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THE CENTRAL DISPENSARY:
A GOOD MANUFACTURING PRACTICE TREND

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ABSTRACT

The design and the operation of a Central Dispensary, the selection of weighing equipment, the methods of classification of raw materials to ensure material stability and operator safety, and the documentation to ensure quality finished product meeting current Good Manufacturing Practice are discussed.

INTRODUCTION

In order to ensure final product quality in any pharmaceutical process, quality must be fabricated into a product during each step in manufacture. Quality of the finished formulation as determined by defined finished product quality control tests cannot be used as the sole definitive criteria upon which batch release is regulated.

One step in the many processes in manufacture of a dosage form is the weighing and measuring of ingredients. This major process in the scheme of manufacture should be finitely controlled (a Standard Operating Procedure written) so that the correct raw material, handled in the correct manner, will be used in its correct proportions in the correct formulation.

In addition to building product quality into the product, the properly run and designed dispensary should also provide protection and safe handling methods to operators. Most pharmaceuticals are potent drugs with defined therapeutic activity and adverse side effects. Product quality morale is difficult to maintain if the safety of the operator is not cared for in the dispensary, production area and quality control laboratories where exposure is maximal.

THE CENTRAL DISPENSARY

The modern trend to weighing or measuring formulation ingredients for Production use, is to establish a Central Dispensary servicing the entire Pharmaceutical Manufacturing Complex.

Advantages

The central dispensary has a number of advantages over the older system where each manufacturing section weighed their own ingredients prior to manufacture. The advantages include:

(a) Much easier to maintain consistency of records.

(b) Only a small group of highly trained personnel are responsible for accurate weighings. No person other than these designated people should perform the initial dispensing.

(c) Less chance of dispensing the wrong material, the wrong grade of material, the wrong lot number of material, a material not yet passed by Quality Control or an out of date material.

(d) Better control of stock. Computer stock control should be linked through the Dispensary to Production Planning , Marketing, and Purchasing so that at all times minimum yet sufficient inventory is maintained.

Design of the Dispensary

The dispensary should be centrally located so that it may equally serve all areas of manufacturing. It must also be located such that there is ready access to the quality control passed bulk materials store and to the drugs of addiction safe.

Design should be such that each weighing balance is situated in a laminar flow balanced cubicle with air flow such that air sweep is from ceiling to rear wall floor filtered exit. This will ensure that dust is kept in the cubicle, cross contamination with other weighing operations being performed in other cubicles will be non-existent.

The cubicle should also be equipped with a dust extraction vacuum drop such that for dusty powder weighing operations, spread of dust is curtailed and after weighing clean up is facilitated. The floors should be of seamless Terazzo® with curvature at the junction of the wall and floor. The walls should be epoxy coated; light fittings and electrical receptacles, water and explosion proof. These latter requirements will allow the complete washdown of the cubicle except for the ceiling. Because air flow should be maintained from the laminar flow ceiling at all times there will be no reason to wash this area down.

Cubicles should be similarly designed for dispensing in the aseptic manufacturing facility.

A low humidity cubicle should also be maintained for weighing of moisture sensitive materials. This cubicle should be directly adjacent to the low humidity manufacturing facility.

The number of cubicles will depend upon the weighing operations of the company, and the accuracy of the balances in hand. Assuming that the weighing operations of the company will require only one balance in each sensitivity range, the layout can then be designed around the sensitivity of the balances purchased.

Weighing Operations

Assuming that the Quality Assurance Department has defined the limit to tolerance of weighing to be 0.1%, e.g., no greater than a 100 mg error is allowed in a 100 gm weighing, then can determine the usable range [illegible] scales using the following formula:

$$\text{Lower end of usable range} = \frac{0.5 \times \text{minimum graduation}}{0.1\%}$$

The above formula assumes that a scale will be read to the nearest minimum graduation and therefore the

maximum amount rounded would be (0.5 x minimum graduation). The lower end of the usable range can be determined to be that point at which the maximum amount rounded (0.5 x minimum graduation) is equal to 0.1% of the scale reading, which is the limit specified by Quality Assurance. The upper end of the range can be simply the scale capacity.

Thus a series of cubicles could be set up having balances as shown in Table 1. Note: The number of cubicles and the recommended weighing ranges will depend upon the brand and scale capacity of the balances purchased.

One, two or more balances of different weight ranges could be positioned in each cubicle. Note, however, that

TABLE 1

Examples of balances that may be employed to allow an acceptable tolerance of 0.1% in all weight ranges expected.

Scale Capacity (kg)	Minimum Graduation (gm)	Usable Ranges (kg)
0.5	0.1	0.05 - 0.5
5	1	0.5 - 5.0
50	10	5 -50
325	100	50 -325
750	500	250 -750

only one weighing operation at a time should be taking place in any one cubicle. Each balance should be labelled with the usable range and dispensers should be familiar with these restrictions. Each balance should be checked before first use each day and a record kept with date and signature.

There are problems associated with establishment of a rigid ruling on weighing as described above as this can lead to loss of flexibility. For instance, flexibility is needed for materials with a low bulk density, for tare weights, for split lots, and for back weighing procedures. Separate Standard Operating Procedures should be written to handle each of the exceptions above.

CLASSIFICATION OF RAW MATERIALS

To ensure both

(a) correct handling of the raw material for reasons of material stability, and

(b) correct handling of the raw material to ensure protection of the dispensary and production staff,

a system for material classification should be instituted.

A system of classification that could be instituted is as follows:

(a) Classify all raw materials into one or more of the categories listed in Table 2.

(b) Colour code each category.

(c) Ensure that a Standard Operating Procedure is written for handling each category.

TABLE 2

Suggested system for categorizing raw materials requiring special handling in the dispensary and in the manufacturing areas.

Classification	Material Handling Characteristics
Class A	Potent Materials requiring air-stream helmet and gloves. Colour coded - red.
Class B	Hazardous Materials requiring careful handling, for example, explosive, highly flammable or corrosive. Colour coded - orange.
Class C	Sterile Materials to be opened in aseptic area only. Colour coded - green.
Class D	Moisture Sensitive Materials to be opened in a low humidity area only. Colour coded - blue.
Class E	Light Sensitive Materials requiring protection from light. Colour coded - brown.
Class F	Items that should be stored in a cool place. Colour coded - white enclosed within a black circle.
Class G	Drugs of Addiction requiring to be weighed in the presence of a Pharmacist. Colour coded - yellow.

IDENTIFICATION

An important aspect of the Central Dispensary Operation is the CORRECT IDENTIFICATION of materials at all times by means of a label or tag bearing:

(a) The raw material code number

(b) The standard name

(c) The company name

(d) Lot number

(e) Quality Control Data showing

  (i) Q.C. Pass sticker, with date of release from quarantine and Q.C. Supervisor's signature.

  (ii) Date for retest.

(f) Raw material handling classifications, i.e. classes A through G.

(g) A handling colour-code dot or dots.

Accompanying each lot of material should be a Raw Materials Bulk Usage Card. This should have listed on it:

(a) all the above items listed under identification,

(b) the number of containers that make up the lot,

(c) the quantities dispensed, to which lot of finished product they were assigned, how much is left, date of dispensing, signature of Dispenser and of Checker.

(d) data such as name, lot number, amount dispensed, and amount remaining could be entered on a computer card so that Purchasing, Planning and the Dispensary have at their fingertips, inventory on hand together with predicted usage.

The initiation of a dispensing step should be upon receipt of a Material Requisition from Production Planning. This should be received in the dispensary about five working days in advance of the date needed. The requisition should state:

(a) the product title, code number, lot number and batch size into which the raw materials will eventually be incorporated.

(b) the description of the material requested, i.e., name, code number, quantity required, and sometimes lot or lot numbers, if inventory control is sophisticated enough to be able to achieve this.

(c) the date required.

(d) the department to which the material is to be delivered.

The material being dispensed should be clearly labelled with the following:

(a) the material name, code number, lot number, handling classification, and colour code.

(b) the name of the product, code number and lot number for which it is intended.

(c) the tare weight, gross weight, and weight of raw material being dispensed.

(d) if two lot numbers are used to make up the quantity desired, the amounts of each and lot numbers should be recorded, as subsequently, this information will be transferred to the Production Ticket.

Upon receipt of the raw material at the site for manufacture, the material should be handled as follows:

(a) check the labelling and indicated weights against those called for in the Production Ticket. If all check then,

(b) weigh the received items to double check gross weight,

(c) add ingredients to formulation and check tare weight. The values obtained should correlate with the values indicated on the Dispenser's Label and the net weight required by the Production Ticket.

(d) the Production Ticket should be signed and checked that the raw material was correct and that it was added to the formulation. The lot numbers of materials used should be recorded on the Production Ticket prior to the signing and check signing.

CONCLUSION

By attacking the problem of design and operation of a central dispensary in a logical manner following some or all the suggestions as posed in this publication, a finite step to building in quality can be effected. There will be less chance of product failure in the finished product Q.C. testing, there will be less chance of product recall due to incorrect, subpotent or contaminated product, and there will be more chance for quickly defining which lots of finished product contained a certain lot of raw material if the necessity arose.

The concept of a central dispensary has merit. Change to this system should be initiated if not in operation already. If a central dispensary concept is already in operation incorporation of suggestions offered here will enhance the assurance of product quality. The necessity for the good manufacturing practice of having an efficient system of dispensing and material control is essential if the Pharmaceutical Industry is to continue it's trend to high quality products always meeting product specifications.

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