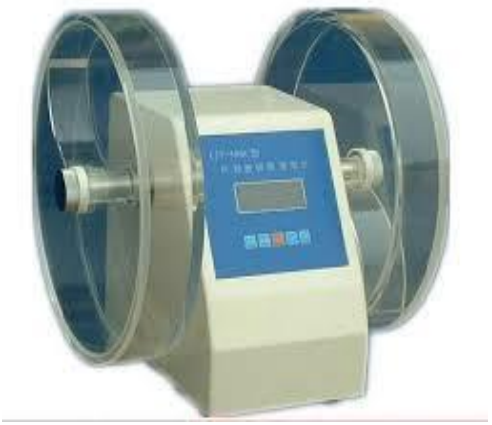
Quality control test of tablet

Name of student's ID number:

Aleen Nasser 1160792

Rawan Hamayel 1161783

Fatima Yasser 1162749



WHAT DOES QULAITY CONTROL (QC) MEAN ?

QULAITY CONTROL (QC):

- It is a small part of QA and it is concerned with sampling, testing and documentation during manufacturing and also after completion of manufacturing .
- Quality control is the monitoring process through which manufacturer measures actual quality performance, compares it with standards and find out the causes of deviation from standard to ensure quality product not once but every time .
- Definition: In general terms, Quality control refers to a procedure or a set of steps taken during the manufacturing of a product to ensure that it meets requirements and that the product is reproducible .

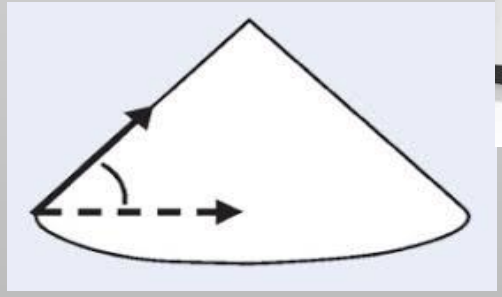
WHAT TYPE QULAITY CONTROL (QC) ?

- In Process Quality Control (IPQC):

Physical parameters of pharmaceutical tablets that are controlled by IPQC tests are temperature, pressure, moisture content, particle size, hardness, loss on drying, disintegration time, color, followability, compactness etc.

❖ **Tests will explain in this presentation:**

- ✓ Sieve analysis
- ✓ Bulk density and tab density
- ✓ Angle of Repose
- ✓ Moisture content



WHAT TYPE QULAITY CONTROL (QC) ?

- Finished Process Quality Control (FPQC):

FPQC test for pharmaceutical tablets are assay, uniformity of content, weight variation, friability test, content of active ingredients, hardness test, disintegration test, dissolution test etc.

❖ **Tests will explain in this presentation:**

✓Dissolution

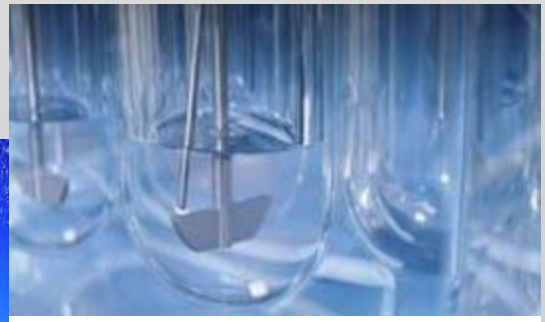
✓ Disintegration

✓ Weight Variation

✓Thickness

✓ Hardness

✓ Friability

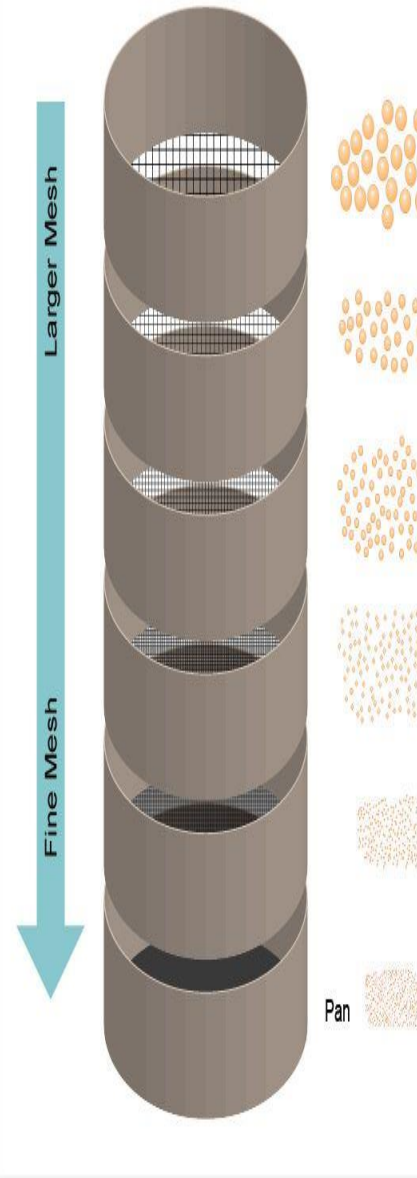



Sieve analysis

Sieve Analysis :

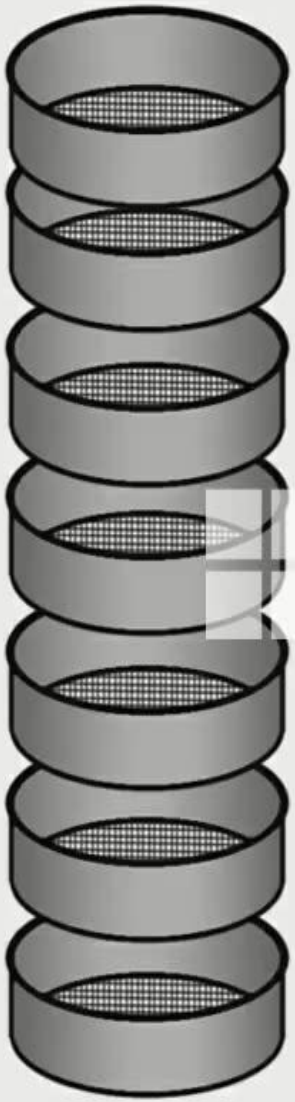
- Sieving is one of the oldest methods of classifying powders and granules by particle size distribution.
- **Among the limitations of the sieving method** :

are the need for an appreciable amount of sample (normally at least 25 g) and difficulty in sieving oily or other cohesive powders that tend to clog the sieve openings.



SIEVING METHODS According to USB :

- Mechanical Agitation _*Dry Sieving Method:*
- Tare each test sieve to the nearest 0.1 g.
- Place an accurately weighed quantity of test specimen on the top (coarsest) sieve, and replace the lid.
- Agitate the nest of sieves for 5 minutes. Then carefully remove each from the nest without loss of material.
- Reweigh each sieve, and determine the weight of material on each sieve. Determine the weight of material in the collecting pan in a similar manner. Reassemble the nest of sieves, and agitate for 5 minutes
- Repeat these steps until the endpoint criteria are met (see *Endpoint Determination* under *Test Sieves*



2 mm

1 mm

600 micron

425 micron

212 micron

150 micron

75 micron

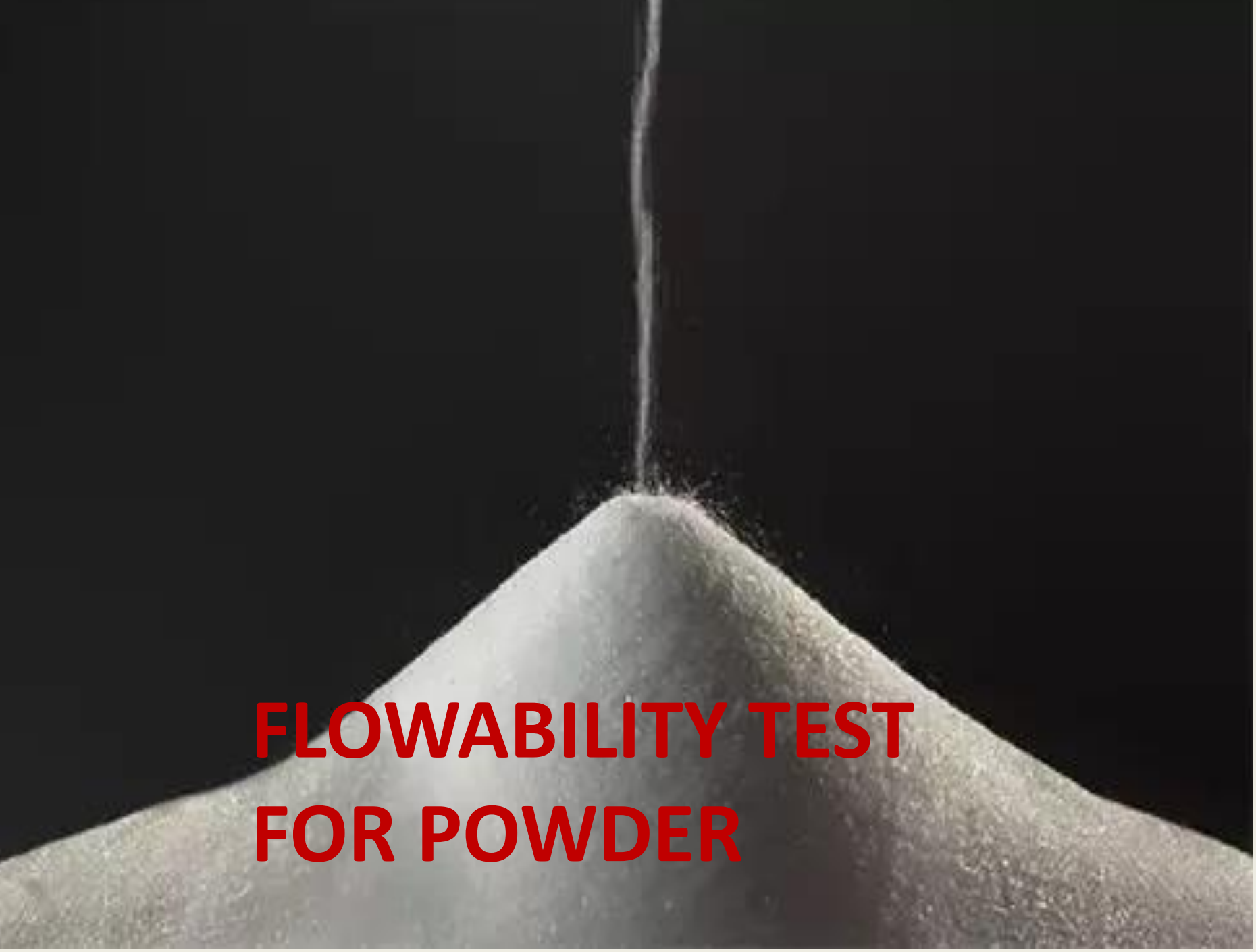
Set of Fine sieves

Endpoint Determination— The test sieving analysis is complete when the weight on any of the test sieves does not change by more than 5% or 0.1 g

- **Air Entrainment Methods**

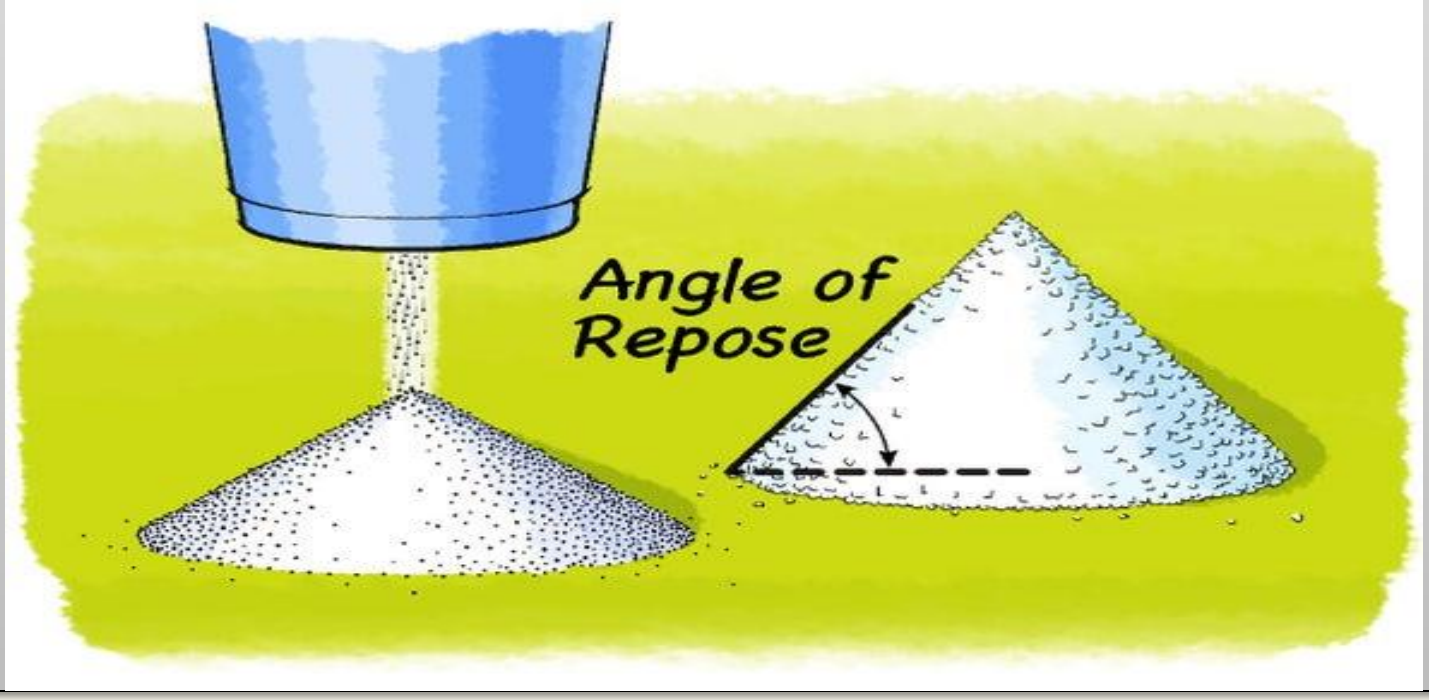
Air jet sieving machines :are ideally suited for very fine powder s which tend to agglomerate and cannot be separated by vibrational sieving

- A system that uses a single sieve at a time
- It uses the same general sieving methodology as that described under the *Dry Sieving Method,* but with a standardized air jet replacing the normal agitation mechanism.


FLOWABILITY TEST
FOR POWDER

Angle of repose

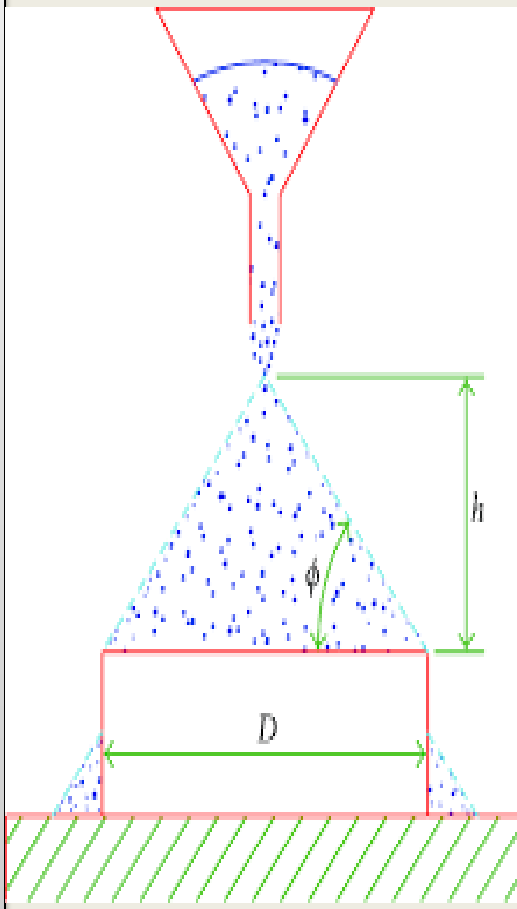
- The angle of repose has been used in several branches of science to characterize the flow properties of solids.
- Angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles.

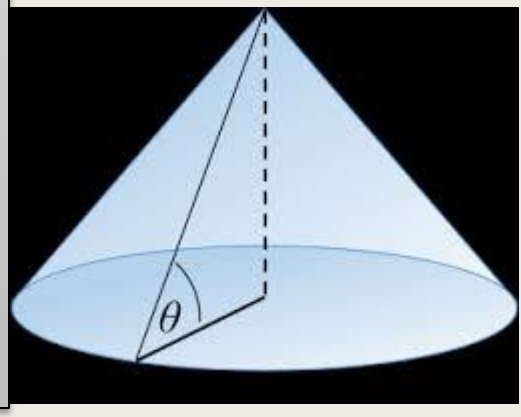


- The most common methods for determining the static angle of repose can be classified on the basis of the following two important experimental variables:

- 1) **The height** of the “funnel” through which the powder passes may be **fixed** relative to the base, or the height may be **varied** as the pile forms.

- (2) **The base** upon which the pile forms may be of **fixed diameter** or the diameter of the powder cone may be allowed to **vary** as the pile forms.





- **Recommended Procedure for Angle of Repose; According to USB :**
- Form the angle of repose on a fixed base with a retaining lip to retain a layer of powder on the base.
- The base should be free of vibration. Vary the height of the funnel to carefully build up a symmetrical cone of powder.
- Care should be taken to prevent vibration as the funnel is moved. The funnel height should be maintained approximately 2–4 cm from the top of the powder pile as it is being formed in order to minimize the impact of falling powder on the tip of the cone.
- If a symmetrical cone of powder cannot be successfully or reproducibly prepared, this method is not appropriate.
- Determine the angle of repose by measuring the height of the cone of powder and calculating the angle of repose, α, from the following equation:

$$\tan(\alpha) = \frac{\text{height}}{0.5\ \text{base}}$$

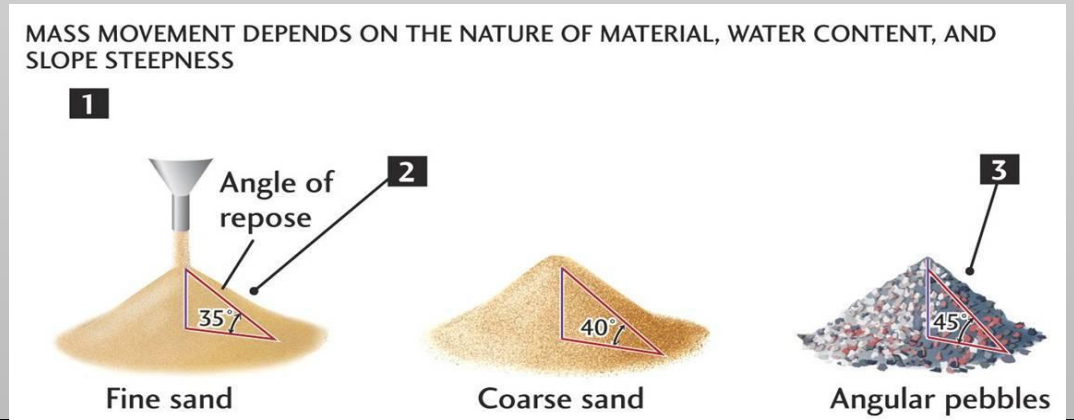


Table 1. Flow Properties and Corresponding Angles of Repose

Flow Property	Angle of Repose (degrees)
Excellent	25–30
Good	31–35
Fair—aid not needed	36–40
Passable—may hang up	41–45
Poor—must agitate, vibrate	46–55
Very poor	56–65
Very, very poor	>66

BULK DENSITY AND TAPPED DENSITY OF POWDERS

bulk density of a powder

- The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the contribution of the interparticulate void volume.

- The bulk density is expressed in grams per mL (g/mL) although the international unit is kilograms per cubic meter (1 g/mL = 1000 kg/m3). It may also be expressed in grams per cubic centimeter (g/cm3).

- The bulk density of a powder is determined by measuring the volume of a known weight of powder sample, that may have been passed through a sieve, into a graduated cylinder (Method I), or a cup (Method II) or a measuring vessel (Method III).

- Method I and Method III are favored.

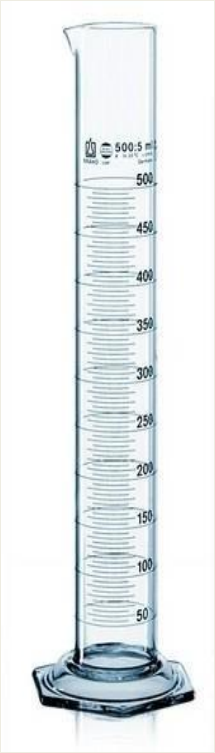
Method I—Measurement in a Graduated Cylinder

Procedure:

- Pass a quantity of material sufficient to complete the test through a sieve with apertures greater than or equal to 1.0 mm, if necessary, to break up agglomerates that may have formed during storage.

- Into a dry graduated 250-mL cylinder (readable to 2 mL), introduce, without compacting, approximately 100 g of test sample, and read the unsettled apparent volume (V0) to the nearest graduated unit.

- Calculate the bulk density in g/mL by the formula m/V0. Generally, replicate determinations are desirable for the determination of this property.



Method II—Measurement in a Volumeter

Procedure:

- Allow an excess of powder to flow through the apparatus into the sample receiving cup until it over-flows, using a minimum of 25 cm3 of powder with the square cup and 35 cm3 of powder with the cylindrical cup.

- Carefully scrape excess powder from the top of the cup by smoothly moving the edge of the blade of a spatula perpendicular to and in contact with the top surface of the cup, taking care to keep the spatula perpendicular to prevent packing or removal of powder from the cup.

- Remove any material from the sides of the cup, and determine the weight. Calculate the bulk density, in g/mL, by the formula: (M)/(V0)

in which V0 is the volume, in mL, of the cup. Record the average of three
determinations using three different powder samples

Method III—Measurement in a Vessel

Procedure:

- Pass a quantity of powder sufficient to complete the test through a 1.0-mm sieve, if necessary, to break up agglomerates that may have formed during storage, and allow the obtained sample to flow freely into the measuring vessel until it overflows.

- Carefully scrape the excess powder from the top of the vessel as described for Method II.

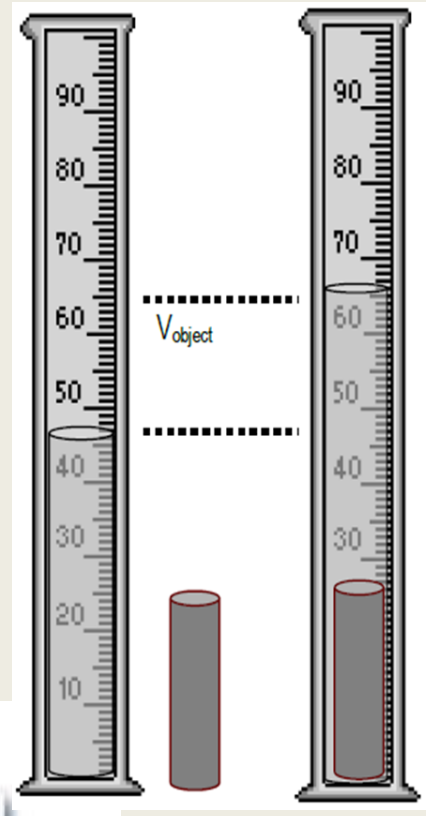
- Determine the weight (M0) of the powder.
- Calculate the bulk density (g/mL) by the formula M0/V0, and record the average of three determinations using three different powder samples.

TAPPED DENSITY OF POWDERS:

The tapped density is an increased bulk density attained after mechanically tapping a container (graduated measuring cylinder or vessel) containing the powder sample.

After observing the initial powder volume or weight, the measuring cylinder or vessel is mechanically tapped, and volume or weight readings are taken until little further volume or weight change is observed.

Calculate the tapped density (g/mL) using the formula m/V_F, in which V_F is the final tapped volume.



Moisture Content

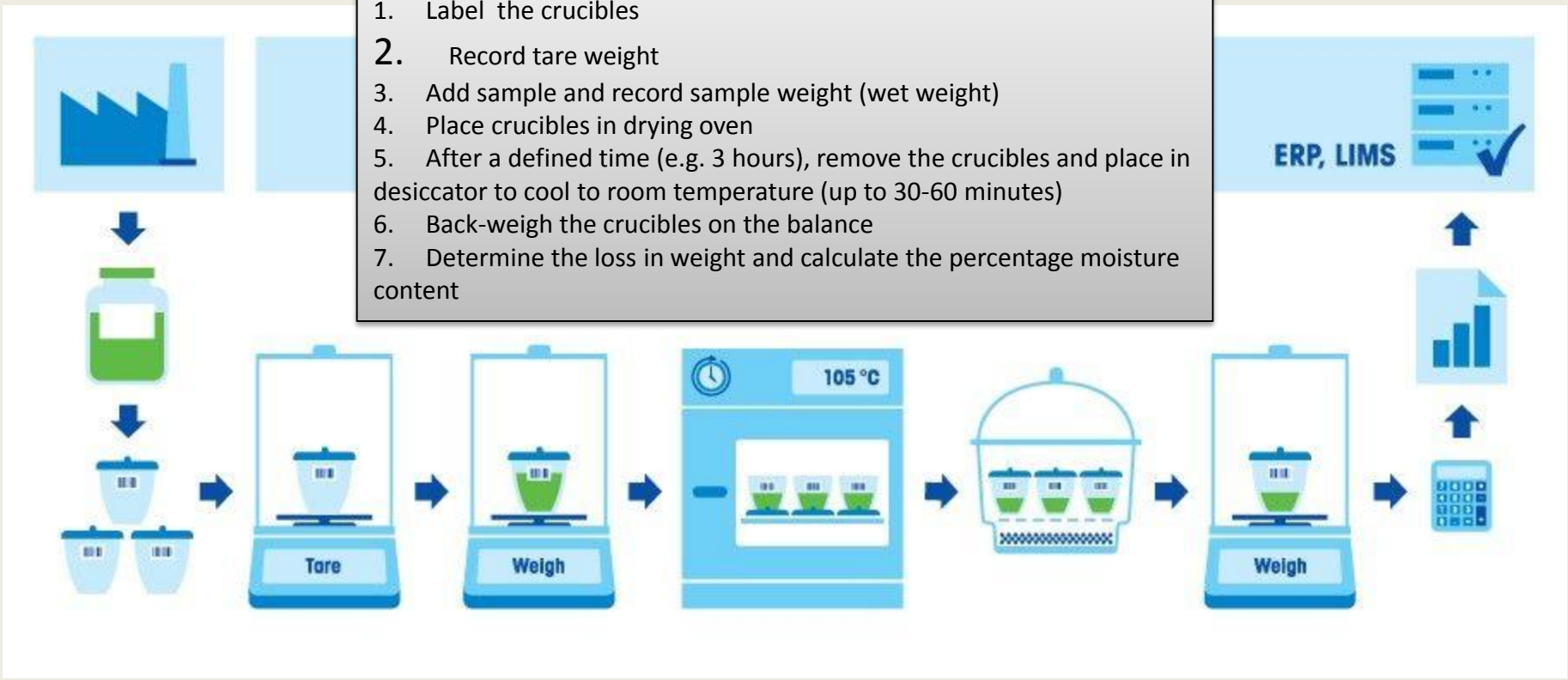
- Moisture content (MC) is a measure of the amount of water found within material at any given time.
- Moisture content is determined via a thermogravimetric approach, i.e. by loss on drying, in which the sample is heated and the weight loss due to evaporation of moisture is recorded.
- moisture content affects the processibility, shelf life, usability and quality of a product.
- Commonly used moisture analysis technologies are the moisture analyzer and the drying oven in combination with a balance

- **Moisture Analyzer**
- Fast results
- Simple operation
- Minimized errors
- Alternative to official method

○ Drying Oven with Balance

- Official method
- No time pressure
- Multiple samples
- Very inhomogeneous samples

1. Label the crucibles
2. Record tare weight
3. Add sample and record sample weight (wet weight)
4. Place crucibles in drying oven
5. After a defined time (e.g. 3 hours), remove the crucibles and place in desiccator to cool to room temperature (up to 30-60 minutes)
6. Back-weigh the crucibles on the balance
7. Determine the loss in weight and calculate the percentage moisture content



Hardness

- Tablet hardness: the force required to break a tablet along its diameter by applying compression loading.
- **Why do we measure hardness?**

- It determine the need for pressure adjustments on the tableting machine.
- Hardness can affect the disintegration.
  - So if the tablet is too hard, it may not disintegrate in the required

    period of time.
  - And if the tablet is too soft, it will not withstand the handling during subsequent processing such as coating or packaging.

- In general, if the tablet hardness is too high, we first check its disintegration before rejecting the patch. And if the disintegration is within limit, we accept the patch.

✓ If Hardness is high + disintegration is within time

- -- accept the batch

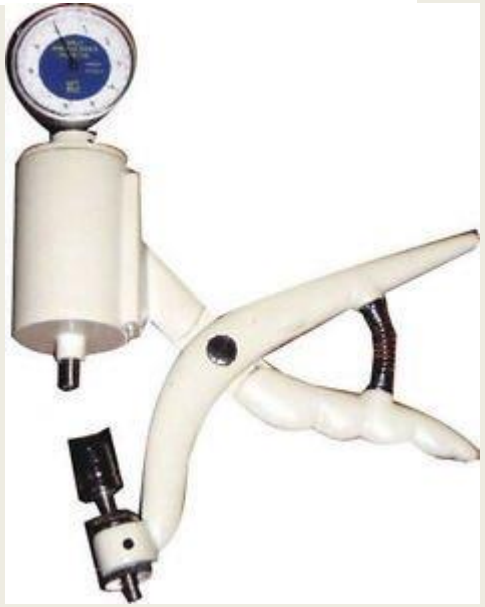
Factor effecting Hardness

- Compression of the tablet and compressive force.
- Amount of binder. (More binder à more hardness)
- Method of granulation in preparing the tablet (wet method gives more hardness than direct method, Slugging method gives the best hardness).

Limits: 5 kilograms minimum and 8 kilograms maximum.

Hardness testers

- manually tester:
- Monsanto tester
- Pfizer tester
- strong cobb hardness tester



- motor driven testers:
- Heberlien schleuniger
- Eweka
- Casburt hardness tester.

Procedure

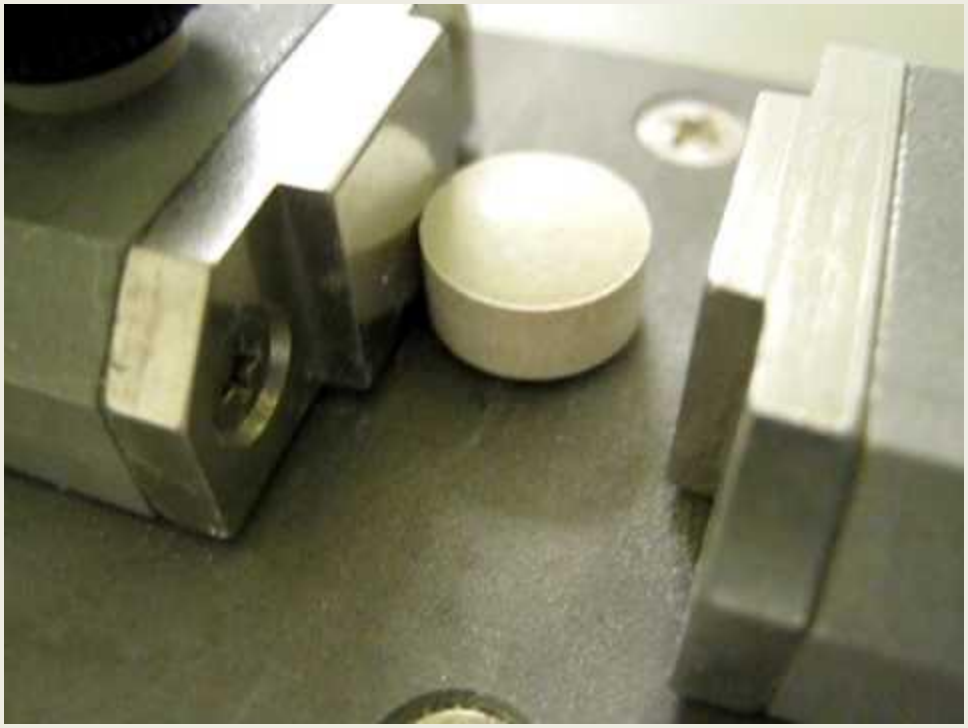
- A tablet is placed between two anvils, force is applied to the anvils, and the crushing strength that just causes the tablet to break is recorded
- Measurements are carried out on 10 tablet (6 tablets as minimum) then take the average hardness

Limits:

Conventional tablets hardness : 2.5- 5 kg/cm2

Dispersible/ chewable tablets hardness: 2.25- 2.5 kg/cm2

Extended release tablets hardness : 5- 7.5 kg/cm



Friability

- Friability: it is the tendency of tablets to chip or break and this can affect the elegance, appearance, consumer acceptance of the tablets, and also add to tablet's weight variation or content uniformity problems.
- The friability test is closely related to the hardness test and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping.
- An instrument called friabilator is used to evaluate the ability of the tablet to withstand abrasion in packaging, handling, and shipping.

- # Procedure :

- For tablets with a unit weight equal to or less than 650 mg, take a sample of whole tablets corresponding as near as possible to 6.5 g.
- For tablets with a unit weight of more than 650 mg, take a sample of 10 whole tablets.
- The tablets should be carefully dedusted prior to testing.
- Accurately weigh the tablet sample, and place the tablets in the drum.
- Rotate the drum 100 times, and remove the tablets.
- Remove any loose dust from the tablets as before, and accurately weigh.

✓ Generally, the test is run once. If obviously cracked, cleaved, or broken tablets are present in the tablet sample after tumbling, the sample fails the test

✓ If the results are difficult to interpret or if the weight loss is greater than the targeted value, the test should be repeated twice and the mean of the three tests determined.

✓ A maximum mean weight loss from the three samples of not more than 1.0% is considered acceptable for most products.

Friability (%loss) = W1- W2/100

- W1 = Initial Weigh 20tablets
- W2 = Weigh 20 tablets after100rotation

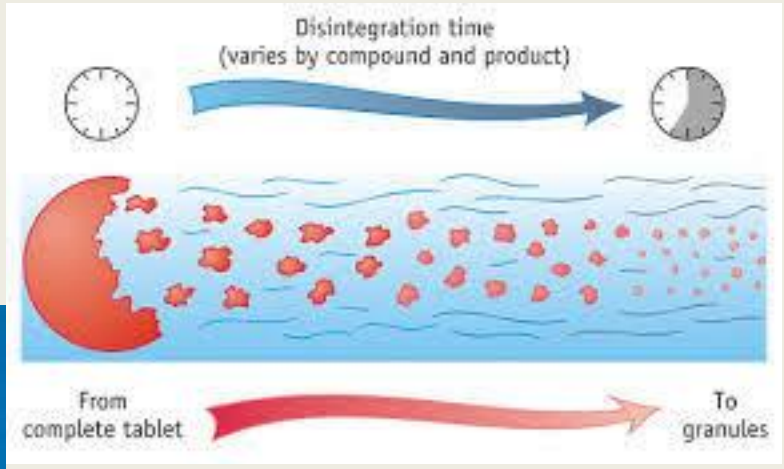
Disintegration

•**Disintegration** is a process in which tablets are break up into granules or smaller particles.

- This test is provided to determine whether tablets disintegrate within the prescribed time when placed in a liquid medium at the experimental conditions
- The time it takes a tablet to disintegrate is measured in a device described in the USP(Thedisintegration apparatus)

- **Six tubes opened at the upper end and closed by a screen at the lower**

- A cylindrical disk of transparent plastic is also used if specified in monograph



The USP disintegration Method:

❖ **Uncoated Tablets**:

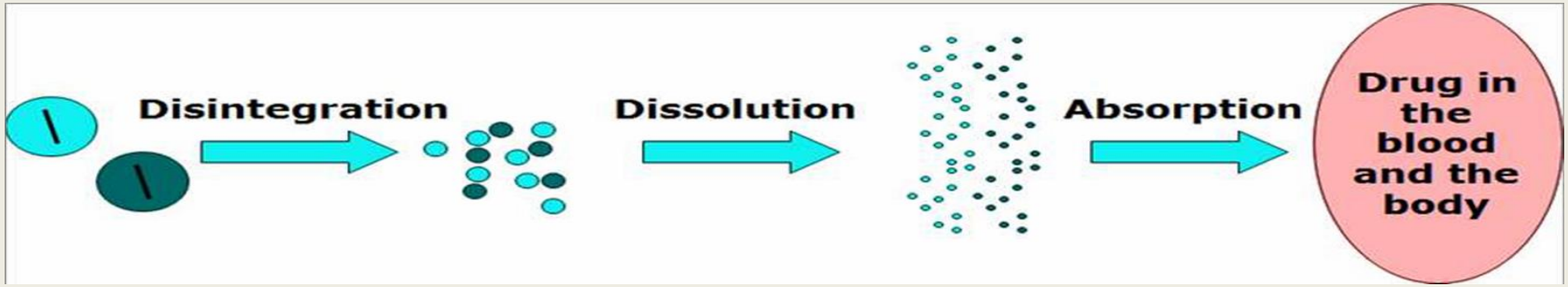
- Place 1 dosage unit in each of the six tubes of the basket and, if prescribed, add a disk.
- Operate the apparatus, using water or the specified medium as the immersion fluid, maintained at 37 ± 2 .
- At the end of the time limit specified in the monograph, lift the basket from the fluid, and observe the tablets all of the tablets have disintegrated completely.
- If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not fewer than 16 of the total of 18 tablets tested are disintegrated.

❖ **Enteric coated tablets** are to show no evidence of disintegration after 1 hour in simulated gastric fluid. These tablets are then tested in simulated intestinal fluid for the time specified in the monograph.

- If 1 or 2 tablets fail to disintegrate completely, repeat the test on 12 additional tablets: not fewer than 16 of the total of 18 tablets tested disintegrate completely.

Dissolutions test

- Dissolution is a process in which a solid substance solubilizes in a given solvent i.e. mass transfer from the solid surface to the liquid phase.
- Rate of dissolution is the amount of drug substance that goes in solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition.



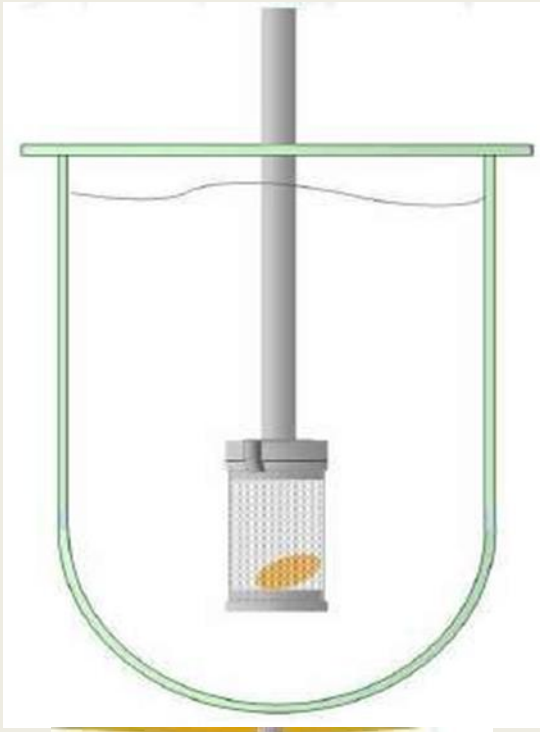
- Dissolution test evaluates the rate and extent that a compound forms a solution under carefully controlled conditions. It helps evaluate the performance of a drug product and indicates when the drug product performs in a substandard fashion.

NEED FOR DISSOLUTION TESTING:

- Evaluation of bioavailability.
- Batch to batch drug release uniformity.
- Development of more efficacious and therapeutically optical dosage forms.
- Ensures quality and stability of the product.
- Product development, quality control, research and application

APPARATUS

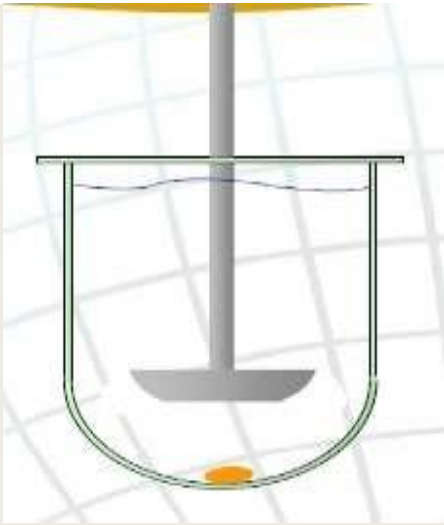
There are 4 apparatuses but mainly apparatus 1 & 2 are used and will be discussed here:



APPARATUS- 1 (ROTATING BASKET)

- The assembly consists of 1- **vessel** made of glass or other inert, transparent material, and it may be covered, 2- **motor**, 3-**metallic drive shaft**, 4- **cylindrical basket**.

USE: Tablets, capsules, delayed release dosage forms, suppositories, floating dosage forms



APPARATUS- 2 (PADDLE)

- The same assembly from Apparatus 1 is used, except that a **paddle formed from a blade and a shaft** is used as the stirring element. And sinkers:-Platinum wire used to prevent tablet/capsule from floating

PROCEDURE

Using Apparatus 1 and Apparatus 2: For immediate release dosage forms:

- Place the stated volume of the Dissolution Medium (±1%) in the vessel. Place 1
  dosage unit in the apparatus, taking care to exclude air bubbles from the surface of the dosage unit, and immediately operate the apparatus at the specified rate.
- Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the Dissolution Medium and the top of the rotating basket or blade, not less than 1 cm from the vessel wall.
- NOTE — Where multiple sampling times are specified, replace the aliquots withdrawn for analysis with equal volumes of fresh Dissolution Medium at 37 °C or,
  where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation.
- Keep the vessel covered for the duration of the test, and verify the temperature of the mixture under test at suitable times.

DISSOLUTION TESTING

Within the time interval specified, or at each of the times stated, withdraw a specimen

Factors affecting Drug Dissolution :-

A. **Factors relating to the physicochemical properties of drug.**

- **Solubility-** Aqueous solubility of drug is a major factor for determines dissolution rates.
- **Particle size** and **effective surface area** of the drug :Greater the effective surface area, more intimate the contact between the solid surface and the aqueous solvent and faster the dissolution.
- **Polymorphism and amorphism**

✓ Stable polymorphs has lower energy state, higher M.P. and least aqueous solubility.

✓ Metastable polymorphs has higher energy state, lower M.P. and higher aqueous solubility.

✓ Amorphous form of drug which has no internal crystal structure represents higher energy state and greater aqueous solubility than crystalline forms.

amorphous > metastable > stable

- **Salt form of the drug-** Dissolution rate of weak acids and weak bases can be enhance by converting them into their salt form

B**. Factors relating to the dosage forms**.

- **Pharmaceutical excipients :(**Diluents , Lubricants , Binders , Disintegrating Agents**)**
- **Manufacturing processes :**Method of granulation , Compression Force

WEIGHT VARIATION TEST:

- The volumetric fill of the die cavity determines the weight of the compressed tablet .
- The weight of the tablet is the quantity of the granulation that contains the labeled amount of the therapeutic ingredient.
- After the tablet machine in operation the weights of the tablets are routinely checked to ensure that proper tablet weights are made.

Procedure :

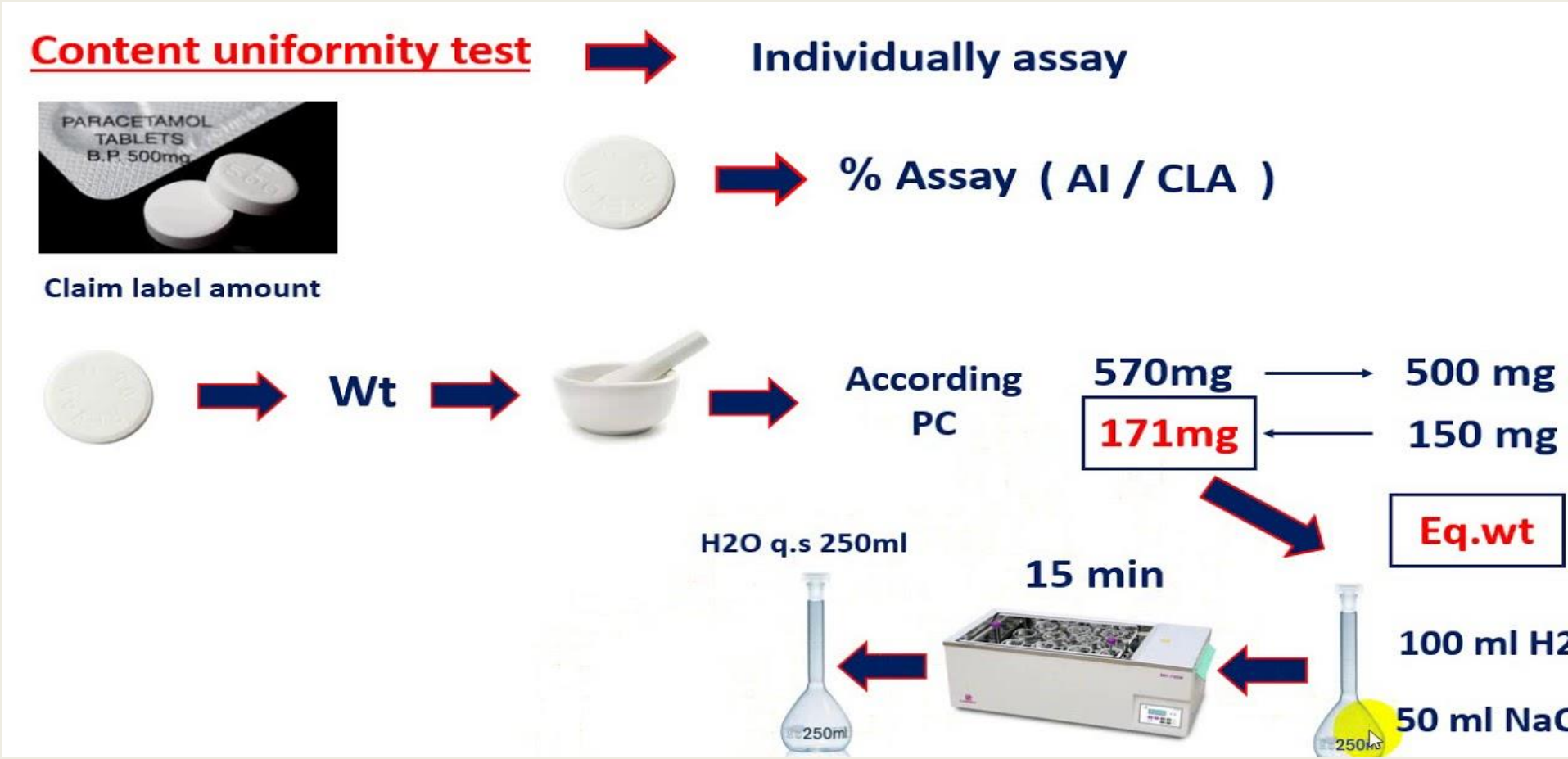
- Take 20 tablets and ,measure the individual weights of each tablets
- Take average weights of 20 tablets
- Compare the individual weight of tablets with avg weight.
- Not more than 2 tablets should deviate from avg weight by percent deviation and none should deviate more than twice the percentage

Table: Weight variation tolerances for uncoated tablets:

Average weight of tablets (mg)	Maximum % difference allowed
130 or less	± 10
130 – 324	± 7.5
More than 324	± 5

Content uniformity

- This test is done to ensure that every tablet contains the amount of drug substance intended with little variation within a batch
- Procedure
- In this test 30 tablets are randomly selected for the sample and at least 10 of them assayed individually
- 9 of the 10 tablets must contain not less than 85% or more than 115% of labeled drug content. 10th tablet may not contain less than 75% or more than 125% of labeled content.
- If this conditions are not meet the tablet remaining from the 30 must be assayed individually and none may fall outside 85 to 115%.



- 9 from 10 tablet (485mg-515mg)
- 1 not exit (475mg-525mg)

References

- The United States pharmacopeia. National formulary. Vol. No. 34(5) . Rockville (MD) United States Pharmacopeial Convention; 2005. Tablet Breaking Force;1217.
- The United States pharmacopeia. National formulary. Vol. No. 34(5) . Lili Wang.United States Pharmacopeial Convention; 2011. DISSOLUTION;711.
- The United States pharmacopeia. National formulary. Vol. No. 30(6) . Robert.H.Rafaver. United States Pharmacopeial Convention; 2002. Particle Size Distribution Estimation by Analytical Sievin;786.
- The United States pharmacopeia. National formulary. Vol. No.34(1)William E.Brown. United States Pharmacopeial Convention; 2002. disintegration;701
- The United States pharmacopeia. National formulary. Vol. No. 28(2)Robert .Rafaver. United States Pharmacopeial Convention; 2004. POWDER FLOW;1174
- The United States pharmacopeia. National formulary. Vol. No. 31(3) .Robert .Rafaver. United States Pharmacopeial Convention; 2012. BULK DENSITY AND TAPPED DENSITY;616
- The United States pharmacopeia. National formulary. Vol. No.34(5)William E .Brown. United States Pharmacopeial Convention; 2004. UNIFORMITY OF DOSAGE UNITS;905
- Allen L. V and Ansel H. C. (2014). *Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems.* Philadelphia: Lippincott Williams and Wilkins.