Seal Quality Test Method Examples

- Residual Seal Force

- RSF Slides courtesy of Roger Asselta, Genesis Packaging Technologies

Seal Quality Tests

- Tests used to **characterize and monitor** the **quality and consistency** of a **seal parameter** providing some assurance of the package's ability to remain integral
- **Parameters monitored** may include
  - Seal quality or characteristic
  - Package materials
  - Package components
  - Sealing process
- **SQT are <u>not</u> leak tests**

Seal Quality Tests

- **Passing SQT ≠ leak-free package**
- Examples
  - **Heat seal strength**
    - A pouch with a strong heat seal peel force may have a pinhole in the pouch face
  - **Closure application force**
    - A well-closed capped bottle may leak due to a scratch on the bottle finish

Seal Quality Tests

- **Failing SQT = package integrity risk**
- Examples
  - **Heat seal strength**
    - A pouch with a weak heat seal peel force is more likely to leak during product life cycle
  - **Closure application force**
    - A loosely capped bottle may leak during shipping
- **SQT and package leak tests work together to ensure package quality**

Seal Quality Tests

- Tests included
  - Closure application and removal force
  - Package burst
  - Package seal strength
  - Residual seal force *
  - Airborne ultrasound
  - Vision inspection (including x-ray)

** J. Ludwig, et al, J Parenteral Sci & Technol, 47, 5, 1993, p. 211, and 49, 5, 1995, p. 253*

Residual Seal Force

Roger Asselta,

Vice President and Senior Advisor

Genesis Packaging Technologies

Residual Seal Force (RSF)

- RSF is the Stress A Compressed Elastomeric Closure Flange Continues to Exert on A Vial Land Sealing Surface after Application of an Aluminum Seal (Crimping).
- USP <1207.3> Seal Quality Test
- Quantifying the RSF is a Test Method for the Indirect Estimation of Elastomeric Closure Compression.
- Sufficient Compression is Essential to Seal Integrity.

RSF Test Method Concept

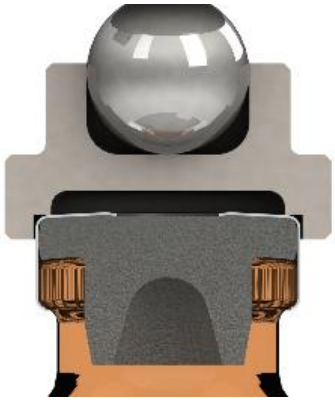
- There is an Optimum Window of Closure Compression
  - Too Little versus Too Much Force
- Poor Compression Cannot be Visually Detected
  - RSF Testing is an Indirect Measure of Compression
- RSF testing is recognized in the recently revised USP <1207> *Sterile Product Packaging – Integrity Evaluation* in section <1207.3> *Package Seal Quality Test Methods*

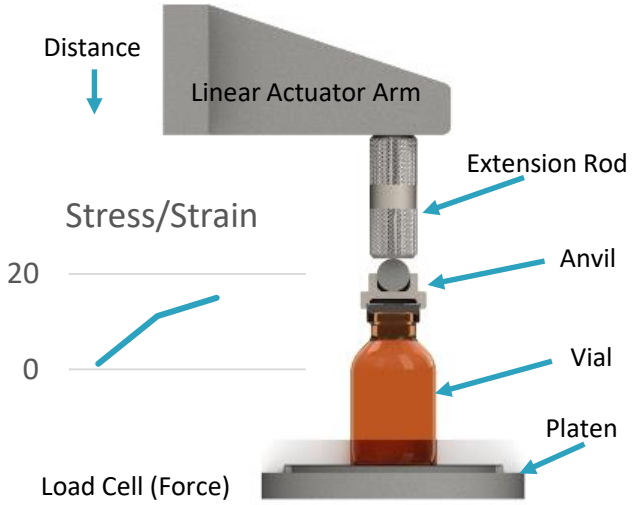
Basis of RSF Testing

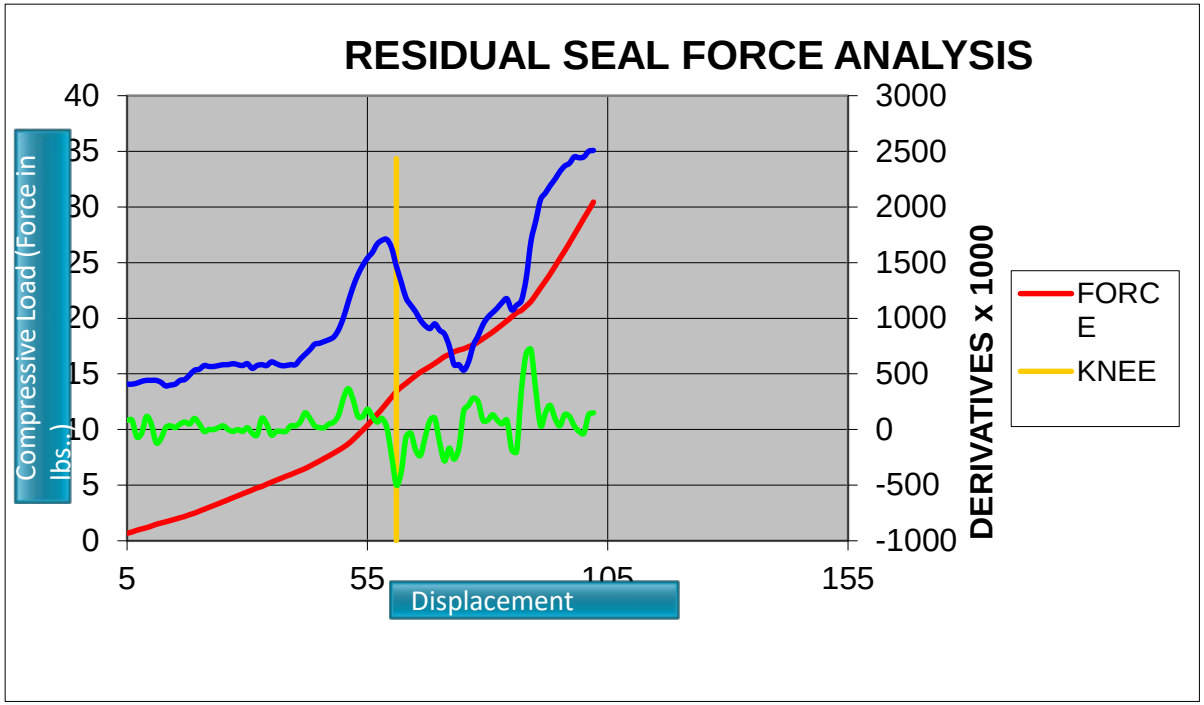
- Upon Capping the Closure Flange is Compressed Against the Vial Land Sealing Surface
- The Closure Acts Like a “Compressed Spring”
- The Tester Exerts Force on the Cap/Stopper
- When the Tester Force Exceeds the Closure Compression Force, Graphically the Stress-Strain Slope (Rate of Change) Drops
- This “Knee” in the Curve Equals the RSF
- >Applied Force at Capping > Closure Compression > RSF

RSF Testers

RSF Tester




Distance
Linear Actuator Arm
Extension Rod
Stress/Strain
20
Anvil
0
Vial
Platen
Load Cell (Force)

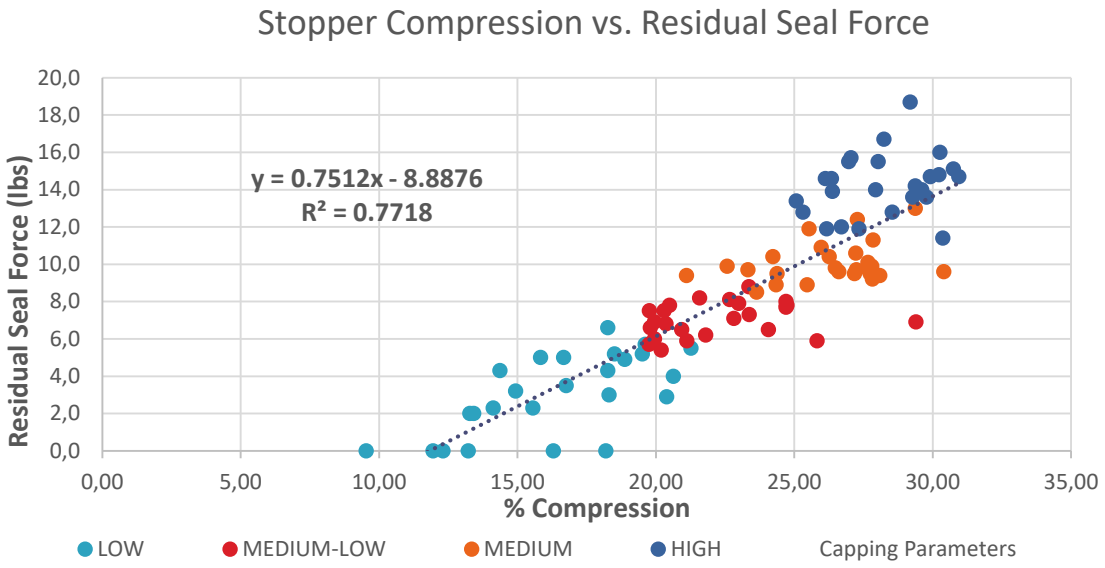


The compression curve (red) is a combination of the viscous and elastic responses to the stress from tester load. "The knee"(yellow) is where additional deformation occurs. An algorithm is applied, using the 1st (blue) and 2nd (green) derivatives to accurately identify that knee.

Significance and Use of RSF Test Method

- Package Development
  - Determine Effects of CCS Component Variables
    - Dimensional Tolerances, Durometer, Cure, Processing etc.
    - Assembled CCS Processing, Distribution, Storage
- Validation
  - *Establish Optimum Capping Parameters*
  - Evaluate Variation
- Production
  - Verify Capping Equipment Set-Up
  - Capping Process Monitor

Correlation of RSF to Compression

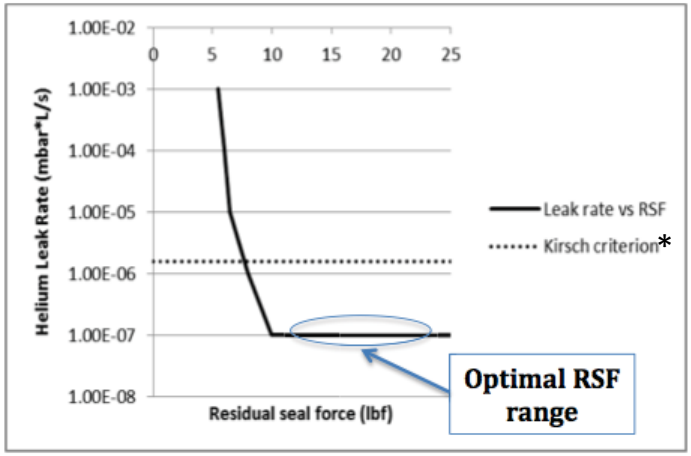


Example: 20mm Serum Soft Stopper

Correlation of RSF to Leak Rate

Tracer gas leakage rate (ASTM F2391) vs Residual seal force

Optimal RSF resulted in consistent leak rates well below the rate predicted for a 0.2µm hole

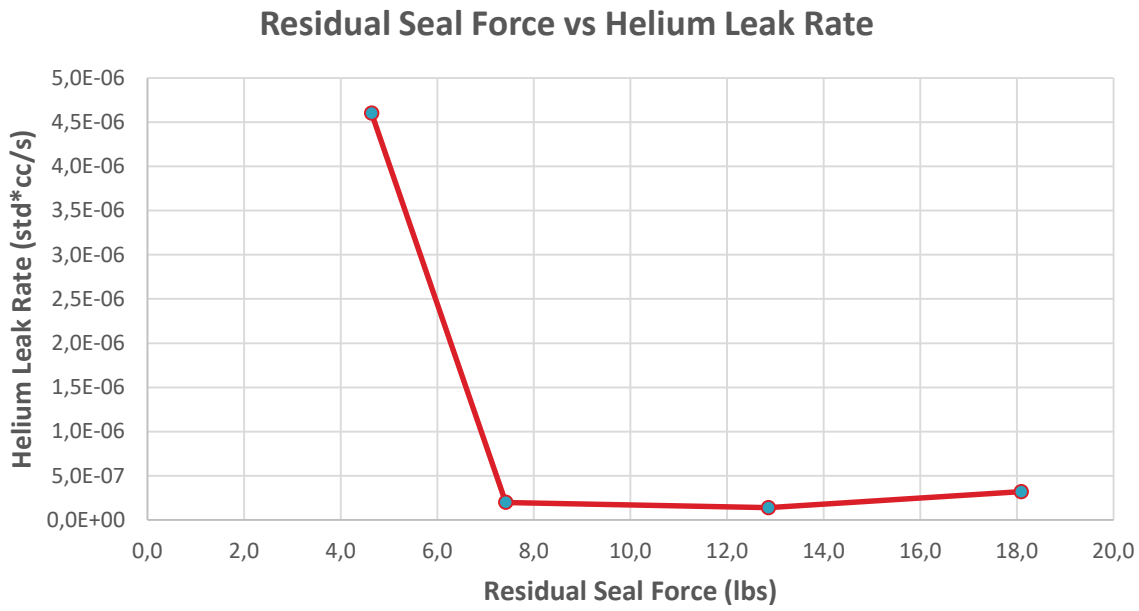


Ref. L Kirsch, L Nguyen, C Moeckly, R Gerth, *Pharmaceutical container/closure integrity II: The relationship between microbial ingress and helium leak rates in rubber-stoppered glass vials,* PDA J Pharm Sci & Tech 51, 1997, 195 – 202

* Microbial ingress is a probability function. Critical leakage rate of log 5.8 or about 0.2-0.3µ

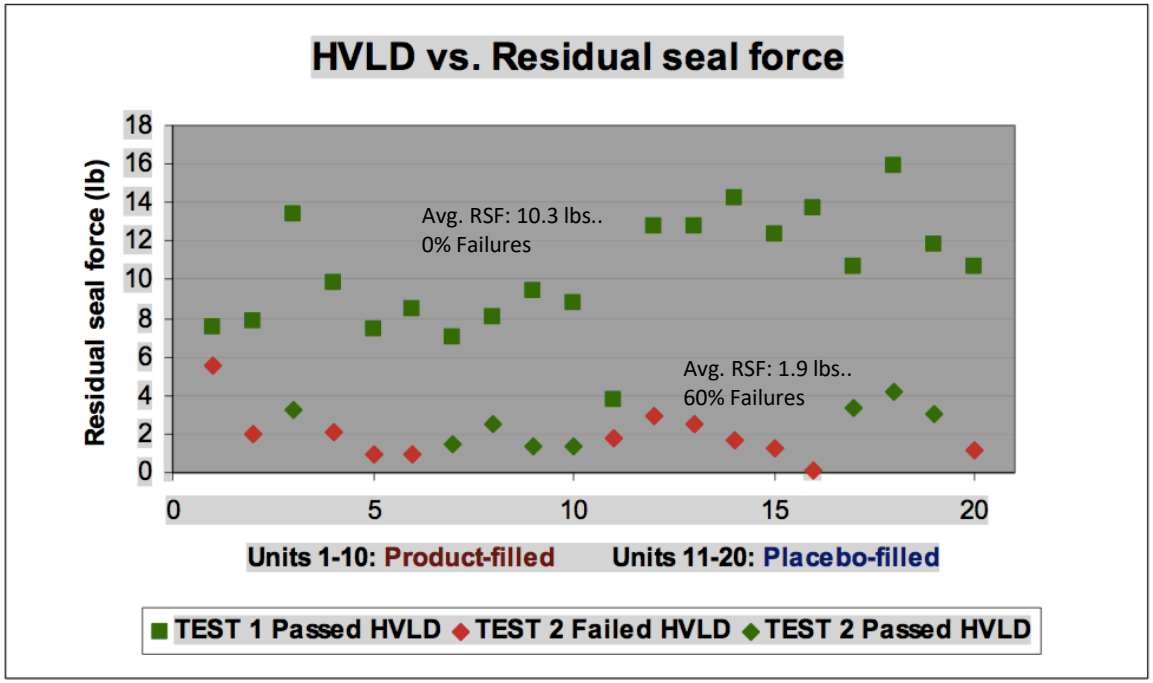
Illustrative purpose only. Courtesy of Dana Guazzo, PhD RxPax

Residual Seal Force vs Helium Leak Rate



HV Leak Detection / RSF

Leakage Failures, High vs. Low RSF



Using RSF Testing

”RSF values may be used in effectively setting up vial cappers and for monitoring the crimping process. With an understanding of compression and leak rate cut-off, RSF can be further used as a predictor of leakage risk.”

S. Orosz and D Guazzo, “Leak Detection and Product Risk Assessment’ presented at PDA Meeting, Mar 2010, Orlando, FL

Using RSF Testing

"The RSF tester can be used to characterize the resulting residual seal force of a capped vial independent of the capping equipment used, which can facilitate the comparison of seal quality of DP units manufactured in different facilities. In addition, a suitable RSF range that would still show full CCI, is recommended specific for each CCS combination and can be established using different capping equipment."

Mathaes, R.; Mahler, H.; Roggo, Y.; et al. Influence of Different Container Closure Systems and Capping Process Parameters on Product Quality and Container Closure Integrity in GMP Drug Product Manufacturing, *PDA J Pharm Sci & Technol 70*, (2016) 109-119