

Good Working Practice – Materials

APIs or Intermediates with Assigned Expiration Dates and which are intended for sale to customers outside of Site do not require reevaluation when stored in finished sealed packages in API manufacturing facilities or Distribution or Logistics Centers.

Reevaluation Intervals for APIs shall be based on accelerated or real-time stability data.

Maximum Reevaluation Intervals for all Materials shall not exceed the following limits, unless supported by analytical data to demonstrate that the material meets established criteria at the time of use:

- One year for intermediates and in-process materials;
- Two (2) years for starting materials and RMs (except for APIs used in Drug Product manufacturing); and
- Five (5) years for packaging materials.

Reevaluation Intervals should relate to any storage conditions stated on the Label and shall be Approved by the Site Quality Team. The Site Quality Team shall consider shorter reevaluation intervals based on the nature of the material (e.g., wet cake intermediates, mother liquor or solvent-based intermediates, dry intermediates).

Reevaluation Dates shall not exceed established expiration dates for materials that have expiration dates.

Materials Without Expiration Dates shall not be reevaluated beyond ten (10) years unless the reevaluation is approved by the Quality Team.

Extension of Reevaluation Dating for APIs beyond five (5) years should be supported with stability data and should be approved by the Site Quality Team.

The Material Status Designation should be changed from approved to Quarantine if by the reevaluation date such reevaluation has not been completed and a new reevaluation date assigned.

Minimum Testing Requirements [e.g., stability indicating tests or Validated release Test Methods (TM)] shall be established by the Site Quality Team for each material to be reevaluated.

Reevaluation Dates shall be able to be readily determined (e.g., appear on material status labels or in a Validated Computerized System).

For Intermediates or APIs that are Intended for Sale and that do not Have an Expiration Date, the reevaluation date shall be indicated on the label and/or Certificate of Analysis (COA).

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- Components;
- Active Pharmaceutical Ingredients (API);
- Returned Goods, including Recalled product;
- Materials determined to be Acceptable for Rework/Reclaim;
- Rejected Materials; and
- Materials with Direct or Potential Indirect Product Contact, including cleaning materials and other items.

This practice document applies to GMP operation sites, manufacturing functions and Logistics Centers responsible for the Production, control, and distribution of Pharmaceutical and Animal Health, drug products, APIs, and medical devices.

Raw Material Lots, Component Lots and Packaging Material Lots, upon receipt, shall undergo the following steps:

- Assigned a Raw Material Lot Number, Component Lot Number, or Packaging Material Lot Numbers;
- Provided status indication or protection; and
- Immediate inspection for, and removal or defacing of any status indicators on the received materials.

Each Container that has been Sampled is to be identified by a readily visible label as having been sampled.

Standard Material Status Categories to be used:

- Approved -materials tested or examined by the Quality Team and declared acceptable by written notice;
- Quarantine -materials expected to be approved, but not yet fully tested or approved;
- Quarantine-HOLD -material, regarding which some evidence exists to suggest might not be approvable for its originally intended purpose, and disposition of which is yet to be determined (Note: Quarantine-HOLD status cannot be assigned to a portion of a Lot unless a new Batch Number or Lot Number is assigned to the questionable portion.);
- Recalled -finished product recalled from the market, final disposition of which has not been determined [may involve other Market Action materials];
- Acceptable for Rework/Reclaim -material that has been declared in writing by the Site Quality Team to be reworkable or reclaimable by following a specific, approved, written procedure;
- Sampled -containers of material that have been sampled and/or evaluated in place (e.g., Near IR); and
- Rejected -material found unsuitable for approval, reclaim, or rework that should therefore be destroyed or returned to a non-Site Supplier.

Approved, Quarantine, and Quarantine-HOLD status labels should identify;

- Date applied, Batch or lot number, and Name of the person who applied the status label
- When Status of a Material is Downgraded, immediate action should be taken

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Receiving and storage procedures for raw materials, components, and packaging materials shall be designed to ensure the identity, quantity, and conformance to Specification of each shipment of each Supplier Lot of material.

This practice applies to GMP production sites and operations responsible for the receipt of raw materials, components, and packaging materials for use in the production of Pharmaceutical or Animal Health products.

Raw Materials, Components, and Packaging Materials shall, upon receipt, be Verified by examination of receipt records and inspection of Labeling and materials to be:

- Free from apparent physical damage and contamination;
- The proper material correctly identified; and
- The correct quantity, according to the matching Site purchase order.

In addition for bulk raw materials received in bulk carriers (e.g., tank trucks or railroad tank cars) that are not pressurized, tamper-evident seals shall be verified as being in place and intact on openings and on capped discharge lines. Where the bulk carrier may also be used for transport of other bulk materials (i.e., non-dedicated tankers), evidence of cleaning (e.g., cleaning certificate) from the prior load shall be examined.

Materials not meeting the above requirements shall not be accepted and the Site Quality Team immediately notified about the unacceptable material.

Following a Successful Inspection or Examination, the received materials shall be promptly stored under Quarantine status, and subsequently sampled by Qualified personnel.

Materials with Direct or Potential Product Contact, such as process or product filters, filter aids, cleaning agents, and lubricants, shall be received in the same manner as raw materials, components, and packaging materials. Sampling and testing requirements for these materials shall be defined by the purchasing specification. Each Supplier Lot of Either Raw Materials, Components, or Packaging Materials shall be assigned a Raw Material Lot Number, Component Lot Number, or a Packaging Material Lot Number, respectively, for each shipment of each supplier lot received.

Raw Materials, Components, and Packaging Materials shall be received for use in site products only if they are purchased from Approved Suppliers.

Intact Container Seals and the Absence of Container, Damage or Evidence of Contamination shall be verified for materials received in bags, drums, or any other container except bulk carriers (e.g., tank truck or railroad tank car) during or immediately after unloading of each container or group of containers.

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A Description of the Sample Received for Testing should be retained as part of the Laboratory Records.

Preparation of Composite Samples or Subdivision of a Sample shall be described in SOPs.

Samples Removed from a Container shall not be returned to the material from which they have been taken, to preserve the integrity of the material that was sampled.

Resampling should be done according to a sampling plan approved by the Site Quality Team.

Use of Samples taken by the supplier prior to shipment (“preshipment” samples or “tailgate” samples) should be approved by the Site Quality Team.

Shipping of Samples to an Off-Site Facility for Testing (i.e., to another Site or an external laboratory) should be performed in a manner that will maintain the integrity of the sample during shipping, including protection from the normal shipping conditions (e.g., moisture, temperature, breakage).

Sample Destruction -after testing is complete, samples shall be destroyed following a written and approved SOP. Samples should be disposed of in a manner that precludes further use as per Environmental Health and Safety (EHS) requirements.

Sampling of Hazardous or Toxic Materials shall be evaluated by Environmental Health and Safety principals, the Site Production Team, and Quality Team for the potential impact on personnel safety and health, and the environment. If a determination is made to not sample such materials, a Certificate of Analysis (COA) should be obtained and reviewed by the Site Quality Team, showing that these raw materials (RM) conform to established specifications.

Containers of Materials to be Sampled shall be cleaned before opening; then opened, sampled, and resealed in a manner that protects the integrity of both the sample and the material being sampled (i.e., prevents mix-ups and contamination from environmental conditions).

Samples for Sterility Testing shall be representative of the entire batch, and include samples from parts of the batch most at risk of contamination. For aseptically filled products, samples shall include containers from the beginning, middle, and end of the batch and after any significant work interruption.

Sample Labels shall contain or reference (e.g., barcode), and are not limited to, the following information:

- Material name and code;
- Batch or Lot Number;
- Date of sampling;
- Sample source (e.g., drum number); and
- Identification of person taking the sample.

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Where an operational Mutual Recognition Agreement (MRA) is in place and reference sample are retained at a manufacturer located in a country outside the EEA, separate retention samples should be kept within the EEA.

7. Storage and Distribution of Drug Products, Medical Devices, and Related Materials

This practice document defines the storage and distribution requirements for Drug Products, Medical Devices and related Production Materials stored at GMP sites or Logistics Centers, and/or transported between sites or from sites to Logistics Centers.

This practice applies to Production Sites and Logistic Centers where Pharmaceutical and Animal Health drug products, medical devices, and related production materials are stored, and/or from which such items are distributed.

Storage Areas with clean, dry, and orderly conditions chosen to ensure quality and security shall be provided for all production materials, drug products, and medical devices. Production materials, drug products, and medical devices shall not be stored unprotected outside buildings.

Environmental Storage Conditions shall be Approved by the Quality Team and shall be based on temperature, humidity, exposure to light, and any other environmental factors known to affect the stored material.

Storage Conditions that Match Temperature and Humidity Requirements (i.e., labeled storage conditions) shall be provided for all production materials, drug products, and medical devices.

Temperature shall be monitored against defined limits and when humidity control is required (e.g., as stated on a Label or Specification), humidity shall also be monitored against defined limits.

Security of Stored Items shall be ensured by establishing and maintaining a system of access control and authorization for entry for each storage area.

Drug Product Lots, Medical Device Lots, and/or Production Materials Lots shall be stored in Dedicated Material Status Areas according to the current status assigned to the material or product.

Storage Off the Floor with Sufficient Cleaning/Inspection Space, or alternative measures for cleaning, shall be provided for all production materials, drug products, and medical devices.

Transport of Production Materials or Products from areas that make penicillins, cephalosporins, other β -lactam antibiotics, or cytotoxic and other highly sensitizing materials to areas that process any other product is prohibited.

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locations.

Returned Goods are to be promptly relocated from the unloading dock to an area dedicated to Returned Goods. Expiry Dates of Drug Products and Medical Devices shall be monitored and products approaching their Expiration Date shall be removed from inventory according to policies and procedures. Drug Product and Medical

Device Distribution Records shall be maintained at the responsible Site and/or Logistic Center that indicate where such products were shipped to and where the products were received from, to enable traceability of the drug products and/or medical devices during a Market Action (e.g., Recall).

Distribution Quality Representative shall be designated for distribution operations. Drug Products and Medical Devices That are Picked and Packed for Shipment shall be verified to ensure accuracy of the shipment. Verification may include a weight check or barcode reader.

Damaged Cases shall be examined to ensure that the product inside is not damaged. It may be necessary to open a damaged case to inspect the product inside. Damaged Product shall be destroyed. Any questions regarding the determination of damaged product shall be directed to the Distribution Quality Representative.

Wooden Pallets are prohibited in areas where product is exposed. A risk assessment is required to justify use of wood pallets in other Production Areas.

Wood Packaging Material (including pallets, crating, packing blocks, drums, cases, load boards, pallet collars, skids) made of coniferous and non-coniferous raw wood, used in international trade shall be treated [e.g., heat (HT) or methyl bromide (MB) fumigation] to eliminate potential Pests in the wood. Such treated wood materials shall be marked to indicate the treatment method used (e.g., HT or MB).

Markings shall be legible, permanent and not transferable, and placed in a visible location on at least two (2) opposite sides of the article being certified. Recycled, remanufactured, or repaired wood packaging material shall be recertified and re-marked.

8. Subdividing Dispensing & Transferring Materials to Production Areas

When Materials are Subdivided into another Container or containers, or when materials are dispensed, the new container(s) shall be fully identified with at least the following:

- Material name and item code;
- Site Batch Number or Lot Number;
- Weight or measure and unit of measure in new container;
- Container number, if applicable;
- Lot or batch for which material is intended to be used (including product name, lot or batch number, and strength if applicable); and

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- Formal agreement between sending and receiving sites including a description of responsibilities;
- Procedures that describe receipt of goods under Quarantine, as a minimum;
- Deviation system and procedures that accommodate use of the material before it is released by the sending site (for example, packaging at risk); and
- Procedures and systems to check that all components are released before next or final stage release is given.

Any transitional shipping site (if any) should be informed of this standard shipment procedure, but need not approve the process.

Exceptional Quarantine Shipments of Finished Products:

The basic requirement for this is a pre-shipment document exchange between the sending and the receiving sites for each lot shipped, using a Quarantine Shipment Form (QSF).

In addition to the requirements listed in this practice document the following controls should be in place:

For all exceptional shipments to a site, before a QSF can be issued:

- The receiving site should have procedures and systems in place to ensure that goods are released by the sending site before final release to the market is given by the receiving site.

In addition, if the receiving site is a 3rd party [e.g., Logistics Service Providers (LSPs) or a local distributor] the following controls should also be in place:

- The 3rd party receiving site is approved, based on:
 - Robust quality systems especially in the areas of training, product segregation, deviation handling, SOPs, and complaint handling;
 - Computerized systems controlling goods;
 - Quality record (audits, incident level);
 - Coverage of Quarantine-shipment in Quality Agreement; (Exceptional Quarantine Shipments of Finished Products.
- There is close Site Quality Assurance (QA) oversight (a person within Site having that responsibility as part of his/her job function) of the 3rd party; and
- The Site QA oversight should approve and takes responsibility for securing each individual Quarantine shipment (part of QSF to be signed by Quality Assurance oversight).

The Quality Manager for the sending site shall be informed about the shipment(s) by issuing a copy of the QSF. For shipments to 3rd parties the responsible Logistics QO

Regional Managers should approve the shipment(s) by signature on the QSF. In addition, any transitional shipping site (if any) shall be informed by receiving a copy of the QSF, but they do not need to approve the shipment.