⟨1207.3⟩ PACKAGE SEAL QUALITY TEST TECHNOLOGIES

1. INTRODUCTION
2. CLOSURE APPLICATION AND REMOVAL TORQUE
3. PACKAGE BURST
4. PACKAGE SEAL STRENGTH
5. RESIDUAL SEAL FORCE
6. AIRBORNE ULTRASOUND

1. INTRODUCTION

The purpose of this chapter is to briefly summarize test methods useful for characterizing and monitoring package seal quality and to guide the reader in their selection and use. These methods are not leak tests but provide additional data regarding package seal characteristics that may affect package integrity and leakage.

"Package seal quality tests" are checks used to characterize and monitor the quality and consistency of a parameter related to the package seal, providing some assurance of the package's ability to maintain integrity. Seal quality tests ensure that seal attributes, package materials, package components, and/or the assembly process are consistently kept within established limits, thus further supporting package integrity. Seal quality tests differ from leak tests in that they provide no information relative to actual package integrity; thus, a package that meets the requirements of a seal quality test may still be defective and leak. For example, a flexible pouch package that passes a seal strength test may leak through a puncture in the pouch face. A bottle that meets closure application and removal torque tests may have a scratch on the bottle finish surface that allows product leakage. In contrast, a pouch or bottle that is poorly assembled could pass leak tests at the time of product manufacture, yet develop leaks later, before reaching the end user.

Therefore, seal quality tests and leak tests work together to ensure package integrity. The package seal quality tests described in this chapter were selected for inclusion on the basis of data in peer-reviewed scientific publications and/or data regarding recognized standard tests (e.g., precision and bias study results). Standard test methods (e.g., ASTM) are referenced where applicable (the reader is advised to utilize the most recent versions). In some cases, the scope of referenced standard test methods does not include the package types of the scope in *Package Integrity Evaluation—Sterile Products* ⟨1207⟩. All methods and literature references are cited to provide benchmark information useful for the application and use of pharmaceutical package seal quality test methods.

Unlike package leak tests, seal quality tests are qualified for use rather than being fully validated. Qualification includes a demonstration of instrument performance and in some cases proof of appropriate instrument set-up specific for the package to be tested.

Finally, this chapter is not intended to provide an exhaustive listing of all seal quality technologies that could be used. Nor is the use of a methodology cited meant to be compulsory. Other qualified tests that are not included in this chapter may be used, as appropriate.

2. CLOSURE APPLICATION AND REMOVAL TORQUE

The closure application torque test measures the force exerted during the application of a screw-thread cap onto a threaded container. Conversely, the closure removal torque test measures the force required to initiate screw-cap removal. The container–closure systems of some ophthalmic solution products are examples of sterile product packaging closed with screw-thread caps.

Cap application torque is kept within an optimum range to prevent leakage from loose caps and to preclude component distortion and compromised seals from over-torqued caps. Cap removal torque is less than application torque due to stress relaxation and closure "back off" that may occur as a function of time and other environmental variables. A properly designed and applied cap will retain sufficient sealing force until the package is opened at the time of use. Caps that back off excessively during shipping, storage, or distribution increase the risk of product leakage. For multiple-dose packages, cap design and application forces should be such that the end-user population may be able to open and reclose the package in a manner that properly preserves the pharmaceutical product.

Reproducibility of application/removal torque test results is improved when tests are performed using automatic instrumentation that applies and removes caps at uniform speeds, with fixtures to lock the bottle and cap into proper test position. Application and removal torque tests are described in several standard test methods that have been written to support various continuous-thread and child-resistant cap designs, including the ASTM methods referenced (*1–7*).

3. PACKAGE BURST

The package burst test is performed by inserting a pressure source into a test package and applying pressure until the package seal(s) burst open. Packages having seals that could be compromised when exposed to a net positive pressure force inside the package may be tested by this method. Such package types include flexible bags and pouches formed by heat-sealing processes.

The package burst strength test result (reported in pressure units) provides an indication of relative seal strength and evaluates the most likely location and mode of package failure when the package is exposed to a pressure differential. However, note that this test method cannot provide a measure of package seal uniformity or overall package integrity.

Package burst tests are described in ASTM F2054 (*8*) and ASTM F1140 (*9*) (Test method A). Method ASTM F2054 uses a restraining plate to limit package expansion during inflation. A restraining plate ensures that the stress is uniformly applied to all seal areas, allowing for identification of the weakest point along the seal. Additional factors can influence the test results, including package inflation rate, tooling dimensions (including gap height), and pressure-sensing mechanisms.

Method ASTM F1140 uses no restraining plate; therefore, this approach provides a snapshot of package performance when challenged with differential pressures in a typical sterilization cycle or distribution environment, for example. However, without restraining plates, stress applied to the package is highest at the middle of the package where the package inflates to the greatest diameter; therefore, the weakest area of the seal may not be identified by this approach. Package inflation rate, as well as pressure-sensing mechanisms and their detection limits, can influence test results.

4. PACKAGE SEAL STRENGTH

The package seal strength test, commonly known as the peel test, measures the force required to peel apart two bonded surfaces. This test is applicable for testing seals between two bonded, flexible surfaces (e.g., a pouch or bag) or between a flexible material and a rigid material (e.g., a lidded tray). Force results provide a measure of seal strength between the bonded surfaces. Maximum seal force, as well as average force to open the seal, may be determined with this method. The results are also useful for monitoring the consistency of package assembly.

The test is performed using a universal stress-strain instrument set to extension force mode, with special tooling for correctly positioning and holding the test sample. The seal strength test is described in ASTM F88 (*10*). Test results are affected by the peel test fixture design, the peel angle, the pull direction, pull speed, and properties of the test sample itself.

5. RESIDUAL SEAL FORCE

The residual seal force (RSF) test provides an indirect measure of the compressive force exerted by an elastomeric closure onto a parenteral vial finish after package assembly (capping). RSF tests can be performed on glass or plastic vial packages of all dimensions. A consistent and sufficiently significant RSF value provides a useful indicator of capping process consistency. RSF is linearly related to closure compression: more tightly capped vials yield higher RSF values.

The RSF test is performed using a universal stress-strain instrument, set to compression force mode, and a metal tool (called a cap anvil) designed to fit on top of the sealed vial package. A constant rate of compressive strain is exerted onto the anvil, which rests on top of the vial package, yielding a typical plot of stress as a function of time (or compressive distance). The point in the stress-response curve immediately before the terminal slope change corresponds to the capped closure’s RSF, reported in either newtons or pound-force units. RSF tests are nondestructive in terms of package integrity. Test results are influenced by cap anvil tooling design, test compression rate, closure viscoelastic properties, closure dimensions, and the inclusion of an aluminum seal plastic top (more reproducible results are possible if plastic tops are removed before testing). Research articles describing the development and application of this method are referenced (*11–14*).

6. AIRBORNE ULTRASOUND

The airborne ultrasound test checks seal quality by passing an ultrasound signal through the sealed area of a package or item. The signal strength transmitted through the package seal under test is compared to that previously established for so-called good package seals. Poorly sealed areas will not transmit as much ultrasonic energy as properly sealed areas.

The types of package seals that can be tested using airborne ultrasound include flexible pouch seals and rigid tray seals made of metallic or plastic laminates. This technology can be used to check for the presence and location of package seal defects such as an incomplete seal, a channel, a wrinkle, or extraneous material inclusion, as well as for package seal bond weakness. The method may be used off-line to perform an *x–y* coordinate scan of a seal area, or it may be used to linearly scan seals during on-line manufacturing processes. Airborne ultrasound is a noncontact testing technology that requires no package preparation and no coupling media, such as a liquid or gel, to propagate sound; thus, it is nondestructive to the package under test.

The airborne ultrasound method is described in ASTM F3004 (*15*). The ASTM method test system is composed of a transducer that provides an ultrasonic signal, a means of holding/transporting the item under test within an air gap between the two transducers, and the detection transducer, which captures the intensity of the signal that passed through the air gap and the item under test. The capability of airborne ultrasound to detect specific package seal quality problems will vary on the basis of package material of construction, seal structure (e.g., smooth versus textured surface), scanning speed, and scanning signal strength.

REFERENCES

1. ASTM D2063/D2063M. Standard test methods for measurement of torque retention for packages with continuous thread closures using non-automated (manual) torque testing equipment. West Conshohocken, PA: ASTM International; 2012.
2. ASTM D3198. Standard test method for application and removal torque of threaded or lug-style closures. West Conshohocken, PA: ASTM International; 2007.
3. ASTM D3469. Standard test methods for measurement of vertical downward forces to disengage type IIA lug-style child-resistant closures. West Conshohocken, PA: ASTM International; 2007.
4. ASTM D3470. Standard test method for measurement of removal lug strippage of type IIA child-resistant closures. West Conshohocken, PA: ASTM International; 2007.
5. ASTM D3472. Standard test method for reverse-ratchet torque of type IA child-resistant closures. West Conshohocken, PA: ASTM International; 2007.

6. ASTM D3810. Standard test method for minimum application torque of type IA child-resistant closures. West Conshohocken, PA: ASTM International; 2007.
7. ASTM D3968. Standard test method for monitoring of rotational torque of type IIIA child-resistant closures. West Conshohocken, PA: ASTM International; 2007.
8. ASTM F2054/F2054M. Standard test method for burst testing of flexible package seals using internal air pressurization within restraining plates. West Conshohocken, PA: ASTM International; 2014.
9. ASTM F1140/F1140M. Standard test methods for internal pressurization failure resistance of unrestrained packages. West Conshohocken, PA: ASTM International; 2013.
10. ASTM F88/F88M. Standard test method for seal strength of flexible barrier materials. West Conshohocken, PA: ASTM International; 2009.
11. Ludwig JD, Nolan PD, Davis CW. Automated method for determining Instron residual seal force of glass vial/rubber stopper closure systems. *PDA J Pharm Sci Technol*. 1993;47(5):211–253.
12. Ludwig JD, Davis CW. Automated method for determining Instron residual seal force of glass vial/rubber closure systems. Part II. 13 mm vials. *PDA J Pharm Sci Technol*. 1995;49(5):253–256.
13. Morton DK, Lordi NG. Residual seal force measurement of parenteral vials. I. Methodology. *J Parenteral Sci Technol.* 1988;42(1):23–29.
14. Morton DK, Lordi NG. Residual seal force measurement of parenteral vials. II. Elastomer evaluation. *J Parenteral Sci Technol.* 1988;42(2):57–61.
15. ASTM F3004. Standard test method for evaluation of seal quality and integrity using airborne ultrasound. West Conshohocken, PA: ASTM International; 2013.