STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Guidelines for the investigation in case of final product rejection	**Effective Date:**
Supersedes: Nil	**Review Date:**
Issue Date:	**Page No.:**

1. **Purpose:** This procedure to be employed when there is reason to believe that a quality problem has arisen.

2. **Scope:** The checklist is to be employed when there is a reason to believe a quality problem has arisen. This checklist includes the review of finished product, test results, specifications, test methods, sampling methods, manufacturing operations, storage facilities, maintenance procedures, vendors and any other factor(s) pertaining to the specific quality problem being investigated.

3. **References , Attachments & Annexures:**
   - 3.1 **References:**
     - 3.1.1 Investigation of Out of Specification Analysis Results SOP
   - 3.2 **Attachments:** NA
   - 3.3 **Annexures:** NA

4. **Responsibilities:**
   - 4.1 **Quality Assurance:**
     - 4.1.1 To inform the Quality Head regarding the Quality Problem.
     - 4.1.2 To prepare and investigate as per guidelines.
   - 4.2 **Quality Head:**
     - 4.2.1 To initiate the investigation
     - 4.2.2 To review investigation report and to action as per guidelines.
   - 4.3 **Regulatory Head, Quality Head and Plant Head:**
     - 4.3.1 To review and approve the SOP.

5. **Distribution:**
   - 5.1 Quality Assurance
   - 5.2 Quality Control
   - 5.3 Production
   - 5.4 Warehouse
   - 5.5 Maintenance

6. **Abbreviation & Definitions of Terms:**
   - 6.1 **Abbreviation :**
     - 6.1.1 **SOP :** Standard Operating Procedures
     - 6.1.2 **QA :** Quality Assurance
   - 6.2 **Definitions of Terms:** NA

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7. **Procedure:**

7.1 **Finished Product analysis/control:**

7.1.1 For each sample, review the in process and finished product test results from the historical batch files.

7.1.1.1 Were all the test results within specification limits?

7.1.1.2 Does there appear to be any unanticipated trends developing such as frequently released batches with deviations, test results shifting in one direction or another, test needing to be frequently repeated?

7.2 Review the stability records and determine the quality status based on the data.

7.2.1 Negative trends?

7.2.2 Is the stability-testing program sufficient in frequency and context?

7.3 Have any batches of this product been rejected? If so, does there appear to be a recurring quality problem.

7.4 In case of batches being rejected, were all of them sufficiently investigated and corrective actions effectuated to prevent recurrence. Check the investigation of Out of Specification results.

7.5 **Specifications, testing and sampling:**

7.5.1 Review all specifications, testing and sampling pertinent to the problem product, update them to current supplement of compendia if required.

7.5.2 Review the current finished product inspections, including testing requirements. Their adequacy in content and the finished product testing requirements.

7.5.3 Review the history of change file for the finished product specifications for any changes made to the specifications or testing requirements and changes if any are properly reviewed for possible effects on quality before approval and effectuation.

7.5.4 In case of non-compendia testing methodologies, sufficient data (validation) to support the use of the test.

7.5.5 Changes in the testing methodologies been thoroughly investigated to assure that the method is still valid for its intended purpose.

7.5.6 Sampling program statically reliable for obtaining information on the quality of the batches.

7.5.7 Do specifications exist for all excipients employed in the manufacture of the product?

7.5.7.1 Are they current and comprehensive enough to assure control of quality?

7.5.7.2 If there a system to assure that sources of supply have the most recent copies of specifications available to them?

7.5.7.3 Is there some form of assurance that the vendor has received the most recent copy of specifications and agrees with them?

7.5.7.4 In cases where certificates of analysis are employed, have these certificates of analysis been qualified for use by verifying the accuracy of vendor's testing programme/ Observations/ Comments.

7.5.8 Investigation as per SOP on Investigation of Out of Specification Analysis Results.

7.6 **Master batch and production records:**

7.6.1 Master batch production records and inspection for the manufacture of each stage of the product and review for the following:

7.6.1.1 The master batch production records are sufficient in content to assure that consistent procedures are followed and appropriate data are recorded.

7.6.1.2 The instructions for manufacturing are organized and easy to understand. Instructions are also written in the vernacular languages to assure that the correct procedures are followed.

7.6.1.3 Changes if any been made to the master production record and instructions been thoroughly investigated and approved by QA before implementation.

7.7 **Manufacturing operations:**

7.7.1 Review the actual manufacturing operations and critique for the following:

7.7.1.1 Production employees operating in a neat, clean, suitably attired, organized and efficient manner to prevent quality problems.

7.7.1.2 Written procedures employed by manufacturing are current.

7.7.1.3 Any changes made to manufacturing procedures or packaging procedures are changes fully evaluated before implementation to assure against negative quality impact.

7.7.1.4 Procedures being properly followed are current.

7.7.1.5 Proper maintenance of production equipment.

7.7.1.6 Have there been any changes to the manufacturing equipment? If so, have such changes been reviewed and approved by QA before implementation?

7.7.1.7 Does there appear to be a sufficient amount of space to perform manufacturing operations?

7.7.1.8 Is the air environment being properly controlled to minimize contamination?

7.7.1.9 Production records are being completed in a competent manner.

7.7.1.10 In cases where a process has been formally validated, has the validation package been taken into consideration when changes have been made?

7.7.1.11 If it has been a number of years, since the initial validation of a manufacturing process, has the process been revalidated to assure that original qualification is still valid?

7.7.1.12 If batches of product are reworked, are the underlying causes of the rework determined? Are actions being pursued to prevent the situations that cause the rework?

7.7.1.13 In cases of rework, have the procedures been approved by the QA?

7.8 **Storage Review:**

7.8.1 Review all areas where product may be stored.

7.8.1.1 Are all of the storage facilities that are employed for the product integrity (i.e. storage temperatures, humidity)?

7.8.1.2 Is the product being stored properly to prevent contamination from other product or storage environments?

7.9 **Engineering/maintenance:**

7.9.1 Review the practices of the engineering and maintenance departments.

7.9.1.1 Are the maintenance procedures for the facility current and being followed?

7.9.1.2 Have any changes been made to the maintenance procedures? If so, whether they have been reviewed and approved by the QA?

7.9.1.3 Have any changes been made to the environmental control systems and water systems?

7.9.1.4 Are the adjacent exterior grounds being properly maintained to assure against inspect and rodent infestation?

7.9.1.5 Are the washing facilities being properly maintained so that employees hygiene is not a contributing factor to a quality problem?

7.9.1.6 Are maintenance and engineering tools, gauges and test equipments being properly maintained to assure accuracy?

7.9.1.7 Are the drawings for equipment and systems properly maintained?

7.10 **Vendors:**

7.10.1 Review the quality history of each chemical and physical item procured to determine whether quality problems have been experienced with any item used in the manufacture of the product.

7.10.2 Has the quality level of all the item been satisfactory?

7.10.3 In case of quality problems from items procured from vendors, have they been thoroughly investigated and appropriate corrective actions pursued to prevent recurrence?

7.10.4 Have any new vendors been added? Were the materials for the new vendors evaluated for impact on product quality.

7.11 **Personnel:**

7.11.1 Have any changes in plant or laboratory personnel? If so, has new employee given proper training?

8. **History:**

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