Nelson Labs™
A Sotera Health company

Packaging Validations – a look at current and future state testing

Agenda

- Purpose/applicable standards
- MDR driven packaging updates
- Common test methods
- Sample size considerations

Purpose of Packaging (Sterile Barrier System)

- Designed to allow necessary sterilization
  - EO
  - Gamma
  - Steam
- Provide an acceptable microbial barrier
- Allow for aseptic presentation

Current Standards

GMP 21 CFR 820.130 Device packaging

- "Each manufacturer shall ensure that device packaging and shipping containers are designed and constructed to protect the device"

ANSI/AAMI/ISO 11607 Packaging for terminally sterilized medical devices

- Part 1: Requirements for materials, sterile barrier systems and packaging
- Part 2: Validation requirements for forming, sealing and

TIR22 Guidance for ANSI/AAMI/ISO 11607, Packaging for terminally sterilized medical devices – Part 1 and Part 2: 2006

ISO/DTS 16775 Packaging for terminally sterilized medical devices – Guidance on the application of ISO 11607-1 and 11607-2

- Provides additional guidance for healthcare facilities on how to implement ISO 11607 -1 and -2

EN 868 parts 2 - 10

Why does it matter…

Definition of medical device:

"products specifically intended for the cleaning, disinfection or sterilization…shall be deemed to be medical devices"

Medical packaging is considered an accessory to the medical device and will be governed by the MDR

- ISO 11607 updated to bring alignments with the definitions within ISO 11139

Highlight of MDR changes on Packaging #1

Devices and manufacturing processes “should be designed to eliminate or reduce …, the risk of infection to the patient,” and the design should “allow for easy handling” and “minimize contamination”.

- ISO 11607 includes a proposal introducing usability evaluations to assess the ability of proper aseptic technique in the intended clinical environment. This usability evaluation will allow for confirmation that requirements in the MDR’s are fulfilled for the packaging function.

Usability - Evaluation of Human Factors Engineering

A package serves as a means of dispensing the product to the end user:

- Design must allow for easy and safe handling while minimizing microbial contamination
- Integrity of the packaging must be clearly evident to the end user (provide a sufficient, reliable tamper-evident seal)
- Correct product identification must be evident

Usability studies allow the manufacturer to mitigate risks associated with the correct use of the package.

Leads to a higher understanding of the factors controlling the quality of user interactions with your product

Usability - Evaluation of Human Factors Engineering

Usability studies of sterile barrier systems for medical devices should provide objective evidence regarding the user interaction.

Include an evaluation of your device's interactive characteristics:

- perceived as usable and appealing
- enables safe and effective interactions

and should measure performance by objective means

- Interviews one-on-one, and group settings
- contextual inquiries

Highlight of MDR changes on Packaging #2

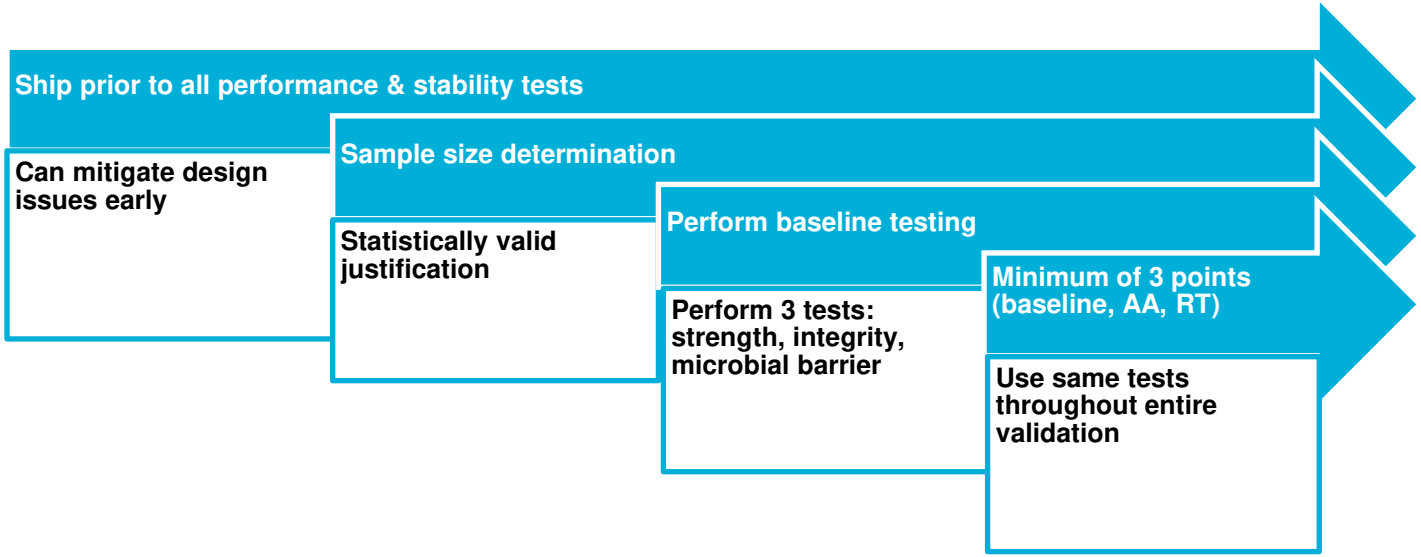
"Devices delivered in a sterile state shall be designed …to ensure that they are sterile when placed on the market and that, unless the packaging …is damaged, they remain sterile, under the transport and storage conditions … until that packaging is opened at the point of use. It shall be ensured that the integrity of that packaging is clearly evident to the final user"

- ISO 11607 updated incorporating a best practice visual inspection and that the integrity of the packaging is clearly evident to the final user
  - Instructions for damaged or unintentionally opened

Additional changes to ISO 11607

- Defining revalidation requirements
  - Changes to material, design, and sterilization
- Update to the test method conformity list
  - Includes declaration of precision and bias statements
- Discussion on differentiating different packaging levels
  - Discussion on the location of the SBS

Basic Packaging Validation Plan

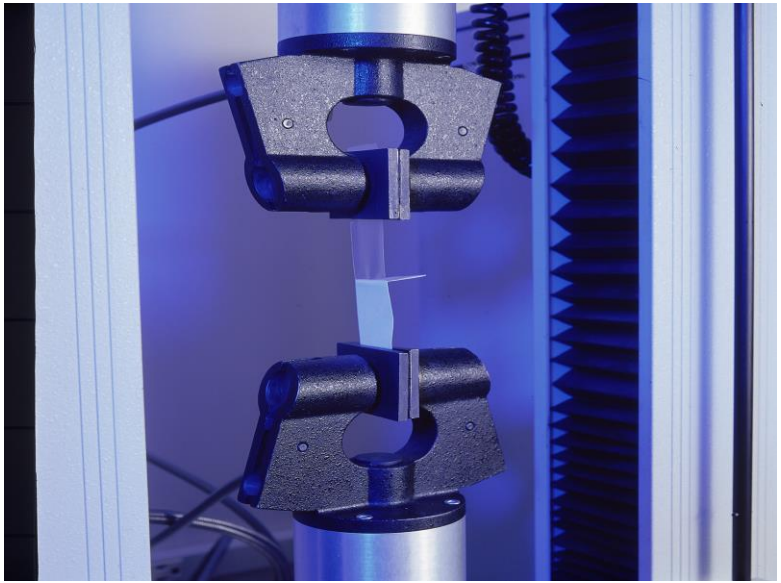


Packaging Test Summary

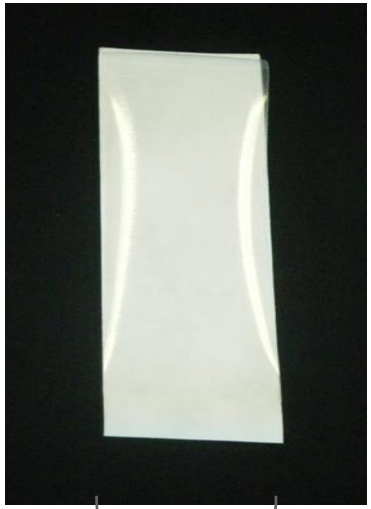
Strength	Integrity	Microbial Barrier
Seal Peel	Visual Inspection	F1608
Burst Test	Dye Migration	Microbial challenge
Creep Test	Dye Immersion	F2638
	Bubble Emission	

ISO 11607

Strength Tests

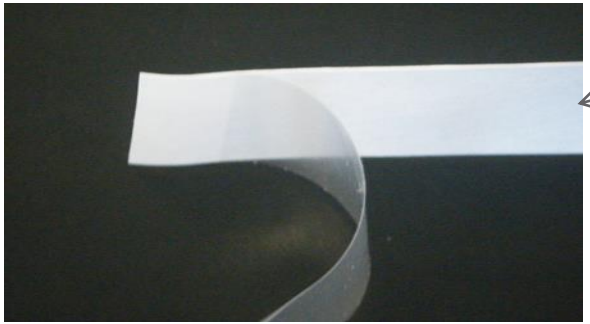


Seal Peel Test



1” across

Identifying the material in each grip, it may have an affect on the results.



Most rigid material in mobile grips

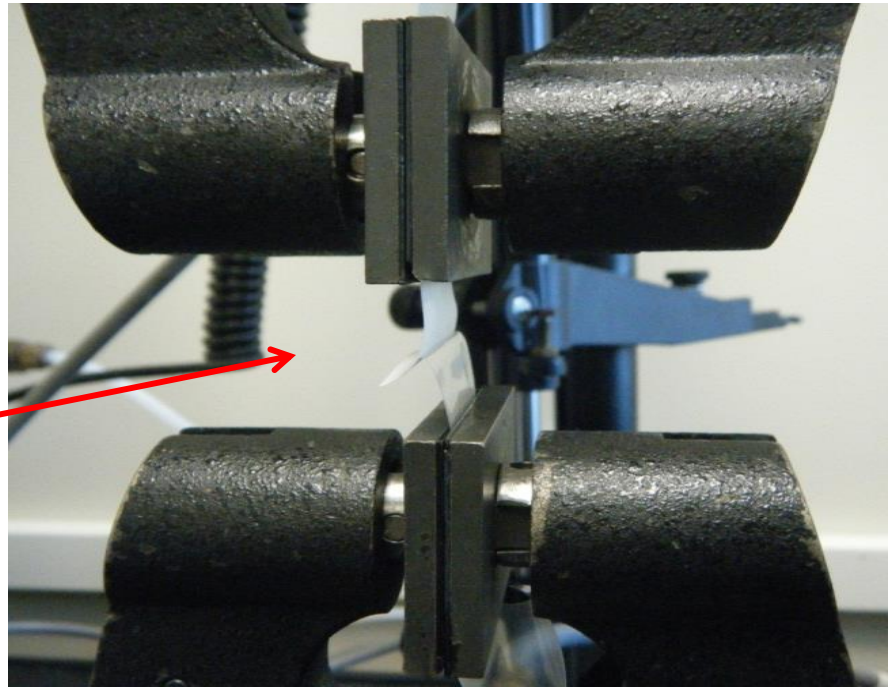
Most flexible in stationary grips

Seal Peel Test - techniques

90° Unsupported

Usually provides the most conservative value (lowest)

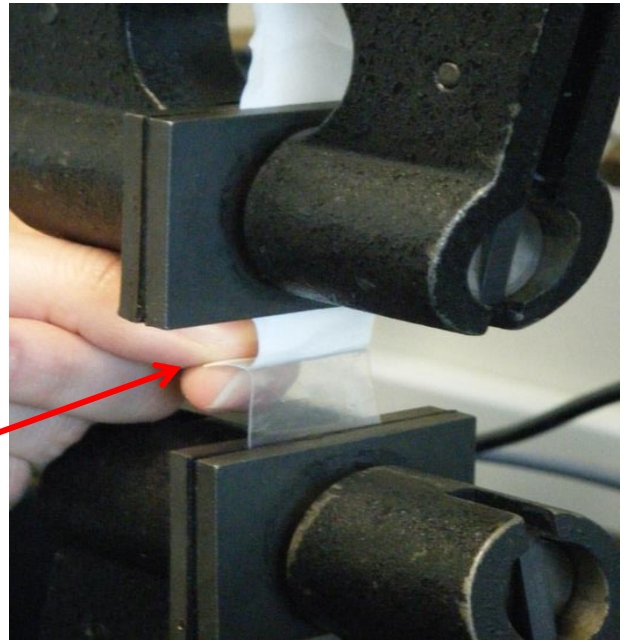
Tail is free floating during the pull



Seal Peel Test - techniques

90° Supported

Tail is manually held with slight pressure during the pull

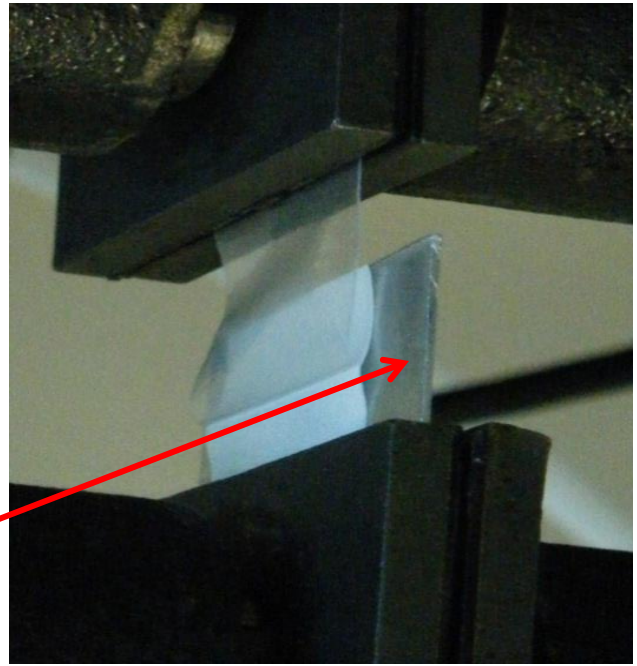


Seal Peel Test - techniques

180° Supported

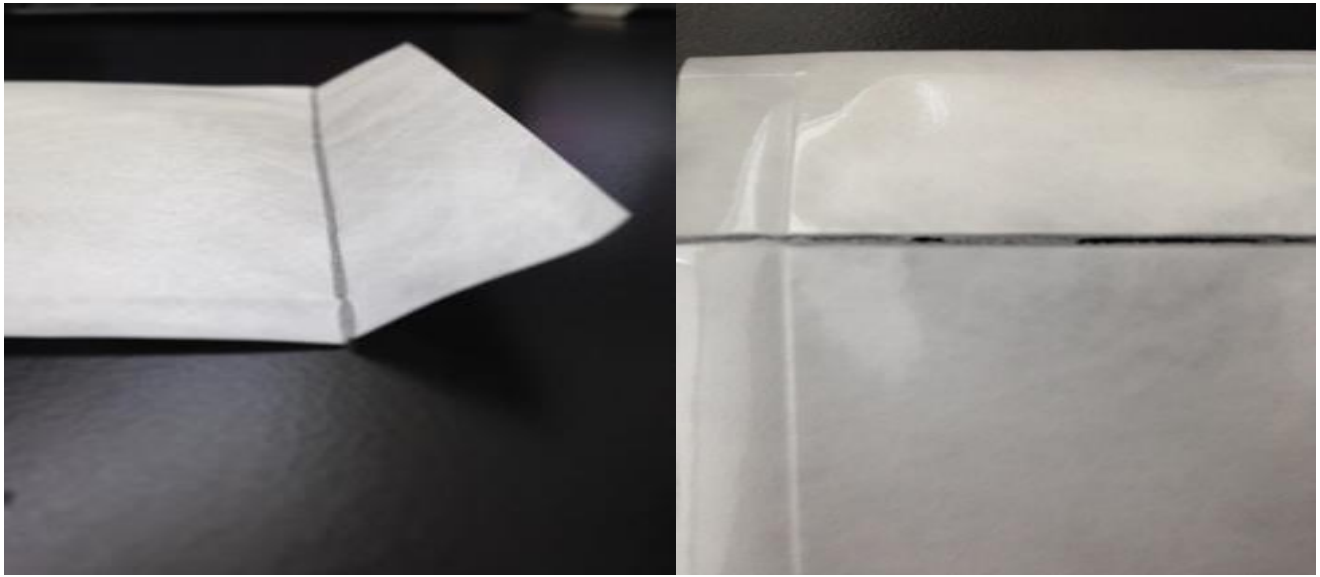
Provides values significantly higher than with tail in 90 ° position. Plate is placed in the stationary grip.

Tail is held with a backing plate during the pull



Seal Peel Test

Seal Peel Test – Failure issues



Over sealed as a result of too high temperatures causing melting/bending of materials and voids in the seals.

Seal Peel Test – Failure issues

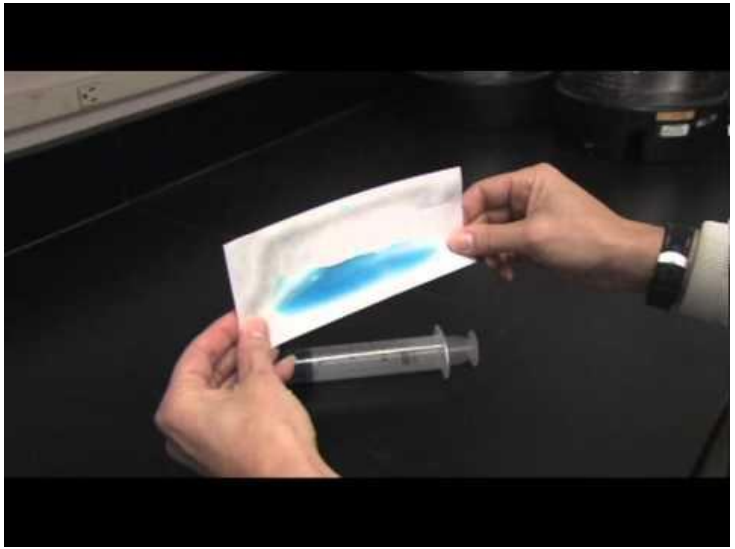
Example of Delamination

Seal Peel Test – Upcoming Changes

- ✓ ASTM F88 updating process for cutting test specimen on trays

ISO 11607

Integrity Tests



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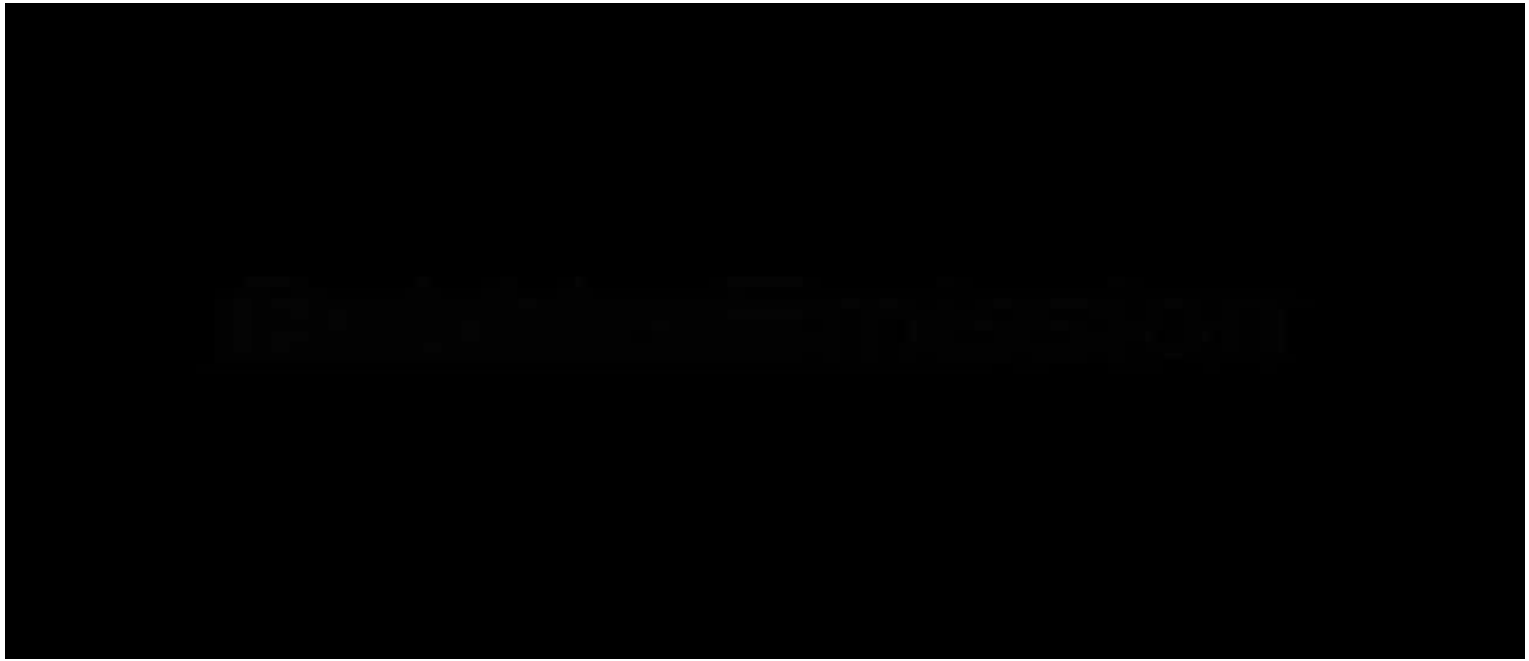
Bubble Emission Test - ASTM F2096

Determines the integrity of the package and the seal

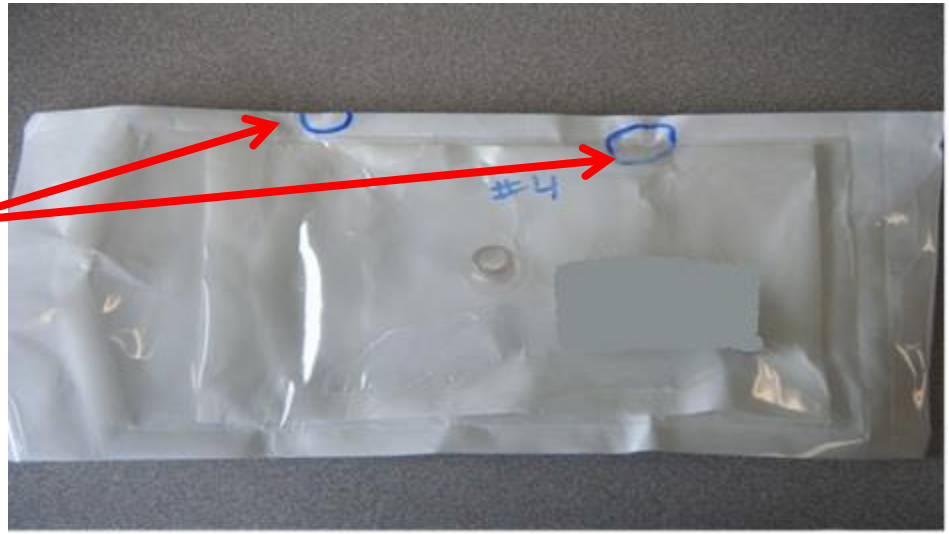
Involves inflating the package and submerging it into water ~1 inch above top surface	Package examined for evidence of seal failure or holes in packaging, demonstrated by continuous bubbles emerging from a single point

Bubble Emission Test



Bubble Emission – Failure Issue

Folds



Can result in sheet separation of the material leading to false failures, this phenomena does not compromise the sterile barrier.

Porous Sterile Barrier Integrity Testing: Failure Anomalies, *Medical Device & Diagnostic Industry* Magazine MDDI Article Index; Jan 2006

ISO 11607

Microbial Tests

Microbial Ranking Test - ASTM F1608

Determines the Log Reduction Value (LRV) of porous material

Sample size must be a minimum of 47mm in width, recommended sample size of 2	Packages placed into a chamber and exposed to a specific organism (*Bacillus*)	Filters are blended and plated to determine titer values

Microbial Ranking Test

Accelerated Aging

Accelerated Aging - ASTM F1980

Purpose/Theory		
Demonstrate the package is not affected by aging to the expected shelf life	Does **not** replace real time aging	Based on the observations of Arrhenius

Accelerated Aging

Justify test conditions and duration	With or Without Product
• Ambient temperature • FDA recommends 25°C • Aging temperature • Relative humidity • < 10-15°C T_g for all polymers–***Caution!***	• The presence of a device can stress a package and affect performance. Use of simulants is not uncommon.

ISO 11607

Sample Size Assessment

Sample Size

ISO 11607 Part 1

"The sampling plans used for selection and testing of packaging systems shall be applicable to the package systems being evaluated. Sampling plans shall be based upon statistically valid rationale."

TIR22

"sampling plans should be applicable to packaging systems, reflective of tolerance, and be based on statistically valid rationale."

ISO 2859-1:1999 Sample Procedures for Inspection by Attributes

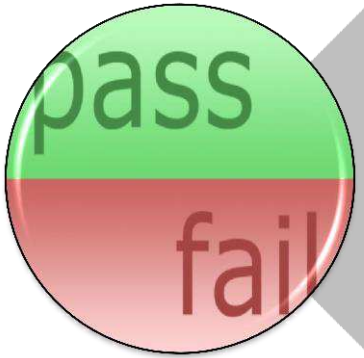
Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection	EN868 series

Sample Size

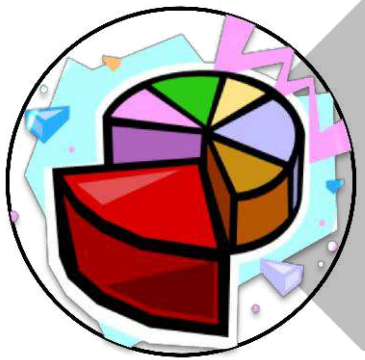
The "right" sample size for a particular application depends on multiple factors, including:

- ✓ Cost considerations (e.g., maximum budget, desire to minimize cost)
- ✓ Minimum acceptable level of deviation (confidence level) – use of Risk Priority Number, patient risk based approach, etc.
- ✓ Test chosen –attribute or variable data output

Sample Size



Attribute (qualitative) data: Data that represents the absence or presence of characteristics. Go/no-go gauging or the presence/absence of a component yield attribute data. Dye migration, bubble emission, etc. incorporates confidence levels.



Variable (quantitative) data: Data that contains a range of quantities. Most measurements yield variable data. Seal peel, burst strength, etc. usually require less samples.

In Summary…

MDR changes in EU are driving packaging updates including:

- Renewed focus on prevention of microbial ingress
- Incorporation of usability studies in design of packaging configuration
- Revalidation requirements

Packaging validations demonstrate 3 specific properties (Strength, Integrity, microbial barrier) throughout establishment of:

- Baseline
- Accelerated aging
- Real time aging

Testing sample size must be established using a Statistically Valid Rationale

THAT'S A WRAP

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