resolved.
EU Volume 4 Part II	Manufacturers of intermediates and/or APIs should have a system for evaluating the suppliers of critical materials.
FDA 21 CFR 820	Purchasing Controls, requires in part: "Evaluate and select potential suppliers, contractors, and consultants on the basis of their ability to meet specified requirements, including quality requirements. The evaluation shall be documented." Define the type and extent of control to be exercised over the product, services, suppliers, contractors, and consultants, based on the evaluation results.
GHTF/SG3 /N17R9:2008	Depending on the risk of the supplied product/service, the manufacturer may plan and perform periodic supplier re-evaluations, regardless of whether problems have been identified. The purpose of this re-evaluation is to assess the supplier's ability (process and output) over time to continue to meet specified product/service requirements as agreed.
ICH Q7A	Manufacturers of intermediates and/or APIs should have a system for evaluating the suppliers of critical materials.
ICH Q10	Monitoring and review the performance of the contract acceptor or the quality of the material from the provider, and the identification and implementation of any essential improvements.

You can rate supplier audits on type of risk (e.g., service provided, supplies purchased, third party certifications). Risk level drives the relation of supply/supplier. The level of risk addresses the supplier situation individually and provides measurable controls around the supplier. Use your internal resources to identify supplier risk during receipt inspection, QC verification, in-process inspection, and final inspection. Example risk levels include:

- Level 1: The highest risk, wherein suppliers have a critical impact on the quality or availability of your product
- Level 2: Significant risk, wherein suppliers have a direct impact on your product, but alternatives are available.
- Level 3: Moderate risk, wherein suppliers have an indirect impact on the product.
- Level 4: Low risk, wherein suppliers have no product impact.

Examples of associated supplier audits based on risk level are shown below:

Level 1	**Action**
High risk supplier/service provider	On-site audit
Level 3	**Action**
Moderate risk supplier	Written audit

Level 4	Action
Low risk supplier	Limited assessment / Audit not applicable

Audit frequency (annual, biennial, triennial) is established based on risk and performance. The frequency may change based on detection inputs from assessment tools. The frequency will also depend on the occurrence of adverse findings and the status of third party certifications.

A pre-defined risk-based decision tree helps maintain consistency and provides justification as to why the audit type, or lack thereof, is chosen.

Risk Assessment for Calibration Subcontractor	Action
Certified to ISO 17025?	Yes= Obtain cert for file No= Written audit
Risk Assessment for Critical Component	
Custom Built product?	Yes=On-site audit No= Go to next question
Certified to ISO? (applicable standard)	Yes= Obtain cert for file No= Written audit

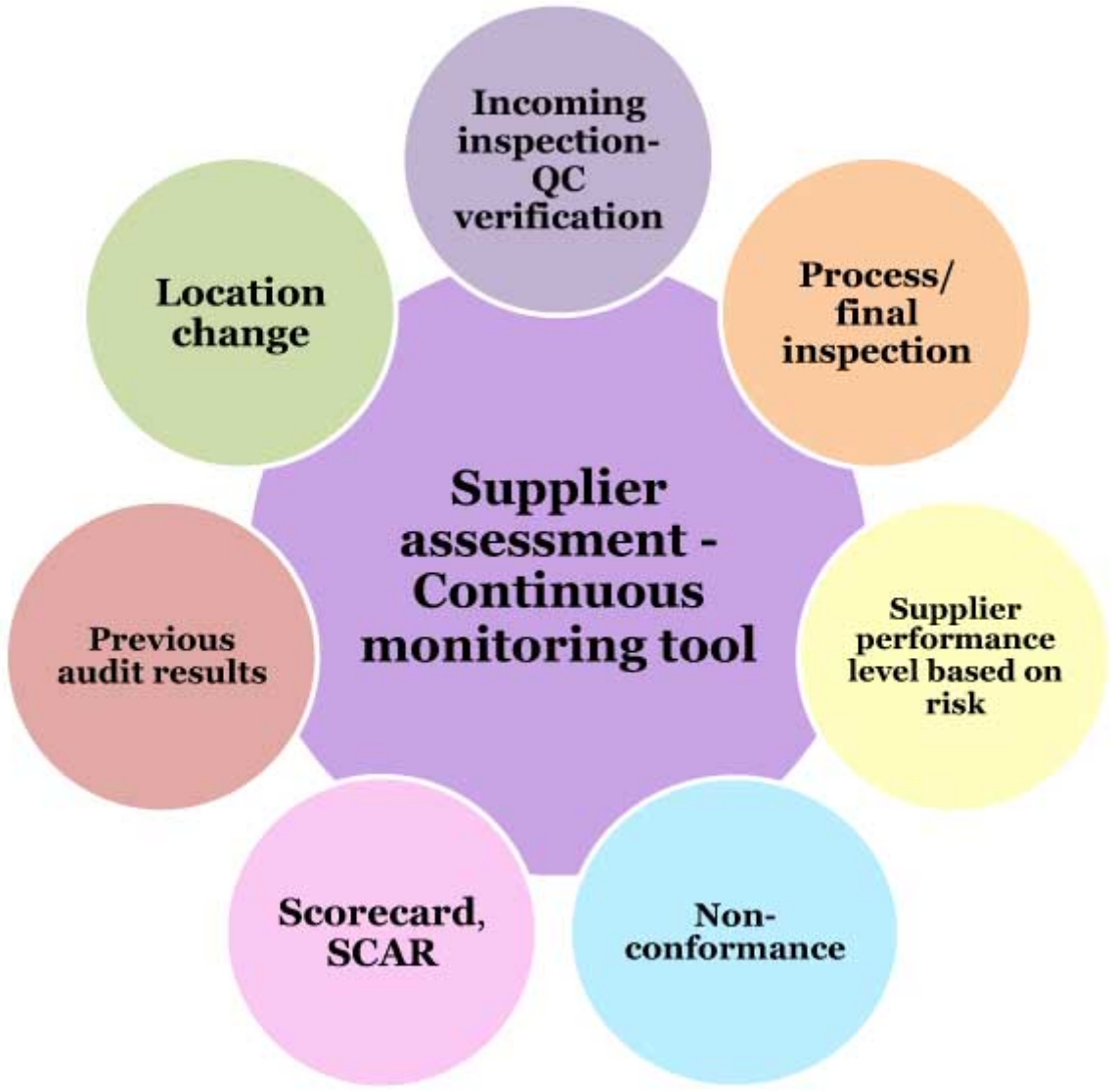
Table III: Quality and Change Management Agreements Comparison Charts

Australian Government- TGA Guidance	Identification of all interactions with the material between leaving the manufacturer's control and the final delivery to the finished medicinal product manufacturer can be useful. Steps to consider: Whether the supplier has a Technical Agreement with the manufacturer and the content of the agreement (e.g. changes to the material, such as the method of manufacture or material supply).
EU Volume 4 Part II	Contract Manufacturers (including Laboratories) There should be a written and approved contract or formal agreement between the contract giver and the contract acceptor that defines in detail the GMP responsibilities, including the quality measures, of each party. Changes in the process, equipment, test methods, specifications, or other contractual requirements should not be made unless the contract giver is informed and approves the changes.
FDA21 CFR 820.50	Establish and maintain purchasing data/documents that describe or reference specified requirements (including notification of change agreements).
GHTF/SG3 /N17R9:2008	The manufacturer and the supplier should have an agreed upon process for evaluating any changes to a validated process and for determining when re-validation should be performed and documented. This needs to be captured in the agreement between the manufacturer and the supplier.
Health Canada GMP Guidelines (GUI-001)	A raw material vendor certification program, if employed, is documented in a standard operating procedure. The program includes: Written agreement outlining the specific responsibilities of each party involved. The agreement specifies that the raw material vendor must inform the drug fabricator of any changes in the processing or specifications of the raw material.
ICH Q7A	General Controls: Manufacturers of intermediates and/or APIs should have a system for evaluating the suppliers of critical materials. Materials should be purchased against an agreed specification, from a supplier, or suppliers, approved by the quality unit(s). If the supplier of a critical material is not the manufacturer of that material, the name and address of that manufacturer should be known by the intermediate and/or API manufacturer.
ICH Q10	(ICH)Q10 Pharmaceutical quality systems guideline gives reference with manufacturer's responsibility to assess suitability and competence of a supplier. Define in writing quality responsibilities.

ISO 13485 7.4.2	Organizations purchasing information (including requirement for supplier records) should define appropriate requirements and communicate them to the supplier to ensure the quality of the purchased product or service. Typically these requirements are formalized in an agreement between the organization and the supplier.

Agreements ensure the quality of purchased products/services. Quality agreements outline the QMS expectations and define each party's responsibility. Change agreements outline the notification requirements for changes thereby assessing impact to the process/product.

Figure 1: Supplier Assessments for Continuous Monitoring.



Supplier scorecards are used to measure and monitor supplier performance. They identify attributes, agreements, factors, attribute ratings, and potential corrective actions. Supplier scorecards leverage each supplier factor in regards to its importance relevant to your business. Rating the supplier from 0–100 can provide a quantitative way to assess the supplier quality as seen in Figure 2.

Figure 2: Example Supplier Scorecard.

ATTRIBUTES	AGREEMENT					FACTOR	ATTRIBUTE RATING
Supplier performed service for which contracted. Quality documentation of studies and reports performed.	1	2	3	4	5	x 6	30
Supplier provided early notification of non-conformance. (Deviations, Amendments)	1	2	3	4	5	x 4	20
Service was performed in the contracted time. (TAT)	1	2	3	4	5	x 4	20
Supplier appropriate and timely resolved Complaints/CAPA (s).	1	2	3	4	5	x 2	10
Supplier provided early notification of schedule changes.	1	2	3	4	5	x 2	10
Service billed as initially bid.	1	2	3	4	5	x 1	5
Cost acceptable	1	2	3	4	5	x 1	5
						SUPPLIER RATING	100
