STANDARD OPERATING PROCEDURE	
Department: Quality Assurance	**SOP No.:**
Title: Operation of Leak Test Apparatus	**Effective Date:**
Supersedes: Nil	**Review Date:**
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1.0 OBJECTIVE:

To lay down a procedure for Operation of Leak Test Apparatus.

2.0 SCOPE:

This SOP is applicable for Operation of Leak Test Apparatus at …….

3.0 RESPONSIBILITY:

Officer/Executive – QA & Production.

4.0 ACCOUNTABILITY:

Head – QA

5.0 DEFINITIONS:

Not Applicable

6.0 PROCEDURE:

6.1 PRINCIPLE:

6.1.1 The dye penetration test under vacuum is used to identify the leakage in vials.

6.1.2 Vacuum is created in the headspace over the dye solution. In case of leakage in the immersed container the air present in the head space of container tend to come out and create low pressure inside the Vials.

6.1.3 When the vacuum is released the dye solution immediately penetrates in the container because of the lower pressure inside the leaked container.

6.2 VACUUM LEAK TEST PROCEDURE FOR COLOUR LESS SOLUTION FILLED & SEALED IN TRANSPARENT CONTAINER (USING METHYLENE BLUE DYE SOLUTION):

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6.2.1 Reagent Preparation:

6.2.1.1 Prepare the Methylene blue dye 2 mg/Liter in WFI, 1% Solution.

6.2.1.2 Transfer the prepared reagent in leak test apparatus flask.

6.2.1.3 **Frequency:** Change the reagent daily.

6.2.2 Procedure

6.2.2.1 Take clean and dry Leak test apparatus having vacuum flasks capacity of 3.0 liters.

6.2.2.2 Open Vacuum flask lid.

6.2.2.3 Remove the perforated disk from the vacuum flask.

6.2.2.4 For Leak testing vials shall be collected after weight adjustments/volume adjustment and sealing adjustment.

6.2.2.5 Collected vials shall be equal to the number of sealing heads.

6.2.2.6 Place the perforated disc properly in to the vacuum flask and ensure all the containers (Vials) should be completely immersed in to the Methylene blue dye solution.

6.2.2.7 Close the vacuum flask lid tightly with the help of rubber gasket.

6.2.2.8 Connect the vacuum pump to leak test apparatus with the help of suitable silicon pipe.

6.2.2.9 Switch on the vacuum pump.

6.2.2.10 Open the vacuum knob and apply the vacuum of 400 mmHg to the flask.

6.2.2.11 Keep the vial for 3 min. under 400 mmHg to 500 mmHg vacuum and then turn the knob off.

6.2.2.12 Close the vacuum knob of apparatus after reached to required vacuum pressure and starts the timer simultaneously.

6.2.2.13 Further hold the vials under vacuum for 2 min. So that dye can penetrate inside the vials, if any leakage is there.

6.2.2.14 Release the vacuum from vacuum flask with the help of vacuum knob after the digital display showing time zero.

6.2.2.15 Ensure the vacuum pressure showing zero reading in vacuum gauge.

6.2.2.16 Open the vacuum lid of vacuum flask and remove the perforated disk.

6.2.2.17 Remove the containers (Vials) from the vacuum flask and wipe with the

tissue paper.

6.2.2.18 Observe the penetration of Methylene blue dye inside the container (Vials) and by visual observation and note the results in BMR.

6.3 TEST PROCEDURE FOR SOLUTION FILLED & SEALED IN OPAQUE/COLOURED CONTAINER OR COLOURED SOLUTION FILLED IN TRANSPARENT CONTAINER:

6.3.1 Collect filled and sealed vials serially from all sealing heads of sealing machine.

6.3.2 Put tissue paper/blotting paper on the cap of the vials up to neck and tighten with rubber band.

6.3.3 Empty the vacuum leak tester flask if methylene blue dye solution present in flask.

6.3.4 Clean& dry the flask with the help of soft lint free cloth to remove moisture and dust particles

6.3.5 Open the lid of vacuum leak tester and remove the perforated disk from the vacuum flask.

6.3.6 Place the filled and sealed vials to be tested in horizontal position.

6.3.7 Place the perforated disc properly in to the vacuum flask and close the lid tightly.

6.3.8 Switch 'ON' the mains power supply of equipments.

6.3.9 Switch 'ON' the mains of the equipments.

6.3.10 Open the vacuum knob and apply the vacuum of 400 mmHg to 500 mmHg for 3 min. by pressing start option key.

6.3.11 Apply gentle force from the top of the desiccator, vacuum start developing which will be indicate on the vacuum gauge fixed on the apparatus.

6.3.12 Close the vacuum knob of apparatus after reached to required vacuum pressure and start the timer simultaneously.

6.3.13 Keep hold the vial for 2 min. under 400 mmHg to 500 mmHg vacuum.

6.3.14 Release the vacuum from vacuum flask with the help of vacuum knob after the digital display showing time zero.

6.3.15 Open the vacuum lid of vacuum flask after confirming that vacuum gauge shows zero and remove the perforated disk.

6.3.16 Take out the vials from desiccator. Check leakage from vials by observing tissue/blotting paper/inside the cap/vial neck after opening the cap.

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6.4 VACUUM LEAK TEST PROCEDURE FOR DRY POWDER INJECTION FILLED & SEALED VIALS (USING METHYLENE BLUE DYE SOLUTION):

6.4.1 Reagent Preparation:

6.4.1.1 Prepare the methylene blue dye 2mg/liter in WFI.

6.4.1.2 Transfer the prepared reagent in leak test apparatus flask.

Frequency: Change the reagent daily basis.

6.4.2 Procedure:

6.4.2.1 Take clean and dry Vacuum leak test apparatus having vacuum flasks capacity of 1000 ml.

6.4.2.2 Open vacuum flask lid.

6.4.2.3 Remove the perforated disk from the vacuum flask.

6.4.2.4 For leak testing vials should be collected after machine setting the empty vials, weight adjustments and sealing adjustment.

6.4.2.5 Collected vials shall be equal to the number of sealing heads.

6.4.2.6 Place the perforated disc properly in to the vacuum flask and ensure all the containers (Vials) should be completely immersed in to the Methylene blue dye solution.

6.4.2.7 Close the vacuum flask lid tightly with the help of rubber gasket.

6.4.2.8 Connect the vacuum pump to leak test apparatus with the help of suitable silicon pipe.

6.4.2.9 Switch on the vacuum pump.

6.4.2.10 Open the vacuum knob and apply the vacuum of 400 mmHg to 500 mmHg to the flask.

6.4.2.11 Keep the vial for 3 min. under 400 mmHg to 500 mmHg vacuum and then turn the knob off.

6.4.2.12 Close the vacuum knob of apparatus after reached to required vacuum pressure and starts the timer simultaneously.

6.4.2.13 Further hold the vials under vacuum for 2 min. So that dye can penetrate inside the vials, it any leakage is there.

6.4.2.14 Release the vacuum from vacuum flask with the help of vacuum knob after the digital

display showing time zero.

6.4.2.15 Ensure the vacuum pressure showing zero reading in vacuum gauge.

6.4.2.16 Remove the containers (Vials) from the vacuum flask and wipe with the tissue paper.

6.4.2.17 Observe the penetration of Methylene blue dye inside the container (Vials).

6.4.2.18 If Methylene blue dye observed inside the vial the Leak test stands "FAIL".

6.4.2.19 In case Leak test "PASS", results shall be verified by opening the vial and neck of vial shall be checked for presence of Methylene blue dye.

6.4.2.20 Record the details in BMR.

6.4.2.21 Records the details as per Annexure-1. (Leak Test Apparatus Log Book)

6.5 VACUUM LEAK TEST PROCEDURE FOR AMPOULES:

6.5.1 Collect filled and sealed ampoules serially from all sealing heads of sealing machine.

6.5.2 Empty the vacuum leak tester flask if methylene blue dye solution present in flask.

6.5.3 Clean & dry the flask with the help of soft lint free cloth to remove moisture and dust particles

6.5.4 Open the lid of vacuum leak tester and remove the perforated disc from the vacuum flask.

6.5.5 Place the filled and sealed ampoules to be tested in inverted position.

6.5.6 Place the perforated disc properly in to the vacuum flask and close the lid tightly.

6.5.7 Switch 'ON' the mains power supply of equipments.

6.5.8 Switch 'ON' the mains of the equipments.

6.5.9 Open the vacuum knob and apply the vacuum of 400 mmHg to 500 mmHg for 3 min. by pressing start option key.

6.5.10 Apply gentle force from the top of the desiccators, vacuum start developing which will be indicate on the vacuum gauge fixed on the apparatus.

6.5.11 Close the vacuum knob of apparatus after reached to required vacuum pressure and starts the timer simultaneously.

6.5.12 Keep hold the ampoules for 2 min. under 400 mmHg to 500 mmHg vacuum.

6.5.13 Release the vacuum from vacuum flask with the help of vacuum knob after the digital display showing time zero.

6.5.14 Open the vacuum lid of vacuum flask after confirming that vacuum gauge shows zero and remove the perforated disk.

6.5.15 Take out the ampoules from desiccator. Check the ampoules by observing presence of any empty ampoule(s), count the number of ampoules and record the details in BMR.

6.5.16 Record the activity of leak test apparatus as per Annexure-I.

6.6 ACCEPTANCE CRITERIA:

6.6.1 For color less solution filled & sealed in transparent container: Solution color of any tested vials should not be changed after test.

6.6.2 For Solution Filled & Sealed in Opaque/Colored Container or Colored Solution Filled in Transparent Container: The sample passes in leak test if no vial's tissue / blotting paper found wet or no solution droplet observed inside the cap / on vial neck after opening the cap.

6.6.3 **For Dry Powder Injection:** Dye should not penetrate in the Vial.

6.6.4 **For Ampoules:** No empty ampoule shall be observed in the apparatus after the vacuum leak test.

6.7 ACTION PLAN IN CASE OF LEAK TEST FAILURE:

6.7.1 If the leak test fails segregate the quantity of filled and sealed vials from the time the test fails, and hold the quantity. These hold vials shall be inspected carefully and short out the defective vials before packing.

6.7.2 Inform to machine operator simultaneously about leak test failure which in turn shall make necessary correction/setting in the machine.

6.7.3 Carry out leak test again after resetting, if the test is satisfactory then only run the machine again.

7.0 ABBREVIATIONS:

QA : Quality Assurance

Ltd. : Limited

No. : Number

IPQA : In-Process Quality Assurance

BMR : Batch Manufacturing Record

SOP : Standard Operating Procedure

DPI : Dry Powder Injection

min. : Minutes

mg : Milligram

ml : Milliliter

mmHg : Millimeter Hydrargyrum

WFI : Water for Injection

8.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Leak Test Apparatus Log Book	

9.0 DISTRIBUTION:

- Master Copy — Quality Assurance Department
- Controlled Copy No. 01 — Quality Assurance

10.0 REFERENCES:

In House

11.0 REVISION HISTORY:

Revision No.	Change Control No.	Details of Changes	Reason of Changes	Effective Date	Done By
00	Not Applicable	Not Applicable	New SOP		

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

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ANNEXURE-I

LEAK TEST APPARATUS LOG BOOK

S.No.	Date	Product Name	Batch Number	Mfg. Date	Exp. Date	Operation Time		Checked by	Verified by	Remarks
						Vacuum Pressure	Hold Time			