Designation: F3169 – 16

Standard Test Method for Leak Detection in Blister Packaging by Vacuum Deflection Method by Laser Measurement[1]

This standard is issued under the fixed designation F3169; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 *Test Packages*—This test method can be applied to non-porous blister packs sealed with flexible films such as those used in pharmaceutical packaging. Such blister packs typically consist of thermoformed polymer or cold formed aluminum trays that contain a number of individual blister pockets into which tablets or capsules are placed. The trays are then sealed with a polymer, paper-backed or foil-based flexible laminate lidding material.

1.2 *Leaks Detected*—This test method detects leaks in blister packs by measuring the deflection of the blister pack surface in response to an applied vacuum. This deflection of the blister pack surface results from the difference in pressure between the gas inside the blister pack and the applied vacuum. Air loss from within a blister pocket as a result of a leak will alter this pressure differential causing a measureable variation in blister pocket deflection. This test method requires that the blister packs are held in appropriate tooling inside a suitable test chamber.

1.3 *Test Results*—Test results are reported qualitatively (pass/fail). Appropriate acceptance criteria for *deflection*, *height*, and *collapse* values are established by comparing non-leaking packs with those containing defects of a known size. Suitably sized defects in the laminate, tray material, and seal can be detected using this test method. The sensitivity of this test method depends upon a range of factors including blister pocket headspace, blister pocket size, lidding material type, lidding material thickness, lidding material tension, printing, surface texture, test conditions, and the values selected for the pass/fail acceptance criteria. The ability of the test to detect 15 µm, 50 µm, and catastrophic sized holes in four blister pack designs was demonstrated in a study.

1.4 The values stated in SI units are to be regarded as standard and no other units of measurement are included in this test method.

1.5 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D996 Terminology of Packaging and Distribution Environments

F17 Terminology Relating to Flexible Barrier Packaging

3. Terminology

3.1 For definitions used in this test method, see Terminologies D996 and F17.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *blister pack, n*—forming material, encapsulated product, and sealed lidding material.

3.2.2 *blister pocket, n*—sealed cavity in the forming material that contains product.

3.2.3 *collapse, n*—difference in height of the blister pocket profile in one plane before and after the reduced vacuum has been applied.

3.2.4 *deflection, n*—difference in height of the blister pocket profile in one plane before and after the initial vacuum has been applied.

3.2.5 *height, n*—difference in height of the blister pocket profile in one plane after initial vacuum when compared against blister pack surface height.

3.2.6 *profile, n*—surface of the lidding material measured at regular intervals across the blister pocket.

4. Summary of Test Method

4.1 The test blister packs are located in the test chamber in appropriate tooling to prevent them from moving under vacuum. The chamber is then sealed and the profile of every

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

blister pocket is measured using an appropriate measurement device such as a laser and actuator (see Fig. 1).

4.2 A vacuum is then applied to the test chamber and each blister pocket measured again. Sealed blister pockets can be identified by the change in measurement between the first and second profiles. This is known as *deflection* and is caused by the pressure difference between the air inside the blister pocket and the air in the chamber caused by the application of vacuum (see Fig. 2).

4.3 The *deflection* of a blister pocket with a gross hole will be minimal as the pressure difference between the air inside and outside of the blister pocket will equalize through the hole.

4.4 The sensitivity of the test can be increased by holding the test samples under vacuum for a period of time and then reducing the vacuum level. After reducing the vacuum, the surface profile of the blister pockets can be measured again and compared with the profiles recorded after the initial vacuum was applied. Reducing the vacuum level causes blister pockets with small holes to have a collapse measurement greater than blister pockets with no defects. This is due to air leaking from any small defects (see Fig. 3).

4.5 The sensitivity of the test is a function of the test parameters chosen, namely vacuum levels, hold time, and the *pass/fail* criteria selected. Blister pack design including headspace and blister pocket size, lidding material, lidding material thickness, lidding material tension, printing, and surface texture can affect test sensitivity. The vacuum levels used are typically in the range of 30 - 60 KPa and are chosen based on setup tests conducted using good blister packs and those containing defects of known size. The required vacuum level depends upon the blister pack design and materials. For example, detecting sub-15 µm defects in small blister pockets sealed with a stiff lidding material typically requires vacuum levels towards the higher end of the standard range. The vacuum level is then reduced and the packs are rescanned after a holding period (typically 10 - 45 s) at this reduced vacuum. The test parameters, including the *pass/fail* criteria, are chosen by comparing the *deflection* and *collapse* values of good blister packs and those containing defects of the required size. Such defects can be produced by using a wire, by laser drilling, or by applying self-adhesive predrilled holes.

4.6 Where blister pockets appear pre-swollen the flat sealed surface of the blister pack is used to project a datum line across the blister pocket from which a change in height under vacuum can be observed. If this height value is small or negative it can be understood that the blister pocket has a gross hole, as the blister pocket has not deflected due to vacuum or positive pressure before testing (see Fig. 4).

4.7 Any blister pocket that falls outside the acceptance criteria for *deflection*, *collapse*, or *height* is recorded as a fail. The ability of the test to detect 15 and 50 µm sized laser drilled holes was verified using four blister pack designs. This method was also used to find large catastrophic defects demonstrated with a 5 mm slit in the lidding material.

4.8 Background noise may occur due to movement of the blister pack under vacuum. Such noise can be minimized by selection of an appropriate measurement device, proper retention of the blister pack, and careful selection of pressures used for testing.

5. Significance and Use

5.1 Leaks in blister packs may affect product quality and such defects can arise from imperfections in the packaging material or bond between the sealed surfaces.

5.2 This method of leak testing is a useful tool as it allows non-destructive and non-subjective leak testing of blister packs. It allows the operator to evaluate how different packaging materials and packaging machine conditions affect the integrity of the packaging. It can also provide indication of unwanted changes in the packaging conditions.

5.3 This type of testing is typically used in pharmaceutical packaging production, during stability trials and for package research and development operations because of its non-destructive nature, cleanliness, and speed.

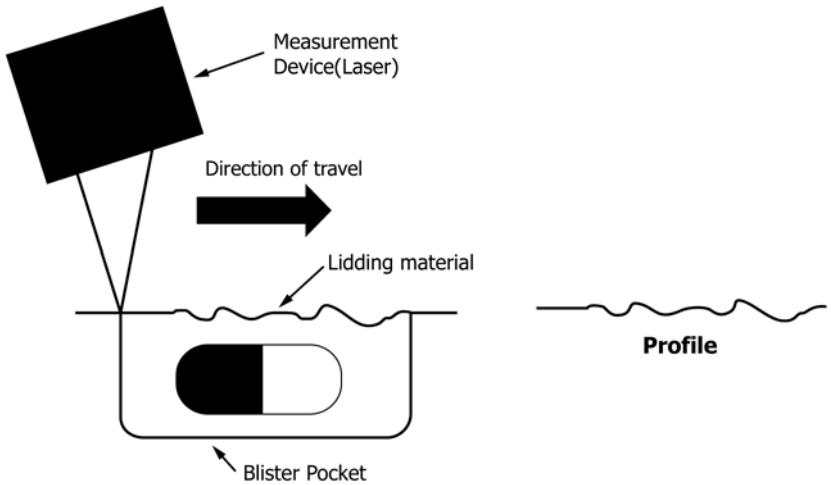


FIG. 1 Profile

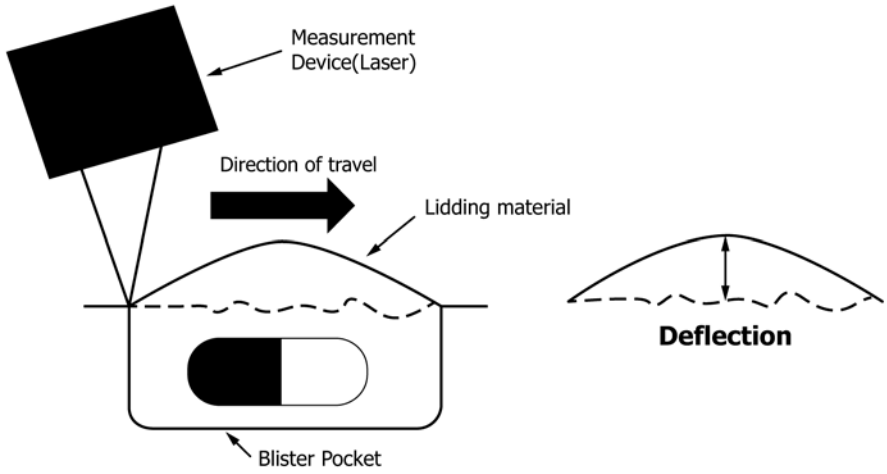


FIG. 2 Deflection

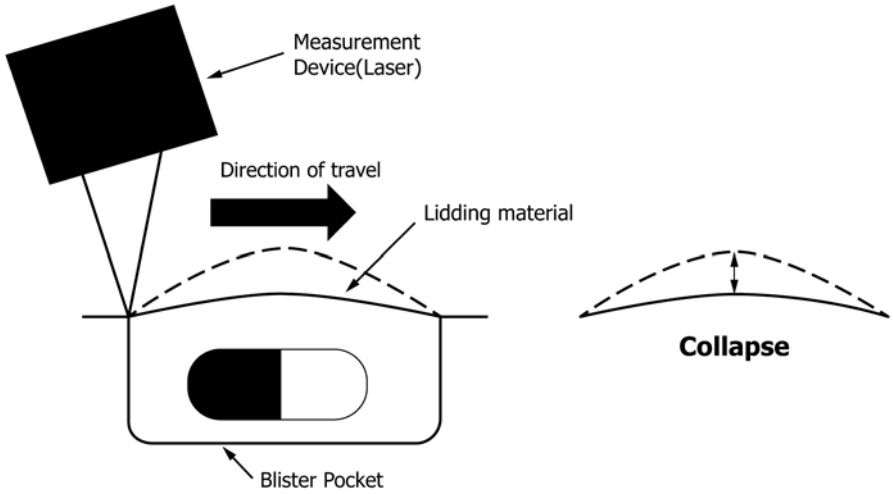


FIG. 3 Collapse

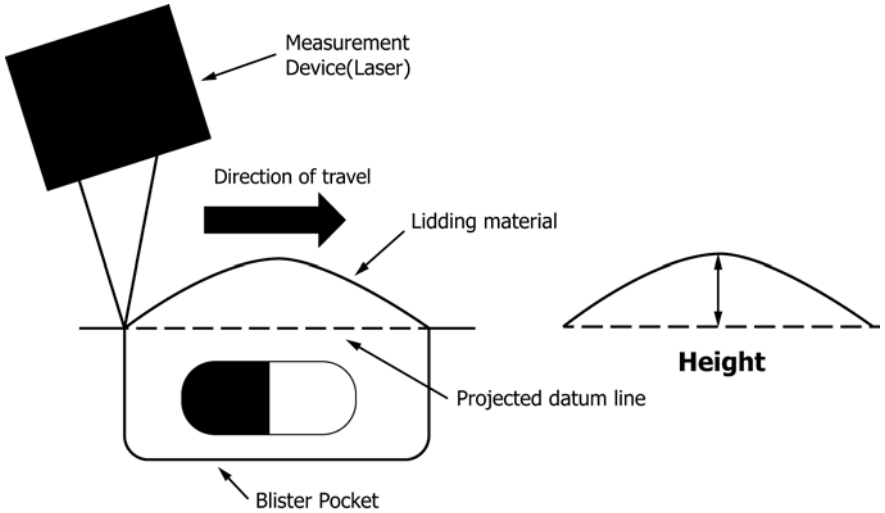


FIG. 4 Height

6. Apparatus

6.1 The leak testing instrumentation consists of a vacuum chamber and measurement device (see Fig. 5).

6.2 *Test Chamber*—The test chamber maintains the blister packs under vacuum, typically at levels between 30 - 60 kPa during the test cycle. It locates the lower and upper tooling,

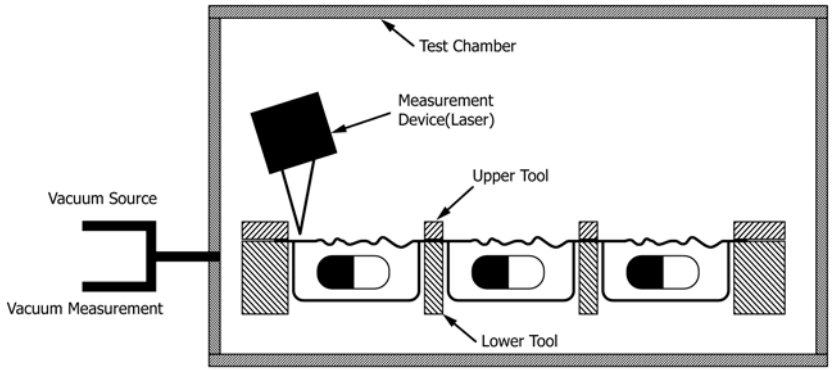


FIG. 5 Leak Testing Instrumentation

allowing the measurement device to accurately pinpoint the blister packs. The test chamber shall be of sufficient size to house the measurement device/devices and allow them to move between all the blister pocket positions.

6.3 *Measurement Device*—The measurement device moves over each pack scanning the surface of every pocket. The profile of the lidding material is measured with reference to a fixed datum. A typical measurement device is a red semiconductor laser with a resolution of 0.05 μm in the *z*-plane at a reference distance of 30 ± 5 mm.

6.4 *Lower Tool*—The lower tool accurately locates the blister packs for testing.

6.5 *Upper Tool*—The upper tool sandwiches the blister packs and ensures that they do not move under vacuum.

6.6 *Vacuum Source*—A suitable vacuum source is selected based on a target vacuum level and the time required to reach the vacuum target.

6.7 *Vacuum Measurement*—A suitable sensor is selected to monitor the vacuum level within the test chamber.

7. Hazards

7.1 As the test chamber is closed it may present a pinch hazard.

7.2 Standard precautions should be followed if using any laser-based measurement device.

8. Preparation of Apparatus

8.1 The test apparatus shall be started and made ready in accordance with the manufacturer's specifications. Assuming the vacuum is being provided by an air driven vacuum pump, utilities required for instrument operation include electrical power and a dry, non-lubricated air supply in accordance with the manufacturer's specifications. Other vacuum sources may be used.

8.2 A suitable set of tooling specific to the blister packs format is also required to ensure that the test samples are retained during the application of the vacuum within the chamber.

9. Calibration and Standardization

9.1 *Vacuum Calibration*—The machine vacuum measurement is calibrated using an external vacuum source and calibrated vacuum meter.

9.2 *Position and Height*—The profile measurement system is calibrated using a test tool that contains slip gauges of known height. The measurement tracking is also calibrated using a test tool with machined features at known *x-y* positions.

10. Procedure

10.1 Turn on instrumentation and check supply pressure.

10.2 Select and install appropriate tooling into test chamber.

10.3 Place test packaging into lower tooling for testing.

10.4 Select appropriate vacuum levels and holding times for leak testing the samples.

10.5 Scan blister pack surface, measuring the initial blister pocket profile.

10.6 Apply initial vacuum level and hold for the chosen set time and rescan the blister pockets.

10.7 Calculate *deflection* (difference in profile before and after vacuum) for each blister pocket. Any blister pockets with *deflection* values below the *pass* criteria are recorded as a *fail*.

10.8 Calculate *height* (difference in datum from sealed surface minus profile after vacuum) for each blister pocket. Any blister pockets with *height* values below the *pass* criteria are recorded as a *fail*.

10.9 If the test method calls for a second reduced vacuum level, the pressure should be increased to this level and the blister packs rescanned after a set time period.

10.10 *Collapse* values (difference in profile between initial and reduced vacuum levels) should be calculated for each blister pocket. Any blister pockets with *collapse* levels above the threshold criteria are recorded as *fails*.

10.11 Record the results, setting aside any failed blister packs for further evaluation where appropriate.

10.12 If a failed blister pack contains product that may contaminate the test chamber or system during the leak test, perform steps to eliminate contaminant from the system.

11. Report

11.1 The test report should include the following information:

11.1.1 A statement that the tests were conducted in accordance with this standard, noting any deviations from the specified test method.

11.1.2 The machine type, serial number, date of calibration, and date of testing.

11.1.3 Blister pack information, including material information, blister pocket size, and free head space (if known).

11.1.4 The specific test procedure used, including the vacuum level and hold times.

11.1.5 The acceptance criteria for *height*, *deflection*, and *collapse*.

11.1.6 *Pass/fail* results for each blister pocket tested and a copy of any software generated data sheets and/or reports produced during the testing.

12. Precision and Bias

NOTE 1—Refer to Table 1 for a summary of the pharmaceutical blister packages used to generate the precision and bias data presented. All of the test equipment used in the studies was manufactured by Sepha Ltd.

NOTE 2—The test results are expressed in qualitative terms (*pass/fail*) and the precision and bias data is presented in terms of percentages of blister pockets meeting the test criteria.

12.1 A study was conducted on three sites in order to ascertain the precision and bias of this test method. The results are shown in Table 2. The ability of the method to detect both 15 and 50 µm sized holes was evaluated using the *tablet* and *capsule* pack designs as described in Table 1. These tests were conducted at three locations, each using a separate instrument. For each of the two pack designs, 25 blister packs were laser drilled for each of the two hole sizes. An independent laboratory verified the holes in a sample of the blister packs by scanning electron microscopy. In addition, any blister packs containing holes which were not detected as leaking or any good blister packs incorrectly identified as leaking were inspected after testing by scanning electron microscopy. A hole was laser drilled in one blister pocket for each of the test blister packs in a random location with the remainder of the blister pockets remaining defect free. All blister pockets were tested. Three replicate tests were performed on each blister pack at each location. The same test blister packs were tested at each location.

TABLE 1 Detailed Specification of Blister Packs Used During Testing

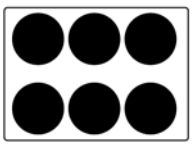
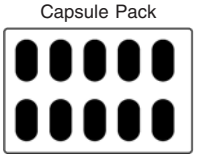
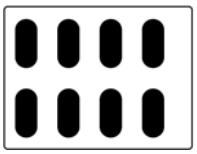
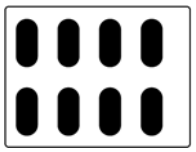
Blister Pack	Materials	Number of Blister Pockets	Blister Pack Size	Blister Pocket Size	Contents Size
Tablet Pack 	250 µm PVC 20 µm Aluminum lidding material	6	97 mm (L) × 70 mm (W)	27 mm (W) × 10 mm (D)	20 mm (W) × 8 mm (D) Standard Convex Tablet
Capsule Pack 	250 µm PVC 20 µm Aluminum lidding material	10	80 mm (L) × 53 mm (W)	18 mm (H) × 9 mm (W) × 6 mm (D)	Size 4 Capsule
Peelable Pack 	125 µm PVC/51µmPCTFE/125 µm PVC 23 µm White Polyester/ 20 µm Aluminum lidding material	8	96 mm (L) × 73 mm (W)	25 mm (H) × 11 mm (W) × 9 mm (D)	Size 0 Capsule
Paper Pack 	125 µm PVC/51 µmPCTFE/125 µm PVC Paper 45 g/m^2/ 25 µm Aluminum lidding material	8	96 mm (L) × 73 mm (W)	25 mm (H) × 11 mm (W) × 9 mm (D)	Size 0 Capsule

TABLE 2 Summary of Precision and Bias Test Results

NOTE 1—This table shows data after the removal of a number of defective incorrectly laser drilled holes.

Blister Pack	Defect Description	Number of Blister Pockets Tested	Total Number of Replicate Tests	Number Failed (Leaks Detected)	Number Passed (No Leaks Detected)	Percentage Accurate
Capsule (10 pockets)	No defect	450	4050	0	4050	100
	15 µm hole	25	225	225	0	100
	50 µm hole	24	216	216	0	100
Tablet (6 pockets)	No defect	235	2115	0	2115	100
	15 µm hole	23	207	173	7	97
	50 µm hole	23	207	207	0	100
Peelable (8 pockets)	No defect	525	2100	0	2100	100
	15 µm hole	25	100	100	0	100
	50 µm hole	25	100	100	0	100
	5 mm slit	25	100	100	0	100
Paper (8 pockets)	No defect	525	2100	2	2098	99.9
	15 µm hole	25	100	100	0	100
	50 µm hole	25	100	100	0	100
	5 mm slit	25	100	100	0	100

12.2 Further testing was conducted on blister packs sealed with a multi-layer peelable lidding material and a paper backed lidding material as shown in Table 1. In this study, blister packs contained 15 or 50µm laser drilled holes or 5mm long cut slit defects in the lidding material. 25 blister packs were prepared for each defect size with one pocket from each blister pack containing the defect in a random blister pocket location. The blister packs were repeat tested four times on a single machine.

13. Keywords

13.1 blister packing; flexible packaging; leak testing; package integrity; pass/fail criteria; pharmaceutical packaging; vacuum leak test