REGULATORY AFFAIRS

DRUG MASTER FILE

POST MARKETING SURVEILLANCE

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Drug Master File

- A drug Master file (DMF) is a submission to the FDA of information, usually concerning the confidential detailed information about chemistry, manufacturing and control (CMC) of a dru product or a component of a drug product.

INTRODUCTION

- The submission of a DMF is not required by law or FDA regulation and a DMF is submitted solely at the discretion of the holder (a person who owns DMF).
- The information contained in the DMF may be used to support an Investigational new Drug Application (IND),a New Drug Application (NDA) ,an Abbreviated New Drug Application (ANDA), another DMF,an export Application or amendments and supplements to any of these.

- This guidelines is intended to provide DMF holders with procedure acceptable to the agency for preparing and submitting a DMF.
- The guidelines discuss type of DMF's the information needed in each type ,the formate of submission to a DMF,the administrative procedures governing review of DMF and the obligation of the DMF holder.
- DMF's are generally created to allow a party other than the holder of the DMF to reference material without disclosing to the party the contents of the file.

TYPES OF DRUG MASTER FILE

Types.	Essential Contents
1.	Manufacturing site, facilities, operating procedure and personnel.
2.	Drug substance and intermediate,. Material used and drug product.
3.	Packaging material
4.	Excipients, flavour,essence ,colorant ,and material used in preparation.
5.	FDA accepted reference information.

Submission to drug Master files

- Each DMF Submission should contain a transmittal letter ,

Administrative information about the submission ,and the specific information to be included in the DMF as described in this section.

- The DMF must be in the English language.whenever a submission contains information in another language,an accurate certified English translation must also be included
- Each page of each copy of the DMF should be dated and consecutively numbered.
- An updated table of contents should be included with each submission..

General information and suggestions to prepare DMF :-

1. **Environmental Assessment**
2. **Stability**
3. **Format, assembly and Delivery**
4. **An original and duplicate are to be submitted for all DMF Submission**

DMF holders and their agents/representative should retain a complete reference copy that is identical to, and maintained in the same chronological order as , their submission to FDA.

5.The original and duplicate copies must be collected ,fully assembled:-. Each volume of a DMF should,in general be no more than 2 inch thick .for multi – volume Submission, number each volume.

6.US standard paper size (8-1/2 by 11 inches) is preferred:-Paper length should not be less than 10 inches nor more than 12 inches. However, it may occasionally be necessary to use individual pages larger than standard paper size to present a floor plan, synthesis diagram,batch formula,or manufacturing instruction.

7.Delivery to FDA.

MASTER FORMULA RECORD

- "A document or set of do documents specifying the starting material with their quantities and the packaging material , together with a description of the procedure and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in- process controls".
- MFR plays an important role in consistency for each batch manufacturing.

PEPARE TO PREPARE MASTER FORMULA RECORD:-

- Production department in association with F and D, shall prepare MFR.
- MFR shall prepared as per the format attached with this SOP.
- MFR shall be divided into two parts:

1. Packaging part
2. Manufacturing part

- The first page of both the section 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 includes in product permission.

- Product description
- Batch size
- Pack size
- Shelf life
- Storage conditions

- Drug shedule.
- Prevent master card number and date.
- Prevent master card effective batch number.
- Reference of changed control number.
- There shall be authorisation of MFR by all the responsible members.
- Batch formula should have the following columns:

Name of ingredients.

Reference of specifications of ingredients.

Quantity to be added.

Overages to be added

Quantity to be added per batch.

POST MARKETING SURVEILLANCE

- Phases of clinical trials-
- PHASE 0 (MICRODOSING)
- PHASE 1
- PHASE 2 (FIRST IN PATIENT – DOSE, DOSAGE FORMS
- PHASE 3 (EFFICACY, ADRs)

INTRODUCTION:-

- Post marketing surveillance refers to any means of obtaining information about product after it has been approved for public use.
- It play an important role to discover an undesirable effect that might prevent at risk.
- It provide additional information on the benefit and risk of the drugs.

BENEFITS OF POST MARKETING MONITORING-

The ability to study the following:

- Low frequency reactions.
- High risk groups
- Long term effects
- Drug- drug / food interactions.

SOURCES OF POST MARKETING SURVEILLANCE INFORMATION-

- Expert user groups
- Customer surveys
- Customer complaints and warranty claims
- Post CE market clinical trials
- Literature review
- The media

METHODS OF SURVEILLANCE

Thus, four types of studies are generally used to identify drugs effect-

1. Controlled clinical trials
2. Spontaneous or voluntary recording
3. Cohort studies
4. Care control studies