

# MFR - INTRODUCTION

## Introduction

- In the 1997 WHO guidance document: “WHO/VSQ/97.01:

A WHO guide to good manufacturing practice (GMP) requirements. **Standard operating procedures and master formulae**

- WHO identifies manufacturing instructions as “**Master Formula** Other terms used in GMP guidelines and regulations are “**Manufacturing Formula**”, “**Master Production and Control Record**”
- An approved master document that describes “**The full process of manufacturing for the batch of product with at least cross-reference to the support operations for a batch of a specific product**”

## Definition

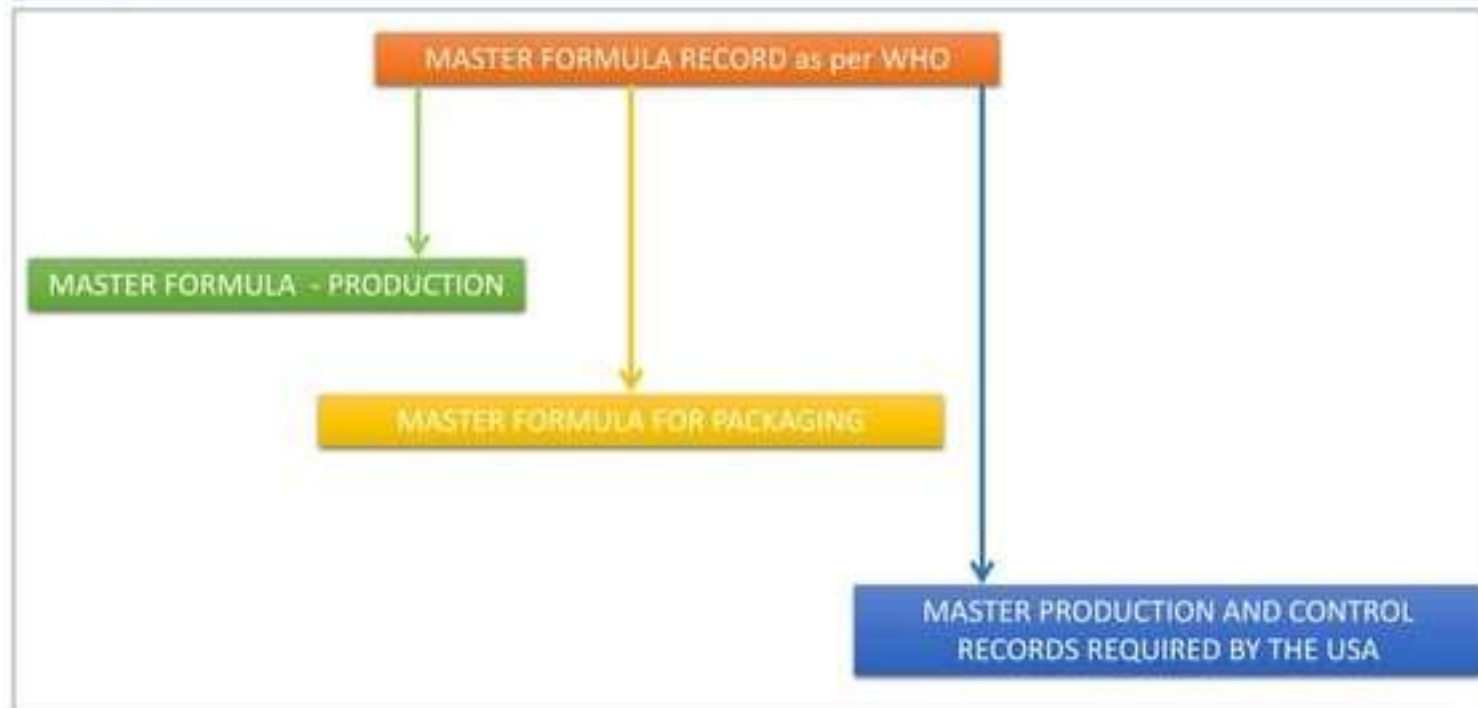
The following are the extracted definitions from several guidelines:

- **WHO GMP Guidelines:** A formally authorized **master formula** should exist for each product and batch size to be manufactured.
- **Health Canada GMP guidelines:** **"MASTER FORMULA** (formula-type) – A document or set of documents specifying the raw materials with their quantities and the packaging materials, together with a detailed description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls."

## US CFR.

- To assure uniformity from batch to batch, **master production and control records** for each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person. The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.

## Required Content of Master Formula:



# MASTER FORMULA RECORD

- ▶ Master Formula Record (MFR) is a master document for any pharmaceutical product.
- ▶ MFR contains all information about the manufacturing process for the product.
- ▶ MFR is prepared by the research and development team of the company.
- ▶ MFR is used as reference standard for preparing batch manufacturing record (BMR) by manufacturing units.
- ▶ MFR is also called Master Manufacturing Record, Master Production Record.

## Definition

“A document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls.”

## Continued...

- ▶ There shall be Master Formula records relating to all manufacturing procedures for each product and batch size to be manufactured. These shall be prepared and endorsed by the competent technical staff i.e. head of production and quality control.
- ▶ MFR plays an important in consistency for each batch manufacturing.



## MFR should include -

### Product Details :

- Name, logo and address of the manufacturing company.
- Dosage form name.
- Brand name.
- Generic name.
- Product code
- Label claim of all ingredients
- Product description
- Batch size
- Pack size and packing style



## ...CONTINUED

- Shelf life
- Storage conditions
- MFR number and date
- Supersede MFR number and date
- Effective batch number
- Authorization by the production and quality assurance head

## ...CONTINUED

**Flow Chart:** Steps of the manufacturing process to be monitored. Flowchart of the material movement from dispensing to the final product to stores.

**Equipment:** Create a list of all required equipment and machines required in the manufacturing process with their capacity.

**Special instructions:** Write down the precautions special instructions to follow during the product manufacturing and packing and these should also be added in the batch manufacturing formula.

## ...CONTINUED

**Calculations:** Include the calculation steps of all active materials to get the 100% of the active material. The calculation shall be done using water or LOD to get 100% potency.

**Manufacturing Process:** Write all steps in all stages of the manufacturing process. All process steps like shifting, milling, lubricating, granulation, compression and coating should be written in detail including the process time and yield.

It also include atmospheric conditions as temperature, humidity, and storage conditions for every step.

## ...CONTINUED

**Packing Process:** List of all packing materials with their quantity is written. Line clearance, reconciliation of printed and unprinted packing materials should be included in details.

**Yield:** Include the theoretical, actual yield and acceptance limit of the batch.

## Procedure to prepare a Master Formula Record:

- ▶ A Master Formula Record is either prepared based upon experience of competent qualified staff like manufacturing chemist or analytical chemist or prepared based upon batch manufacturing record of a batch size.
- ▶ We can't ignore Master formula record at any level. Once Master Formula Record is prepared, it is transferred to previous staff to new staff. It is followed as standard documents for processing a batch. Master Formula record is consider as standard for making a Batch Manufacturing Record.

# SOP for preparation of the Master Formula Record:

## RESPONSIBLE DEPARTMENTS:

Primary Responsibility:

F&D and Production Department

Secondary Responsibility:

Quality Assurance Department

## ACCOUNTABILITY:

Head-Quality Assurance shall be responsible for implementation of SOP.

## STEPS TO PREPARE A MASTER FORMULA RECORD:

- ▶ Production Department in association with F&D, shall prepare MFR.
- ▶ MFR shall prepared as per the format attached with this SOP.
- ▶ MFR shall be divided into two parts:
  - ▶ Packaging part
  - ▶ Manufacturing part



- ▶ The first page of both the sections shall have following details:

Name, address and logo of the company

Dosage form

Brand name

Generic name

Product code

Label claim : this should include all ingredients and text included in product permission

- ▶ Product Description
- ▶ Batch Size
- ▶ Pack Size
- ▶ Shelf Life
- ▶ Storage conditions
- ▶ Drug Schedule: whether schedule H or schedule G drug.
- ▶ Superseded Master card number and Date.
- ▶ Present Master card number and Date.
- ▶ Present Master card effective Batch number.
- ▶ Reference of changed control number.
- ▶ There shall be authorization of Master Formula Record by all the responsible members

- ▶ The secondary page of manufacturing section shall include-Process steps to be monitored.
- ▶ Subsequent pages shall include the processes to be monitored. The stage wise movement of material in a form of flow chart.
- ▶ The list of equipment, machines ,utensils to be used, shall be described.
- ▶ The subsequent page shall include any special precautions to be taken for the product during manufacturing and packing. The same page should also include Batch Manufacturing Formula.

- ▶ Batch Formula should have the following columns:
  - ▶ Serial number
  - ▶ Name of ingredients
  - ▶ Reference of specifications of ingredients
  - ▶ Quantity to be added (in mg/ml or per tablet or per capsule or per gm. as the case may be)
  - ▶ Overages to be added(in %)
  - ▶ Quantity to be added per batch or per lot

Below that give the calculation step for every active material, ensuring that the active material shall be compensated for assay values less than 100% which could be due to less potency or higher moisture content.

- At the end of every important stage, include a statement of the yield with the acceptable limits.
- Include in-process quality checks during and at the end of important steps and stages with their limits.
- The process shall include the process equipment to be used. The methods or the reference of the methods/procedures to employed for preparing, cleaning, assembling, operating the various equipments shall be given.
- Include detailed stepwise processing instructions(example: checks on materials, pretreatments, sequence for adding materials, mixing times, temperatures, humidity etc.)
- Includes the requirements for storage conditions of the products.

- The packaging part of MFR should include complete list of all the packaging materials required for a standard batch size, including quantities, sizes and types.
- Include line clearance checking during batch cording and batch packaging operations.
- Includes reconciliation of printed and unprinted packaging materials with acceptable limits.
- Includes destruction of excess or rejected printed packaging materials
- Includes description of packaging operation including any significant subsidiary operations and equipments to be used.



**MASTER FORMULA RECORD**

PRODUCT CODE: 001/1/2012		MASTER BMR No.: MFR/S.R.TAB/001		PAGE: 1	
<b>DICLOFENAC-Na TABLET(100 mg)</b>					
BATCH No.	:	_____			
BATCH SIZE	:	1,20,000 TABLETS			
MFG. DATE	:	_____			
EXP. DATE	:	_____			
LABEL CLAIM	:	Each Uncoated Tablet Contains.			
		INGREDIENTS	QTY FOR EACH BATCH	OVERAGES ADDED	
			40.00 Kg		
		Powdered Sugar	47.00 kg		
		Cetyl Alcohol	23.00 kg		
		Acronil	1.20 kg		
		Polyvinyl	2.40 kg		
		Pyrolidone			
		Magnesium Stearate	1.20 kg		
REFERENCE OF MASTER FORMULA RECORD	:	MFR/S.R.TAB/01			
MANUFACTURING DATE	:	_____			
REVISION No.	:	_____			
REVIEW PERIOD	:	2 YEARS			
EXPIRY DATE	:	_____			
PACK	:	Blister Package			
MFG. LICENCE No.	:	_____			
BMR ISSUED BY & DATE		_____		BMR RECEIVED BY & DATE	
Q.A.:		_____		PRODUCTION: _____	

PREPARED BY	CHECKED BY	APPROVED BY	AUTHORIZED BY
QA OFFICER	PRODUCTION MANAGER	QA MANAGER	GM QA/QC



*THANK YOU*