STANDARD OPERATING PROCEDURE

Title: Operation of Leak Test Apparatus

SOP No.:		**Department:**	Production	
		Effective 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 in production department.

3.0 RESPONSIBILITY:

Operating Person-Production

4.0 ACCOUNTABILITY:

Head - Production

5.0 ABBREVIATIONS:

BMR	Batch Manufacturing Record
IPQA	In process Quality Assurance
Ltd.	Limited
mg	milligram
mm	millimeter
Pvt.	Private
QA	Quality Assurance
SOP	Standard Operating Procedure
WFI	Water for Injection
Hg	Mercury

6.0 PROCEDURE:

Note:

- Number of sealing heads available in sealing machine of DPI, Three Piece (I block) and Three Piece (Q block) sections :-

S.No.	Section	No. of sealing heads
1.	DPI	04
2.	Three Piece (I block)	08
3.	Three Piece (Q block)	16

- In-process test sample shall be discarded after completion of leak test.

6.1 Vacuum Leak Test Procedure For Dry Powder Filled & Sealed Glass Vials And Clear Three Piece Plastic Vial (Using Methylene Blue Dye Solution):

6.1.1 Principle:

6.1.1.1 The dye penetration test under vacuum is used to identity leakage in vials.

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

6.1.1.3 When the vacuum is released the dye solution immediately penetrates in the Vials because of the lower pressure inside the leak Vials.

6.1.2 Reagent Preparation:

6.1.2.1 Prepare the Methylene blue dye 2 mg/Liter in WFI and record the details as per annexure-II "Methylene Blue Solution Preparation Record"

6.1.2.2 Transfer the prepared reagent in leak test apparatus flask.

6.1.2.3 **Frequency:** Change the reagent on daily basis.

6.1.3 Procedure:

6.1.3.1 Clean and dry Vacuum leak test apparatus having vacuum flasks.

6.1.3.2 Open vacuum flask lid.

6.1.3.3 Remove the perforated disk from the vacuum flask.

6.1.3.4 For leak testing vials should be collected after filling and sealing operation.

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

6.1.3.6 QA/Production officer shall collect the vials from sealing machine and provide the number as per the sealing sequence with permanent marker.

6.1.3.7 Place the vials into the Methylene blue solution in leak test apparatus flask.

6.1.3.8 Now Place the perforated disc properly into the vacuum flask and ensure all the Vials should be completely immersed in to the Methylene blue dye solution.

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

6.1.3.10 Switch on the vacuum pump.

6.1.3.11 Open the vacuum knob and apply the vacuum of -300 mm Hg to the flask.

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

6.1.3.13 Hold the vials at pressure -300 mm Hg for 120 Seconds. So that dye can penetrate inside the vials, if any leakage is there.

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

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

6.1.3.16 Remove the Vials from the vacuum flask and wipe with the tissue paper.

6.1.3.17 Observe the penetration of Methylene blue dye solution inside the vials by visual observation and note the results in respective BMR & Log Book.

6.2 Test Procedure for Solution Filled & Sealed in Opaque/ Coloured Container or Coloured Solution Filled in Transparent Container:

6.2.1 Procedure:

6.2.1.1 Collect filled and sealed vials serially from all sealing heads of sealing machine and mark the sealing head number on each vial by permanent marker.

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

6.2.1.3 Empty the vacuum leak tester flask if Methylene Blue dye solution present in flask.

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

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

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

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

6.2.1.8 Switch ‘ON’ the mains power supply of equipments.

6.2.1.9 Switch ‘ON’ the mains of the equipments.

6.2.1.10 Open the vacuum knob and apply the vacuum of 300 mm Hg to the flask by pressing start option key.

6.2.1.11 Apply gentle force from the top of the desiccators, vacuum will indicate on the vacuum gauge fixed on the apparatus.

6.2.1.12 Close the vacuum knob of apparatus after reached to require vacuum pressure set the timer for 2 minutes and starts the timer simultaneously.

6.2.1.13 Keep hold the vial for 2minutes under 300 mm Hg vacuum.

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

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

6.2.1.16 Take out the vials from desiccator. Check leakage from vials by observing tissue/ blotting paper / inside the cap / vial neck after opening the cap. Vials by visual observation and note the results in BMR and **Annexure-I** “Cleaning and Utilization Log for Leak Test Apparatus”

6.3 Acceptance Criteria:

6.3.1 For Dry Powder Filled & Sealed In Glass Vials:

No penetration of dye solution observed / lumps formation of inside any of the vial after completion of leak test.

6.3.2 For Three Piece Filled & Sealed Plastic Vials:

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.

6.4 Action Plan in Case of Leak Test Failure:

6.4.1 If the leak test fails, repeat the test with new vials from each sealing head at same machine setting (for confirmation) and inform to machine operator simultaneously about leak test failure which in turn shall make necessary correction/setting in the machine (if required).

6.4.2 After that segregate the quantities 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.

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

6.5 Cleaning of Leak Test Apparatus:

6.5.1 Drain the methylene blue solution filled in the leak test apparatus.

6.5.2 Wipe the internal and external surface of leak test apparatus using 70% IPA solution and lint free mop.

6.5.3 Record the cleaning activity in annexure-I "Cleaning and Utilization Log for Leak Test Apparatus"

6.5.4 Frequency of cleaning is at the end of the day or whenever required.

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Cleaning and Utilization Log for Leak Test Apparatus	
Annexure-II	Methylene Blue Solution Preparation Record	

ENCLOSURES: SOP Training Record

8.0 DISTRIBUTION:

- Controlled Copy No. 01 Quality Assurance
- Controlled Copy No. 02 Production
- Master Copy Quality Assurance

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9.0 REFERENCE:

Not Applicable.

10.0 REVISION HISTORY:

CHANGE HISTORY LOG

Revision No.	Change Control No.	Details of Changes	Reason for Change	Effective Date	Updated By

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ANNEXURE – I
CLEANING AND UTILIZATION LOG FOR LEAK TEST APPARATUS

Name Equipment : **ID No.:**

Area : **Block:**

S.No.	Date	Activity/ Product Name Batch No. details	Time		Observation	Done By Sign & Date	Remarks
			Start	End			

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ANNEXURE – II
METHYLENE BLUE SOLUTION PREPARATION RECORD

S.No.	Date	Weight of Methylene Blue	Volume of WFI used	Done By	Checked By	Remarks