Procedure

MASTER PRODUCTION RECORD
BATCH PRODUCTION RECORD

AUTHOR

Quality Assurance Assistant	Signature……

VERIFICATION

Quality Assurance Manager	Signature …….

AUTHORIZATION

Quality Assurance Manager	Signature ……. Date 22.04.2013

Expiry Date **22/04/2015**

Re-Approvals Form

REAPPROVED ON _____
EXPIRES ON _____
QUALITY ASSURANCE _____

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0. Revision Matrix

REVISION	DATE	UPDATE CARRIED OUT AND REASON FOR UPDATE
01		. Date Rev. 00 Withdrawn
02		Date Rev. 01 Withdrawn
03		Date Rev. 02 Withdrawn
04		Date Rev. 03 Withdrawn
05		Date Rev. 04 Withdrawn
06		Date Rev. 05 Withdrawn
07		Date Rev. 06 Withdrawn
08		Date Rev. 07 Withdrawn
09		Date Rev. 08 Withdrawn

1. Scope and Application

To determine the content and methods of preparation and management of the document containing the instructions and information necessary to manufacture the products.
The procedure applies to all substances manufactured and / or packaged at the company: if different operating conditions exist for a product, each of these must have a corresponding Master Production Record.
Each processing step has a Master Production Record with its own code.

2. Definition

Batch: a specific quantity of material, produced in a specific process, which is expected to have the characteristics of homogeneity within specific predetermined limits. The batch size can be defined based on the quantity or the time required for production.

3. Responsibility

Drafting of the Master Production Record: Production Manager/Assistant.
Approval and Verification of Master Production Record: Production, Quality Control, Quality Assurance.

4. Master Production Record

The Master Production Record is the original document that contains all the information necessary for the manufacture of products.
Each process or process step must have its own Master Production Record.

These documents must be approved and signed (with data) on the title page and the first page by the persons referred to in the responsibility section above.

Each Master Production Record is kept by Quality Assurance, who reproduce it in order to output the processing sheets for that product.
The Master Production Record is set so that the actual sequence of operations, checks and controls are clearly recorded. It is required that individual operations are listed and numbered consecutively with clear spaces for inputting the necessary records, including the date and time of execution, the initials of the person who executes the operations and the supervisor’s check in operations involving the loading of raw materials and at critical points shown in bold.

Any change to the method of manufacture must be approved by the same functions that have approved the previous edition. Upon issuance and distribution, all copies of the previous edition should be recalled and destroyed.

The first two pages of the Master Production Record consist of the cover page and the revisions matrix, as described in procedure G.SOP.001 "Documentation Management."

Additional information to be included in the Master are:
- Master code and date of issue,
- Page number in the form "Page X of Y ", where X is the sequence number and Y is the total

In all the pages of the Master, the following information shall be indicated in bold:
- Product identification data: name, code and batch number.

The documentation table of contents and the table of weights in the Master, must also contain the following information in bold:
- The date of preparation, expiration, and retest;
- standard theoretical yield (ST), standard theoretical yield range (ST), theoretical yield, theoretical yield range.

The bill of materials within the Master also shows the date of preparation, expiration, and retest of the product in bold.

The Master is organized in four sections:
- Documentation Table of Contents,
- Bill of materials,
- Work Instructions,
- Weighing and Sampling Record Sheet.

• Documentation Table of Contents

The Documentation Table of Contents contains the following information:
- List of documents attached to the processing sheet;
- Space for checking for compliance by Production Manager/Assistant.

Production signature is not related to the verification of cleaning operations, whose verification is attested by Production signature at the end of the cleaning operations themselves.

In the case of a finished product, the product shall be released only if there is an authorization by the persons mentioned (Production, Quality Assurance and Quality Control).
In the case of an intermediate, the product shall be released if there is an authorization by Production.

• Bill of Materials

It consists of the Manufacturing formula for the batch, set in tabular form. In addition to the manufacturing order number, the bill of materials contains the following information for each raw material to be used in the process:
- Name, Code, Batch Number;

- Theoretical quantity (with an indication of any fractions) - indicate the theoretical amount to be dispensed with three decimal places for the starting materials;
- Assigned amount (with an indication of any fractions) and final verification signature of the Production Manager or his assistant and a second supervisor. An indication of the number of drums prepared in the case that an MPR dictates that the product has to be dried in several parts;
- Total quantity dispensed in the warehouse with the operator's signature and date;
- Total amount loaded and operator's signature and date;
- Quantity returned to Warehouse with signature and date of compilation (only in the case where a raw material is a gas, for which the amount set up in the Warehouse may not coincide with that assigned and in the case where one of the raw materials is used only in certain operating conditions reported in the MPR, thus making it impossible to establish before the exact quantity of the raw material to be prepared in the Warehouse);
- Signature and date to verify the dispensing of goods by Quality Assurance/Warehouse Supervisor (must be another person than the one doing the dispensing) before delivery to the departments;
- Signature and date of receipt and supervision of such goods in the department by the Production Manager, his assistants or in their absence of an operator. This is done with the intention of verifying the indicated expiration/ retest date, the correct labeling, proper cleaning and integrity of the drums and the consistency of the weights brought into production with those defined in the Bill of Materials.

At the time of use, the raw materials are weighed by the operators before being loaded into the reactor. After the loading, the container is weighed again and the net weight calculated.
In the case of fractions, these are checked for the expiration/retest date indicated in the analysis bulletin and the correspondence of the weights assigned in the bill of materials with that brought in production.
Based on the experience gained so far, an acceptability range of 0.4% on the amount of Starting Materials prepared and loaded with respect to the assigned amount is permitted. In this case it is not necessary readjust the amount of other materials provided.
In the case in which a raw material is a gas, for which the amount dispensed in the warehouse may not coincide with that assigned, or in the case where one of the raw materials is used on the basis of certain operating conditions reported in the MPR, so that the amount dispensed may be higher than that used, there may be a certain amount returned to the Warehouse, in which case the following information should also be reported:
- Signature and date of examination of the goods to return it in stock by the supervisor who controls the correspondence of the contents with those reported in the bill of materials;
- Signature and date of receipt and supervision of the return of materials in the Warehouse and verification of the correspondence between the data reported in the bill of materials and the returns that have been delivered.

In the case in which the MPR so requires, the preparation of the solvent to be used for the plant cleaning can be done in a single container: all fractions

contained in it must be indicated in the "fraction identification labels" applied on the container itself. These labels shall be filled in the manner defined in M.SPC.001 procedure taking into account that the tare weight of the container is made initially, before filling the container, so only the label related to the first "fraction" can indicate both the tare weight, the net weight of the product and the final gross weight. In all the labels for other "fractions", it is possible to specify only the net weight of the product, for this reason "zero" or "n.a." has to be reported on the tare and gross weight.

• Processing Instructions

This contains the operative instructions for the production of that product.

Checks and inspections
- Description and identity of the location and main machinery and equipment to use;
- Description of work clothing and any PPE to use;
- Description of preliminary tests to be performed on premises, equipment, environmental conditions, products, materials, and availability of personal protective equipment provided and any printed materials (refer to the relevant operating procedures) with spaces designed for registration of the verification;
- When multiple operations are shown, the operator carrying out the operations has the task of coordination as they are performed.

Process Instructions
- Sequence and method of adding individual commodities, identified by name and quantity;
- The activities to be carried out and the operative conditions to be applied;
- Precautions to be taken during the critical stages of the process;
- All parametric operating conditions (time and temperature) to be expressed in terms of numbers and their respective tolerance ranges, with any spaces designed for their record. In particular, with regard to the drying step, limits must be imposed for the vacuum and temperature must be recorded at regular time intervals.
- All in-process controls to be carried out during the processing of products, materials, and machinery. For each control, spaces must be assigned to input the necessary annotations and/or to give reference for any control documents to be attached (chromatograms, spectra, etc.) compiled with the control's code, name and batch number of the product, date and time of the inspection, signature.
- All the activities to be carried out for the plant cleaning must be preceded by a coarse removal of all residuals and a visual supervision should be carried out.

• Weighing and Sampling Record Sheet

This is divided in two parts:
- Weighing Record,
- Sampling Record.

• Weighing Record Sheet

This record sheet contains a table representing the weighing operations and contains the following information:
- Numerical list of containers;
- Tare weight of each container;
- Gross and net weight of each packaged container;
- Code and batch number of the bags used for packaging;
- Date and initials of the operator who made the packaging;
- Total weight;
- Instructions to calculate the yield (total weight (kg) / weight of last dry (kg));
- Signature of the Supervisor.

In the case of MPRs which provide for the drying of the product in multiple stages, each phase of product discharge from the dryer is documented on the weighing record.

Sampling module

This is in tabular form and used at the time of sampling. This contains the following information:
- Required materials,
- Sample size,
- Sampling date and initials of the sampler.

There will also be a space for notes at the end of each processing stage in which to report any anomalies or deviations from the approved instructions.
Production is required to assess whether these anomalies or deviations have an impact on the quality of the product or of the operations performed: if so a deviation must be open, in accordance with the procedure G.SOP.018 "Deviation Management".
In any case, Production is required to communicate such anomalies or deviation to Quality Assurance at the time of their occurrence.

5. Batch Production Record

Based on every Master Production Record, there are working documents for each time the Master is applied. These are the Batch Production Records, which faithfully reproduce the original Master.

The Batch Production Record is issued by Quality Assurance (or in his absence by a Production Supervisor), who must include the following information upon issue:
- Date of issue;
- Batch Number of the product to be produced.

Upon issue Quality Assurance sign each page and no further changes can be made to the operative instructions defined in the Batch Production Record.

In addition to the Batch Record, Quality Assurance (or in his absence a Production Supervisor) also emits identification labels to be affixed to containers of the packaged product.

The batch number and amount of each component of departure (Commodities and Materials) are reported by Production Supervisor.

From its emission, the Batch Record materially follows the various stages of the process, from the preparation of materials to the packaging of finished product, and is compiled in real time in all its parts.

Closing the Batch Record: In the case of an intermediate, at the end of the process recorded in the document, this batch record must be verified and approved (signed and dated) by Production prior to commencing with the next step. In the case of a finished product, at the end of the process recorded in the document, this batch record must be verified and approved (signed and dated) by Production, Quality Assurance and Quality Control.

Quality Assurance is required to formally verify the entire Batch Record by signing and dating for approval. This approval coincides with the authorization to use/sale and the release of the product on the market.

If the last step of manufacturing is performed externally, the release of the product is guaranteed by Quality Assurance that signs for approval the Packing List, based on the data reported in the Bulletin and in the Certificate of Analysis.

The documents making up each batch record (possibly also including a copy of the Analysis Request and Bulletin) shall be collected and assembled in a binder with the cash flow of documentation as the title, in order to avoid confusion between documents from different batches.

The labels "Cleaned Following Maintenance" (P.SOP.010/All.05) and the labels "Clean" (FORM 23) must be attached to the equipment at the end of each cleaning process and also to the Batch Record of the product whose production has to be carried out in that equipment after its cleaning.

The Batch Records are stored by Batch Number and are kept in a secure and controlled access area by Quality Assurance for 10 years.