

# **STRENGTH AND INTEGRITY – The Basics of Medical Package Testing**

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## **Chapter 1: An Overview**

The release of a terminally sterilized medical device or product to the marketplace is the culmination of monumental design and development effort. Efficient, effective and safe usage characteristics are critical. Once the product has met its own design criteria, the package in which it is enclosed must form a single functional entity with the product that performs to the highest level in the end user's application. Package testing enables validation of the packaging design and process, and provides documentation of ongoing conformance to specifications. This will in turn assure the maintenance of the sterile barrier around the product, protecting it from contamination.

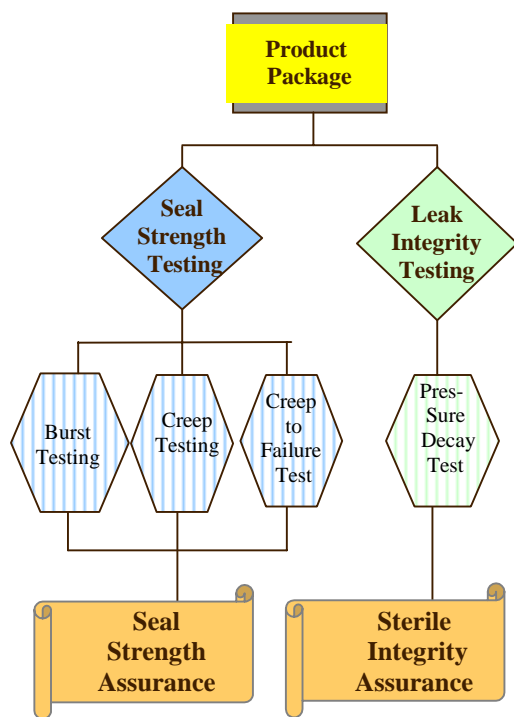
Terminally sterilized medical product packaging occurs in a variety of forms. Product may be contained in pouches of various configurations constructed of porous or non-porous material, rigid thermoformed trays with Tyvek® or film lids, bottles with induction welded seals, or blister packs, all needing verification that their sterile barrier characteristics are not compromised. In addition, under certain circumstances, items once considered single-use devices may be reused; the FDA has indicated that it will regulate reprocessors of SUDs in the same manner as original device manufacturers. As the packaging design engineer or project manager for a medical device or product, it is incumbent on you to obtain FDA approval of the protocol you used in validating your packaging system.

Guidance in determining your course of action can be found in ANSI/AAMI/ISO 11607-1997, *Packaging for Terminally Sterilized Medical Devices*. This document is an international standard providing a guideline for the designing, processing and testing of final product packages through which you can develop the documentation necessary to validate your package design and its conformance to specifications. The FDA considers ISO 11607 to be the paradigm for validation protocol for medical device packaging.

It is helpful to define several terms before proceeding with our discussion. Based on usage suggested in AAMI TIR No. 22-1998 (relative to ISO11607), the combined test and inspection results for a requirement provide *verification* that specific requirements have been met at a point in time. A combination of verifications for a capability assessment of how well equipment, a process, or a product can perform at a point in time provides a *qualification*. The combination of appropriate qualifications and objective evidence that these processes consistently produce product meeting predetermined specifications constitutes *validation*. In other words, validation implies that design, equipment, processes and materials are all working together to provide

consistently acceptable product. According to ISO11607, the validation process mandates documentary evidence obtained by calibrated instruments that your equipment can and does deliver results within specified tolerances under established operating conditions.

The package validation protocol must be approached in stages, each of which becomes an issue when designing your package test systems. The first consideration involves the selection and qualification of the materials to be used in the package. Depending upon the application, specific performance requirements are considered essential for sterile barrier packaging materials. For example, a package with peelable seals, in addition to having minimum physical properties such as tensile strength, porosity and burst strength, must demonstrate a minimum specified seal strength (4.1.5.c). Formed packages have additional requirements for specifications for seal width, burst and/or seal strength (4.1.6.2), and packages suitable for sterilization must conform to tolerances appropriate to the sterilization method utilized (4.2.1.1.4). Once your package has been subjected to a formal material qualification, objective evidence is needed that your package forming/sealing process consistently produces results meeting specifications, and the “Golden Rule” of all testing – if you can’t measure it, you can’t control it – applies here. To qualify your manufacturing process, it is necessary that verifications include the establishment of upper and lower processing limits, that valid test methods for quality attributes (such as seal strength) are in place, and that procedures have been established to ensure process control. These verifications are obtained through careful, well-designed package testing procedures.



The objective of package testing is twofold: first, to ensure the integrity of the sealed package, and second, to assure that no weaknesses in the sealed areas of the package permit leaks to develop during sterilization, normal handling, transportation and storage. Terminally sterilized medical packaging must provide a microbial barrier between the medical device and the external environment, and this barrier must be maintained against physical, chemical or microbial challenges. To assure that the package performs adequately, determination must be made that the sterile package is able to maintain the integrity of both the seals and the materials under stress. This implies, and ISO11607 confirms, that a validatable package testing system must include both *package integrity testing* and *seal strength testing*, two complementary but very different procedures. **Package** integrity is defined as the “unimpaired physical condition of a final package” (3.12). This attribute may be thought of as a “leak test”

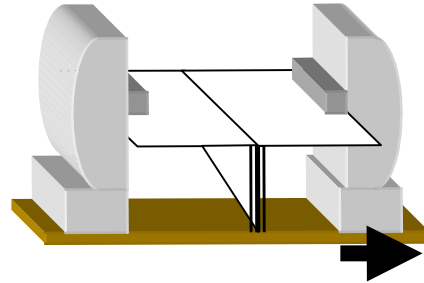
of the package – is there a failure in the materials or process which allows contamination to enter? Seal strength testing, on the other hand, measures an attribute of the seal, which is designed to ensure that the seal presents a microbial barrier to at least the same extent as the rest of the packaging. Seal Strength can also be required to assure that a proper entry method is maintained; for example, peelable seals for sterile presentation in the operating field.

**Seal Strength Testing** evaluates the mechanical strength of the seal. This seal attribute will assure proper bonding to maintain **package** integrity throughout the life of the package. The Seal Strength also provides assurance of control of the “peelable” characteristic of the package.

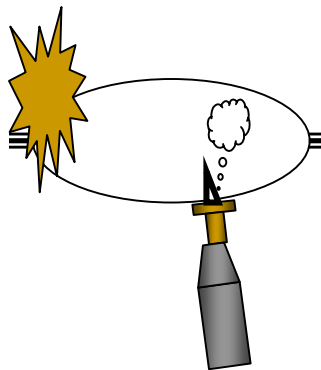
Seal  
Strength  
Testing

ISO-11607 refers to two methods which may be used to determine seal strength, tensile strength testing and burst or creep pressure (inflation) testing.

*Tensile Seal Strength Testing (ASTM F88)* uses a defined width sample of a package perimeter seal. A moving jaw pulls the sample apart at a constant speed while measuring the resistance force during the seal separation. The tensile test is particularly suited to peelable packages. A significant advantage to this test is its sensitivity, and a disadvantage is that in the majority of cases a perimeter seal is sampled only at several locations and a total package seal strength measure is not obtained.



*Inflation Seal Strength Testing (ASTM F1140 and F2054)* includes burst, creep and creep-to-failure testing. Burst testing pressurizes the entire package and captures the peak rupture pressure. This test provides a whole-package minimum seal strength and also indicates the weakest seal area, and is equally applicable to peelable and non-peelable seals. In a Creep test, the package is pressurized to a predetermined level (less than that required to burst the package) and held over a defined time period, resulting in a pass/fail attribute test result; in the Creep to Failure test the creep pressure is held until the seal fails. The variable here is the time to failure, a variable that like the burst pressure can be quantified and used to monitor the process of seal manufacture.



Flexible packages under pressure will deform and transmit stress to the seal in addition to the pressure forces. These added stresses may affect the location of seal rupture. Restraining plates counteract these wall stresses, leaving only the pressure forces around the seal perimeter (ASTM 2054).

Package Integrity Testing involves physical testing of the total package with the goal of ascertaining that the package will protect the contents from damage and maintain sterile package integrity (6.4). ISO-11607 indicates the use of microbial challenge tests to confirm the ability of the package to prevent the ingress of microorganisms. Examples of these tests include materials tests and whole package biological aerosol challenge tests. Although in fairly common usage, microbial challenge tests are not always the most appropriate test of package integrity. The HIMA Study published in *MD&DI (August/ Sept 1995)* indicates that microbial challenge tests are not reliable measures of

Package  
Integrity  
Testing

whole package integrity and that physical test methods reliably find defects when properly applied. ISO-11607 indicates as well that validated physical test methods are acceptable for determining microbial barrier properties (4.2.3.3.2). Examples of physical test methods reviewed in ISO 11607 include Internal Pressure Testing (bubble test), Dye Penetration (a visual test), Gas Sensing (trace gas pressurization) and vacuum leak tests (blue dye test).

The FDA has accepted certain test methods produced by industry consensus organizations as being valid. No further validation of the test method is required, a project time saver. The FDA Consensus List of physical test methods provides the easiest approach for the design engineer, in that the recommended tests do not necessarily need to be re-validated (see Table 1).

Table 1 FDA Consensus List of Physical Test Methods	
<i>ASTM D3078</i>	Standard Test Method for Determination of Leaks in Flexible Packaging by Bubble Emission
<i>ASTM F1886</i>	Standard Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection
<i>ASTM F1929</i>	Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration
<i>ASTM F1585</i>	Standard Guide for Integrity Testing of Porous Barrier Medical Packages
<i>ASTM F1608</i>	Standard Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method)

When considering whole-package physical integrity tests, the engineer must consider material issues, package design, and the attributes of the enclosed medical device. Of primary importance is whether the barrier materials are in whole or in part porous. Another issue is whether a destructive or non-destructive test is more appropriate for your package. More mundane but equally important is your budget for test equipment. There are a number of industry-available

methods tailored to the answers to these questions. These methods vary in sensitivity and applicability as well as cost, but because they are not currently on the FDA Consensus List these test methods need to be validated for your particular application. A discussion of these methods will follow in a subsequent article.

Shelf life testing (sterile package integrity maintenance) is a final consideration for the test designer. Once your package has proved to be acceptable in providing a sterile barrier for your medical device, it is essential that your materials and seals do not deteriorate over time or become weakened by normal transport and storage stresses. According to ISO-11607, the same functional tests you have put in place – both seal strength tests and package integrity tests - can be used to evaluate the package’s ability to maintain sterile package integrity over time (6.4.3). Accelerated aging tests may be used, but only in conjunction with real-time testing.

Assurance that your package will provide an effective, consistent sterile barrier for your medical device requires a well-designed, thoroughly documented test protocol evaluating **both seal strength and package integrity testing**. ISO-11607 provides a guideline, but the tailoring of your testing program to your particular product and package requires understanding of your package and of the way various seal and package tests function. In the two chapters to follow,

we will look closely at both Seal Strength Testing and Package Integrity Testing. Various test methods will be discussed in great detail, including their applicability to particular packaging materials, package configurations and materials. We will also look closely at fixturing designed to adapt certain test methods to your product, including restraining plates, methods of access to sealed packages, and techniques to test seal strength of pouches before they are filled and sealed.

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# STRENGTH AND INTEGRITY – The Basics of Medical Package Testing

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## Chapter 2: Inflation Seal Strength Testing

The objective of package testing for medical packages is twofold: first, to ensure the integrity of the sealed package, and second, to assure that no weaknesses in the sealed areas of the package permit leaks to develop during sterilization, normal handling, transportation and storage. Testing of a medical package must yield a comprehensive view of its ability to provide and maintain a sterile barrier around the medical device or product. According to ANSI/AAMI/ISO11607-1997 *Packaging for terminally sterilized medical devices*, both seal strength testing and package integrity testing are needed in order to properly validate your design and document your conformance to specifications. In this article we will look closely at seal strength testing.

Seal strength testing evaluates the mechanical strength of the seal, assuring proper bonding to maintain **package integrity** throughout the life of the package. Package integrity implies the maintenance of the sterile barrier property of the package. It is important to understand that *seal strength* and *package integrity* are distinctly separate objectives of the package testing process.

Seal strength is a package attribute; data acquired can be used to validate the package design as adequate for maintenance of integrity, to monitor process performance, and to confirm shelf life performance. The seal strength also provides assurance of control of the “peelable” characteristic of the package. There are two basic types of seal strength testing addressed in ISO-11607: tensile strength testing and burst or creep (inflation) testing.

Tensile seal strength testing (ASTM F88) uses a defined width sample (25.4mm) of the package seal perimeter. A jaw moving at a defined constant rate 10 to 12 in/min. pulls the seal apart while measuring the resistance force during seal separation. A typical seal strength plot is shown in Figure 1.

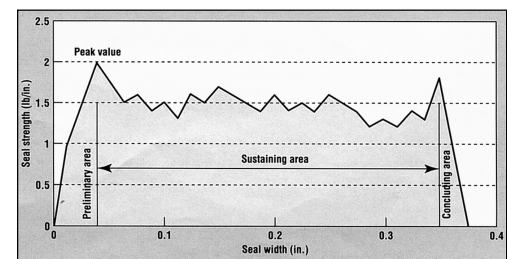


Figure 1: Typical tensile strength test plot

This test is particularly applicable to peelable medical package seals. It has the advantage of determining the force required by the end user to open a peelable package as well as providing force data that can be used in validation and control of the sealing process. Interpretation of the tensile seal strength result and plot is an important factor in reporting results. The resultant plot may show a higher peak force on the initiation of the test followed by a relatively constant force region during the peel apart of the seal and may be concluded with another higher peak. It is vital to the test result interpretation that the test report include the region of measurement; that is, peak initial force, sustaining region force or average energy (area under the curve). More help in interpreting the results can be found in ASTM F-88.

Another important reporting factor is the configuration of the sample support. Samples may be run with a free or supported seal, called a tail (see Figure 2). Both methods are acceptable but it is important to note



that the stress/ strain curves or results are NOT equivalent. In the “free tail” method, the angle of peel is constantly varying from 90 degrees to greater than 90 degrees. In the “supported tail”, the tail is restrained by the use of a fixture to keep the angle of peel at 180 degrees. The force result will vary depending on the support condition. Test results cannot be compared for different support conditions.

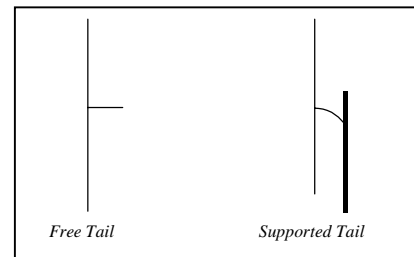


Figure 2: “Free” vs. “Supported” Tail Tensile Test Design

The tensile seal strength test is a valuable testing tool for seal evaluation. Its limitations are that only single sections of a seal are evaluated at one time, thus not providing information on whole package integrity and the process of testing is relatively slow for process control considerations. Its strengths are specific force results for peelable packages and wide usage within the industry.

*Inflation Seal Strength Testing (ASTM F1140 and F2054)*, including burst, creep and creep-to-failure testing, requires pressurizing the entire package and measuring the peak rupture pressure (burst test) or the time to failure at a constantly held pressure (creep and creep-to-failure test). These tests provide a whole-package minimum seal strength and are equally applicable to peelable and non-peelable seals. Inflation tests are applicable to most package forms such as pouches, header bags, lidded trays, flexible or rigid blisters and laminated or rolled tubes.

Although no universal mathematical relationship has been defined between inflation and tensile seal strength tests, research has been done on pouch forms that establishes a good correlation between restrained plate inflation testing – discussed later in this article – and tensile testing in locating the minimum seal strength area. (Franks, Stephen H. and Donald S. Barcan. “Examining the Relationship of Tensile and Inflation Seal Strength Tests in Medical Pouches”. © 1999, Donbar Industries, Inc. & TM Electronics, Inc.).

### Burst Test

Whole package inflation tests are categorized as *burst tests*, *creep tests* or *creep-to-failure tests* (ASTM F1140 or F2054). To perform a burst test, a package is inflated at a uniform rate until the seal separates at the point of greatest weakness. The burst test is a peak inflation pressure test. It is a variable test; the variable is the back pressure inside the package at the instant of seal rupture. Figure 3 is a graphic plot of a burst test provided by the TM Electronics BT-1000 Package Tester, showing the characteristic burst curve. In this illustration, the tested part burst at a pressure of 176.0 In H<sub>2</sub>O. The burst pressure result is a variable statistic that can be utilized to document process development and process control through the use of tools such as upper and lower control limits.

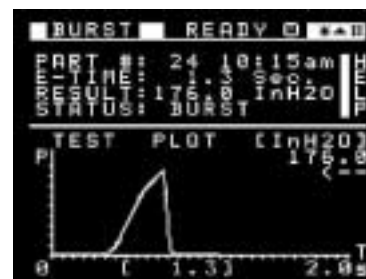


Figure 3: Burst Test Graph

In the burst test, air is introduced into the package at a predetermined pressure and flow rate (see Figure 4). Control of inflation rate is important in a burst test to ensure consistent conditions for the test method, similar to the tensile test method. The porosity (or lack thereof) of the package material determines the inflation rate for the burst test. Because air escapes through the walls of a porous package during inflation, the flow rate must be increased to compensate for the lost air through the walls and create the back pressure in the porous package. This pressure creates the force to rupture the seal.

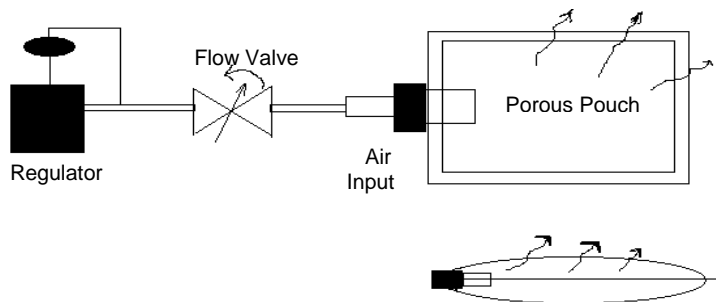


Figure 4 – where does inflation pressure come from?

Limitations of the burst test are that package characteristics will vary the resultant value. For example, the character of the seal itself is a factor; peelable seals will part under a lower pressure than the non-peelable seals found in formed packages. The size of the package will influence the resultant value; burst values of a large package will be lower than that of a smaller package. Unrestrained packages may have material failures before the seal

fails. These issues are not a factor when testing a single style package with consistent methodology and are offset by the speed of the test, which provides access to process data in seconds. The burst test does not require sample preparation and can be run with minimum operator training.

### Whole Package Creep Tests

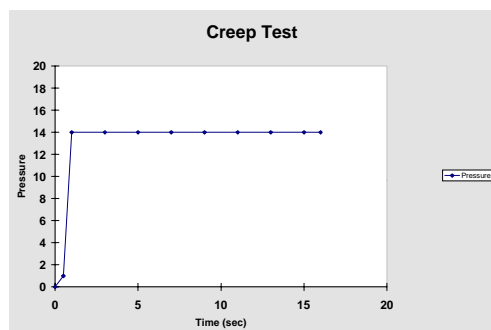


Figure 5: Typical Creep Test Plot

The Creep Test is a second general type of whole package inflation seal strength test. In the Creep Test, a whole package is inflated to a constant pressure, which is then held for a specified time, resulting in a pass/fail result (see Figure 5). Early users of the method for peelable seals used the test as an analogy for the pressure difference on the seals seen in the ETO sterilization and air transport cycles. The Creep test provides a test for slow shear of the adhesive bond similar to a dead weight hanging on the seal. It is important to first determine the burst strength of the package; a suggested

starting pressure for peelable seals in ASTM F1140 is to begin evaluating your seal with a creep pressure that is about

80% of the burst value. Different seal adhesive systems may require a lower creep test pressure to be effective, for example, pressure sensitive adhesives. Inflation rate of the test is not critical as long as the initial fill is not so fast to shock the seal or too slow to cause an effectively longer test time.

Shortcomings of the Creep Test include the need for the operator to visually examine the seal at the end of the test to declare the amount of seal peel for process control and the lack of a variable statistic upon which to perform process control analysis.

The Creep-to-failure Test (CTF) is a variation on the Creep Test that addresses these weaknesses. In the Creep-to-failure Test, the test pressure on the inflated package is held until the seal actually fails, yielding an end point value (a variable statistic), *time to failure*, and pinpointing the area of greatest weakness in the seal (ASTM F1140 method b2). Time to failure can then be used in SPC or SQC methods.



To achieve sensitive, repeatable results using both burst and creep inflation tests, test equipment must be used that takes into consideration the configuration of the package. Completely sealed packages need an access probe to inflate the package. This probe may require reinforcement to prevent material splitting at the entry point. Open pouches (sealed on only three sides) are sealed with a mechanical clamp to pressurize the three formed pouch seals. Figure 6 illustrates one method of closing an open package for seal strength testing as well as a device designed to provide reinforced and a leak-tight air path into a completely sealed package.

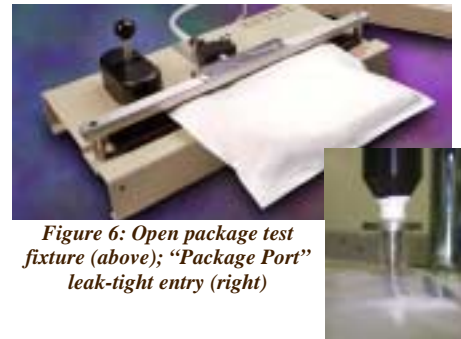


Figure 6: Open package test fixture (above); "Package Port" leak-tight entry (right)

Inflation seal strength testing on unrestrained packages, ASTM F1140, provides a fast and effective method of evaluating package seal strength. A shortcoming of this method is that there are no specific standards for a package's inflation seal strength, since the seal strength values are relative to the package size, geometry, materials and bonding agents, although tests have proven over time to provide consistent process data on a package that is tested under consistent, repeatable conditions. In addition, shortcomings of the unrestrained method are recognized for geometry effects of the package on the interpretation of test results. For example, pouches with a long side seal will generally fail on the long seal unless a heater failure has occurred on the shorter seal or chevron. Unsupported tray lid seals may fail at points only relative to their geometry. Very flexible package materials may deform with pressurization to an extent that makes seal testing difficult. To address these problems, it may be advisable to use restraining plates for your inflation testing.

#### *Restrained Package Testing (ASTM 2054)*

So far we have discussed seal strength testing of packages unrestrained in any axis (ASTM F1140). *Restrained package testing* is a refinement that has several advantages: it has been shown in pouches to define the minimum seal strength area more consistently, provides more consistent loading on the package seal, and incidentally correlates well with tensile seal strength tests in defining the minimum seal strength area.

The geometry of the package under test affects the distribution of internal pressure forces on the package surface and seals. A pouch-form package unrestrained in any axis exhibits circumferential hoop stress when internal pressure is applied (Figure 7a). When the package is restrained, the load application is distributed directly on the seal area, and, because material stretching and deformation is minimized, the test forces are more uniformly applied (Figures 7b and 7c). In addition, package restraint has a direct relationship to burst pressures: the wider the gap between restraining plates, the lower the average burst pressure, with unrestrained packages yielding the lowest burst pressure of all (figure

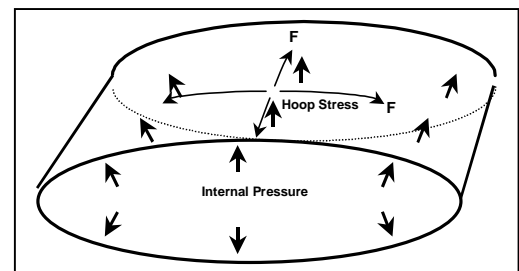


Figure 7a: Circumferential Hoop Stress

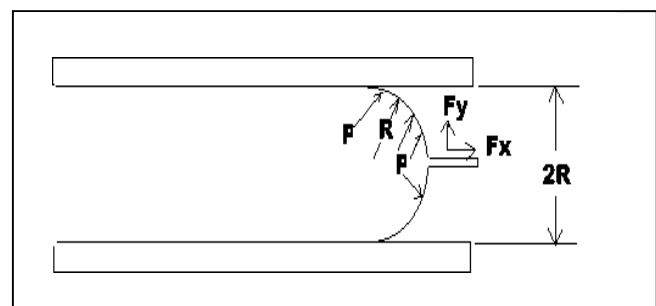


Figure 7b: Restrained plate test forces (bags)

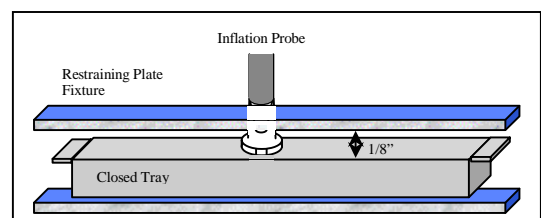


Figure 7c: Restrained plate test forces (trays)

7d). The most important factor in the interpretation of results is that all conditions in the package test method are consistent. One must not compare results of different packages or different test conditions on the package, such as restraining plate gap, when analyzing data. Establish a set of test conditions for each package and reproduce those conditions consistently.

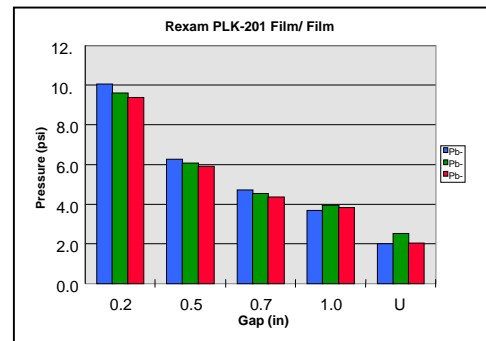


Figure 7d: Plot of Burst Pressure vs. Gap

Figure 8 illustrates a restrained package fixture. Use of package restraints must be approached with caution; because of pressures exerted on the plates, extreme care must be taken that fixtures are designed to withstand the forces applied by the inflated package (Franks, Stephen. “Calculating Factors of Safety for Package Burst and Creep Test Fixtures”. *Medical Device & Diagnostic Industry*, June, 1998).

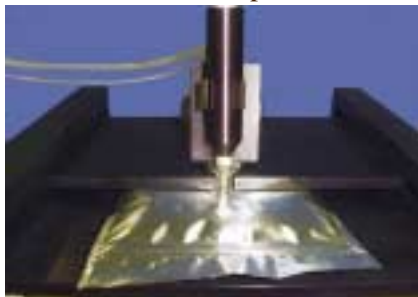


Figure 8: Pouch in restraining fixture

Inflation seal strength test results provide an excellent tool for process control. Inflation Burst test results, creep-to-failure and tensile data are all amenable for use in control charts, and provide quantitative data required by ISO-11607 for package validation. Furthermore, ASTM test methods ASTM F88, Standard Test Method for Seal Strength of Flexible Barrier Materials and ASTM

F1140, Standard Test Methods for Failure Resistance of Unrestrained and Nonrigid Packages for Medical Applications, are accepted FDA Consensus Standards. ASTM F2054, Standard Test Methods for Burst Testing of Flexible Package Seals Using Internal Pressure within Restraining Plates, has been submitted for FDA acceptance.

But this is only half of the story. Seal strength testing is only one part of the ISO-11607 recommendations; *Package Integrity Testing* is the other part. In the concluding chapter of this series, to be presented soon, we will look at various methods of **physical package integrity testing**

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