QUALITY CONTROL TEST FOR CONTAINERS AND CLOSURES

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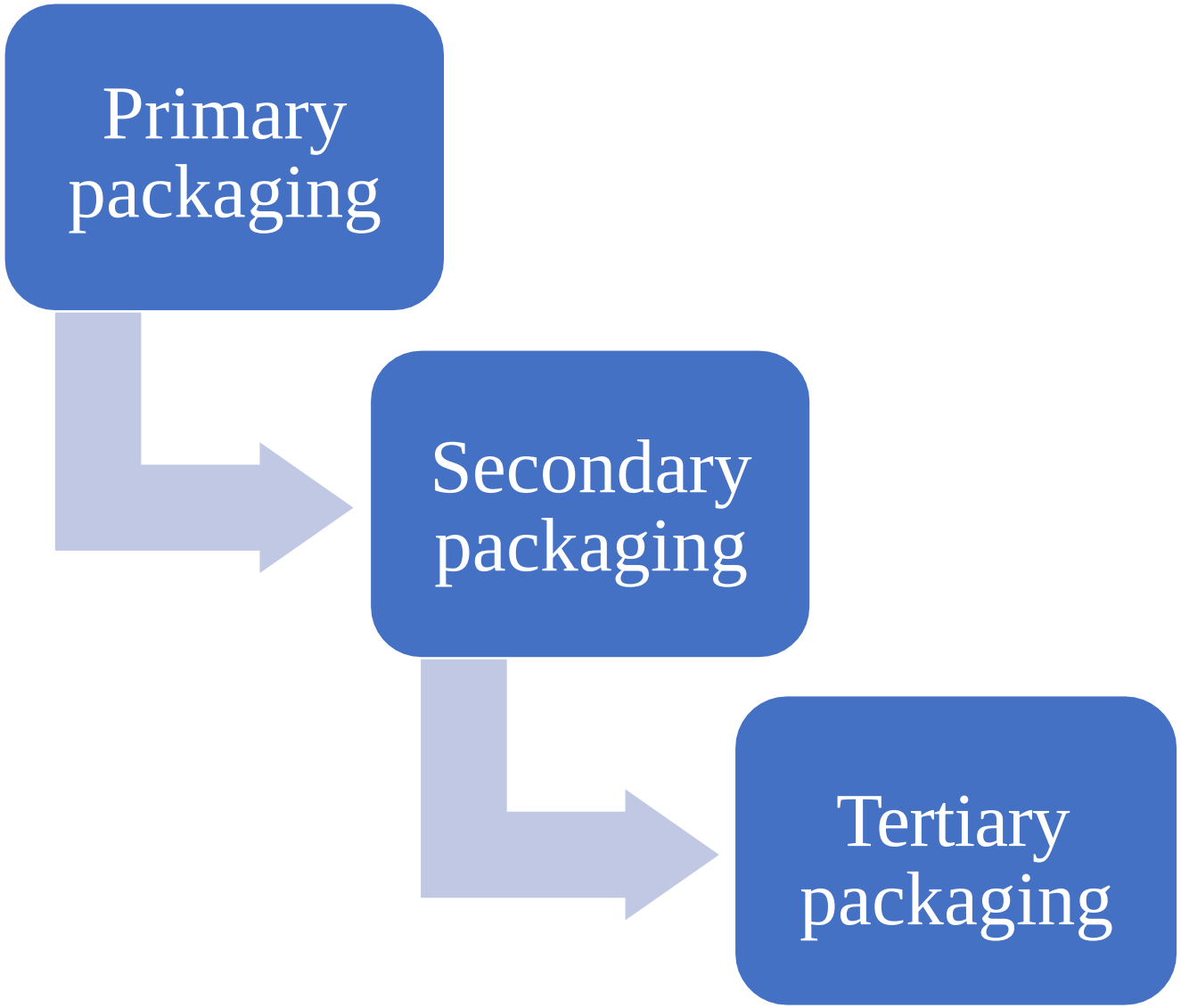
Definition

- Packaging is the science, art and technology of enclosing or protecting products for distribution, storage , sale and use.

Packaging types



Primary packaging

Secondary packaging

Transit packaging

primary	• Direct contact with product • Maintain product quality
secondary	• Contains product and primary pack • Presentation, protection
tertiary	• Transport shipping ,warehouse storage, bulk handling

CONTAINERS

- It is refers to storage media in which product is placed and enclosed & it is in direct contact with drug.(glass and plastic)

TESTS ON CONTAINERS

QUALITY CONTROL TESTS FOR GLASS CONTAINERS

A. Powdered glass test
B. Water attack test
C. Hydrolytic resistance test
D. Arsenic test
E. Thermal shock test
F. Internal bursting pressure test
G. Leakage test

QUALITY CONTROL TEST FOR PLASTIC CONTAINERS

A. Water vapour permeability
B. Light transparency test
C. Clarity or aqueous extract

TYPES OF GLASS:

TYPE I

Neutral or borosilicate glass

TYPE II

Treated soda lime glass

TYPE III

Soda lime glass

TYPE IV

General purpose soda lime glass

QUALITY CONTROL TESTS FOR GLASS CONTAINERS

(A)Powdered Glass Test:

- It is done to estimate the amount of alkali leached from the powdered glass which usually happens at the elevated temperatures.
- When the glass is powdered, leaching of alkali is enhanced, which can be titrated with 0.02 N sulphuric acid using methyl red as an indicator.

STEP 1: Preparation of glass specimen:

Few containers are rinsed thoroughly with purified water and dried with stream of clean air.

Ground in a mortar to a fine powder and passed through sieve no. 20 & 50.

STEP 2 : Washing the specimen:

10gm of the above specimen is taken into 250ml conical flask and washed with 30 ml acetone.

↓

the washing is repeated

↓

the acetone is decanted and dried after which it is used within 48 hr.

PROCEDURE:

10 gm of sample is added with 50ml of high purity water in a conical flask → Placed in autoclave at 121°C ± 2°C for 30min. → Cooled under running water → The solution is decanted into another flask ↓ The sample(residue) is washed again with 15ml high purity water and again decanted ← Titrated immediately with 0.02 N sulphuric acid using 5 drops of methyl red as an indicator ← Record the volume of 0.02N sulphuric acid

(B)WATER ATTCAK TEST (USP):

- This test is performed on intact containers.
- This is only for treated soda lime glass containers under the controlled humidity conditions which neutralize the surface alkali and glass will become chemically more resistant. Principle involved is whether the alkali leached or not from the surface of the container.

PROCEDURE:

Rinse 3 or more containers twice with high purity water

↓

Fill each container to 90% of its overflow capacity with water

↓

Cap all the flask, autoclave at 121°C for 30min.

Then it is cooled and the liquid is decanted which is titrated with 0.02N sulphuric acid using methyl red as an indicator

↓

Measure the volume of sulphuric acid

↓

Volume should not exceed that indicated in table

TABLE : types of glass and their test limits

Types of glass	General description of glass	Type of test	Limits size , ml	Limits (ml of 0.02N)
I	Highly resistant, Borosilicate glass	Powdered glass	All	1.0
II	Treated soda-lime glass	Water attack	100 or less	0.7
			Over 100	0.2
III	Soda-lime glass	Powdered glass	All	8.5
IV	General -purpose soda-lime glass	Powdered glass	All	15.0

(C) HYDROLYTIC RESISTANCE OF GLASS CONTAINER:

Rinse each container at least 3times with CO_2 free water and fill with the same to their filling volume. fill & cover the vials and bottles and keep in autoclave.

↓

Heat to 100°C for 10min. & allow the steam to issue from the vent cork.

↓

Rise the temp. from 100°C to 121°C over 20min. maintain the temp. at 121°C to 122°C for 60min.Lower the temp. from 121°C to 100° C over 40min.

↓

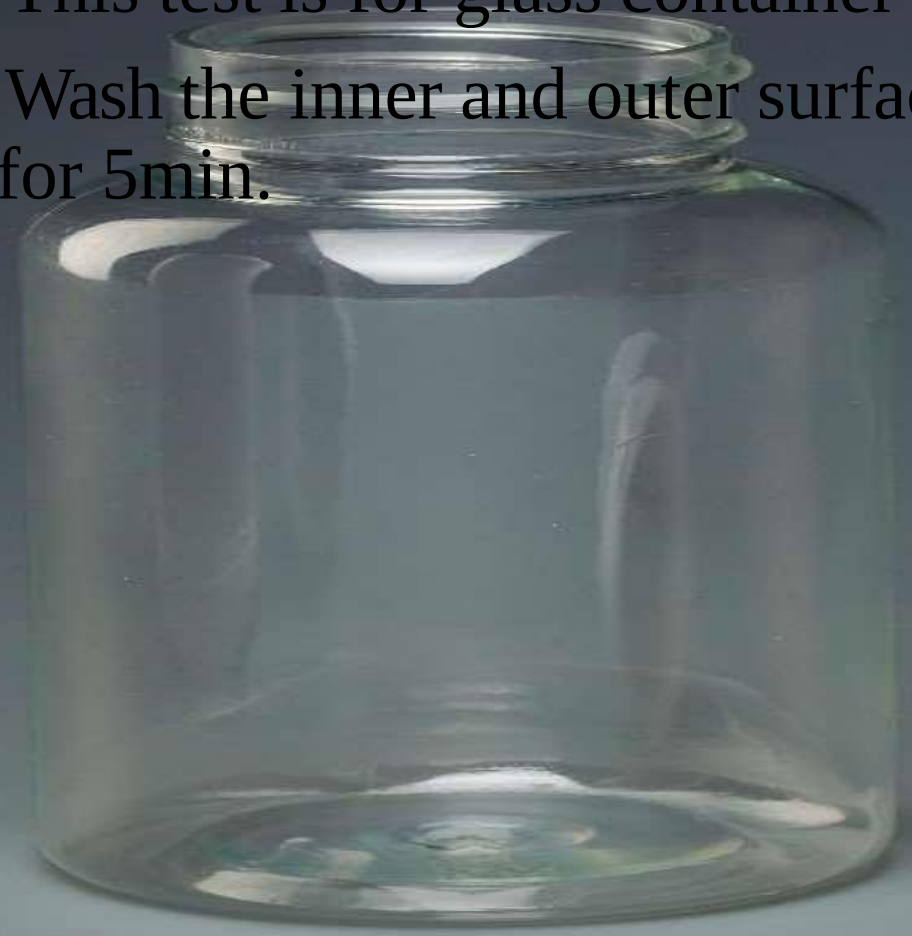
Remove the container from autoclave, cool & combine the liquids being examined. Measure the volume of test solution into a conical flask and titrate with 0.01N HCL using methyl red as an indicator. Perform blank with water and the difference between the titration represents the volume of HCL consumed by the test solution.

❑ Acceptance criteria as per I.P.

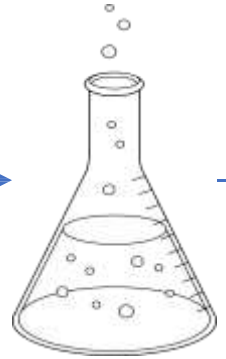
Nominal capacity of container (ml)	Number of containers to be used	Volume of test solution to be used for titration (ml)
5 or less	at least 10	50.0
6 to 30	at least 5	50.0
More than 30	at least 3	100.0

(D) ARSENIC TEST:

- This test is for glass container intended for aqueous parenteral.
- Wash the inner and outer surface of container with fresh distilled water for 5min.



Pipette out 10ml solution from combined contents of all ampoules



Add 10ml HNO_3 to dryness on the water bath

dry the residue in an oven at 130°C for 30min, cool

add 10ml hydrogen molybdate reagent

Swirl to dissolve & heat under water bath & reflux for 25min

Cool at room temp

determine the absorbance at 840nm

Do the blank with 10ml hydrogen molybdate

The absorbance of the test solution should not exceed the absorbance obtained by repeating the determination using 0.1ml of arsenic standard solution (10ppm) in place of test solution.

(E) THERMAL SHOCK TEST:

Place the samples in upright position in a tray. Immense the tray into a hot water for a few time & transfers to cold water bath, temp. of both are closely controlled.

Examine cracks or breaks before and after the test. The amount of thermal shock a bottle can withstand depends on its size, design and glass distribution.

Small bottles withstand a temp. differential of 60 to 80°C . A typical test uses 45°C temp. difference between hot and cold water.

(F) INTERNAL BURSTING PRESSURE TEST:

The most common instrument used is American glass research increment pressure tester. The test bottle is filled with water and placed inside the test chamber. A scaling head is applied and internal pressure automatically raised by a series of increment each of which is held for a set of time. The bottle can be checked to a preselected pressure level and the test continues until the container finally bursts.

(G) LEAKAGE TEST :

Drug fill container is placed in a container filled with coloured solution(due to the addition of dye)

↓

Which is at high pressure compared to the pressure inside the glass container so that the coloured solution enters the container if any cracks or any breakage is present.

↓

So leakage is there.

QUALITY CONTROL TESTS FOR GLASS CONTAINERS

1. **Powdered glass test:**

   Done to estimate the amount of alkali leached from the powdered glass, which usually happens at elevated temperatures.

Sample containers are rinsed with purified water and dried.

↓

The containers are grinded in a mortar to a fine powder and passed through sieve no. 20 and 50.

↓

10gm of the sample is washed with acetone and dried.

↓

50 ml of purified water is added to the dried sample and autoclaved at 121°C for 30 mins and cooled and decanted.

↓

The decanted liquid is titrated with 0.02 N H_2SO_4 using methyl red as indicator.

2. Hydrolytic resistance of glass containers:

Each container is rinsed at least three times with CO_2 free water and filled with the same to their filling volume.

↓

Vials and bottles are covered and autoclaved at 100°C for 10 mins.

↓

The temp. is risen from 100°C to 121°C over 20 mins.

↓

The temp. is maintained at 121°C to 122°C for 60 mins.

↓

The containers are cooled and the liquids are combined and volume measured.

↓

It is titrated with 0.01M HCl using methyl red as an indicator.

Capacity of container [corresponding to 90 per cent average overflow volume (ml)]	Volume of 0.01M hydrochloric acid per 100 ml of test solution	
	Type I or II glass (ml)	Type III glass (ml)
Not more than 1	2.0	20.0
More than 1 but not more than 2	1.8	17.6
More than 2 but not more than 5	1.3	13.2
More than 5 but not more than 10	1.0	10.2
More than 10 but not more than 20	0.80	8.1
More than 20 but not more than 50	0.60	6.1
More than 50 but not more than 100	0.50	4.8
More than 100 but not more than 200	0.40	3.8
More than 200 but not more than 500	0.30	2.9
More than 500	0.20	2.2

3. Arsenic test:

This test is for glass containers intended for aqueous parenterals.

The inner and outer surface of container is washed with fresh distilled water for 5 min.

↓

Then similar steps are followed as performed in the hydrolytic test, previously described, till obtaining the final combined solution.

↓

10ml from the final combined volume is pipetted out and to it 10 ml of HNO_3 is added and dried in an oven at 130°C.

↓

10ml of hydrogen molybdate is added and refluxed for 25 mins.

↓

It is cooled and absorbance is measured at 840nm.

↓

The absorbance of the test solution should be less than the absorbance obtained using 0.1ml of arsenic standard solution (10ppm).

QUALITY CONTROL TESTS FOR PLASTIC CONTAINERS FOR NON-PARENTERAL PREPARATIONS

1. Leakage test:

10 containers are filled with water and fitted with intended closures.

↓

They are kept inverted at room temperature for 24 hours.

↓

The test is said to be passed if there is no sign of leakage from any container.

2. Collapsibility test:

- This test is applicable to containers which are to be squeezed in order to remove the contents.
- A container by collapsing inward during use, yield at least 90% of its normal contents at the required rate of flow at ambient temperature.

3. Clarity of aqueous extract:

A suitable container is taken at random, and unlabeled, unmarked and non-laminated portions is selected.

↓

These portions are cut into strips, none of which has a total surface area of $20cm^2$.

↓

The strips are washed free from extraneous matter by shaking them with at least two separate portions of distilled water for about 30 secs.

↓

The processed sample is taken in to the flask, previously cleaned with chromic acid and rinsed with distilled water.

↓

250ml of distilled water is added to the flask, covered and autoclaved at 121°C for 30 mins.

↓

The extract is cooled and examined. It should be colorless and free from turbidity.

QUALITY CONTROL TESTS FOR CLOSURES

Preparation of sample:

- The closures are washed in 0.2% w/v of anionic surface active agents for 5 mins.
- Rinsed five times with distilled water and 200ml water is added.
- Subjected to autoclave at 119°C to 123°C for 20-30 mins covering with aluminum foil.
- Cooled and solution is separated from closures (Solution A).

1. **Residue on evaporation:**
    - 50ml of Solution A is evaporated to dryness on a water bath and dried at 105°C.
    - The residue weighs not more than 4 mg.

2. Sterilisation test:

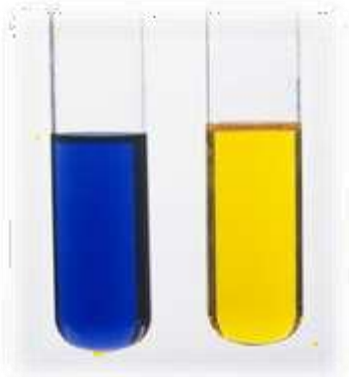
The closures used for the preparation of the sample solution shall not soften or become tacky and there shall be no visual change in the closure.

3. pH of aqueous extract:

To 20ml of solution A, 0.1ml of bromothymol blue solution is added.

↓

NMT 0.3ml of 0.01M NaOH or 0.8ml of 0.01M HCl is rqd. to change the color of the solution to blue or yellow respt.



4. Self stability test:

Pierced ten times with hypodermic needle

↓

Immersed in 0.1% methylene blue solution and subjected to a pressure of about 27 KPa

↓

Restored to ATM pressure and made to stand for 30mins

↓

Traces of colored solution should not be found.

QUALITY CONTROL TESTS FOR CARTONS

1. **Compression:**
   - Used to assess the strength of erected package there by estimating the degree of protection that it confers on the contents.
   - This is useful for products with no inherent strength in one plane or another.

2. **Carton opening force:**
   - The carton should spring open in to its original shape without a need for unreasonable force.
   - If the carton does not spring open or buckles in on itself, it may cause problems on cartooning machine.

QUALITY CONTROL TESTS FOR PAPER AND BOARD

Test conditions:

Temperature- 23 ± 1°C ; Relative humidity- 50±2%

Name of the test	*Description*
Moisture content	All the substances will be measured at temperature specified for test
Folding endurance	Fold the test piece back and forth until rupture occurs
Air permeability	Important for using light weight uncoated paper on machine having vacuum pick up system.
Tensile strength	The max tensile force per unit width that a paper or board will withstand before breaking.
Tear strength	The mean force required to continue the tearing of an initial cut in a single sheet of paper.
Stiffness	Degree of resistance offered by paper/board when it is bent.
Burst resistance	The max uniformly distributed pressure, applied at right angles to the surface that a test piece of paper and board will stand under conditions of test. Hydraulic pressure is applied to diaphragm, bulging it until test piece bursts.

➢ QUALITY CONTROL TEST FOR PLASTIC CONTAINERS

➢ Plastic containers are light in weight and non-breakable, but they have high permeability for water vapour.

➢ Indian pharmacopoeia prescribes Leakage test for plastic containers.

➢ These test are applicable for both injectable and non-injectable.

➢ Water vapour permeability test of Indian Pharmacopoeia is applicable for injectable preparation.

(A)WATER VAPOUR PERMEABILITY (IP 1996)(only applicable for injectable preparation):

Fill 5 containers with normal volume of water and seal the bottle with aluminium foil

↓

Weigh each container

↓

Allow to stand for 14days at RH of 60 ±5% at 20° to 25°C

↓

Reweigh the container and check loss of weight in each container should not be more than 0.2%

(B)LIGHT TRANSPARENCY TEST:

- The observed light transmission for plastic containers for products intended for oral or topical administration does not exceed 10% at any wavelength in the range from 290nm to 450nm.
- This test is to determine the effect of light passing through the bottle wall on the product stability and appearance.

APPARATUS: Spectrophotometer, adapted for measuring the amount of light transmitted by either transparent or translucent glass or plastic materials.

PROCEDURE: Cut circular sections from 2 or more areas of the container. Wash and dry each sample taking care not to scratch the surfaces.

- Mount the specimen on the Spectrophotometer and measure the transmittance of the section.

(C)CLARITY OF AQUEOUS EXTRACT:

- Select unlabelled portion from a suitable containers → Cut these portions into strips and Wash it with extraneous matter by shaking with two separate portions of distilled water for about 20sec.

- after Transfer to flask – previously washed with chromic acid mixture and rinsed with distilled water add 250ml distilled water and Cover the flask and autoclave at 121°C, 30min.

- carry out the blank determination using 250ml dist. Water.
- Cool and examine the extract, it should be Colourless & free from turbidity.

Conclusion:

- The testing of packaging materials is almost requirement for any pharmaceutical industry.
- The material of a package affects quality, stability and efficacy of drug product.
- The cost of material of a package should be as low as possible without compromising the quality of product.
- It should pass the specification of tests before it reached the local markets and made available to the consumers of product.

CLOSURES :

- It is a device tightly pack the container to exclude O_2 , CO_2, moisture, microorganism , prevent loss of water and volatile substance from the product during transport and handling.
- It is part of container system but does not come in contact with drug.(aluminium, rubber)

TYPES OF CLOSURES:

(1)Rubber closures

(2)Caps and overseals

- Screw cap
- Crown cap
- Snap on
- Friction fit

(3)Special types

- Tamper- evident
- Dispensing
- Child resistant

QUALITY CONTROL TEST FOR CLOSURES

Preparation of sample(solution A):

wash closures in 0.2%w/v of anionic surface active agent for 5min. Rinse 5 times with dist. water

add 200ml water and is subjected to autoclave at 119 to 123°C for 20 to 30min. covering with aluminium foil.

Cool and separate solution from closure(sol.-A).

(A)FRAGMENTATION TEST:

For closures for aqueous preparations, place a volume of water corresponding to the nominal volume 4ml in each of 12 clean vials

↓

Close the vials with the “prepared” closures and allow to stand for 16hours

↓

For closures for dry preparations, close 12 clean vials with the “prepared” closures

↓

Using a hypodermic needle with an external diameter of 0.8mm inject 1ml of water into the vial and remove 1ml of air.

↓

pass the liquid in the vials through a filter with a pores size 0.5µm.

Carry out this operation 4 times with new needle each time.

No. of fragments is NMT to except in the case of butyl rubber closures where the total no. of fragments is NMT 15.

(B)STERILTY TEST:

- when treated closures are subjected to sterilization test at 64-66° C and a pressure of about 0.7 KPa for 24hr.

(C) SELF – SEALABILTY:

- This test is applicable to closures intended to be used with water

Close the vials with the ‘prepared’ closures

For each closures, use a new hypodermic needle with an external diameter of 0.8 mm & piece the closure 10 times, each time are different site.

Immense the vials upright in a 0.1% w/v solution of methylene blue & reduce the external pressure by 27PKa for 10min.

Restore the atmospheric pressure and leave the vials immersed for 30minutes. Rinse the outside of the vials

None of the vials contains any trace of coloured solution.

$_{P}$H OF AQUEOUS EXTRACT:

20ml of solution A is added with 0.1 ml bromothymol blue when it is added with a small amount of 0.01 M NaOH which changes the colour from blue to yellow. The volume of NaOH required is NMT 0.3 ml and if it is done with HCL, the volume of HCL needed should NMT 0.8ml.

(E) LIGHT ABSORPTION TEST:

It must be done within 4hrs of preparing solution A.

It is filtered through 0.5µ filter and its absorbance is measured at 220 to 360nm.

Blank is done without closures and absorbance is NMT 2.0.

(F) RESIDUE ON EVAPORATION:

50ml of solution A is evaporated to dryness at 105°C.

Then weigh the residue NMT 4mg.

(G) REDUCING SUBSTANCES:

20ml of solution A

1ml of 1M H_2SO_4

20ml of 0.002M $KMnO_4$

→ boil for 3min then cool →

add 1gm of potassium iodide which is titrated with sodium thio-sulphate using starch as an indicator

↓

Blank is done and the difference between titration volumes is NMT 0.7ml

QUALITY CONTROL TEST OF STRIP AND BLISTERS:

3/4th of water is poured in desiccators

placed inside the desiccators and vacuum is applied

After sometime vacuum was released, strips and blisters were taken out

The water present over the outer surface of the package was wiped off with tissue paper.

The contents of strips and blister packages were removed and the presence of moisture was checked

If there is no leakage, the contents will not be wetted. This indicates the perfect sealing of the packages.

REFERENCE:

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- The Theory and Practice of Industrial Pharmacy by Leon Lachman

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