Auditing a Packaging and Labeling Operation

Goals

When you have completed this module, you should be able to:

- Perform a packaging and labeling audit.
- Know and understand which of the worldwide requirements apply to packaging and labeling operations.
- Use a range of information tools, including the contents of this module to the Intranet, in support of a packaging and labeling audit.
- Recognize compliance or non-compliance of regulations pertaining to packaging and labeling requirements.

Definitions

Blinding: A procedure in which one or more parties to the Clinical Study are kept unaware of the treatment assignment(s) until code break after clean file.

Cleaning: Operation which terminates a production process, incl. dismantling and wet cleaning of the equipment as well as removal of all materials, products and documentation from the equipment and room/surrounding area. The cleaning must be finished by a documented check by a second person.

Cut labeling: labels that have been cut from a sheet and are individual labels.

Gang-printed labeling: labeling derived from a sheet of material on which more than one item of labeling is printed. (see example below)

Line-clearance: Operation which must be made immediately before a production process is started. Line-clearance includes:

- Verifying that the Cleaning has been performed at termination of the previous batch
- A documented check that the equipment/area is still in a clean status

The operation above must be performed by a person not involved in the Cleaning of the line/area.

Over-labeling: The addition of a label, usually to a primary pack or carton, to obscure the original labeling and supersede it with the text on the added label.

Over-printing: where text and objects in the foreground print directly on top of any background objects. An example of label overprinting would be printing the expiration date on the label.

Packaging material: Any material employed in the packaging of an API, intermediate or formulated product, excluding any packaging material used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

Packaging records: the complete collection of documentation associated with the packaging of a lot of drug product.

- Directions for sampling
- Handling and storage requirements
- Special handling requirements
- Where appropriate, an example of the relevant packaging supplies and labeling with the lot number and expiration date affixed

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On-line Controls

On-line controls for the packaging line must be in place. Items that should be checked before, during, or after operations are that:

- lines and equipment have been cleared of bulk material, labeling and packaging materials, and documentation from previous operations, including any computer screens or systems holding information pertinent to the batch.
- the general appearance of finished packages is satisfactory
- the packages are complete
- the correct product and packaging materials are being used
- over-printed details are correct and clearly readable
- all line monitors, indicators, and readers are working or have worked correctly

Special attention should be paid to checking the accuracy of variable information, such as batch numbers and expiration dates to packaging components on line. Printed and embossed information on packaging materials must be clear, easy to read, and resistant to fading or erasing.

In process test equipment e.g. Leak test equipment to realize integrity of blister sealing should be on the equipment and maintenance schedule. The in process testing should be completed as appropriate to demonstrate the integrity on the blister is maintained throughout the packing order. Any failures should be documented, investigated and appropriate actions taken.

Special controls should be applied to the management of trial and experimental packing work to ensure the same level of compliance and assurance is applied for this type of work around packing, documentation and labeling compared to routine work.

Sampling

Samples taken away from the line should never be returned to the line. They should be placed in dedicated containers, clearly marked.

Labeling

The use of cut labels should be discouraged or minimized. If cut labeling (and other loose packaging components with a pre-printed Lot Number and Expiration Date) is used, packaging and labeling operations must following special control procedures. All cut labels must be stored and transported in a secured container.

Controls used for routine labeling activities include

- Use of appropriate electronic or electromechanical equipment to conduct a 100% examination for correct labeling during or after completion of finishing operations.
- Use of a visual inspection to conduct a 100% examination for correct labeling during or after completion of finishing operations or hand-applied labeling. Such

- Verify that written approved procedures exist and are current.
- Verify that incoming packaging components have a unique reference number for identification.
- Verify that samples of incoming packaging and labeling components are tested/inspected and undergo an approval process.
- Verify that materials that fail to meet acceptance specifications are rejected and quarantined.
- Ensure that documentation exists for the receipt of each shipment of different labeling and packaging material which includes:
  - receipt
  - examination or testing
  - status (either accepted or rejected).

- Ensure that a control system is in place for implementing changes in packaging and labeling operations.
  - Verify that there is an approved, written change control procedure in place.
  - Verify that changes are consistent with the Authorization to Market and are monitored within a change control system.
  - Verify that there is a system for the control of all master documents
  - For master documents,
    - ensure that the Packaging Order is an accurate version of the master packaging instructions that were approved in the authorization to market document for the drug product.
    - verify that working copies of a master document are only released after a signature had been obtained.
    - ensure that changes to the master packaging order are reviewed, authorized, and issued by the appropriate department following the approved change control procedure..
    - verify that only qualified individuals may make changes to a document.
    - verify that these individuals have signed the document verifying its accuracy.
  - For in-process individual Packaging Orders (working copy):
    - ensure only authorized personnel make changes to the document.
    - ensure that only authorized personnel document and approve the changes.
    - ensure that the changed Packaging Order has been signed by qualified individuals who verify its accuracy.
    - when changes have been made to an individual Packaging Order, ensure that employees using this order have been notified or the document marked to indicate the changes.

- Ensure that that there is some type of 100 percent electronic or visual verification or dedicated lines for finished product cut labels, similar in appearance, which are used for immediate labeling on the lines.
  - Verify that any electronic code readers, label counters and similar devices are checked for proper operation.
  - Verify that computer systems used to control inspection equipment are secure, and designed to prevent unauthorized changes by mechanics and operators.
  - Verify that procedures exist emphasizing the strict control of on-line printing and the use of cut labels.
  - Verify that product and packaging components are checked for:
    - sufficient quantity.
    - identification.

