Designation: F3287 – 17ε1

Standard Test Method for Nondestructive Detection of Leaks in Packages by Mass Extraction Method[1,2]

This standard is issued under the fixed designation F3287; 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.

ε[1] NOTE—Editorial corrections were made in May 2018.

1. Scope

1.1 This method provides a nondestructive means to detect holes (leaks) in a variety of non-porous rigid and semi-rigid packages.

1.2 This test method detects package leaks by measuring the mass flow extracted from a package while the package is enclosed inside an evacuated test chamber. The test system is a closed system during the leakage measurement portion of the test cycle. The closed system includes a vacuum reservoir, Intelligent Molecular Flow Sensor (IMFS), and vacuum test chamber. Mass extracted from the test package into the vacuum test chamber flows to the vacuum reservoir through the IMFS to equalize the system. Mass flow rate from the vacuum chamber to the vacuum reservoir is measured by the IMFS. Based on the conservation of mass law, mass flow into the closed system is equal to the mass loss from the test package. The test system is capable of producing quantitative (variable data) or qualitative (pass/fail) results depending on the requirements.

1.2.1 Headspace gas leakage defects equivalent to a 1µm diameter glass micropipette (sharp edge defect) can be detected at a 95% confidence level.

1.2.2 Liquid leakage defects equivalent to a 1µm diameter glass micropipette can be detected at a 95% confidence level for glass vials and LDPE bottles. Liquid leakage defects equivalent to a 2 µm diameter glass micropipette can be detected for glass syringes.

1.3 *Units*—The values stated in SI units are to be regarded as standard. Pressure units are expressed as Pa, mbar, or Torr.

1.4 *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, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.5 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[3]

E177 Practice for Use of the Terms Precision and Bias in ASTM Test Methods

E691 Practice for Conducting an Interlaboratory Study to Determine the Precision of a Test Method

F17 Terminology Relating to Primary Barrier Packaging

2.2 *ISO Standard:*[4]

ISO/IEC 17025 General requirements for the competence of testing and calibration laboratories

3. Terminology

3.1 For terminology related to primary barrier packaging, see Terminology F17.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *baseline flow measurement, n*—measured flow rate for a negative control test package. Measured flow is largely attributed to characteristics of the package (material type, labels, etc.).

3.2.2 *blank master part, n*—a piece of metal tooling with similar volume and shape as the actual test package. This is used to represent a leak free package.

[1] This test method is under the jurisdiction of ASTM Committee F02 on Primary Barrier Packaging and is the direct responsibility of Subcommittee F02.40 on Package Integrity.

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[2] Mass Extraction is covered by patents (**1**, **2**). If you are aware of an alternative(s) to the patented item, please attach to your ballot return a description of the alternatives. All suggestions will be considered by the committee. If alternatives are identified, the committee shall reconsider whether the patented item is necessary. The committee, in making its decision, shall follow Regulation 15.

[3] 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.

[4] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

3.2.3 *chamber base, n*—lower portion of a vacuum test chamber that is connected to the mass extraction test instrument. Chamber base commonly includes an o-ring to seal the chamber lid onto the base. The chamber base also contains a nest to contain the test package. Nest configuration is dependent on test package features.

3.2.4 *chamber lid, n*—upper portion of a vacuum test chamber. The chamber lid commonly conforms to the portion of the test package that extends above the chamber base.

3.2.5 *container closure integrity test (CCIT), n*—a method to determine if a package is sealed to a specified level.

3.2.6 *glass micropipette, n*—a thin glass tube that includes a specific diameter within ±20% of specification at the tip of the capillary tube. Micropipettes are independently qualified by supplier. Flow paths of this nature are commonly designated as sharp edge (SE) holes. This can be used to represent a hole of a specific diameter when inserted into a package.

3.2.7 *gross leak (GL) check, n*—preliminary step in the leak detection process where chamber pressure is measured before the chamber is fully evacuated. This step is intended to detect major issues (e.g. missing cap, chamber lid not installed, missing part, etc.).

3.2.8 *intelligent molecular flow sensor (IMFS), n*—mass flow measurement sensor that is capable of operating in the transitional and molecular flow regimes measuring mass flow, pressure (vacuum) and temperature (**3**). The IMFS is independently calibrated against traceable standards per the requirements of ISO 17025.

3.2.9 *large leak check (LLC), n*—preliminary step in the leak detection process where the mass exiting the chamber is measured before the chamber is fully evacuated. This step is intended to detect leaks large enough to allow the test package to be evacuated as the vacuum test chamber is evacuated in preparation for the fine leak test. This step is also intended to detect liquid leakage or spillage early in the process to minimize system drying (moisture removal) requirements. Refer to Section 10 for additional details regarding the drying process. The size of defect that would be detected in this test step is largely dependent on target fine leak detection level.

3.2.10 *leak, n*—a hole, void, or defect in the wall or mated components of a package capable of passing aerosols (microorganisms or inert), liquid, or vapor from one side of the wall to the other. These can be passed under action of pressure and/or concentration differential across the wall and is independent of quantity of fluid flowing. Real life leaks are random and typically irregular shaped with given throat area (smallest cross section area) and length.

3.2.11 *leak artifact, n*—a test package that includes a manufactured defect. For this method, leak artifacts are packages that include a glass micropipette to simulate a package leak with a similar cross sectional area as real life leaks. The glass micropipette is encapsulated inside a syringe needle and inserted into the needle so its tip is near the needle sharp point as shown in Fig. 1. The metal needle provides mechanical protection to the fragile micropipette. Leak artifact flow rates were verified using airflow NIST traceable standards in compliance with the requirements of ISO 17025 to assure their integrity and size.

3.2.12 *leak test signature, n*—flow curve that displays the flow rate for the test package through the test cycle.

3.2.13 *mass extraction instrument, n*—complete instrument with automated test circuit, IMFS sensor, and controls to complete mass extraction testing (**3**).

3.2.14 *negative control, n*—intact (known good) test package.

3.2.15 *rigid packages, n*—test packages that maintain their shape with very minimal deflection under vacuum.

3.2.16 *semi-rigid packages, n*—test packages that deform under vacuum but return to original shape once vacuum is removed.

3.2.17 *verification orifice, n*—calibrated leak device built into the mass extraction instrument includes a small calibrated leak used for periodic test system challenges.

3.2.18 *water for injection (WFI), n*—water purified by distillation or a purification process that is equivalent or superior to distillation in the removal of chemicals and microorganisms.

4. Summary of Test Method

4.1 The test package is placed inside a vacuum test chamber and the vacuum test chamber evacuated. The test system includes a vacuum reservoir, IMFS, and vacuum test chamber. Fig. 2 illustrates the mass extraction test concept (**3**). Once the test system is evacuated to the appropriate level, the system is isolated from the vacuum source. Mass extracted from the test package into the vacuum test chamber through any leaks present in the package will flow to the vacuum reservoir. The IMFS measures mass flowing from the vacuum test chamber into the vacuum reservoir. The mass flow is proportional to the

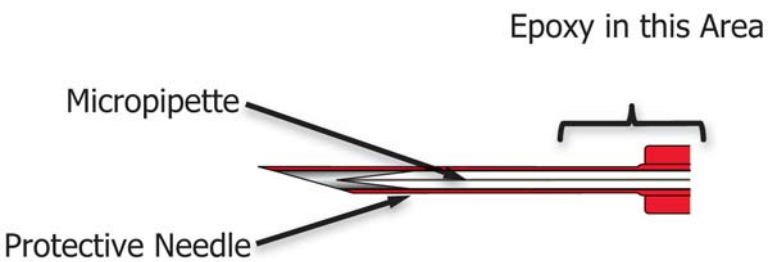

FIG. 1 Micropipette Epoxied Inside Protective Needle

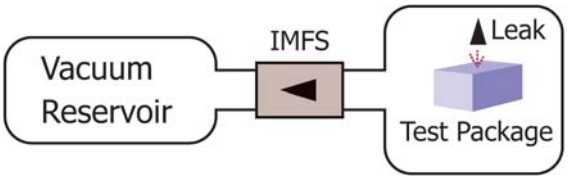

FIG. 2 Mass Extraction Test System Overview

defect geometry at the given differential pressure. The measured gas flow results from leaks from the headspace volume or liquid (e,g, water) leaks exposed to the vacuum inside the chamber. Since the vacuum pressure is lower than the boiling point of water at 20 ± 5 ºC, the liquid will boil resulting in liquid vapor and air gas flow mixture.

4.2 Test system sensitivity is dependent on IMFS full scale range, vacuum test chamber design, package material type, and test system set-up parameters. Test system set-up parameters can vary significantly based on required sensitivity, test package material type, test package volume (size), and amount of package deflection that occurs when vacuum is applied. Materials can release mass into the vacuum test chamber due to outgassing. The effects of outgassing on final mass flow rate can be minimized by lengthening the evacuation time before the final mass flow rate is measured or raising the vacuum level to a higher absolute pressure. In special cases (e.g. large volume flexible packaging or some label materials) test package preparation may be required to minimize package volatiles. In cases where a component can move when vacuum is applied (e.g. Syringe or Cartridge stoppers), it is important to design the vacuum test chamber to limit movement. Outward movement of components during the test cycle will change the volume inside the vacuum test chamber and can cause flow to move to the reservoir which could simulate a leaking package or false positive.

4.3 Test chamber and test parameters must be designed to detect large holes in packages (holes ≥ 70-100µm in diameter). This is particularly significant for dry products where the internal free volume inside the test package is evacuated. Large leak detection for liquid filled packages is important to minimize introduction of liquid into the test system. Proper chamber design and additional test steps are required prior to the fine leak test to detect the larger defects early in the evacuation process.

NOTE 1—A detailed description of the test steps, along with a sample test signature, are included in Annex A1. This additional information helps to clarify the actions taken prior to fine leak measurements and precautions taken in advance of fine leak measurement to ensure leaks of all sizes are detected.

5. Significance and Use

5.1 Leaks in medical, pharmaceutical, or food product packages can affect product quality and consumer safety. Such leaks can arise from imperfections in package material or between mated components designed to seal the package. Defects can allow unwanted gas (e.g. oxygen or water vapor), particulates, liquids, or microbiological contaminants into or out of the package. Package defect detection can be a critical part of ensuring product quality and consumer safety. Use of a physical CCI test method for sterile products can be used to assure the stability of the package sterility property during transportation and product shelf life.

5.2 Mass extraction is a useful non-destructive test method for testing a wide variety of packages. Package shape and dimensions that can be tested using mass extraction are essentially unlimited, as long as a vacuum test chamber can be designed and manufactured to accommodate the package.

5.3 This method produces quantitative flow measurement results that are useful in comparing package sealing properties, different batches of product, material properties, and combinations of process parameters.

5.4 Applications for mass extraction range from manually loaded and operated machines to automatic unattended work cells. This method can be applied for audit testing or 100% in-line testing.

NOTE 2—Leak test methods that rely on gas or vapor transport, such as mass extraction, are not able to detect defects if they become plugged by solid or nonvolatile matter. Plugging is possible by exposure to environmental contaminants. In some cases, the packaged product itself can clog defects. For example, leak paths may become blocked by suspended solids, gelatinous matter or dried-out solutions. Product clogging propensity is a function of the product formulation, defect size and geometry, and may be linked to product storage and handling conditions as well as the time allotted to defect exposure. An investigation into the impact of repeated test condition exposure on defect plugging is recommended if product-package units are to be subject to repeated leak testing. Clogging is a complex phenomenon that is not well characterized or understood. Care must be taken to ensure that any CCI test method based on gas or vapor transport through the leak path is appropriate for the intended product.

6. Apparatus

6.1 *Mass Extraction Leak Detection Apparatus*—Mass extraction apparatus includes a vacuum test chamber connected to a test instrument that includes an IMFS. The system also requires a vacuum reservoir, vacuum generation package (pump, mixing tank, and regulator), and dry gas vent. Fig. 3 includes a system photo and Fig. 4 includes a system overview showing the main components of a test system.

6.2 *Vacuum Test Chamber*—Vacuum test chambers typically consist of a chamber base and lid. The chamber base connects to the mass extraction instrument and contains an o-ring to seal the base to upper chamber. The chamber base also serves as a nest to locate the test package. The chamber lid tightly seals to the chamber base and conforms to the portion of the package that extends above the chamber base. It is critical to minimize free volume inside the chamber in order to optimize test time and maximize test system sensitivity. For this method, the vacuum test chamber free volume ranged from 60% to 107% of the test package volume. Fig. 5 illustrates 2 piece test chambers designed for testing glass vials and LDPE bottles.

6.2.1 *Complex Vacuum Test Chamber*—In cases where the test package includes components that could move under vacuum, the test setup must include features to restrict movement. In this case the vacuum test chamber includes tooling to restrict movement of the stopper. Fig. 6 illustrates a syringe chamber where the stopper movement is restricted to minimize movement.

Photograph supplied by Advanced Test Concepts, Inc. (ATC, Inc.).

FIG. 3 Mass Extraction System

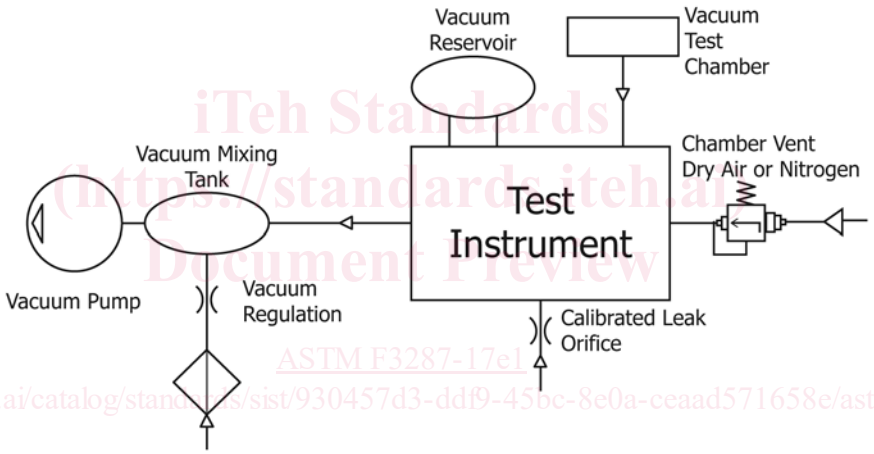

FIG. 4 Mass Extraction System Overview (1, 2)

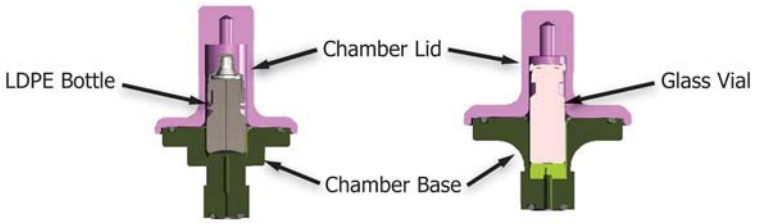

FIG. 5 Example Vacuum Test Chambers

6.3 *Mass Extraction Instrument*—The mass extraction instrument includes several valves required to automatically evacuate and isolate the test chamber, pressure sensors to monitor both system and test chamber pressure, and the IMFS to measure flow and temperature. These components are required to automatically complete the various test steps and checks outlined in Annex A1.

NOTE 3—IMFS full scale range and maximum operating pressure are configured for the application. Multiple IMFS configurations are available depending on the application requirements.

6.4 *Vacuum Generation System*—A high quality (capable of achieving a minimum ultimate vacuum of 10× lower than the desired vacuum level) vacuum pump is the main component in the vacuum generation system. Size and type of pump are determined by application, location where the system will be operated (cleanliness requirements), and required cycle rate. The vacuum level must be raised from the ultimate vacuum of

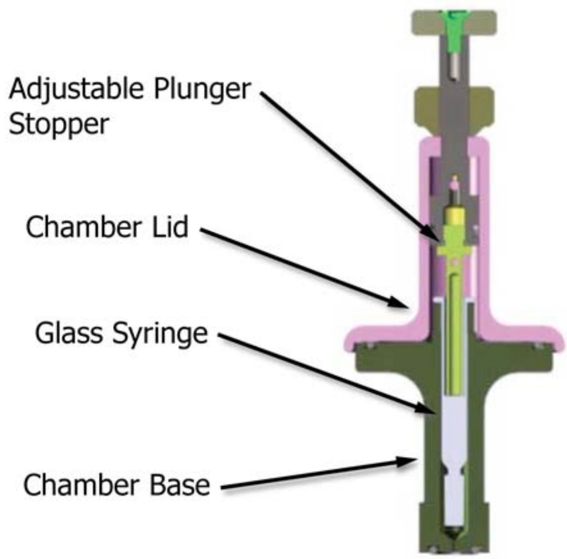

FIG. 6 Syringe Vacuum Test Chamber

the pump to the desired test pressure. This vacuum level is established by bleeding air into the system using a vacuum regulation device. Common tolerance for the vacuum level is ±66 Pa. However, vacuum level tolerance can vary significantly depending on application.

6.5 *Chamber Vent*—Venting the vacuum test chamber with clean dry gas is important for consistent long term operation. Venting the chamber with atmospheric air can introduce test result variation due to varying moisture content of the atmospheric air along with particulates. If the atmosphere around the system is well controlled, clean, and dry, it is possible to use atmospheric air to vent the vacuum test chamber.

7. Hazards

7.1 Manual operation of this equipment presents no hazards. In cases where mass extraction is integrated into an automated work cell and vacuum test chambers are opened and closed automatically, care must be taken to ensure that all pinch points are appropriately guarded.

8. Preparation of Apparatus

8.1 The apparatus must be started and made ready per the manufacturer's specifications. Utilities required for the instruments operation include 120/220VAC power and dry compressed air or gas at 551 kPa (80 psig) minimum.

8.2 A vacuum test chamber and/or volume fillers designed and manufactured for the test package is required.

9. Calibration and Standardization

9.1 The mass extraction instrument is initially calibrated by the manufacturer using traceable flow, pressure, and temperature standards according to ISO 17025 requirements. Repeat calibration frequency is user defined but is commonly completed annually. There are no requirements for daily, weekly, or monthly calibration before use.

9.2 The systems baseline leak tightness verification using the master blank part prior to use is recommended by the manufacturer, but is not required. This ensures that there are no significant system leaks and that the tooling has not been damaged since last use. Frequency of baseline verification checks should be defined by the user. The blank master part or master intact packages can be used to verify system performance after a failed test result.

9.3 Test parameters must be established and qualified for each package type along with corresponding vacuum test chamber prior to use. The master blank part or negative control packages can be used for development of test parameters. Test parameters are defined during the development process to achieve adequate differentiation (separation) between the master blank and known leak. The known leak is commonly achieved using the built in verification orifice or manufactured leak artifact.

9.4 The system includes a calibrated NIST traceable verification orifice that can be used in conjunction with the blank or negative control packages to simulate a gas leak. Gas flow detection sensitivity can be determined using the calibrated leak orifice. This built in verification orifice can be used to periodically challenge the system by completing a test cycle with the verification orifice included in the test circuit. This verification orifice typically represents the leak tightness required for the package being tested. The test cycle should fail when the verification orifice is included in the circuit.

9.5 System verification should be completed on a regular basis. Verification includes manually (or remotely through digital I/O) opening the calibrated leak orifice into the circuit, loading the blank master part or negative control packages, and performing a normal leak test cycle. The calibrated leak orifice should be turned off and test cycle run a second time. Results of these tests can be used to determine if the system is operating per manufacturer's specifications.

10. Procedure

10.1 *Initial Package Set-up:*

10.1.1 Prior to initiating leak test cycles, it is suggested that the instrument calibration date should be verified to ensure that the instruments calibration is valid.

10.1.2 Load appropriate test parameters for the desired test set-ups into the test instrument (see section 9.3). Verify that all parameters were properly programmed into the instrument.

10.1.3 Verify vacuum generation system operation to ensure vacuum level was within specified range as determined during parameter qualification.

10.1.4 Cycle the test instrument multiple times, typically 3-5 cycles, with the system isolated (capped without vacuum chamber) to ensure that the system is leak free within the manufacturer's recommendation. This step is not required for regular operation but can be applied as needed to ensure that the system is operating within specification.

10.1.5 Install the appropriate vacuum test chamber and volume filler (if applicable) for package being tested along with the blank master part. Complete a test cycle on the vacuum test chamber 5 to 10 times without exhausting between

test cycles to ensure that the tooling was installed properly, tooling was not damaged since last use, there are no system leaks, and to condition (remove surface moisture) the tooling under vacuum conditions.

10.1.5.1 Results for conditioning cycles must be under parameters established by the manufacturer when the tooling was qualified in order to proceed with CCIT cycles.

10.2 *Routine Testing:*

10.2.1 Load the test package into the chamber base and install the chamber lid.

10.2.2 Start the test cycle.

10.2.3 Record the test result. For cases of gross leak and large leak, variable fine leak results are not available. Fine leak results are not available since the test cycle is automatically stopped before the fine leak step of the test cycle.

NOTE 4—Unusual results can occur due to operator error (e.g., not installing chamber lid or test package properly) and can result in the system vacuum level becoming unstable. If this occurs, the blank should be loaded and test cycle run until results meet manufacturer's recommendations for the system.

NOTE 5—Test packages that rupture or include large defects may allow product to enter the vacuum test chamber. Vacuum test chambers are typically designed to prevent any liquid contamination from entering the test instrument. Filtration is also included to minimize the potential for dry product to enter the instrument. Any contamination must be removed from the vacuum test chamber per manufacturer's recommendations prior to running any additional test cycles. Liquid contamination will boil and dry out with no damage to the mass extraction instrument if performed per manufacturer's recommendations. Subsequent failed test results may occur if chamber is not thoroughly dried and all moisture removed. The test system is thoroughly dried once a test cycle can be completed using the blank master part with a result under the limit established by the manufacturer. Acceptable limits for a thoroughly dry system depend on test parameters, tooling design, and test instrumentation used for CCI test.

NOTE 6—Test chamber product decontamination may be required depending on product being tested and safety requirements.

10.2.4 Load another test package and repeat the sequence.

10.3 *System Shutdown:*

10.3.1 When the system will be idle for an extended period of time, it is beneficial to turn off the vacuum pump to reduce pump wear. Shutting down the system properly will minimize time required to prepare the system for next use. To properly shut down the system the following steps should be completed:

10.3.1.1 Complete a test cycle with the blank master part inside the vacuum test chamber. Do not vent the chamber after the test is complete.

10.3.1.2 Remove the compressed air supply from the system. This is commonly accomplished by actuating the manual pneumatic dump valve. This closes all of the air pilot valves and maintains vacuum inside the test circuit.

10.3.1.3 Turn off the vacuum pump.

11. Report

11.1 For regulated products, multiple critical process parameters should be recorded for each test cycle run. Data collection can be facilitated automatically using a qualified PC program connected to the instrument's Ethernet or RS232 communication port. Recommended data to be collected:

11.1.1 Operating vacuum level and tolerance expressed in mbar, Pa, or Torr.

11.1.2 *Test Cycle Step Timing and Limits*—For example, this could include: Pre-Evacuation1 Time, Gross Vacuum Limit, Pre-Evacuation2 Time, Evacuation1 Time, Stability1 Time, Large Leak Check Limit, Evacuation2 Time, Stability Time.

11.1.3 Mass Extraction Accept/Reject Limit expressed in µg/min to define allowable mass exiting the test package.

11.2 All deviations from the recommended procedure must be documented.

12. Precision and Bias

NOTE 7—Each individual test result did not produce a quantitative result. Test cycles that stopped in the initial test steps (see Annex A1 for a detailed description of test steps) were simply failed and produced a qualitative result. Test parameters can be optimized for target detection levels based on package specifications and requirements. Tables 1-4 include the qualitative e results for all tests. Tables 5-7 include quantitative results.

NOTE 8—Mass Extraction test instruments used in this Interlaboratory study were manufactured by Advanced Test Concepts, Inc. (ATC, Inc.), Indianapolis, Indiana, USA. Mass Extraction instruments are available in a wide range of configuration to meet various detection limits and test package configurations. Every instrument is not suitable for every application. Instruments full scale range is determined based on target sensitivity level and package properties.

12.1 The precision of this test method is based on an interlaboratory study ILS#1178 Nondestructive Detection of Leaks using Mass Extraction Method, conducted in 2015. Four laboratories tested 3 different package types. Each of the 4 laboratories used a different test instrument with the same measurement range (same part number). Instruments used for completion of ILS were in use from 2 to 6 years in each of the respective laboratories. For each package type, a sample set

TABLE 1 Gas Leak Detection Results—Glass Vial 2mL

NOTE 1—Liquid filled glass vials that included a 10µm micropipette were removed from the sample population due to liquid leakage into vacuum test chamber during CCIT.

Package Description	Number of Samples	Number of Replicate Tests	Number of Failed Tests (Defects Detected)	Number of Passed Tests (No Defects Detected)	Success Rate (% Accurate)
No Defect – Liquid Filled – Negative Control	10	120	0	120	100%
No Defect – Air Filled – Negative Control	10	120	0	120	100%
1 µm micropipette – Liquid Filled	3	36	36	0	100%
1 µm micropipette – Air Filled	3	36	36	0	100%
2 µm micropipette – Liquid Filled	3	36	36	0	100%
2 µm micropipette – Air Filled	3	36	36	0	100%
5 µm micropipette – Liquid Filled	3	36	36	0	100%
5 µm micropipette – Air Filled	3	36	36	0	100%
10 µm micropipette – Air Filled	3	36	36	0	100%