BSR/PDA Standard 01-201x, Enhanced Purchasing Controls to Support the Bio-Pharmaceutical, Pharmaceutical, Medical Devices and Combination Products Industries

Draft stage

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Martin VanTrieste, CivicaRX

Susan Schniepp, Consultant

Deepak Aggarwal, Center for Drug Evaluation and Research (CDER), FDA

Hal Baseman, Valsource

Jose Caraballo, Bayer

Jim Fries, Rx-360

Victor R. Gaines, Center for Drug Evaluation and Research (CDER), FDA

Roisin Hickey, Hovine

Kim HuynhBa, Pharmalytic (Ret)

Dan Kazzaz, Secure Exchange Solutions

Lee Leichter, P/L Biomedical

Janeen SkutnikWilkinson, Biogen

Richard M Stout, Adaptimmune

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1. Introduction

Historically, not all organizations have systems that ensure shared responsibilities for making purchasing decisions or define who is accountable for purchasing decisions and/or what measures/justifications or other controls/criteria are in place to maintain product quality. The focus of regulatory authorities on the responsibility of the Quality Unit for purchasing controls, consistent with the structure and text of the pharmaceutical CGMP regulation may provide the false impression to functions within companies other than Quality that they do not share in this responsibility.

Some medical products regulators do not exercise their authorities to inspect the areas of a firm where purchasing decisions are made, giving false assurance that this area is not subject to the same measures and controls to ensure product quality implying that this area is not subject to the same product quality controls and measures. The following quote from the Preamble to 1978 US GMPs indicates that the government is concerned about purchasing decisions that prioritize cost over quality and can be used to justify a standard.[1]

"These regulations were promulgated under the authority of section 501(a)(2)(B) of the act, which was passed by the Congress in 1962 in order to assure that no drug product available to consumers was adulterated. The requirements of the regulations are a reasonable and necessary step toward that goal. They do not inhibit competition, but rather enhance it by assuring that no manufacturer can reduce costs by eliminating those steps integral to the prevention of adulterated products. Thus, the consumer is assured that all marketed drugs meet the essential standards of identity, strength, quality, and purity; and consequently, selection of drugs by the consumer (directly or with the advice or a physician of pharmacist) will be based on fair principles of competition and free enterprise."

Purchasing / procuring / sourcing organizations have not been under routine regulatory CGMP scrutiny. In rare cases when purchasing controls were evaluated, it resulted from inspecting a quality unit or a manufacturing site, where the Quality Unit was solely held accountable. For example, a typical inspectional observation related to these issues begins "The Quality Unit failed to…". These responsibilities and authorities should be shared cross-functionally; however, accountability can only rest with one individual. The following enhanced controls place accountability with the proper individual within an organization, and to put those accountable purchasing / procuring / sourcing organizations under increased regulatory scrutiny via routine regulatory inspections. There is a saying that is a well-accepted leadership principle "When Everyone is Accountable, No One is Accountable" and that leaders are accountable for their teams' actions. Therefore, in the USA FDA Medical Device Quality Systems CGMPs that there is an entire section on Management Responsibility (21 CFR 820.20). [2]

The above citations are the minimum requirements which can be exceeded as part of each manufacturer's internal policies and procedures.

The lack of enforcement of regulations applicable to purchasing controls may have contributed to gaps in compliance including adequately defining appropriate internal responsibilities, authorities, and accountabilities. Current Pharmaceutical and Biotechnology manufacturer organizations, as required by CGMPs,[3] might focus on the quality control unit as the most responsible authority. Also, CGMPs primarily focuses on the control of components and drug product containers and closures through control of receipt and testing, and typical with CGMPs, there are no prescriptive requirements for the control of the suppliers themselves as these should be defined as appropriate by each manufacturer.

Current US law (CGMP regulations for Medical Devices and Combination Products)[2] requires robust systems for ensuring that manufacturers perform and document the evaluation and approval of potential suppliers, contract manufacturers, and consultants based on their ability to meet specified requirements, including quality and supply requirements. These CGMPs also require that the manufacturers have a supplier qualification program and maintain a list of approved suppliers. Also, CGMPs require that each manufacturer establish and maintain data that clearly describes or references the specified requirements including quality requirements. And where possible, an agreement should identify suppliers, contractors,

and consultants to agree to define when and how to inform the manufacturer of changes in the product or service.

CGMPs apply to the entire commercial product lifecycle, from the inception of the Design[4] through the discontinuation of the product. And although the regulations make it clear that the responsibility for meeting CGMPs rests the quality control unit, the expectation is that senior management of the company is at least equally or more responsible.[5] With the advent of ICH Q8, Q9 and Q10[6], guidance has been provided to pharmaceutical manufacturers to embrace those concepts that are already requirements for Medical Devices and Combination Products. Also, the legal conditions for establishing supplier requirements have changed with the passage of the Food and Drug Administration Safety and Innovation Act (FDASIA) in 2012.[7] FDA has heightened awareness of raw material and excipient suppliers and expectations include robust controls for oversight and management to ensure the supply chain is legitimate and materials sourced are safe and meet specifications. Therefore, there is a need for standard guidance for the selection and control of suppliers of purchased goods and services that can impact product quality and patient safety.

2. Scope

The purpose of this document is to ensure that there is an awareness of the requirements for purchasing controls for a specific material, component, product or service throughout the product lifecycle and that the responsibility for compliance at all stages is shared throughout the entire organizations, with final responsibility falling to the management of the company. Current quality management systems can be made more effective in preventing counterfeit, substandard or adulterated materials from entering the market and potentially harming patients. This could be achieved by implementation of adequate systems that better defines purchasing controls responsibilities, authorities and accountabilities and risk-based approaches in general.

The procedures shall describe the operating instructions and best practices for manufacturers of FDA regulated products. It is intended to expand on the requirements already defined under FDA regulations for pharmaceutical products, medical devices, and combination products and ICH guidance.

Note: Products subject to regulation outside of the USA may benefit from the concepts within this standard.

This standard represents current thinking on the topic and should be viewed only as recommendations, unless activities in the standard are specified by a regulatory or statutory requirement. An alternative approach might be appropriate if the approach satisfies the requirements. Therefore, in the USA FDA Medical Device Quality Systems CGMPs that there is an entire section on Management Responsibility (21 CFR 820.20). [2]

3. Normative references

The procedures shall describe the operating instructions and best practices for manufacturers of FDA regulated products. It is intended to expand on the requirements already defined under FDA regulations for pharmaceutical products, medical devices, and combination products and ICH guidances.

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4. Terms and definitions

- Approved Suppliers – These are suppliers that have been formally approved under the Purchasing control system for a specific material, component, product or service.

- Biopharmaceuticals – A pharmaceutical derived from biological sources and especially one produced by biotechnology.[8]

- Chief Procurement Officer (CPO) – the individual within the organization who is responsible for the management, administration, and supervision of the company's acquisition programs.

  Note: In small organizations, this could be an individual with multiple responsibilities.

- Combination Product – Combination products are defined in 21 CFR 3.2(e).[9]

- Contract – A written business arrangement for the supply of goods or services at a fixed price.[5] There should be a written Contract covering the outsourced activities, the products, services or operations to which they are related, and any technical arrangements made in connection with it.[10]

- Contract Acceptor – The organization that accepts a contract to produce product or provide services.[11]

- Contract Giver – The organization that engages with an outsource facility to produce product or provide services. [11]

- Drug Product – The finished dosage form that contains a drug substance, generally, but not necessarily in association with other active or inactive ingredients.[12*]

- Firm – A business enterprise.[9]

- Good Manufacturing Practices (GMPs) or Current Good Manufacturing Practices (CGMPs) – GMPs refer to the Current Good Manufacturing Practice regulations, policies and guidance enforced by the US FDA.

- Medical Devices – An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

  (1) Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,

  (2) Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

  (3) Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon

being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).[13]

- Manufacturer – A company that has been granted FDA clinical or marketing authorization for the study or commercialization of a regulated product such as pharmaceuticals, bio-pharmaceuticals, combination products or medical devices (including virtual companies).

- Outsourcing or Extramural Facilities – An extramural independent contract facility such as testing laboratories, contract manufacturers, contract packers or labelers, etc., and CGMP regards extramural facilities as an extension of the manufacturer's own facility.[14]

- Pharmaceuticals – A medication (also referred to as medicine, pharmaceutical drug, or simply drug) is a drug used to diagnose, cure, treat, or prevent disease.[15]

- Phased Appropriate Good Manufacturing Practice - A graded approach to good manufacturing practices (CGMP) throughout the product lifecycle, as CGMP expectations increase in scope and become more stringent from the discovery/R&D stage through clinical trials to commercial launch and to be continued with process verification, these activities should also match the development phase of the API (or drug product).[16]

- Purchasing Controls – Procedures each manufacturer should establish and maintain to ensure that all purchased or otherwise received product and services conform to specified requirements.[17]

- Quality Agreement – A comprehensive written agreement between parties involved in the contract manufacturing of drugs that defines and establishes each party's manufacturing activities in terms of how each will comply with CGMP. In general, the quality agreement should clearly state which party — the owner or the contract facility or both — carries out and is responsible for specific CGMP activities.[18]

- Shall – Indicates a requirement.[19]

- Should – Indicates a recommendation.[20]

- Supplier – An all-encompassing term that refers to a person or organization that provides something needed such as: products or services such as contractors, consultants, service providers, service to design, manufacture, store, distribute, etc. for pharmaceutical, bio-pharmaceutical, combination products and medical devices.

- Supply Agreements – A written agreement between a supplier and a buyer for supply and purchase of products. The agreement specifies the terms upon which the parties agree to supply and purchase products from each other. The agreement makes the buyer and seller understand their responsibilities and obligations under the agreement. The supplier supplies the products and the buyer purchases these products for business purposes according to the terms agreed under the product supply agreement.[21]

- Supply Chain – A system of organizations, people, activities, information, and resources involved in moving a product or service from supplier to customer.[22]

- Virtual Companies – Companies follow a model in which they typically employ few people (e.g., <50) and outsource most operations case by case to third-party organizations. However, virtual

companies if they hold the FDA approval to market a regulated product are still accountable for the quality of the product.

- Virtual Companies – Virtual FDA Regulated companies are companies that accomplish most if not all of their operations (e.g., research, development, and management) through outside, contract organizations.

  Note: Virtual companies, if they hold the FDA approval to study or market a regulated product, are fully accountable for the quality of the product and compliance of all suppliers to appropriate GMPs or quality systems.

5. Acronyms

ANSI	American National Standards Institute
FDA	United Stated Food and Drug Administration
CGMP	(current) Good Manufacturing Practice
ICH	International Council of Harmonization
ISO	International Standards Organization

6. Procedure or Process

Organizations shall comply with FDA regulations. Organizations should comply with ISO standards, ICH, International Medical Device Regulators Forum (IMDRF) (previously Global Harmonization Task Force)[23] Guidance documents. FDA and other regulatory guidance documents that are non-binding should be considered when developing purchasing controls. All activities shall include all functions involved in the supplier and purchasing process, including quality and as appropriate Subject Matter Experts, at each stage of the process. The decision to add, change or eliminate a supplier must be a cross-functional decision based on objective data and risk-based approaches.

The following summarizes the key elements of the supplier selection, qualification, approval, management and control process.

1. Determination of Need for New Supplier

The need for a new supplier can come at any stage of development or commercialization. The reasons can include:

(1) The need for a new part, component, material or service;

(2) replacement of an existing supplier due to cost, supply, quality or other issues;

(3) for a second source to an existing supplier

When the part, component, material or service is unique, it may be necessary to research and contact multiple suppliers to help develop refine the needs and requirements and identify the specific capabilities of each potential supplier before initiating the supplier selection process. However, other than a Confidential Disclosure Agreement (CDA), no agreement or commitment should be made before the supplier selection process has been completed.

2. Supplier Selection, Qualification and Approval[24]

Each manufacturer shall:

1. Evaluate and select potential suppliers, contract manufactures, and consultants on the basis of their ability to meet specified requirements, including quality and supply requirements. The evaluation should be documented.

2. Qualify and approve suppliers for the specific product or services they are to provide. The scope and depth of the activities necessary to approve each supplier should be based on risk to product quality and ultimately to patient safety, and where necessary can include initial qualification/approval audits. The approval process can be abbreviated for off-the-shelf parts but should be more intensive for custom materials, parts or services or single source suppliers' parts or services or single source suppliers.

3. Establish and maintain records of acceptable and unacceptable suppliers, contract manufacturers, and consultants.

3. Supplier Control

Each manufacturer shall:

1. Define the type and extent of control to be exercised over the product, services, suppliers, contract manufactures, and consultants, based on risk and the evaluation results.

2. Establish and maintain documentation that clearly describes or references the specified requirements, including quality and supply requirements, for purchased or otherwise received product and services.

3. As part of the Control strategy, using a documented risk-based approach, determine the necessity, duration, scope and frequency for auditing each supplier, contract manufacture and consultant.

4. Document the Supplier and Company responsibilities in a in a written Contract or Quality Agreement between the Contract Giver and the Contract Acceptor which clearly establishes the duties of each party.

5. Where possible ensure the supplier agrees to notify the manufacturer of changes in the product or service prior to implementation for major/critical changes, so that manufacturers may determine whether the changes may affect the quality of drug product, medical device or combination product. Notification requirements for minor changes might be defined in the quality agreement.

6. Where possible, the contract should include metrics to reflect the quality and other related performance criteria of suppliers.

   Note: It is recommended that the Quality Agreement or quality related contractual terms and quality related expectations be negotiated and established prior to the finalization of commercial terms. It is recommended that the Quality Agreement of quality related contractual terms note response and remedy for failure to meet quality requirements and where specified, metrics.

4. Supplier Monitoring

The performance of each supplier shall be monitored and performance against quality and other related performance criteria (i.e. supply, cost, customer service). This performance shall be reviewed and part of Management Review.

Where the performance is unacceptable, the supplier should be required to identify most probable potential root cause and initiate corrective actions, and if not successful, disqualified and removed from the approved supplier.

7. Responsibilities, Duties and Activities to Meet This Standard

It may be advisable to establish a position, such as a Chief Procurement Officer or equivalent to be responsible for the entire process, with the intent to ensure seamless and continued compliance from supplier identification throughout the procurement process.

A Chief Procurement Officer or equivalent would be the individual within one method or organizational structure that can help a company ensure compliance throughout the procurement process as for the license holder of a marketing authorization for a drug product, combination product or medical device to designate a Chief Procurement Officer or equivalent.

It is envisioned that a Chief Procurement Officer is the individual within organization who can be responsible for the management, administration, and supervision of the company's CGMP acquisition programs, supporting activities including, but not limited to Phased Appropriate Good Manufacturing Practice regulations for:

(1) product development;

(2) clinical study supplies;

(3) quality control;

(4) manufacturing drug products, medical devices, combination products;

(5) processing drug products, medical devices, combination products;

(6) packaging drug products, medical devices, combination products;

(7) storage of drug products, medical devices, combination products;

(8) and distribution of drug products, medical devices, combination products.

7.1 The Chief Procurement Officer duties

1. The Chief Procurement Officer may lead, direct, and manage the procurement organization.

2. The Chief Procurement Officer understand the business requirements, and buys products and services at:

    - At the right price
    - From the right source
    - At the right specification that meets users' needs
    - In the right quantity
    - For delivery at the right time

3. The Chief Procurement Officer should be involved early in the supplier selection process to be effective.

4. The Chief Procurement Officer with cross-functional advice, where appropriate from R&D, Product Development, Engineering, Quality, Operations and other functions, oversees contracting for goods, outsourcing or extramural facilities operations and services and manages the purchase of supplies,

equipment, materials and outsourcing services from approved firms for use in cGMP activities. It is his or her responsibility to source goods and services, and to select suppliers that can meet scientifically justified specifications including quality requirements, ensuring a consistent supply of goods and services.

5. It is important that the Chief Procurement Officer oversee the initial selection of any firm, no matter how early in the development process to ensure his accountability.

6. The Chief Procurement Officer is accountable for assisting in identifying and selecting appropriate suppliers that produce quality products or services, which includes a robust and reliable supply chain. Where a supplier cannot meet quality or supply requirements the Chief Procurement Officer is accountable for assessing the risk to product quality posed by deficiency and taking immediate actions to remedy the non-conformance, which shall be documented in a CAPA (Corrective and Preventive Actions) plans. Risk based actions to address the non-conformance should be recommended by other cross-functional members that could include R&D, Product Development, Engineering, Operations, Supply Chain Professionals, Quality Professionals, Qualified Persons, Responsible Persons, etc. as specified in the company's Quality Risk Management policies and procedures.

7. The Chief Procurement Officer, in consultation and with input from other appropriate company functions, including Product Development, Quality, Engineering, Operations, and other functions, is responsible for the evaluation of suppliers, contract manufacturer, and consultants should be conducted. The Chief Procurement Officer should establish and maintain the requirements, including quality and supply requirements that should be met by suppliers, contract manufactures, and consultants.

8. The Chief Procurement Officer should establish and maintain procedures to ensure that all purchased or otherwise received products and services conform to scientifically specified requirements assuring product quality, which includes a robust and reliable supply chain. These procedures should be documented and formalized as Standard Operation Procedures.

9. The Chief Procurement Officer should promptly notify the appropriate medical products regulator if required by legislation, regulation, policy or guidance if the remediation cannot be performed to prevent substandard quality or product shortages potentially impacting patients.

10. Since the Chief Procurement Officer and the firm's procurement organization may have inherent conflicts of interest of cost versus quality, the following activities should be performed outside the jurisdiction of the Chief Procurement Officer that do not report to the Chief Procurement Officer and is separate from procurement organization:

    - Development of scientifically sound specifications should occur in an independent product development or technical support organization.

    - Approval of scientifically sound specification shall be performed by an independent quality unit or quality professional.

    - Approval of CAPAs should be performed by an independent quality unit or quality professional.

    - Approval of Standard Operating Procedures utilized by the procurement organization should be approved by an independent quality unit or quality professional.

    - Approval of supplier selection should be performed by an independent quality unit or quality professional.

    - The frequency, duration and type of evaluation of suppliers is determined and approved by an independent quality unit or quality professional.

- Approval of the list of acceptable suppliers shall be approved by an independent quality unit or quality professional.

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