

Good Working Practice 07 - Quality Systems Management

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Topics:

- 1. Batch Record and Device History Record (DHR) Review**
- 2. Deviation Reporting**
- 3. Quality Risk Management (QRM)**
- 4. Medical Device Corrective Action, Preventive Action (CAPA)**
- 5. Documentation Practices**
- 6. Stop Distribution**
- 7. Disposition of Production Materials and Finished Products**
- 8. Market Actions**
- 9. Quality Assessment for Reworking Active Pharmaceutical Ingredients and Drug Products**
- 10. Assigning Expiration Dates**
- 11. Annual Product Records Review**
- 12. GMP Training**
- 13. Returned Goods**
- 14. Quality Agreements**
- 15. Product Complaints**
- 16. Change Control Management**

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- Documentation of manufacturing line cleaning and clearance;
 - Documentation of packaging line cleaning and clearance; and
 - Documentation of final quantity manufactured and packaged.
- If a data entry field on a batch record or DHR is not filled or is missing data, an explanation must be documented in the batch record or DHR. If no explanation is provided, a deviation investigation must be initiated.

Missing Data for Critical Process Parameters shall only be allowed to be added to the batch record or DHR after a deviation has been initiated, the reason for the batch record or DHR missing the data is investigated and there is independent documented evidence to support the information. If the data are added, the person adding the data shall sign and date the addition and reference the supporting documented evidence. The step shall also be reviewed, signed and dated by the Quality Team.

2. Deviation Reporting

- Deviations to approved Production, Testing, or Distribution Procedures for Active Pharmaceutical Ingredients (API), Drug Products, Medical Devices, Consumer Health Care (CHC), Animal Health, and cosmetic products produced by a GMP site or confirmed Out-Of-Specification (OOS) Results obtained during testing of such products shall be documented, Investigated and Disposition to be made.
- Planned temporary deviations shall be approved prior to initiation of the deviation. Planned permanent changes shall be addressed by the change management system.
- Each colleague is responsible for identifying deviations and reporting incidents to department supervision.
- The Site Quality Team shall be notified of all deviations.
- Planned Temporary or Unplanned Deviations shall be documented in a Deviation Report (DR).
- The Supervisor responsible for the department where the Deviation occurred shall document the results of the investigation of the deviation in the DR, review the DR and forward the report to the Site Quality Team. Either the DR form or a site-specific form that meets the requirements of this procedure shall be used.
- The DR shall be approved by the Site Quality Team.
- The DR shall:
 - Be assigned a unique number;
 - Document any decision regarding the need for any Market Action for a Batch/Lot already approved and distributed
 - Contain a final statement regarding product quality;
 - Contain a conclusion regarding the probable disposition (Approved, Rejected, or Reprocessed) for a lot/batch that has not been assigned a final disposition; and
 - Be tracked and Trended by the Site Quality Team.
- The Site Quality Team shall evaluate deviations (planned temporary and unplanned) and assess the potential impact to product quality.
- Final Disposition of a Batch/Lot shall not be assigned until the DR has received final approval.
- Responsibility for Batch Disposition is vested with the Site Quality Team.
- All Unplanned Deviations shall be investigated by the Supervisor of the department where the deviation occurred and the Site Quality Team, with assistance from other experts, as needed.
- The Site Quality Team shall call for an expanded investigation through the establishment of a Cross-Functional Team (CFT) using Root Cause Methodology, when one of the following situations occur:

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- Are outside quality action criteria but within regulatory limits, a lot/batch may be recommended for approval or reprocessed following review of the DR and concurrence with the Site Quality Team; or
- Are outside Alert Levels but within Action Levels, no action is required, other than to be aware that a potential deviation may be developing.
- The Original DR shall be filed in the batch/lot Record when an API or drug product is involved and in the Device History Record (DHR) when a medical device is involved. Alternatively, the assigned DR number shall be referenced in the respective batch/lot record or DHR when the original report is filed in a central file system administered by the Site Quality Team.

When DR is not batch/lot related it shall be filed in the specific product/subject file.

- The site system used to track DRs shall include all identified corrective and preventive actions.
- When All Corrective and Preventive Actions are Complete, the Site Quality Team shall perform the final close-out of the DR by confirming that all actions were completed and documented.
- The Site Quality Team shall trend DRs by deviation category, product, and/or root cause at least annually. The trends shall be reviewed by the SMT, when there is a trend identified, a corrective action shall be put in place.
- When an Electronic System is used at the site to track Corrective Actions, the system shall track the close-out of the corrective action and the tracking number shall be included on the original DR. It is then not necessary for the Site Quality Team to document final close-out on the original DR.

For a Drug Product or API manufactured outside the European Community (EC) or Canada and imported into the EC or Canada, copies of all relevant DRs, with quality or Regulatory Impact, must be forwarded by the sending Site Quality Team to the receiving Site Quality Team (who is a Qualified Person in the EC). Deviations concerning quality or regulatory issues must be approved by the receiving Site Quality Team prior to release to the EC or Canada.

3. Quality Risk Management (QRM)

This working practice provides the necessary components of an acceptable QRM methodology, to support and complement existing procedure and standard requirements.

QRM is a broad methodology, with multiple approaches and applicability. The application of QRM methodology, and the corresponding level of documentation, varies, depending on the individual circumstances.

QRM includes systematic processes designed to coordinate, facilitate and improve science-based decision-making with respect to risk.

- The Extent to Which QRM is used and Documented shall be consistent with the complexity and/or criticality of the issue to be addressed. Use of QRM in a quality, Good Manufacturing Practice (GMP), or regulatory decision shall be documented and Approved by the Site Quality Team.
- If Use of QRM is Specified in a procedure, the process or methodology, and resulting decision, must be documented and approved by the Site Quality Team.
- When QRM is used:
 - The Site Quality Team has oversight responsibility for all QRM activities [e.g., QRM Standard Operating Procedures (SOP)] and decisions at the Site
 - The Site Quality Team shall continue to use the notification, escalation, and review processes; and

Appendix 1: Common Risk Management Tools and Methods and Examples of Their Usage in Pharmaceutical Quality Risk Management.

Note: This is not an exhaustive list and is intended for illustrative purposes only. These methods may also be used in circumstances not included in this list.

Risk Management Tool/Methodology	Description and Examples of Application
<p>Failure Mode Effects Analysis (FMEA)</p>	<p>Description: Evaluates potential failure modes for processes, and the likely effect on outcomes and/or product performance. Once failure modes are known, risk reduction can be used to eliminate, reduce, or control potential failures. Relies upon product and process understanding. Output is a relative “risk score” for each failure mode.</p> <p>Examples: Evaluate equipment and facilities; analyze a manufacturing process to identify high risk steps/critical parameters.</p>
<p>Failure Mode, Effects and Criticality Analysis (FMECA)</p>	<p>Description: FMECA extends FMEA to incorporate the degree of severity for consequences and the respective probability/detect-ability of each consequence. Product/process specifications should be established to utilize FMECA</p> <p>Examples: Typically used in failures, and risks associated with manufacturing processes.</p>
<p>Fault Tree Analysis (FTA)</p>	<p>Description: FTA is a method to identify all root causes of an assumed failure or problem. The method evaluates system/sub-system failures one at a time, but can combine multiple causes of failure by identifying causal chains. FTA relies upon process understanding to identify causal factors.</p> <p>Examples: Investigating complaints or deviations.</p>

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- Personnel directly responsible for assuring the quality of the applicable product or the prevention of such problems;
- Management; and
- Regulatory Authorities and/or Notified Bodies.

The Impact of a Nonconformity on other production units, Lots or similar products shall be assessed. A documented investigation shall include evaluation of, and not limited to, the following:

- Manufacturing processes;
- Quality processes;
- Failed components;
- Design related issues; and
- Process anomalies.

Design Deficiencies detected as a result of a nonconformity investigation shall be corrected in accordance with the documented Design Control and change control standards and procedures.

CAPA Documentation shall include:

- Description of the nonconformity, including identification of the Batch or lot affected;
- Scope of the nonconformity including any other product, batches, or lots potentially impacted by the nonconformity;
- Risk or hazard assessment associated with the nonconformity;
- Root cause investigation;
- Corrective actions taken (short-term and long-term);
- Preventive actions taken (short-term and long-term);
- Conclusion, including Disposition of the impacted batch (es) or lot(s);
- Verification or validation to demonstrate effectiveness;
- Follow-up;
- Identification of person(s) conducting the investigation;
- Date of investigation;
- Signature of Site Quality Team approving the CAPA report and date of Approval.

5. Documentation Practices

This practice defines the requirements for systems for control, implementation, maintenance and archival of Good Manufacturing Practice (GMP) - Related Documents and GMP - Related Records. These systems must assure that such documents and records are adequate, Approved and in compliance with applicable GMP and Site requirements.

Documentation Practices shall be established and maintained that define the requirements for GMP-related documents and records including, but not limited to, the following:

- Documents applicable to Active Pharmaceutical Ingredients (API), Drug Products, and Medical Devices:
 - Direct Impact System facility, utility, and equipment drawings;
 - Stability and Validation Protocols and reports
 - Material Control Documents (MCD); and
 - Test Methods (TM); and
- Records applicable to APIs, Drug Products, and Medical Devices:
 - Equipment Cleaning, Maintenance, and Use Logs;
 - Training Records;
 - Complaint Records;
 - Distribution Records;
 - Change Control Records;
 - Records of Market Actions;
 - Laboratory Test Records;
 - Equipment and Instrument Calibration Records;
 - Deviation Investigation Records; and
 - Batch Production Records and Control Records;

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distributed in Canada shall be maintained on the premises of the relevant Canadian fabricator, packager, labeler, importer, or distributor.

6. Stop Distribution

- This guidance applies to all Drug Products, Active Pharmaceutical Ingredients (API), and Medical Devices in transit, at a GMP site, Logistics Centers or with Contract Vendors, intended for commercial distribution, when a Disposition status change is required after initial product release and while any portion of the product is still under Site or Site contractor control.

The term "Logistics Centers", for purposes of procedure, includes all locations where Site products are received, stored, or shipped prior to entering the market place and are controlled by Site.

Any product Lot, or portion thereof, subject to a Stop Distribution that has been further distributed outside of Site control (e.g. to customers) must be considered by the Site Quality Team for possible Market Actions

- This procedure applies to all GMP Sites and Logistics Centers responsible for the control and distribution of Pharmaceutical, Animal Health and Site Consumer Healthcare drug products, APIs, and medical devices.
- Potentially Significant Problems, for which a Stop Distribution shall be considered, include and are not limited to, the following:
 - An Out-of-Specification (OOS) Result for stability studies, complaint analysis, or other Investigations related to marketed lots when no readily apparent Assignable Cause is found upon completion of the Laboratory Investigation (LI);
 - Evidence of microbiological contamination;
 - Any significant chemical, physical, or other change or deterioration of the product;
 - Notification of product tampering;
 - Information concerning any incident that causes the drug product or its Labeling to be incorrect;
 - A Product Complaint; and
 - A Deviation that could potentially impact product quality.
- Any Site Colleague who observes a situation that might require a Stop Distribution shall report the matter at once to a Supervisor and/or the Site Quality Team, who shall immediately inform the responsible Manufacturing Site Quality Team.
- In the Event of a Potential Stop Distribution at a Contract Vendor, the Director/Team Leader Contract Operations Quality Assurance shall assume the responsibilities described in this procedure for the Site Quality Team.
- The Site Quality Team shall be responsible for the following actions upon receipt of a verbal or written observation that describes a potential problem:
 - Initiate and conduct a Quality Assurance (QA) Investigation of the observation;
 - Verify that a potential problem exists;
 - Determine how many and which Batches/lots are affected;
 - Determine Primary Receiving Locations to which the lots have been shipped;
 - Prepare a Stop Distribution Notice (SDN) to authorize status change from Approved to Quarantine-HOLD;
 - Sign and date a master copy of the SDN;
 - Ensure that status changes are made physically and by entries to all computer/paper inventories of the concerned lot(s) at the location where the batches/lots are held;
 - Inform other members of Site Management who may have need for the information;
 - Initiate any further actions that result from the investigation; and
 - Alert the Site Quality Review Team.
- An SDN shall be issued by the Site Quality Team to Managers of Primary Logistics Locations receiving inventory of lots or batches involved, when a Stop Distribution needs to be put into effect. The SDN must be in a written form. The SDN shall be signed and dated by the sender and copies transmitted by e-mail or fax in a way that provides readability of the signatures (in

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be conveyed to Managers of all storage locations using SDN after it has been signed and dated by the Site Quality Team.

- Receipt of the SDN Assigning Final Product Disposition shall be acknowledged by each recipient of any of the lots or batches concerned to the Site Quality Team after first adjusting inventory status indications physically and in the inventory data systems. The Site Quality Team shall track all such returned acknowledgements to ensure that action is completed.
- Sources of Notification to the Site Quality Team that a Stop Distribution might be needed shall include, and are not limited to:
 - Site employees;
 - Contract labs or manufacturers;
 - Auditors or investigators;
 - Suppliers; or
 - Customers.
- Employees shall report to their supervisors all observations of unusual appearance, properties, or test results related to finished products. Supervisors shall, in turn, confirm and report such observations directly to the Site Quality Team.
- For SDN Document Management and Tracking Purposes SDN Numbers shall be assigned as follows: [SD -Country/Site Code-YY-XX], where SD stands for Stop Distribution, Country/Site Code is a two-character alphanumeric code that identifies each GMP site, YY represents the year and XX represents a sequential number assigned at the Site. The same SDN Number is to be used at least for the initial SDN and all follow-up SDNs (e.g., indicating final product disposition), and may be used optionally for subsequent follow-up documents.
- Lot Status in the Inventory Control Computer Systems at the Production Site shall be changed from Approved to Quarantine-HOLD by the Site Quality Team to prevent shipment of any Quarantine-HOLD material with a customer order. Corresponding changes are to be made at all other affected locations using independent inventory control systems.
- The SDN, prepared by the Site Quality Team, shall include the following information:
 - SDN Number;
 - Date;
 - Product Name;
 - Lot Number(s);
 - Product Code(s)/Item Code(s);
 - Date and time (local) of initial observation;
 - Name of the Site Quality Team responsible for the Manufacturing Site;
 - Statement to the effect that the "Product Status is changed from Approved to Quarantine-HOLD";
 - Reason for the SDN; and
 - Signature of Site Quality Team authorizing the SDN and date signed.
- Recipients of the SDN shall include, at least, the following:
 - A. For Action:
 - All affected Site Logistics Centers:
 - Managers;
 - Quality Operations (QO) representatives; and
 - Materials Managers;
 - Manufacturing Site Materials Management Managers;
 - Any other Site location to which any of the concerned batch(s)/lot(s) have been sent;
 - All affected contract manufacturers, labelers, or packagers;
 - Logistics Center Managers assigned to affected Contract Distribution Centers; and
 - Authorized Site Contact at the contract vendor when a contract vendor facility is involved.
 - B. For Awareness, Information, and Possible Action:
 - Quality Operations Regional Leaders (QORLs) and Quality Operations Area Leaders
 - Vice President/Area Team Leader -Manufacturing;
 - Center Supply Chain Management;
 - Qualified Person(s) for the applicable impacted countries; and
 - Director/Team Leader Logistics Quality.

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- Disposition of APIs, Drug Products, and Medical Devices by the Site Quality Team shall include a review and assessment of batch manufacturing, packaging, and testing records to assure the records are complete and accurate.
- Disposition of medical devices shall also include a review of batch/lot documentation to ensure that all activities required by the Device Master Record (DMR) have been completed.
- The Site Quality Team shall also review the following information associated with the production of a batch:
 - Deviation investigation reports [e.g., Laboratory Investigation Report (LIR) and Quality Deviation Report (DR) have been completed and approved
 - Any applicable change control;
 - Correct Expiration Date or Re-evaluation Interval has been assigned to the finished product; and
 - Results from examination of the final finished pack, when required.
- In Addition to the Requirements in this article, Disposition of Sterile APIs, Sterile Drug Products and Sterile Medical Devices shall include a review of environmental and personnel monitoring records.
- The Product Disposition shall be documented, signed (written or electronic), and dated by the Quality Team representative making the disposition decision, and included in the batch record or DHR. Such dispositions include, but are not limited to, the following:
 - Approved,
 - Quarantine,
 - Quarantine-Hold,
 - Acceptable for Rework/Reclaim, and
 - Rejected.

In addition to the above items, the disposition shall also document the actual quantity of materials being assigned the disposition.

- If Only a Portion of the Batch or Lot is to be Approved, the quantity of the material that was assigned a disposition other than approved (e.g., Quarantined-Hold, Acceptable for Rework/Reclaim or Rejected) shall be verified to have been segregated from the portion of the batch or lot that is to be approved prior to the approval of the rest of the batch or lot.
- For Prospective Validation, validation reports must be approved prior to product release and distribution of validation batches in accordance with the established site validation requirements.
- A Quality Agreement with a Contract Vendor shall specify the requirements for approval of products produced by the contract vendor.

The duties of the Qualified Person(s) include ensuring:

- Each batch of medicinal products manufactured within the European Community have been produced and tested/checked in accordance with the local regulatory directives and the marketing authorisation.
- For medicinal products manufactured outside the European Community, a Qualified Person must ensure that each imported batch has undergone, in the importing country required testing.

8. Market Actions

Market Action Procedure shall be available at each GMP site that produces, stores or distributes Drug Products, Active Pharmaceutical Ingredients (API) or Medical Device and within each Business Unit responsible for any Market Action activities. The Market Action procedure must be capable of being initiated promptly and at any time. The procedure shall include an outline of actions required to address the following Market Action types as they apply to the markets involved:

- Product Recall,
- Market Withdrawal, and/or

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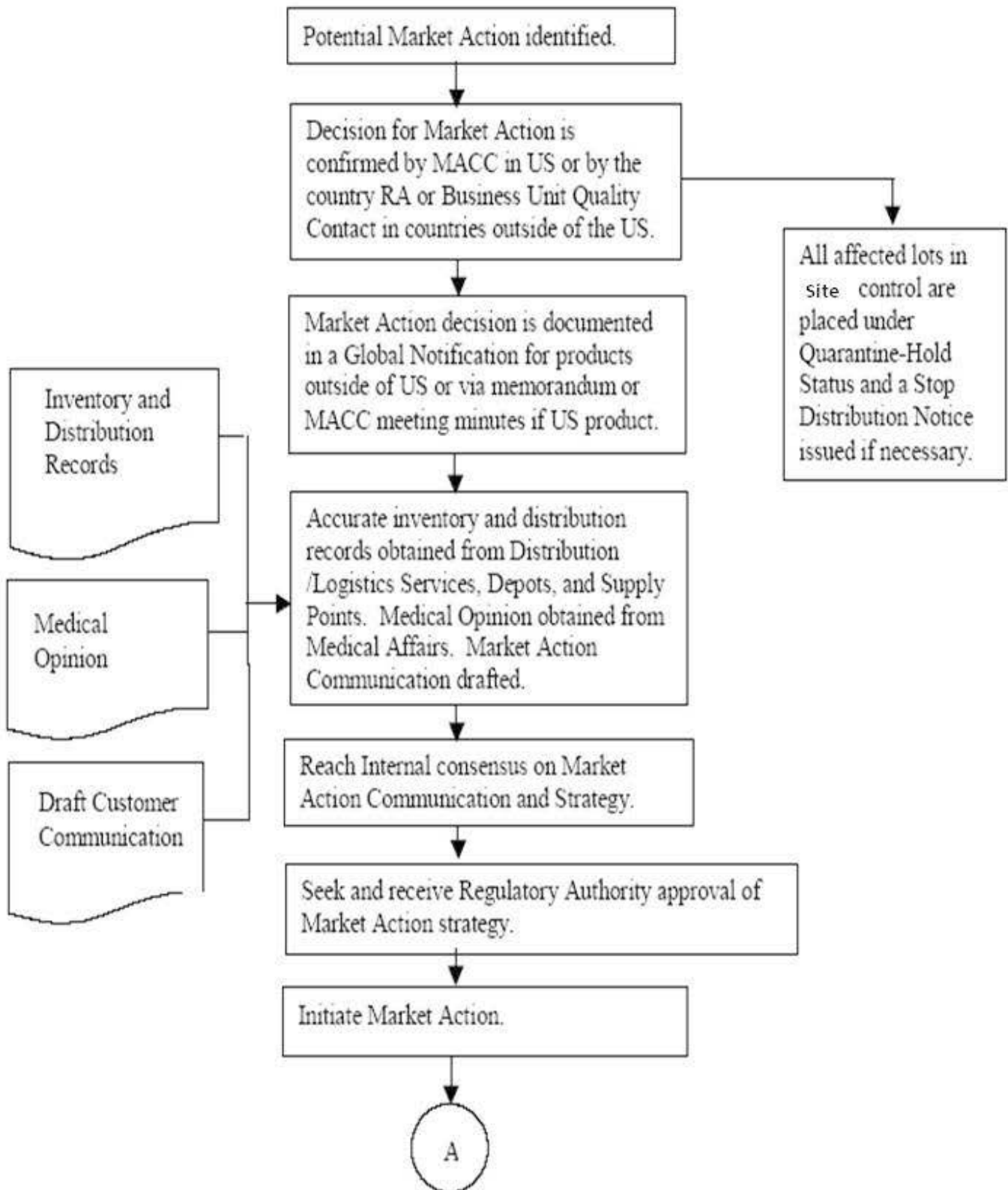
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Final responsibility for lot/batch Disposition is vested with the Site Quality Team.

- For Contract Manufacturers Involved in a Market Action, the Director/Team Leader Contract Operations Quality Assurance (COQA) and/or the responsible Site Quality Team shall serve as the primary liaison between the responsible Market Action Leaders and the contract manufacturer.
- When Public Information Releases are required, a draft shall be sent to the applicable Country General Counsel (Legal), Regulatory Affairs, Business Unit Quality Contact, Marketing, Medical Affairs, and Media Relations for review and authorization.
- Effectiveness Checks, when required by regulations, shall be conducted to verify that customers have received Market Action notifications and have taken the specified action.
- A Market Action Final Report shall be prepared by the Market Action Leader and issued as defined by the Market Action Procedure at the completion of the Market Action to, at least, the following:
 - Regulatory Authorities; and
 - Responsible management principals [e.g., Quality Operations, Regulatory Affairs, Medical Affairs, Qualified Person (QP), Marketing, Country General Counsel].
- Market Actions shall be considered in a number of situations including, but not limited to, the following:
 - Results of a Product Complaint Investigation,
 - Review of product retention samples of a distributed product lot,
 - Material erroneously released to stock without Quality Team authorization,
 - Mislabeled marketed product,
 - Failure of a marketed product lot to meet Specifications, or
 - Request or mandate from a Regulatory Team.
- When a Potential Market Action is Identified, a Stop Distribution Notice (SDN) shall be issued for all affected lots and the affected lots shall be placed under Quarantine-Hold status.
- The Market Action Leader in conjunction with the Site Quality Team is responsible to ensure the following activities are completed:
 - Inform and/or involve the concerned Country Regulatory Affairs Managers and Country Qualified Person(s) in relevant Market Action activities;
 - Consultation with Regulatory Authorities, in country of manufacture and country of distribution, on Market Action activity;
 - Identification of the product and Lot Numbers involved and the time period when the affected lot(s) was/were distributed;
 - Preparation of the draft Market Action communication;
 - Preparation of the draft public information releases for review by applicable Country General Counsel (Legal), Regulatory Affairs, Business Unit Quality Contact, Marketing, Medical Affairs, and Media Relations;
 - Notification of Site Global Research and Development principals of Market Actions, which could affect clinical studies;
 - Coordination of Market Action communications;
 - Determination of the depth (i.e., level of product distribution) of the Market Action (e.g., wholesale, retail/pharmacy, patient);
 - Verification that a complete record of all returned material is maintained by the receiving locations;
 - Determination of the method and level of Effectiveness Checks, as required;
 - Preparation of all status reports, where required and final reports related to the Market Action;
 - Maintenance of records of all Site-related Market Actions in accordance with established record retention standards and procedures;
 - Verification of proper disposition of returned product; and
 - Coordination and/or execution of Effectiveness Checks as required.
- Country or Area Medical Affairs and/or Safety Representatives shall assess the health and safety risks associated with the product being considered for a Market Action and shall advise the responsible Market Action Leader and country RA principals. Factors to be considered by the Medical Affairs and/or Safety representative include, and are not limited to, the following:
 - Whether any disease or injuries have already occurred from the use of the product;

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Figure 1 – Market Action Flow



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Expiration Dates for Drug Products and APIs shall be defined:

- By the month and year that result from adding the approved expiration dating period to the Manufacture Date or to the release date of the Batch/Lot, if the release date is within thirty (30) calendar days of the manufacture date; or
- As defined in the regulatory filing for the product. The expiration date assignment format shall be based on the requirements for the product market.

For APIs, the Expiration Date of the Blended Batch shall be based on the manufacturing date of the oldest tailings or batch in the blend.

For Drug Products Containing reprocessed drug products, the expiration date shall be based on the manufacture date of the oldest reprocessed lot used in the production lot.

Where more than one drug product lot with different Manufacture Dates are packaged together (e.g. 1, 2, 4, 8mg of a product blistered and sealed into one card), the expiration date of the complete package must not exceed that of the product lot with the shortest remaining expiration period used in the package.

Maximum Expiration Dating for drug products shall not exceed five (5) years.

Extension of Expiration Dating for already manufactured and packaged drug product may be performed based on the following criteria:

- Continuous, controlled real-time stability program has shown the product to be stable to support the extended expiration dating;
- Concurrent testing of the product shows little drift from the original test data and is within the release Specification; and
- Regulatory approval for the extension has been granted through Product Change Management System.

For Drug Products that require reconstitution, labeling shall include expiration information for both the un-reconstituted and reconstituted drug product.

For Drug Products requiring an expiration rate assignment prior to manufacturing the Expiration Date shall be assigned based on a documented planned manufacturing date and approved by the Quality Assurance.

Prior to packaging the drug product, the assigned expiration date must be verified against the actual manufacture date to be within the acceptable expiry period established by stability studies.

Expiration Date assignments shall be documented and maintained as part of the batch or lot record.

Quality Assurance shall:

- Ensure that the expiration date for each lot is based on a predefined time period commencing on the manufacture date or release date;
- Ensure that the expiration dating period is filed and has regulatory approval;
- Approve the expiration date assigned; and
- Ensure that the product is labeled with the assigned expiration date before the lot is released for commercial distribution.

Changes to expiration date must be processed either through the planned permanent changes, or through one-time temporary changes or Deviations.

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- Validation summary.
- In addition, for products that have a US FDA approved, active NDA, the number of Batches/Lots requiring an NDA-Field Alert Report versus the number of batches manufactured shall be included in the Annual Product Records Review. A summary of the Assignable Causes for any NDA-Field Alert Reports shall also be included in the report.
- The Supporting Data for the Annual Product Records Review must be compiled by each Production and Quality Department Head and sent to the site Quality Team.
- The Quality Team shall ensure that the Annual Product Records Reviews are completed, approved and action items tracked. Where required by local regulations, the Qualified Person (QP) shall also ensure that Annual Record Reviews and Annual Product Reviews are performed and are accurate.
- Site Management shall be notified of all significant issues discovered during Annual Product Records Reviews through a system of sequential or concurrent notifications.
- Annual Product Records Reviews shall be maintained by the site Quality Team and the documents retained according to the site records retention policy.

Regulatory Exceptions:

- The Term “NDA-Field Alert Report” is a US FDA term. Other terms and procedures may be used for similar forms of notification to non-US Regulatory Authorities. For some kinds of data (e.g. analytical tests results, yields, environmental controls) it is recommended that records in a manner permitting trend evaluation be kept.
- Complaint records are regularly reviewed for any indication of specific or recurring problems that require attention. The same procedures are applied to recalls.
- Written records required by this part shall be maintained so that data therein can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures. Written procedures shall be established and followed for such evaluations and shall include provisions for:
 - (1) A review of a representative number of batches, whether approved or rejected and where applicable, records associated with the batch.
 - (2) A review of complaints, recalls, returned or salvaged drug products and investigations conducted under §211.192 (CFR) for each drug product.
- Reserve samples from representative sample lots or batches selected by acceptable statistical procedures shall be examined visually at least once a year for evidence of deterioration unless visual examination would affect the integrity of the reserve sample. Any evidence of reserve sample deterioration shall be investigated in accordance with §211.192 (CFR). The results of the examination shall be recorded and maintained with other stability data on the drug product.
- Regular periodic or rolling quality reviews of all licensed medicinal products, including export only products, should be conducted with the objective of verifying the consistency of the existing process, the appropriateness of current specifications for both starting materials and finished product to highlight any trends and to identify product and process improvements. Such reviews should normally be conducted and documented annually, taking into account previous reviews, and should include at least:
 - (i) A review of starting materials and packaging materials used for the product, especially those from new sources.
 - (ii) A review of Marketing Authorisation variations submitted/granted/refused, including those for third country (export only) dossiers.
 - (iii) For new marketing authorisations and variations to marketing authorisations, a review of post-marketing commitments.
 - (iv) The qualification status of relevant equipment and utilities, e.g. HVAC, water, compressed gases, etc.

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- Reason for the return;
- Length of time the product was out of Site control as defined in local or area SOP;
- Whether the product is within Expiration Date or Re-evaluation date;
- Physical appearance of the returned material; and
- Integrity of the product packaging and shipping carton including any tamper-evident seals.

The following information shall be considered for making final disposition, if available:

- Storage conditions history;
- Transport history;
- Pedigree Letter; and
- Meets minimum unit of sale requirements.

The Manufacturing Site Quality Team shall be consulted if the conditions (e.g., time and temperature) to which the returned goods have been exposed were outside of established requirements or if testing and an Investigation are warranted. The criteria for selecting the testing and the results must be documented as part of the disposition. The Manufacturing Site Quality Team must approve the results of any testing performed.

- Human health pharmaceuticals Returned Goods may be re-shelved only when GMP site receives them within 30 calendar days after shipment by Site.
- Animal health pharmaceuticals Returned Products may be re-shelved only when GMP site receives them within 48 hours after shipment by GMP site for biologicals and 45 calendar days for pharmaceuticals.
- Some Products may have shorter time requirements to qualify for re-shelving, or may not be allowed to be re-shelved under any conditions. Such time limits must be observed when determining criteria for re-shelving and shall be defined in SOPs at Logistics Centers and GMP sites as applicable to the products.
- Returned Goods shall be classified and processed as one of the following:
 - Quarantine-Hold (Potentially Re-shelvable) - product is being held pending inspection and/or testing;
 - Acceptable for Rework - product must be relabeled, repackaged, or Reprocessed;
 - Approved (Re-shelvable) - product can be restocked as available inventory; or
 - Rejected - product will be destroyed.
- Destruction of Returned Goods shall comply with Site standards and all local waste regulations.
- Records of Returned Goods must include, and are not limited to, the following:
 - Original shipping date(s);
 - Date of return;
 - Reason for return;
 - Person returning the product;
 - Product name and strength;
 - Batch Number or Lot Number;
 - Quantity returned;
 - Expiration date or re-evaluation date;
 - Name and address of Consignee or contact information identifying those responsible for the materials while out of Site custody;
 - Results of any inspection or evaluation performed;
 - Pedigree letter (if available); and
 - Final disposition.
- If Product is Returned to Stock, inventory records must be adjusted to accurately reflect finished product stock.
- For Contract Logistics Centers, the responsible Site Quality Team shall assure that the contractor has a comparable system in place to evaluate returned goods.