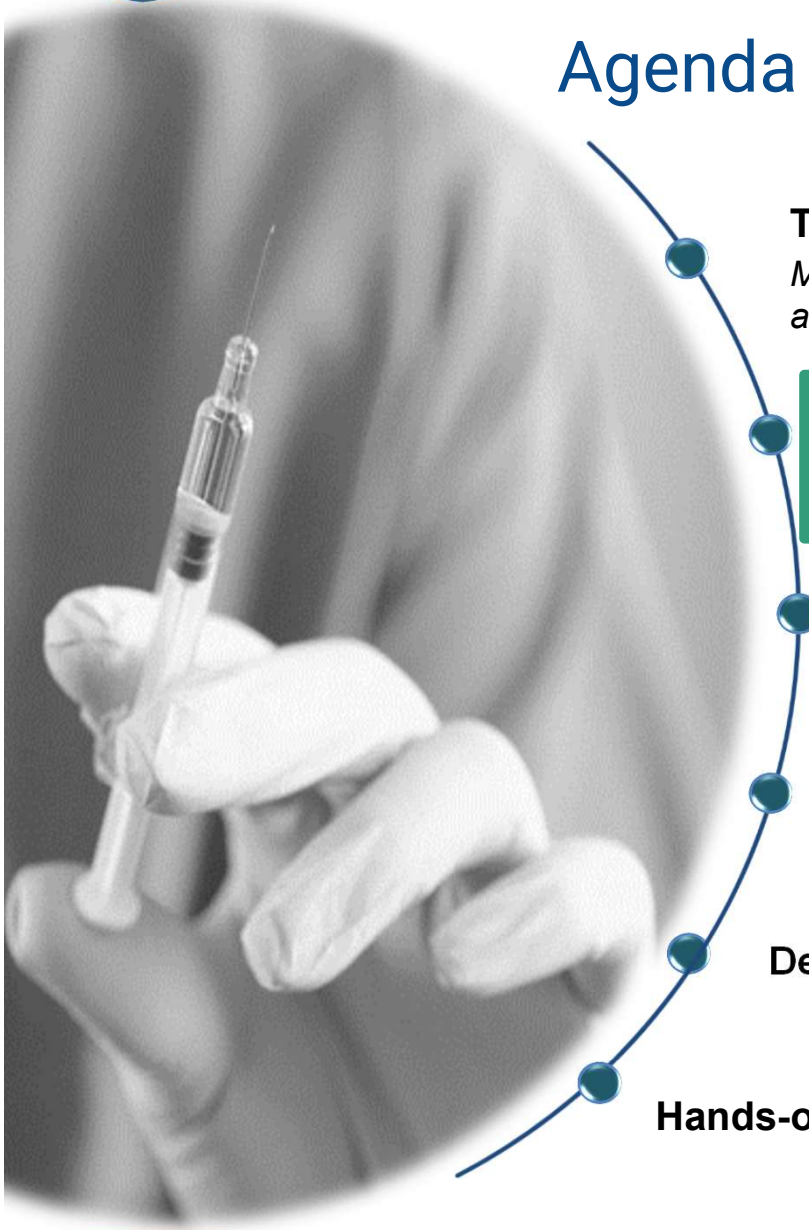
All about Pre-filled Syringe Systems

From Initial Development to Final Fill Finish

Christa Jansen-Otten

Venice, April 21st 2023 – DAY 2



Agenda – DAY 2

The "Ready-to Fill" Syringe
Material • Shape • Properties • Siliconization • Impact of different drug • Nest and Tub • Needles and LL • backstops • Rods • Regulatory Guidelines

Plunger Stoppers, Needle Shields, Tip Caps
Materials • Properties • Functionality • Production • Regulatory

Manufacturing Aspects in Fill & Finish and Assembly
Bulk versus Nested • Nest Sizes • Rod insertion • Handling of Syringes, Labeling • Glass to Glass Contact

Assembly of Syringes and Administration Devices
Pen Injectors • Safety systems • Autoinjectors • Manual vs Automated

Design Independent Assembly

Hands-on Session 2, Mind map, Lottery

Customer Impact - Demands on Packaging Components are Increasing

Vial Components

PFS Components

Cartridge Components

- Particulate reduction/foreign matter
- Concerns regarding extractables/leachables
  - Ultra-clean components needed
  - New ways to deliver medicine
- Functional performance of components
  - High-speed lines
  - Complex devices
- Moisture Vapor Transmission Rate
- Container closure integrity (CCI)
- New manufacturing approach
  - Flexibility
  - Time to market
  - Total cost of ownership (TCO) focused
- Functional performance of components
  - High-speed lines
  - Complex devices

Considerations in Selection of PFS Components

COMPATIBILITY WITH DRUG	APPLICATION – MANUAL OR AUTO SYSTEM	CONTAINER CLOSURE INTEGRIETY (CCI)	QUALITY SPECIFICATIONS	FINISHIING
• Type of drug • pH • Viscosity • Excipients	• Break loose & glide force requirements • Accuracy of delivery volume	• Interference fit of plunger with barrel • Sealing ribs and their function • Preservation of drug potency and sterility	• Particulate level – visible & sub-visible • Dimensional control • Endotoxin level • Bioburden level • Visual defects	• Mode of sterilization • Lubricity • Consistency

Rubber material

Why Use a Rubber Material?

Sealing properties that maintain container – closure seal integrity over time.

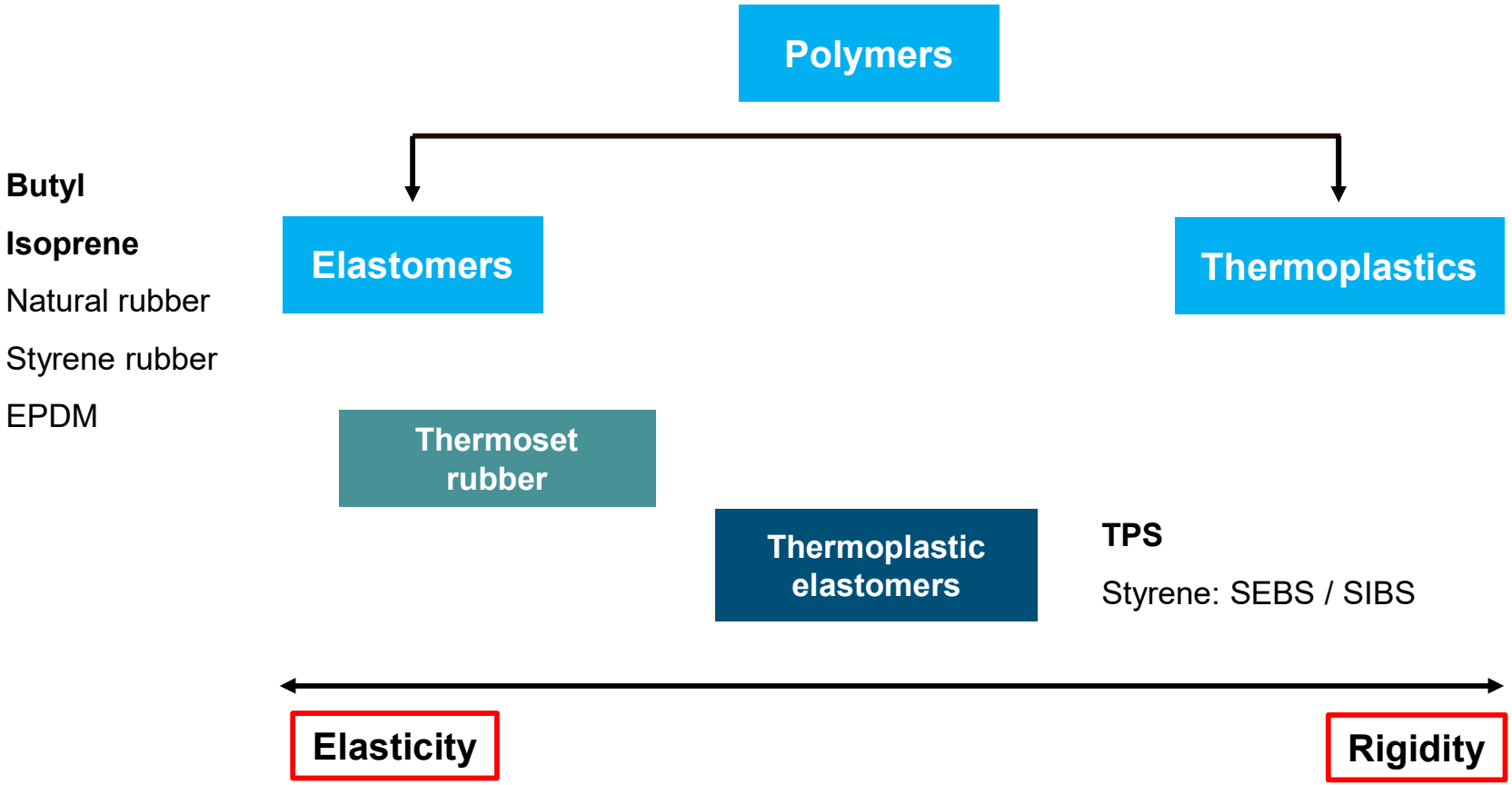
Physically and chemically compatible with different sterilization methods.

Different range of material permeability.

Compatible in long-term contact with drugs.

Wide range of product designs

Polymers: thermosets and thermoplastics

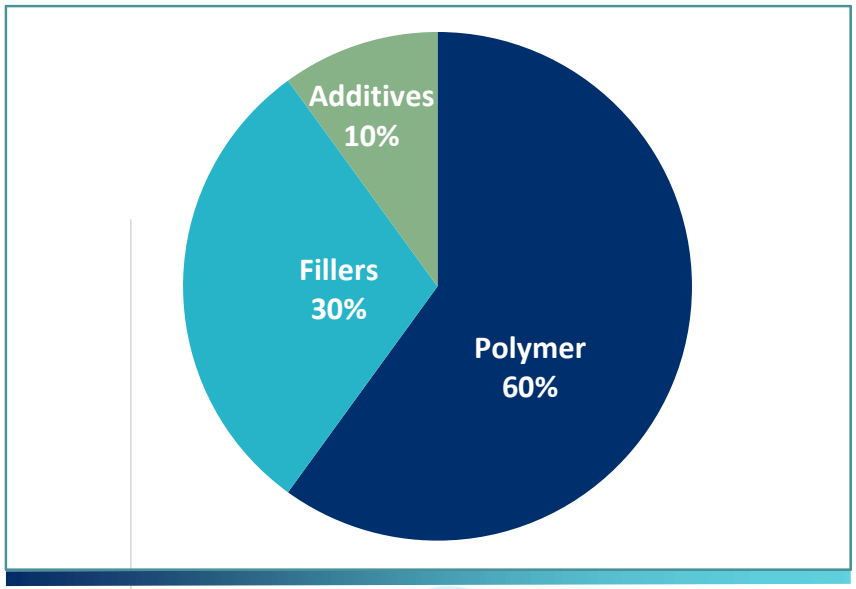


Main Elastomer Types Used for Parenteral Applications

- Natural Rubber (NR) – from Hevea Brasiliensis
- **Isoprene Rubber (IR)** – synthetic equivalent to NR
- Styrene-Butadiene-Rubber (SBR)
- Butadiene Rubber (BR)
- Nitrile Rubber (NBR)
- Ethylene-Propylene Rubber (EPM/EPDM)
- **Isobutylene Isoprene Rubber** (IIR, Butyl Rubber)
- **Halogenated Butyl Rubber** (XIIR) – Br, Cl

Elastomers Closures General Composition

Approximate Composition of an Elastomer Component



Additives

can be curing agents, antioxidants, accelerators, activators, protective agents, colorants, plasticizers, acid scavengers, light and heat stabilizers, lubricants, anti-static agents, etc.

Fillers

are mainly defining the physical properties

→ Ask your supplier for potential extractable lists

Elastomeric Formulations for Pharmaceutical Use - Properties Butyls/Halobutyls

1. Application: stoppers, plungers, cartridge seals and tip caps
2. High elasticity
3. Low potential E&L[1] for good drug compatibility
4. Low moisture and gas permeation rates
5. Steam and gamma sterilizable
6. JP, USP, EP compliant[2]
7. Low fragmentation / corning
8. Optimal penetrability/good resealing properties

[1]extractables & leachables [2]design dependent

Elastomeric Formulations for Pharmaceutical Use - Properties synthetic Polyisoprene

1. Application: needle shields/rigid needle shields, tip caps plungers, cartridge seals (laminates)
2. High elasticity
3. Low potential E&L[1] for good drug compatibility
4. Good permeability rates towards moisture and gases (ETO[2])
5. Steam, gamma and EtO sterilizable
6. USP, EP compliant
7. Low fragmentation / corning
8. Ozone resistance (low cracking), no blooming, no frosting

[1]extractables & leachables
[2]Ethylene oxide

Potential Issues: Needle Shields and Tip Caps

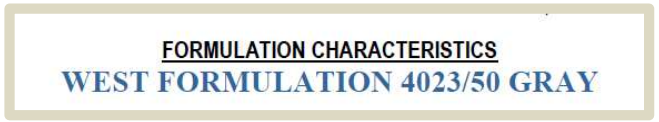
Ozone Cracking

Frosting (Bloom)

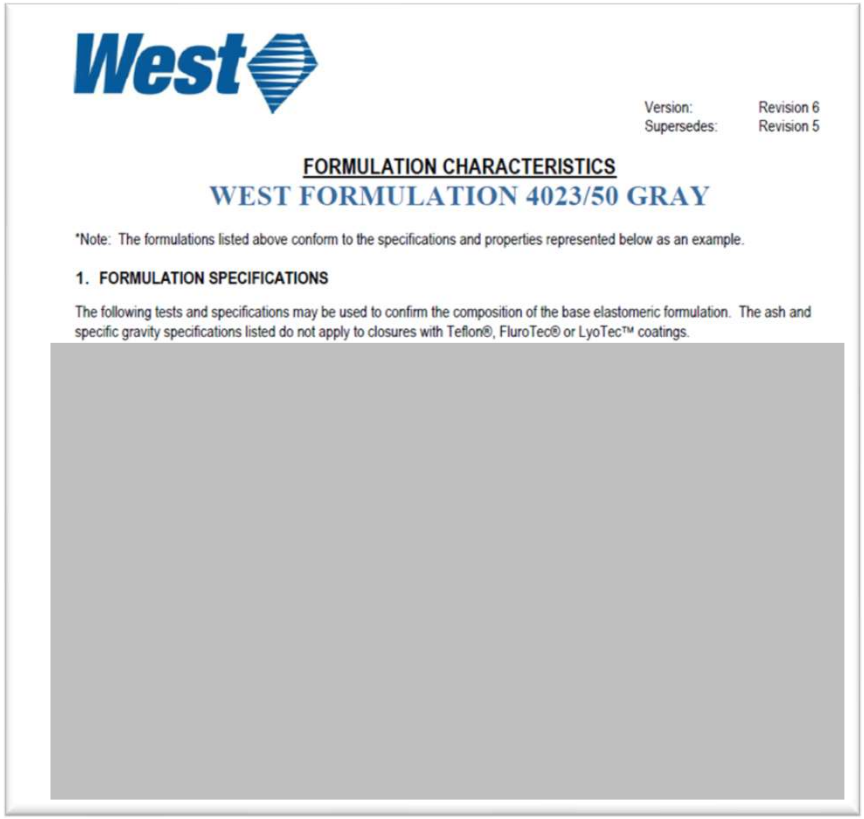
Supporting Documents

Supporting Documents: Example

- Technical drawings
- Formulation Characteristics
- Elastomer Formulation Biocompatibility
- Technical Bulletins and Reports
- Theoretical Material Extractable List
- VeriSure® Extractable Technical Package
- Material Characterization Package
- Regulatory Compliance Bulletins
- Product Specifications
- DMF
- Certificates



Formulation Documents: Example



West

Version: Revision 6
Supersedes: Revision 5

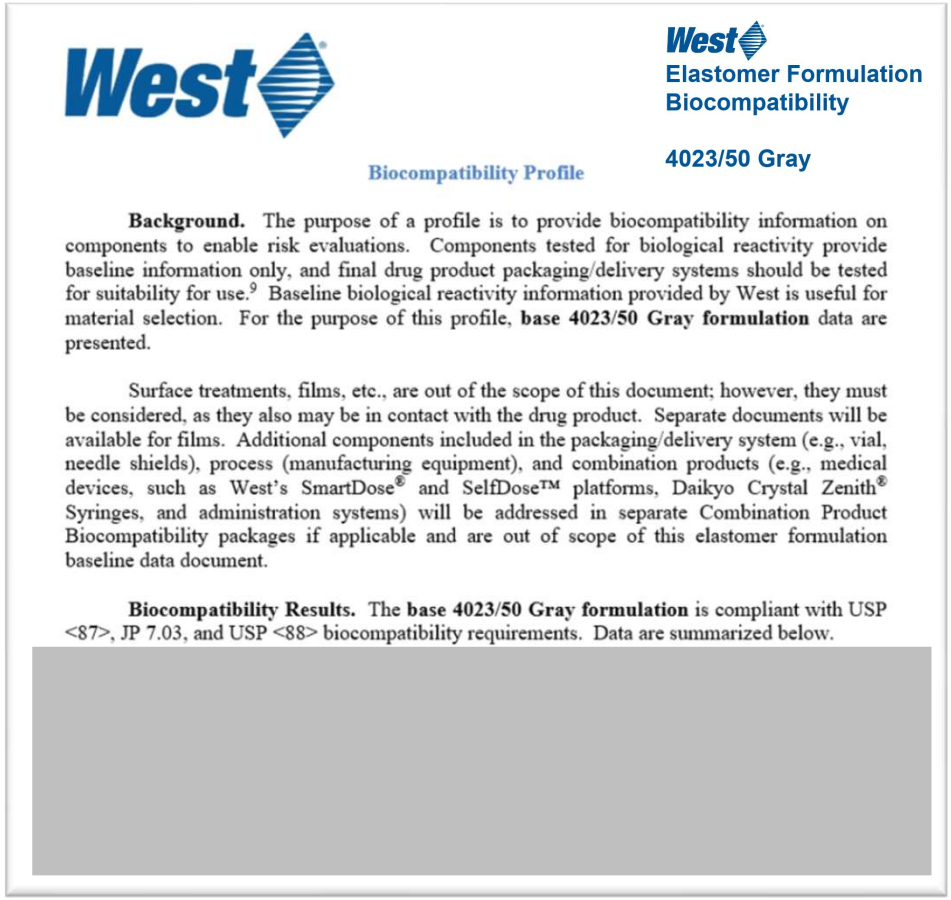
FORMULATION CHARACTERISTICS

WEST FORMULATION 4023/50 GRAY

*Note: The formulations listed above conform to the specifications and properties represented below as an example.

1. FORMULATION SPECIFICATIONS

The following tests and specifications may be used to confirm the composition of the base elastomeric formulation. The ash and specific gravity specifications listed do not apply to closures with Teflon®, FluroTec® or LyoTec™ coatings.



West

West
Elastomer Formulation
Biocompatibility

4023/50 Gray

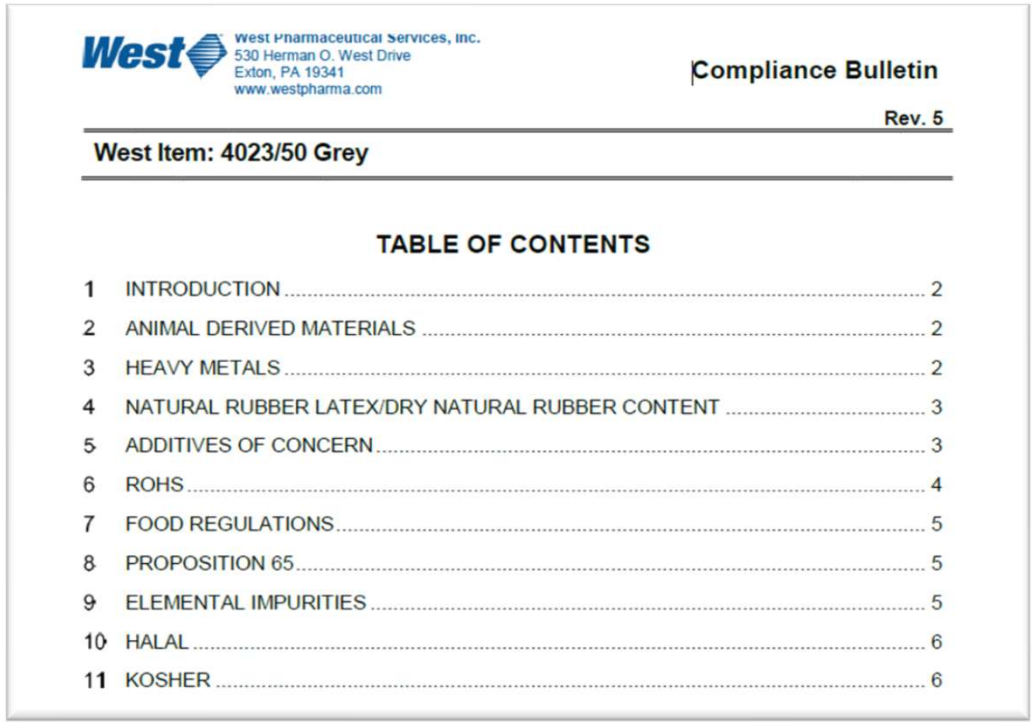
Biocompatibility Profile

Background. The purpose of a profile is to provide biocompatibility information on components to enable risk evaluations. Components tested for biological reactivity provide baseline information only, and final drug product packaging/delivery systems should be tested for suitability for use.[9] Baseline biological reactivity information provided by West is useful for material selection. For the purpose of this profile, **base 4023/50 Gray formulation** data are presented.

Surface treatments, films, etc., are out of the scope of this document; however, they must be considered, as they also may be in contact with the drug product. Separate documents will be available for films. Additional components included in the packaging/delivery system (e.g., vial, needle shields), process (manufacturing equipment), and combination products (e.g., medical devices, such as West's SmartDose® and SelfDose™ platforms, Daikyo Crystal Zenith® Syringes, and administration systems) will be addressed in separate Combination Product Biocompatibility packages if applicable and are out of scope of this elastomer formulation baseline data document.

Biocompatibility Results. The **base 4023/50 Gray formulation** is compliant with USP <87>, JP 7.03, and USP <88> biocompatibility requirements. Data are summarized below.

Formulation Documents: Example



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Compliance Bulletin

Rev. 5

West Item: 4023/50 Grey

TABLE OF CONTENTS

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By your side
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530 Herman O. West Drive • Exton, PA 19341
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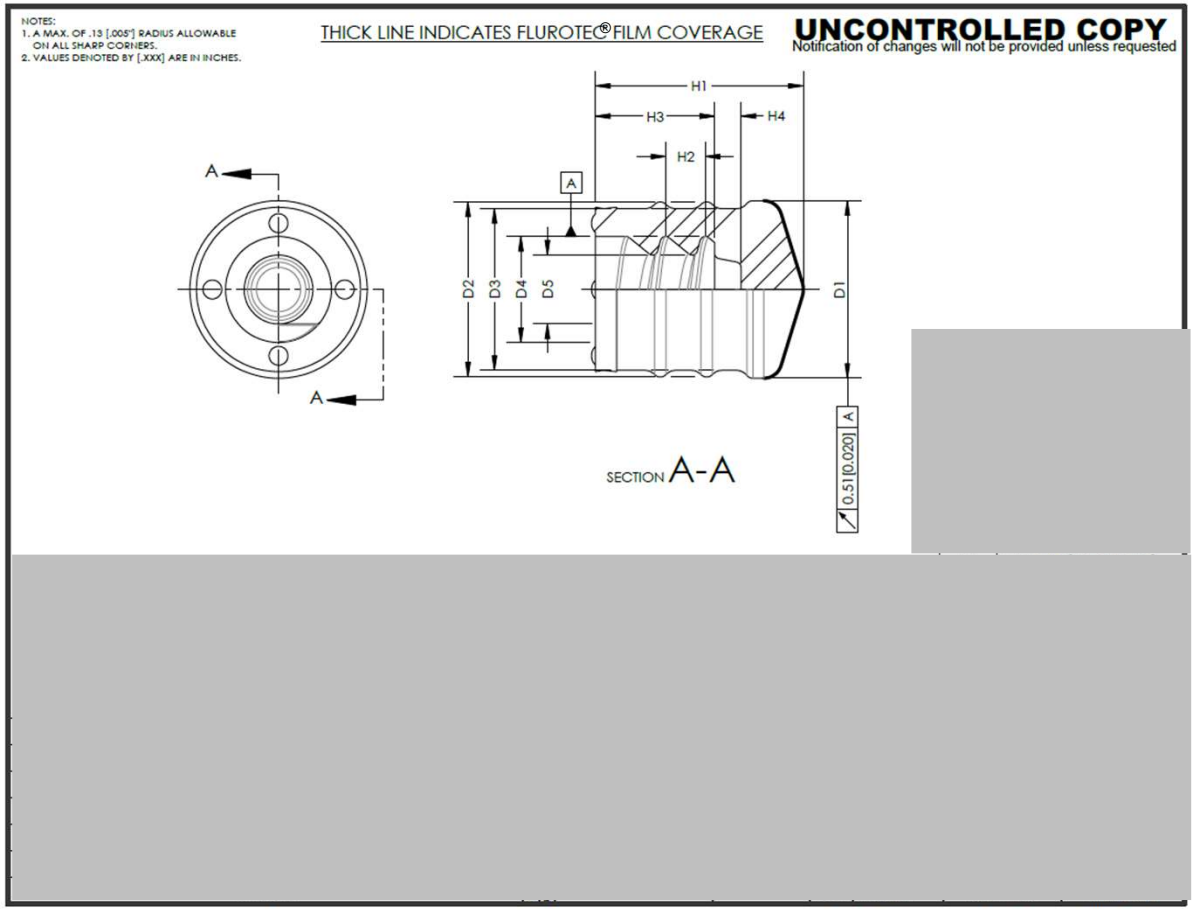
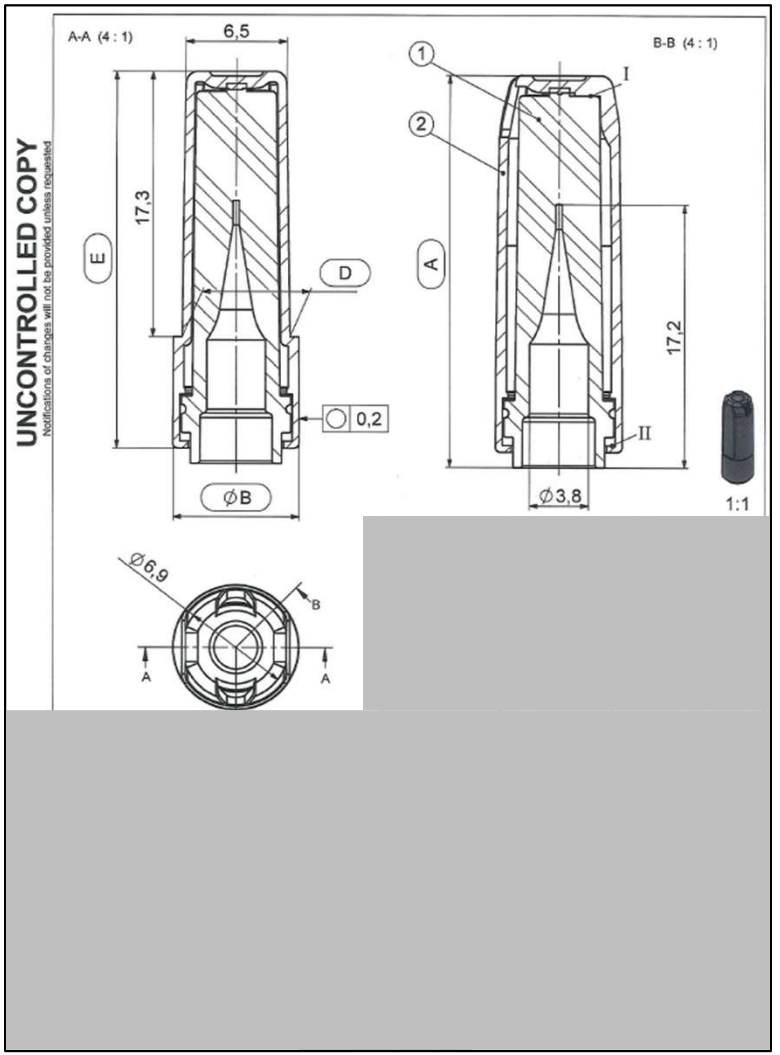
Theoretical Material Extractables List: 4023/50 Gray

Below is a summary of the potential chemical entities that could be extracted from West elastomer formulation 4023/50 Gray based on the materials that are used in the formulation. Since each drug application is unique, it is possible to form new reaction products from the closure or from a combination of the closure and the drug product components.

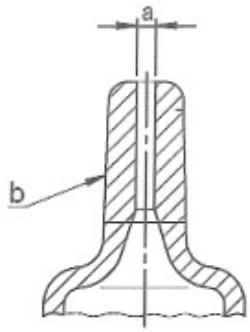
Uncontrolled Drawings: Example



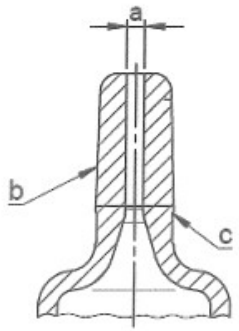


Rigid Needle Shields and Tip Cap

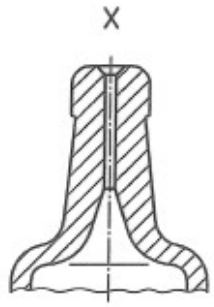
Pre-filled Head Designs ISO 11040-4 require different closure design solutions



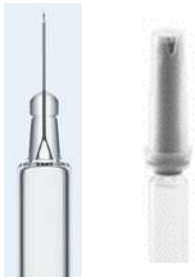
Head design of glass barrel with a 6% Luer cone



Head design of glass barrel with a 6% Luer cone for Luer Lock (LL)



Head design of glass barrel with staked needle



West Rigid Needle Shields

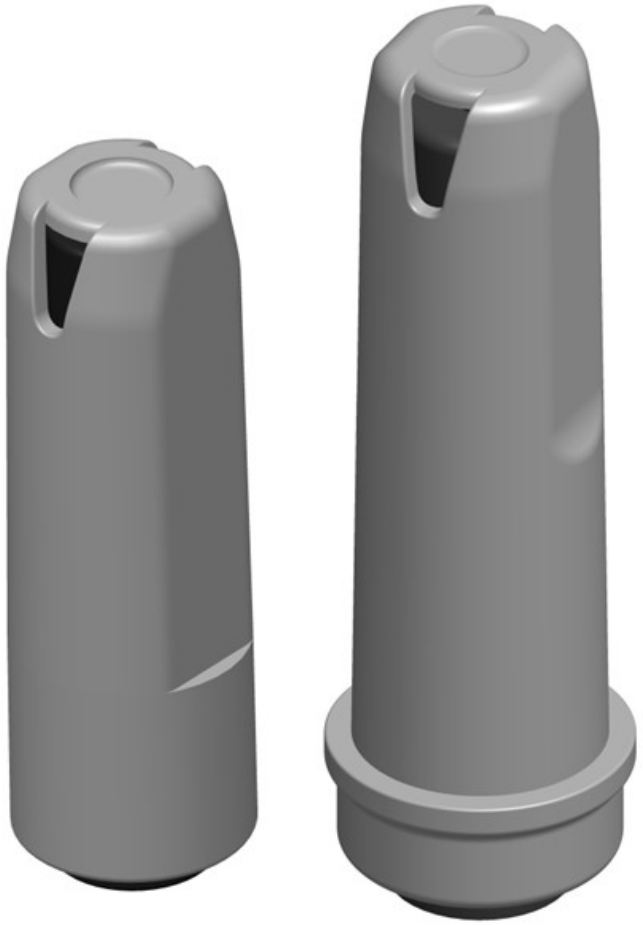
Rigid PP Shell		Soft Rubber Part		Assembled RNS
	+		=	

Rigid Needle Shields [RNS] are a safe & efficient closuring system for Prefilled Syringes with staked needles

Design Examples of Rigid Needle Shields

RNS ½'' [13 mm]

Needle length used for subcutaneous drug injection (into the tissue layer between the skin and the muscle)



RNS ⅝'' [16 mm]

Needle length used for intramuscular drug injection (deep into the muscles)

Solution

- Designed for existing assembly machine and filling equipment.
- Fits to ISO Norm 11040-4 glass syringe with staked needle
- Suitable also for polymer (e.g. COP) syringe
- Compatible with safety devices
- High gas permeation rubber formulation combined with sterilization windows of the rigid shell allowing effective sterilization by EtO or steam

Advantages of Rigid Needle Shields vs Soft Needle Shields

Process

- Easier distribution & orientation on syringe assembly equipment
- Compatible with safety devices

Protection

- Reduces risk of needle tip damage and deformation, the rigidity helps straight removal, no compression during removal

Handling Final Use

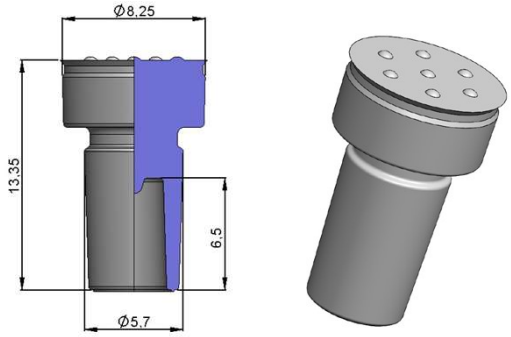
- Easier and safer de-shielding through its optimized design and comfortable haptic for health care professionals and patients
- Considered as more user friendly by Health Care Professionals
- Easier to de-shield when used with auto-injectors

Appearance

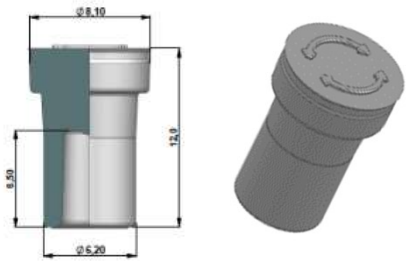
- More valuable appearance
- No visible defects of soft NS e.g., “banana” effect

Rigid Needle Shields are the preferred closure for staked needle syringes

Example of various Tip Caps for Luer and Luer Lock Syringe



Tip Cap to be inserted a rigid plastic cap # 3155



Easy Turn Tip Cap # 3131

Mushroom Rip Cap # 3379

Multiple rubber formulation options (halobutyl and synthetic isoprenes)

Barrier Film & Coatings

Films and Coating Technologies

Film – sheet (e.g., PTFE, ETFE) that is laminated to elastomeric component during the molding process

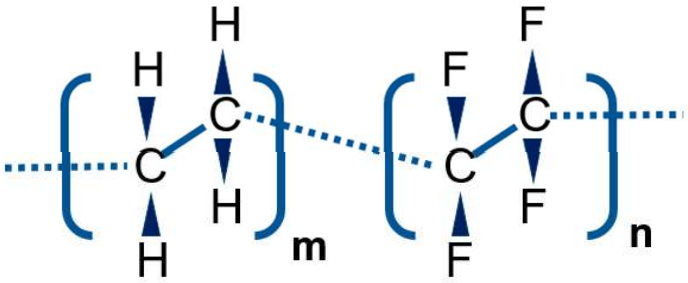
- Barrier function, e.g., FluroTec™ film

Coating – liquid or vapor that is sprayed, tumbled or vapor deposited onto the elastomeric component

- Lubricity, e.g., B2-Coating
- Lubricity and barrier function

Film properties

The blue color indicates FluroTec™ film



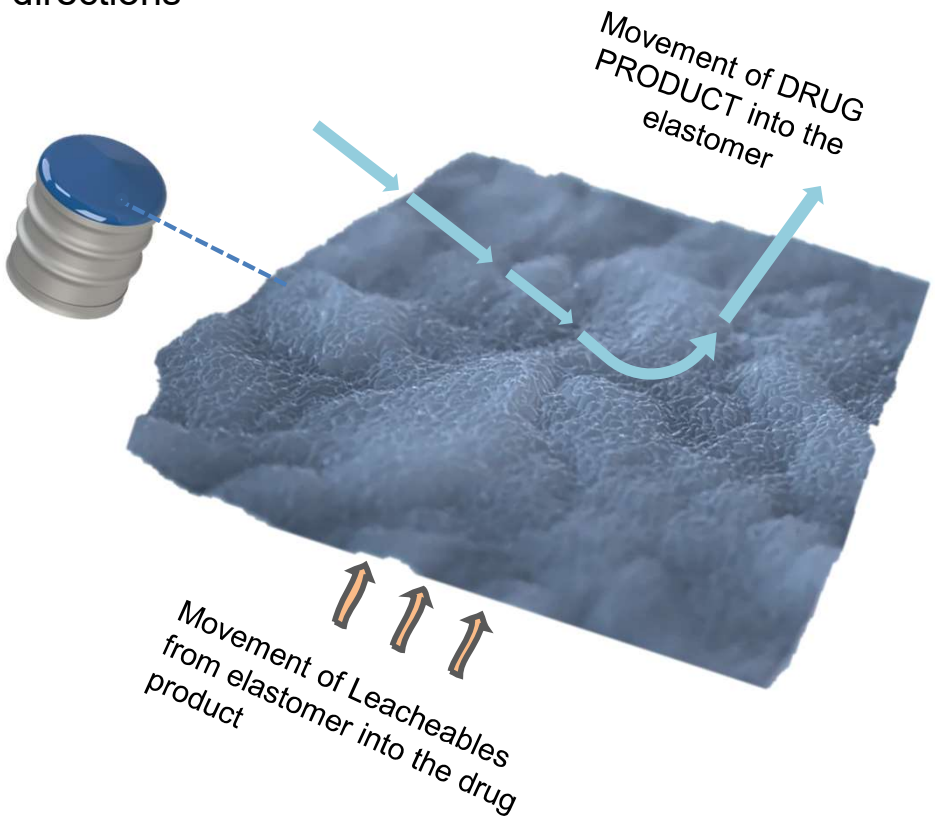
Structure of Poly(ethylene tetrafluoroethylene) (ETFE)

FluroTec™ film is

- based on poly(ethylene tetrafluoroethylene)
- smooth surface
- very adherent to elastomers (either bromo- or chloro-butyl)
- translucent
- compatible with sterilization by either:
  - autoclave
  - gamma irradiation
- Applied during the compression molding process

Film has a low level of Interaction

ETFE acting as a barrier reduces transport in two directions

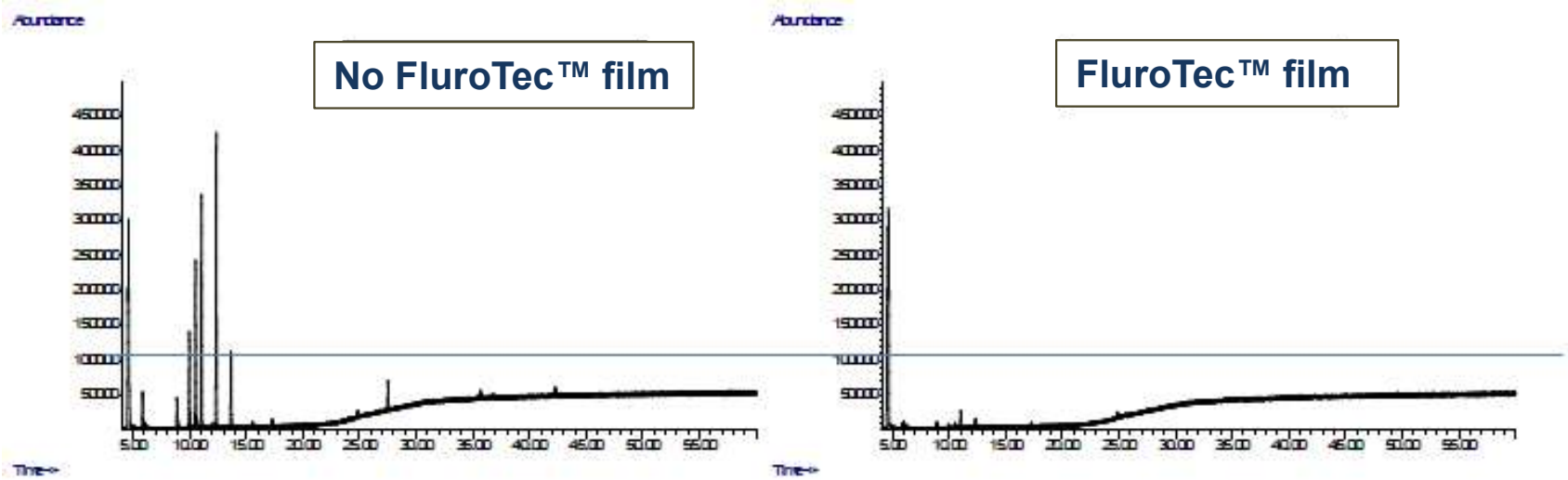


FluroTec™ film

- No reactive functional groups
- chemically inert – mitigates chemical migration
- resistant to degradation
- supports reduction in absorbance

Very Low Surface Energy → Very Low Level of Interaction!

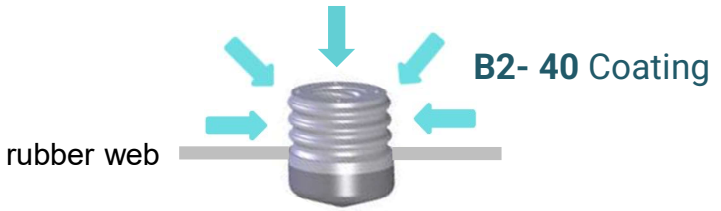
Fluoropolymer film coating Significantly Reduce Leachables



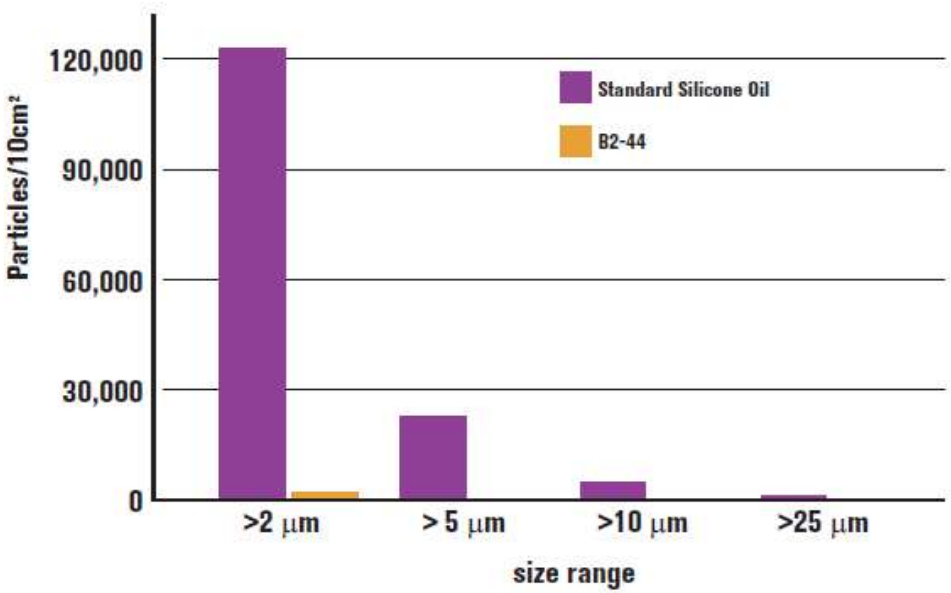
- **The drawn blue line indicates an estimated identification threshold of 0.5 µg/unit, which is below the Product Quality Research Institute recommended safety concern threshold for parenteral drug products**
- **Non-laminated elastomers showed approximately eight volatile organic compound (VOC) peaks estimated to be > 0.5 µg/unit**
- **Elastomers with FluroTec™ film did not show any peaks > 0.5 µg/unit [blue line]**

Most marketed biopharmaceuticals use fluorpolymer-coated component technology (FluroTec® film)

Lubricity coating



B2-coating vs. Traditional Silicone Oil
- Sub visible Particles -



B2-Coating

- Cross-linkable high and low molecular weight polydimethylsiloxane coating
- Applied to the surface of rubber stoppers and syringe components
- Low levels of extractable silicone oil
- Reduced particulate count
- Does not alter chemical and biological stopper/plunger properties
- Enhanced machinability

Study extract from Technical Report TR 2000/026 B2-Coating Quantitative Particle Analysis

Lubricity Coating: Classical Silicone Oil

Polydimethylsiloxane *DuPont™ Liveo™ 360 Medical Fluid** added during washing operation into the washing drum:

- 350 centistokes → USA
- 1000 centistokes → Europe

ADVANTAGES	DISADVANTAGES
• Commonly used • Applied during wash cycle • Low cost	• Particles/droplets may be found in drug product • Silicone level may be inconsistent if process is not validated

* Example of silicone oil used by West

Plungers

Facilitating Life Cycle: Seamless Transition from Vial to Prefilled Syringe format

Multi Dose Vial [MDVs]

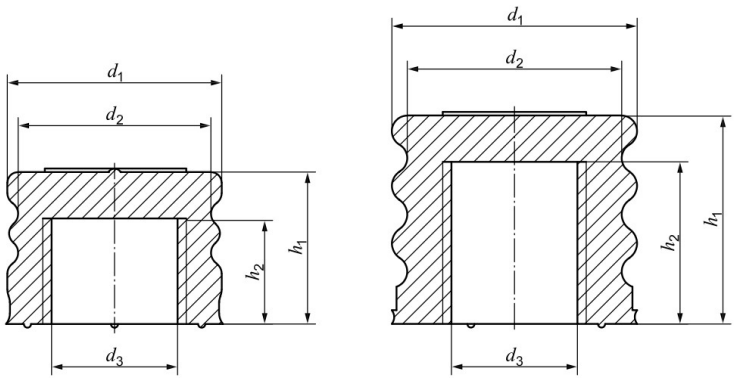
Single Dose PFS

- **The Same** Rubber Formulation
- **The Same** Lubricant [B2-coating]
- **The Same** Fluoropolymer Film lamination
- **The Same** Manufacturing Technology
- **The Same** Quality

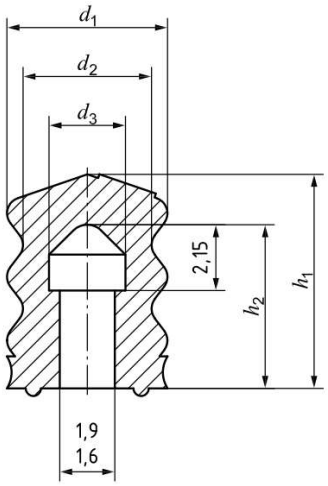
Main requirements for Prefillable Syringes Plungers

- Delivers a smooth injection profile [break loose & glide forces profile]
- Compatibility with the drug product
- Compatible with gamma-irradiation and final steam sterilization treatment
- Compatible with glass and plastic (COC/COP) barrels
- Good compression set properties
- Maintains Container closure Integrity
- Well performance on fill-finish equipment
- Optimized Break Loose & Extrusion Profile
- Low Part-to-Part Variability

Plunger ISO 11040-5



b) Plunger stopper with thread (PST)



a) Plunger stopper with snap lid (PSL)

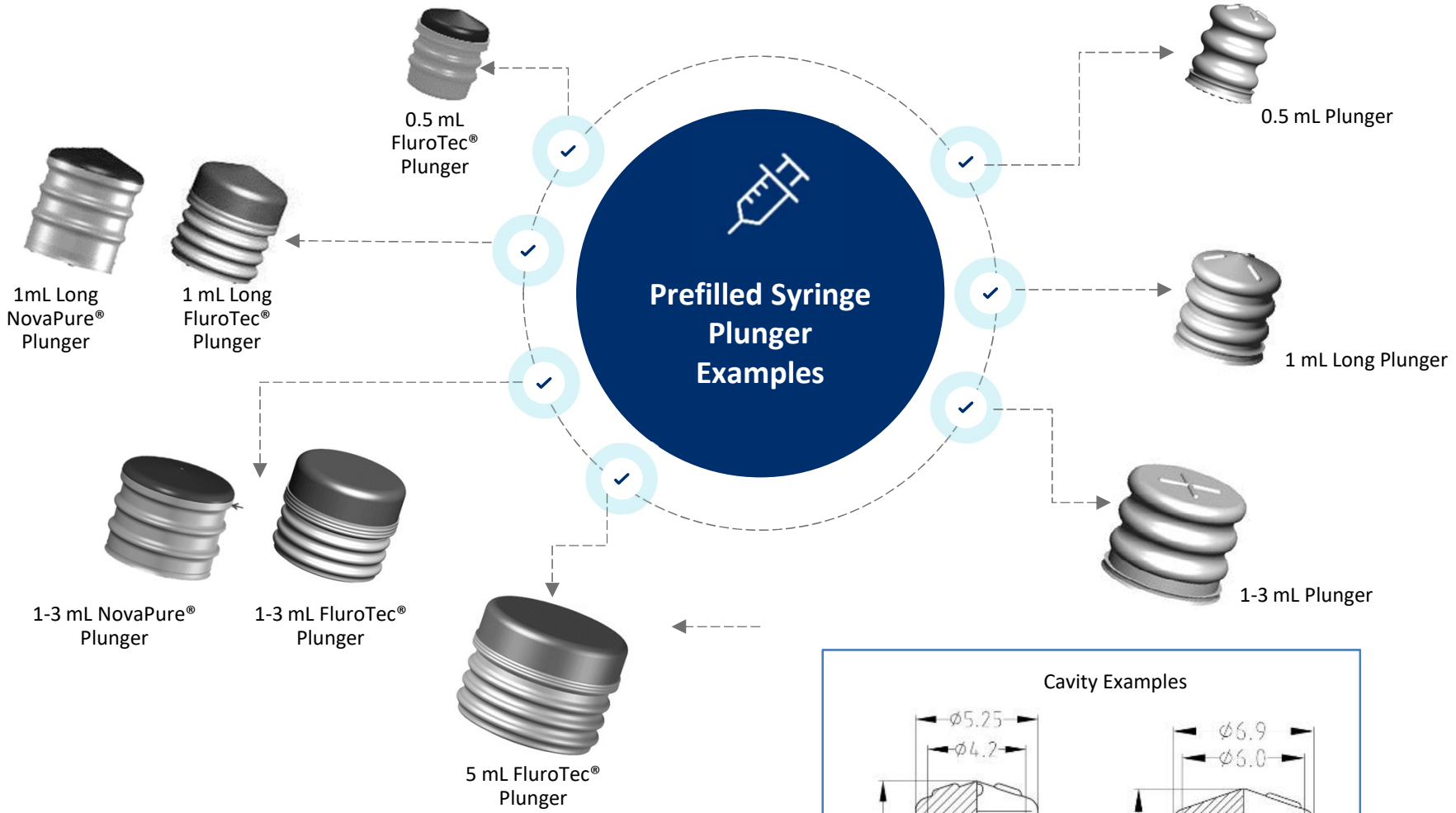
Nominal inner diameter d_2[b]	Nominal volume ml	Type	d_1[a] nom.	d_1[a] tol.	d_2[a] nom.	d_2[a] tol.	d_3[a] nom.	d_3[a] tol.	h_1[a] nom.	h_1[a] tol.	h_2[a] nom.	h_2[a] tol.
4,65 ± 0,1	0,5	PSL	5,2 to 5,3	±0,1	4,1 to 4,2	±0,15	2,5	±0,2	6,85 to 7,0	±0,4	5,3	±0,35
6,35 ± 0,1	1 (long)	PST	6,8 to 7		5,9 to 6		2,6		7,65 to 7,85		4,5	±0,3
8,65 ± 0,2	1 to 3		9,05 to 9,25		7,6 to 8		4,7		7,7 to 7,85		4	
11,85 ± 0,2	5		12,5 to 12,7		10,5 to 11,15		5,2 to 5,6	±0,25	8,5		6,0	
14,25 ± 0,2	10		15 to 15,3		13,5 to 13,75		7,4 to 7,6		8,5 to 10		6 to 6,2	
19,05 ± 0,2	20		19,9 to 20,1	±0,15	18,4 to 18,6		10,7		13,45 to 13,50		7	

[a] The nominal diameter shall be agreed upon between the manufacturer and the user within the given range.

[b] In accordance with ISO 11040-4.

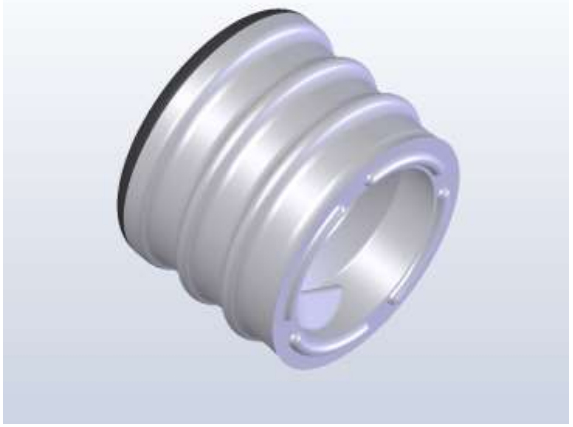
West standard components are compatible with ISO glass barrels

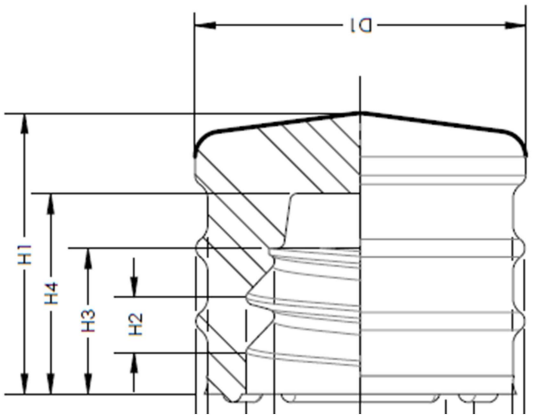
Example of Prefillable Syringe Plungers - Portfolio at West



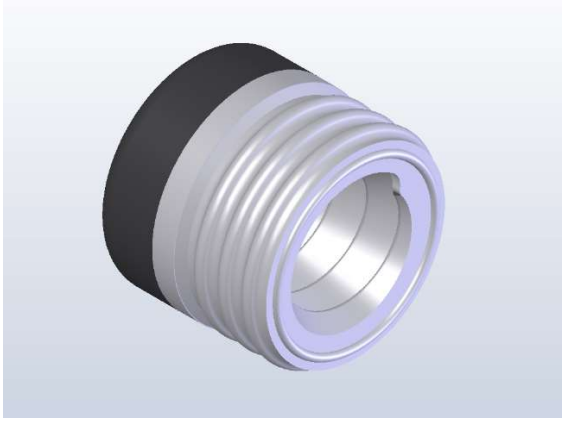
Examples of Prefilled Syringe plunger designs

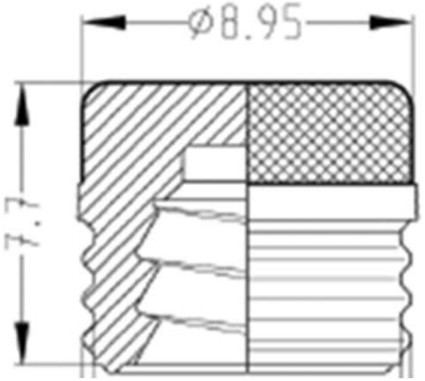
1-3 mL NovaPure® Plunger



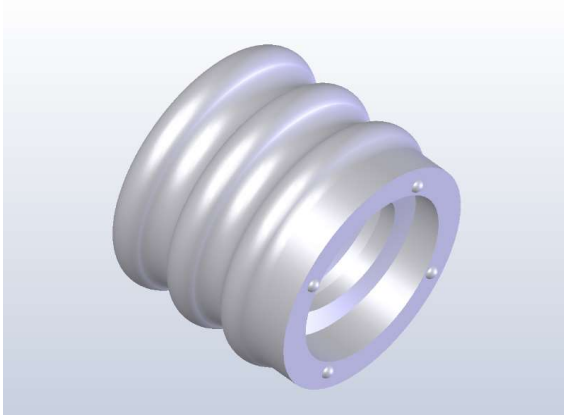


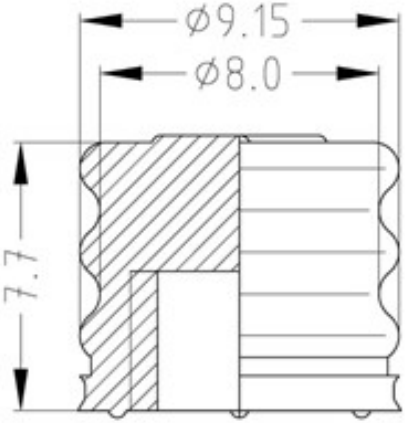
1-3 ml FluroTec® Plunger #2345





1-3 ml Plunger #2116

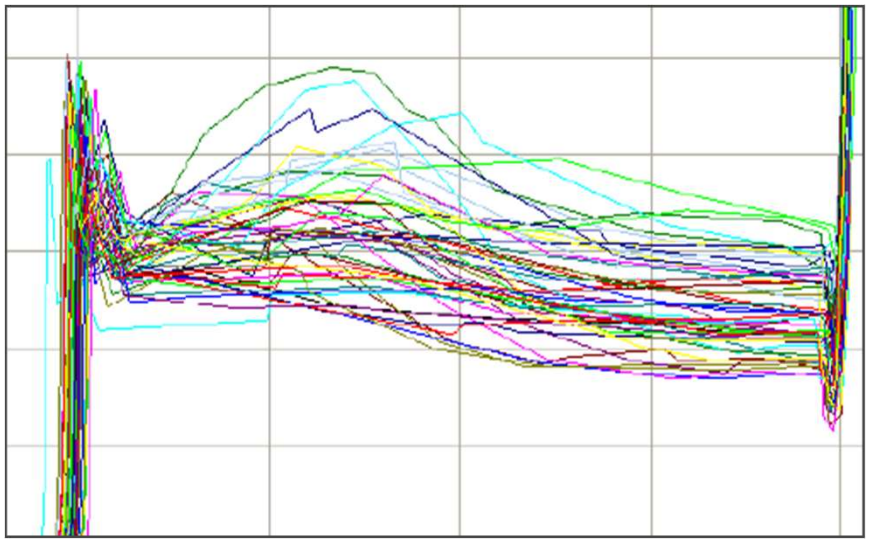




Manual PFS to Auto-injector Challenges

Challenges

- Complex container closure
- Designed for manual injection
- Top variations to overcome
  - Dimensional
  - Silicone oil
  - Break loose and gliding force



Syringe functionality with high variability

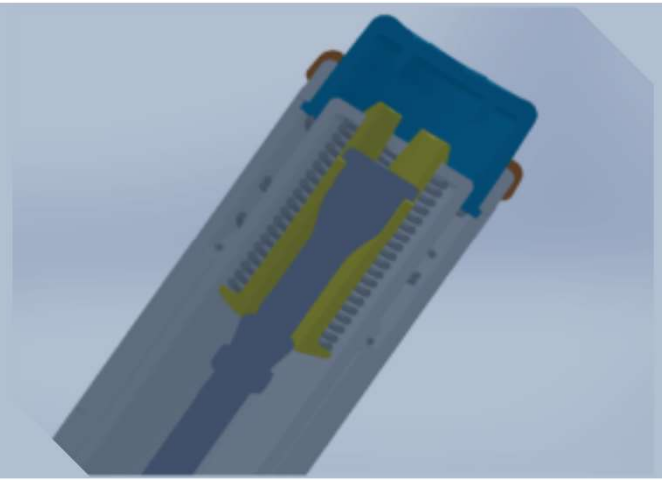
Auto-injector Reliability Risks

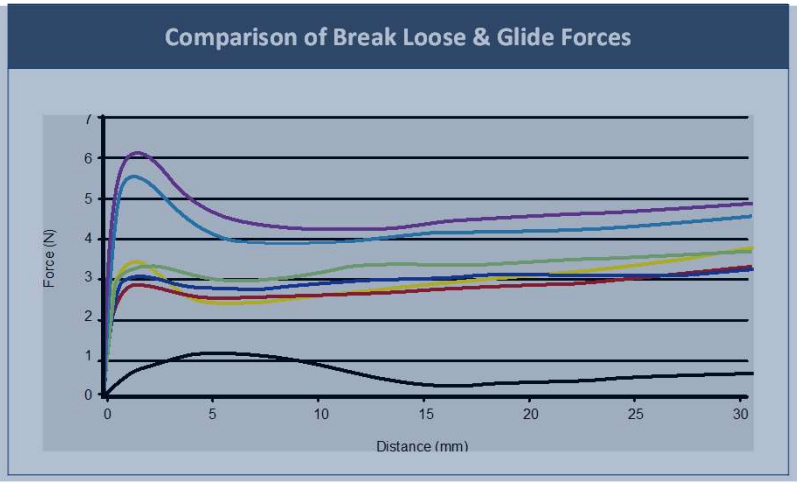
If injection times vary between doses with an auto-injector:

- Patient may stop dose if too long
- Patient may question quality of the product

Critical design factors must be considered, especially functional compatibility

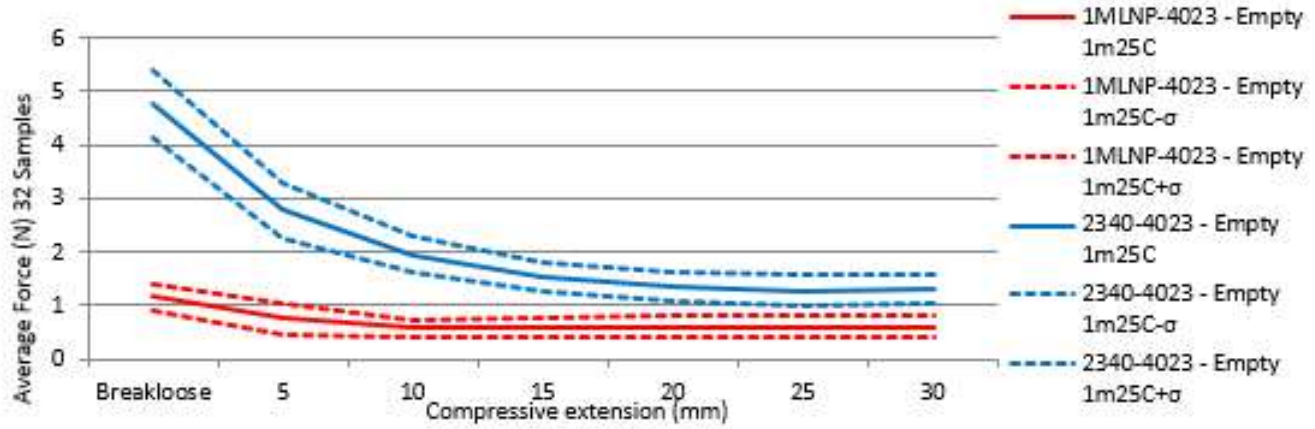
- Break lose and glide forces (max/min)
- Spring falling rate forces (max/min)



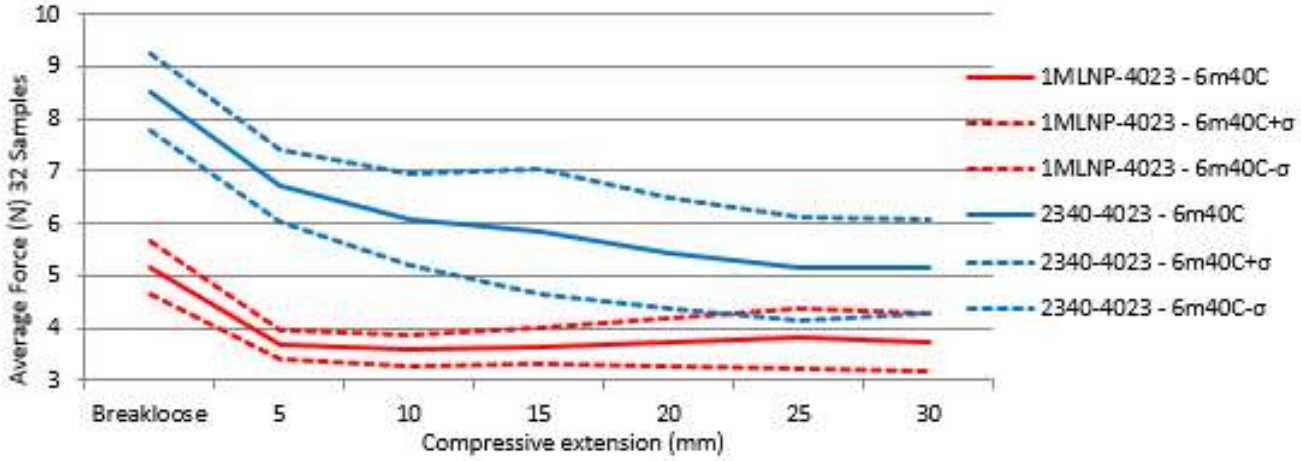


Performance: two different laminated 1 ml long Plungers

Empty

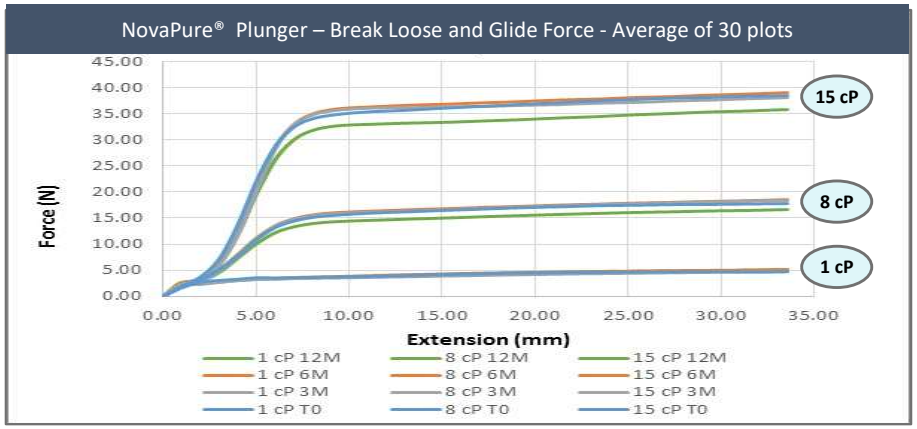


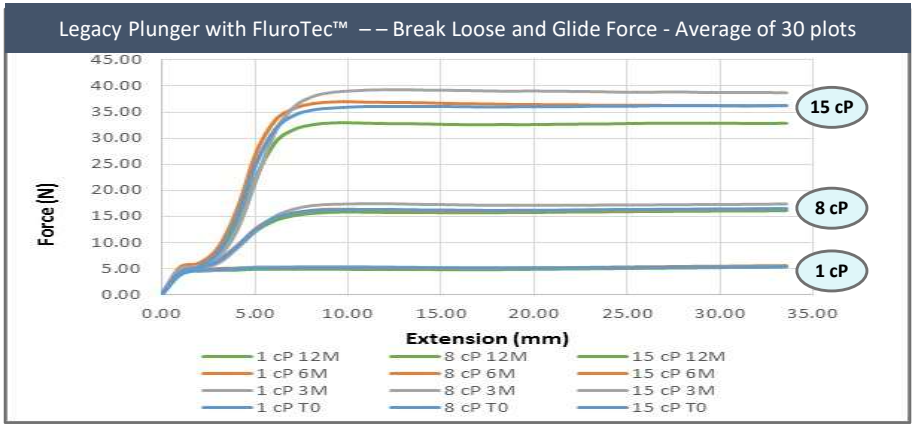
Water Filled



Source: West TR 2013/147

Break-loose and Glide Force - 1 ml Long Plungers Curves represent averages of 30 plots - Example





Time	Fluid Viscosity	NP Plunger Force [N]	Legacy Plunger Force [N]	% lower (with NP)
T0	1cP	1.63	3.68	55.8 %
	8cP	1.77	4.23	58.2 %
	15cP	1.89	4.00	52.7 %
3M	1cP	2.16	4.55	52.5 %
	8cP	2.31	4.64	50.3 %
	15cP	2.35	4.89	52.0%
6M	1cP	2.05	4.45	54.1 %
	8cP	2.55	4.34	41.2 %
	15cP	2.20	5.21	57.8 %
12M	1cP	2.63	4.71	44.3 %
	8cP	2.53	4.43	43.1 %
	15cP	2.39	4.55	47.6 %

- Break-loose forces are on average **50% lower for NovaPure® plungers at all viscosities and all timepoints**
- **Less variability over time with NovaPure® plungers especially for high viscosities**

Break Loose Forces at 1 mm extension

Study Extract: TR 2018/191

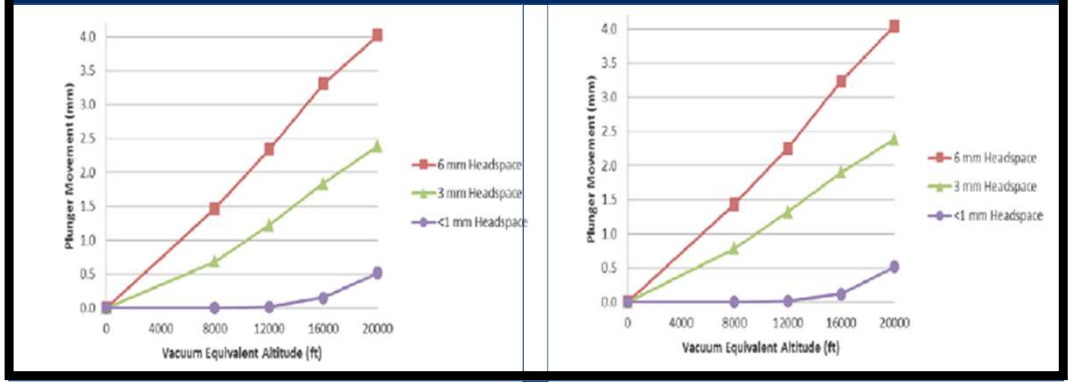
Evaluation of Plunger Movement During Transit Conditions- Example

West Plungers Evaluated: 1-3 ml FluroTec™ film laminated plunger and 1-3 mL NovaPure® plunger

- Headspace Values
  - 6 mm (exaggerated vent-tube placement)
  - 3 mm (typical vent-tube placement)
  - <1 mm (typical vacuum placement)

Altitude	Significance
8,000 ft	Pressurized Jet
12,000 ft	Mountain Passes
16,000 ft	Unpressurized Jet
20,000 ft	Highest Cargo Jet Altitude on Record

NovaPure® 1-3mL | **1-3 ml FluroTec™ film laminated#2345**

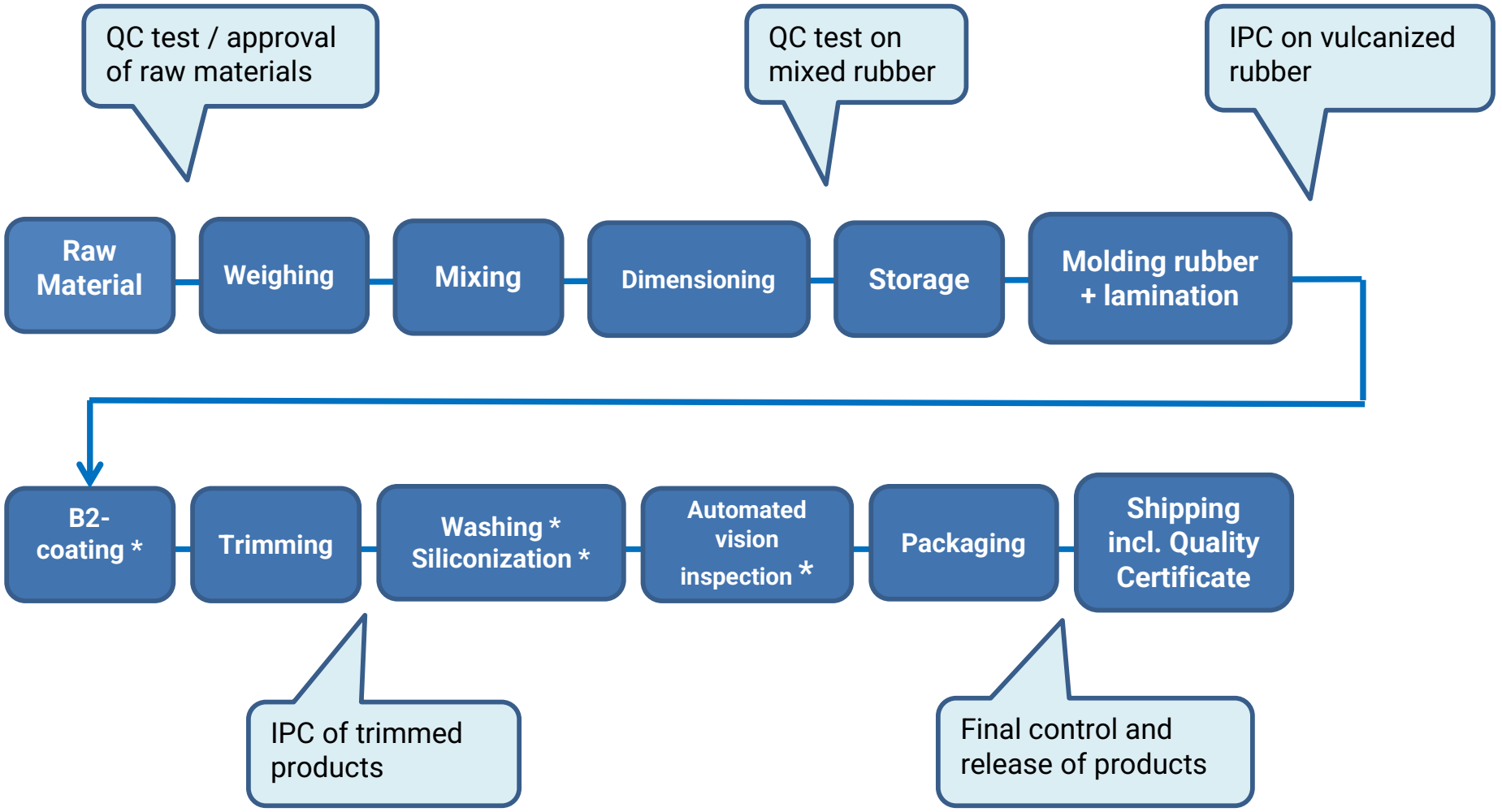


- Linear correlation between pressure and movement
- Higher headspace volume leads to stronger movement
- NovaPure® and legacy plunger performance is comparable

Extract of Study – technical report available – TR 2016-172

Processing

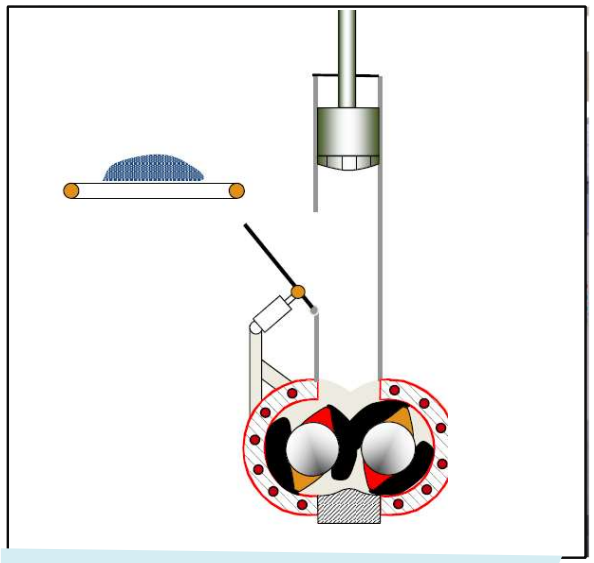
Production Overview [Plungers]



* optional upon request

Manufacturing Process

Internal Mixer



Mixer all components are mixed by turning rotors

- Shearing the elastomer, squeezing out air, Incorporating all material
- Critical parameters are specific for the individual formulations: rotor speed, temperature, time, filling volume, etc.
- Caution not to start vulcanization

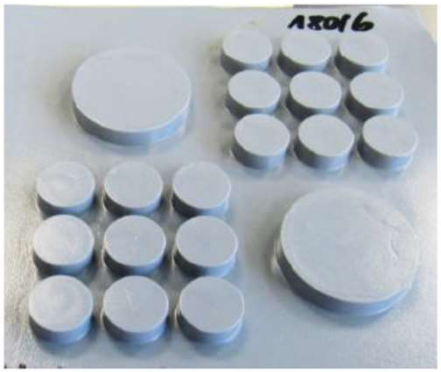
Open Mill

Mill additional homogenization of the mixture by compactors

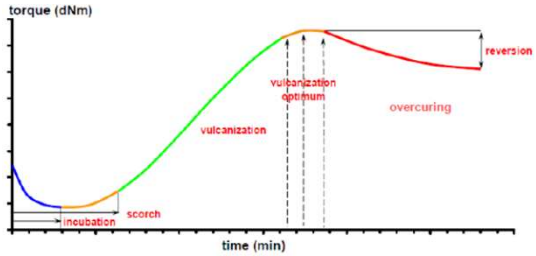
- Squeezing out air, cooling down
- Caution not to start vulcanization
- Elastomer mixture is collected in “puppets”

Mixing Control (Mill Control)

Curing of ISO – standard sample for testing purposes	
specific gravity	per batch
Shore A of vulcanized sample	per batch
dispersion of vulcanized sample	per batch
color of vulcanized sample	per batch
ash content	every 10th batch plus 1st and last
rheology of the compound	every 5th batch plus 1st and last



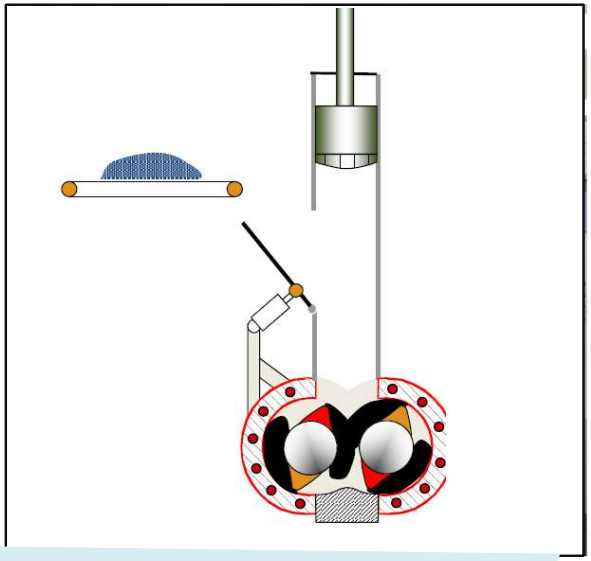
Vulcanized Test buttons



Rheology Curve

Manufacturing Process

Internal Mixer



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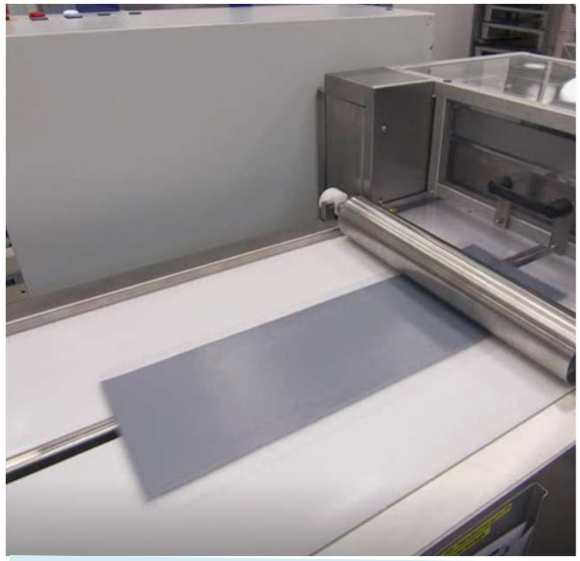
Open Mill

Mill additional homogenization of the mixture by compactors

- Squeezing out air, cooling down
- Caution not to start vulcanization
- Elastomer mixture is collected in “puppets”

Calendaring & Dimensioning

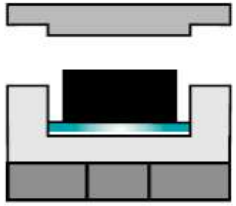


- “Puppets” are finally cooled down in rollers
- Cooling & Cutting
- Coasted into webs with defined thickness and width
- Webs are led to relax for some time

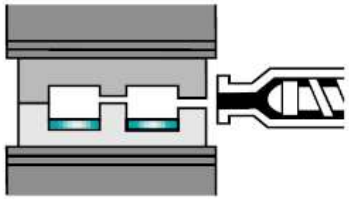
Pharmaceutical Rubber Manufacturing

Different 'shapes' need different molding technology:

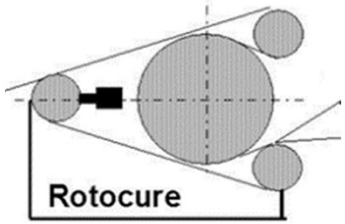
- Compression Molding (CM)
  e.g. Plungers, stoppers, disk
  .



- Precision Injection Molding (PIM)
  e.g Needle shields …



- Rotocure (Sheeting Material)
  e.g. Lined seals…

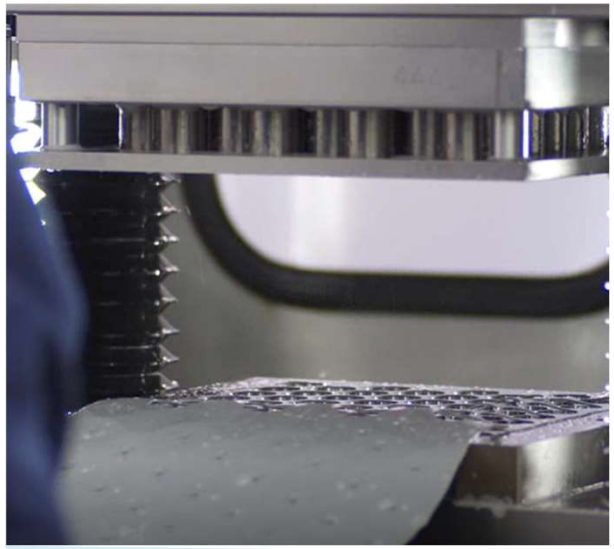


Manufacturing Process

Compression Molding

- Compression and Precision Injection Molding
- Vulcanization takes place
- Critical parameters are specific for the individual formulations: press speed, temperature, time, vacuum, etc.

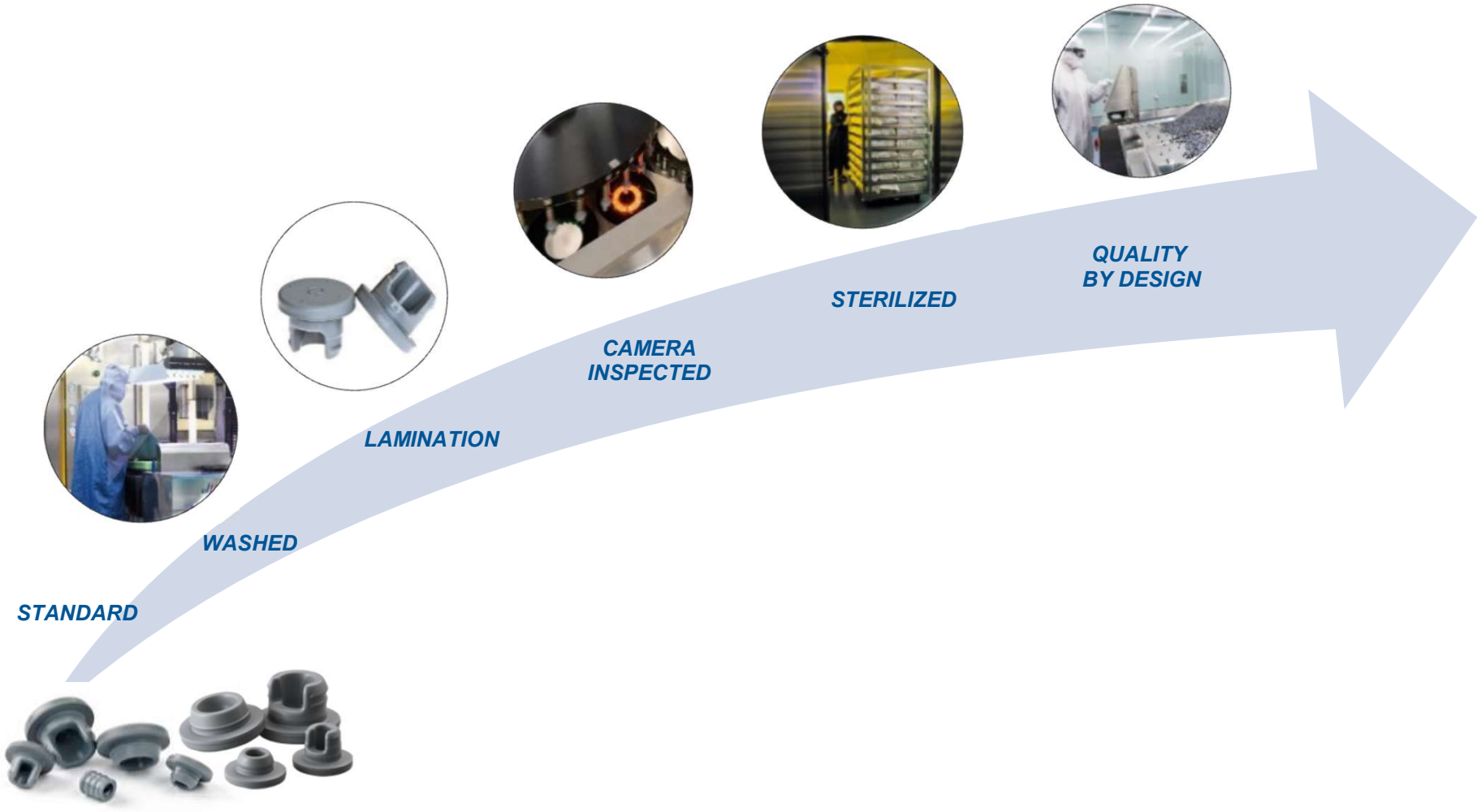
Trimming



- Trim presses designed for cleanroom manufacturing
- Enhanced trim dies to lower particle contamination
- Automated control of web positioning
- Automated web spraying for lubrication

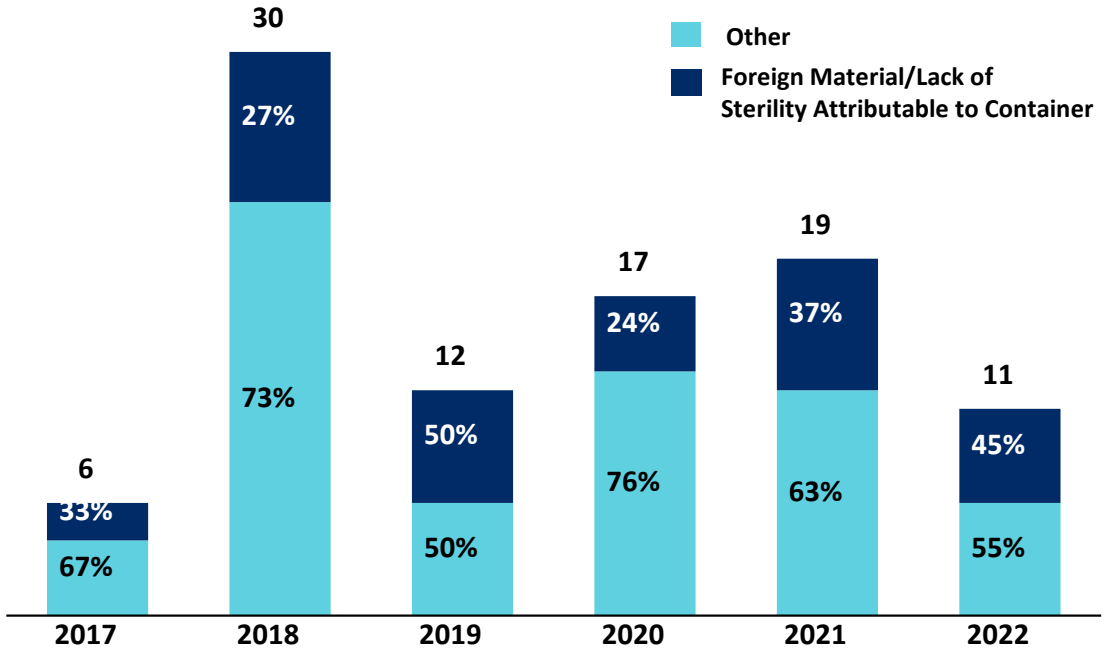
- Single parts transferred to Washing operations

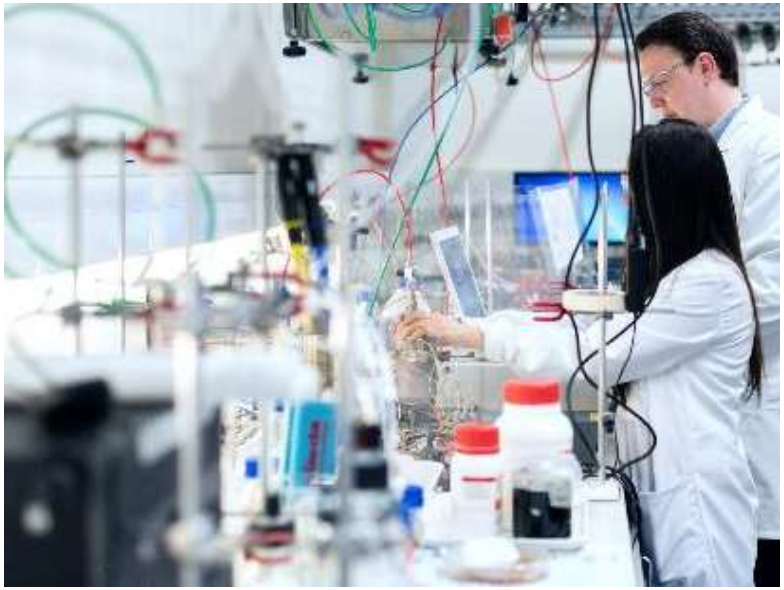
Differentiated Solutions: Increasing Quality & Inspection



Particulates and Lack of Sterility Cause Most Product Recalls

Reason For Injectable Product Recalls[1]





34% of recalls are due to particulate or lack of sterility attributable to container closure.

Regulatory agencies driving for better product quality

[1] *https://www.fda.gov/drugs/drug-safety-and-availability/drug-recalls (Accessed September 1, 2022) and https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/recalls-biologics (Accessed September 1, 2022)*

Finishing: Pharmaceutical Wash Process

- Validated process according to GMP to demonstrate an endotoxin content reduction by at least 99.9% (3.0 $\log_{10}$).
- Components are unloaded from the washer in a Zone 5 clean room
- All associated process data is filed in Drug Master Files (DMF) with FDA and Health Canada.
- **Particulate, bioburden and endotoxin are reported in the quality certificate provided with every batch**

NOVAPURE

WestarSELECT

Product Specification for Particulate Matter

Westar™ Select treatment particulate matter specification

Specification	Westar™ Select
Particulate between 25-50 µm	≤ 13 particles / 10 cm^2
Particulate between 50-100 µm	≤ 3.5 particles / 10 cm^2
Particulate > 100 µm	≤ 0.5 particles / 10 cm^2
PCI	≤ 1.9 PCI

The manufacturing and validation approach support the capability to produce elastomeric components that meet established specifications for particulate matter.

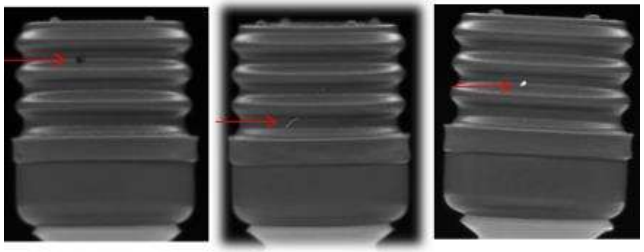
NovaPure® component best-in-class particle specifications

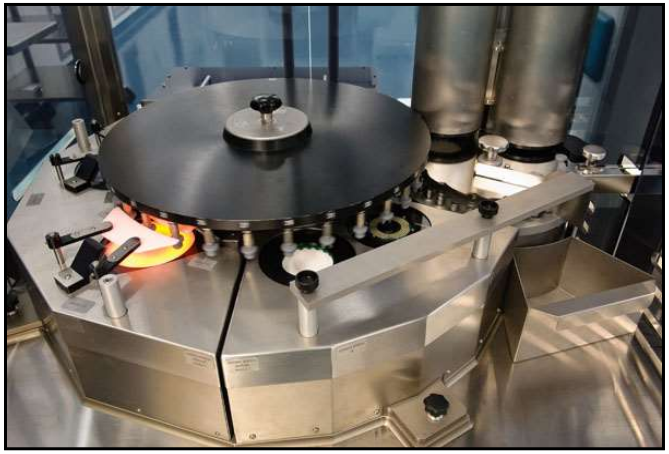
Specification	NovaPure®
Particulate ≥5µm ≤10µm	≤ 100.0 particles / 10cm^2
Particulate ≥10µm ≤25µm	≤ 60.0 particles / 10cm^2
Particulate ≥25µm ≤50µm	≤ 10.0 particles / 10cm^2
Particulate ≥50µm ≤100µm	≤ 1.0 particles / 10cm^2
Particulate ≥100µm	≤ 0.2 particles / 10cm^2

Note: Particulate specifications may differ from the above depending on the packaging materials selected.

- Developed with in-depth product & process knowledge
- Higher level of performance with minimal variability for packaging components

End-of-Line Defect Reduction

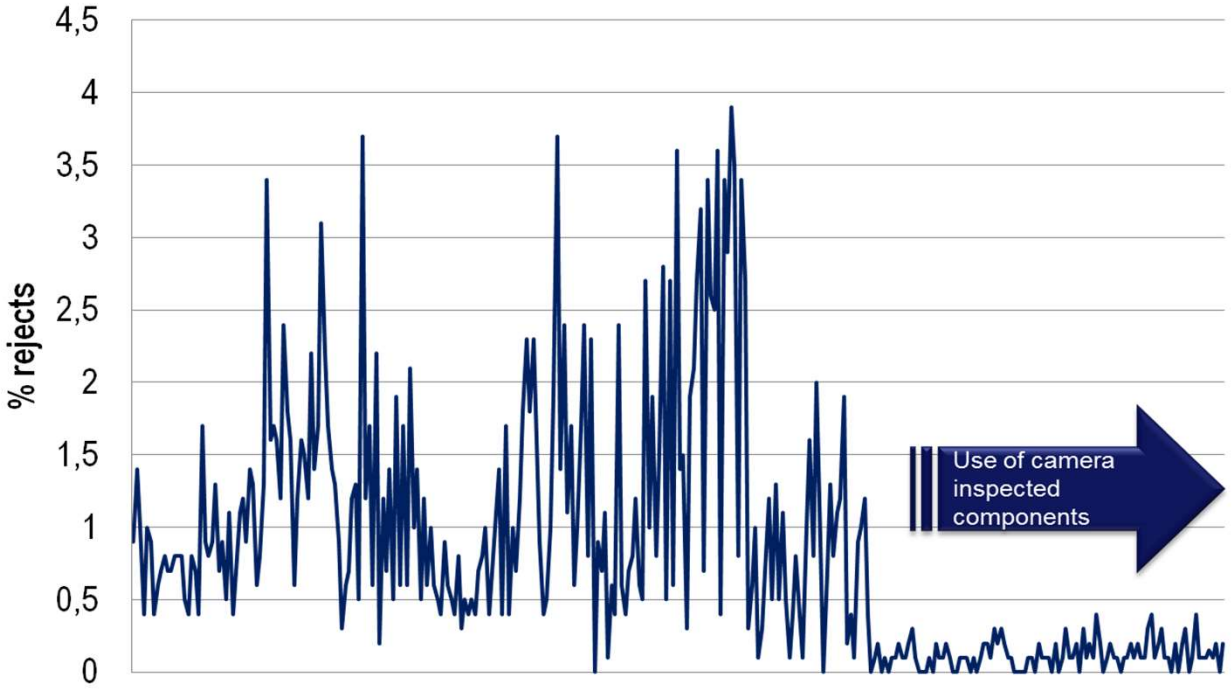




100% Camera Inspection of rubber components

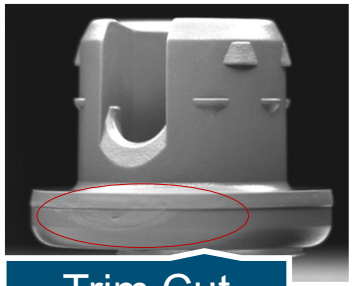
technical report available – TR 2016-172

Case Study: End-of-line drug filled units reject trend



Automated vision inspection verification: defects examples

Flow Line

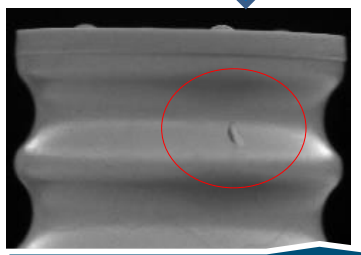


Trim Cut

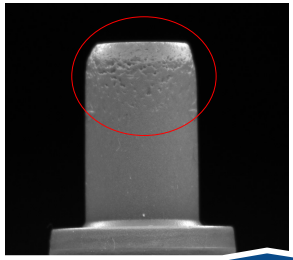
FluroTec™ film wrinkles and torn FT

Manufacturing Defects

Eccentric Trim



Damaged Cavity



Molding non-fills

Automated vision inspection verification: defects examples

Fiber

Mixing dispersion issue

Hairlike

Dispersion/Contamination related

Rubber flash

Embedded foreign matter

Sterilization process

Steam sterilization

- Plungers, stoppers and lined seals
- The sterilization process is validated to assure a minimum SAL of 10^{-6} and in line with
  - ISO 17665-1 and 17665-2
- Steam processed elastomer formulations exhibit less degradation

Gamma sterilization

- Plungers
- The sterilization process is validated to assure a minimum SAL of 10^{-6} and in line with
  - ISO 11137-1 and ISO 11137-2
- Gamma processing might impact degradation of the elastomeric formulation

Sterility assurance is reported in the quality certificate coming with every batch

Manufacturing Process

Secondary Packaging

Secondary Packaging - Flexibility for Filling Needs

- Filled bags are offered in ready-to-use (RU) quality by either steam or gamma validated processes
- The ported bag packaging system is qualified to maintain the package integrity and stability of the components throughout the recommended shelf-life period. Verification includes shipping distribution simulation studies.

Image courtesy of Bausch+Stroebel.
Used with permission

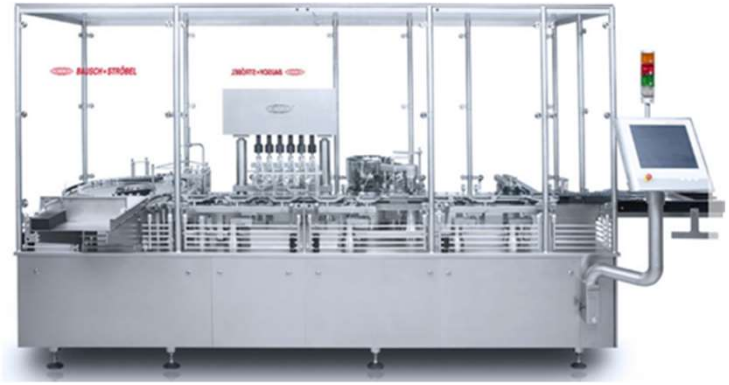


Image courtesy of Bausch+Stroebel.
Used with permission

High-quality packaging materials

- Reduction of particle load of primary packaging → tighter specification
- Ease of use
- Pinhole resistant – physical – stress
- Plastic cartons & plastic pallets
- Qualified to maintain the package integrity and stability of the components throughout the recommended shelf-life period. Verification includes shipping distribution simulation studies

Ready-to-Use Packaging Solutions

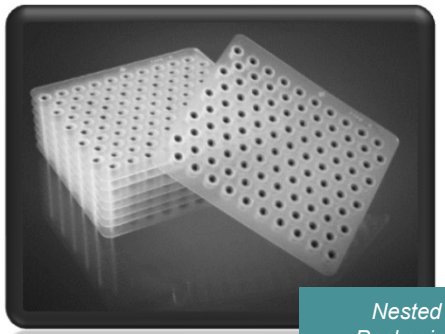
Bulk Packaging System (Gamma)

Not commercially available – Under Development Tub Nested Plungers

STERILIZABLEBAG™ Packaging System Small Pack or Commercial

Sartorius Stedim Biotech (SSB) 110mm BioSafe™ System (Steam and Gamma)

Getinge-La Calhene (GLC) 190mm DPTE-BetaBag® System (Steam and Gamma)



Nested Packaging System (Gamma)

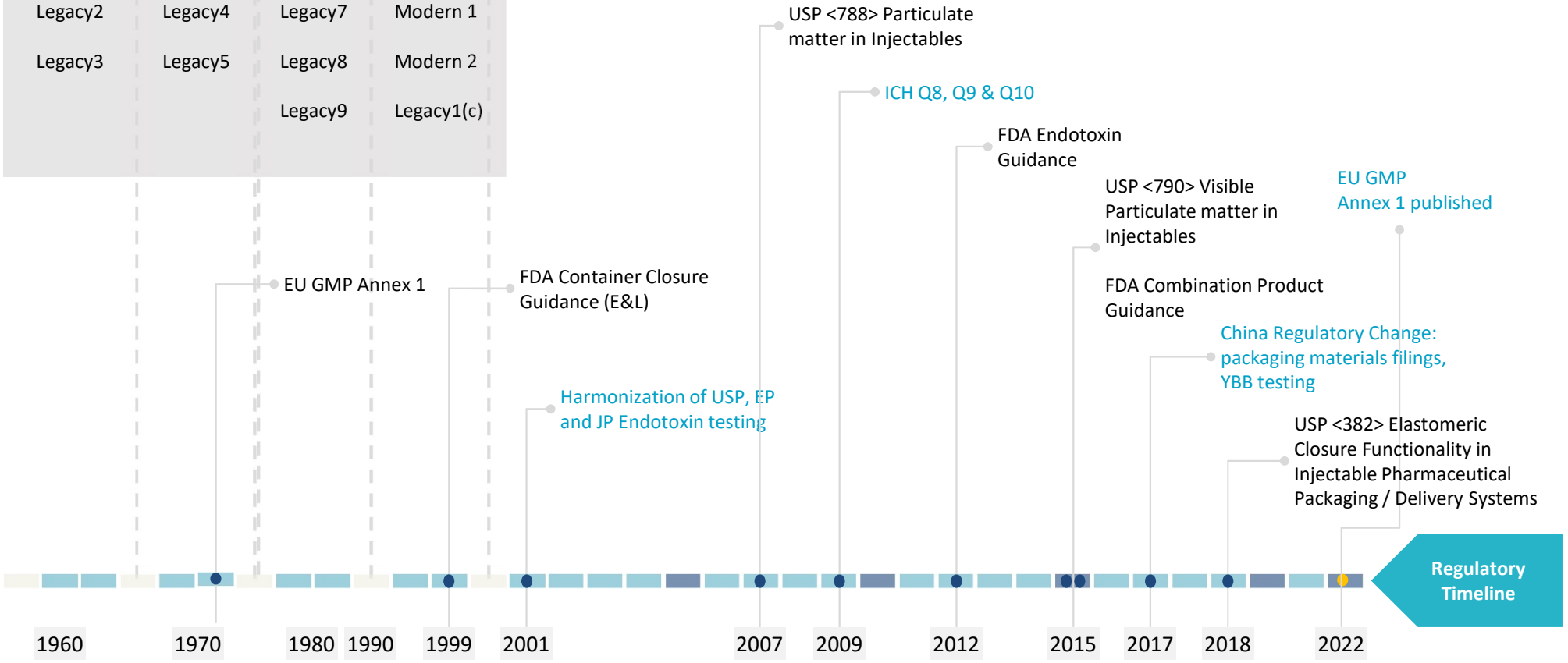
Please note, not all product offerings are available in these packaging formats

Relevant Compendial Chapters and Standards

Regulations Are Evolving

Legacy Formula Timeline (examples only)

Legacy1	Legacy1(b)	Legacy6	Legacy 10
Legacy2	Legacy4	Legacy7	Modern 1
Legacy3	Legacy5	Legacy8	Modern 2
		Legacy9	Legacy1(c)



Global Comparison of Elastomer Chapters

Purpose	Paragraph	USP <381>	Ph Eur 3.2.9	JP 7.03	YBB
Introduction	Definition of Elastomer Types	✓	✓	-	✓
Identification	e.g. IR, ash test	✓	✓	✓	✓
Physico-chemical Tests	Appearance of solution, absorbance, etc. ..	✓	✓	✓	✓
Potential Extractable	Ammonium, Volatile Sulfides	✓	✓	✓	✓
Functionality Tests*	Fragmentation, self-sealing, …	✓	✓	-	✓

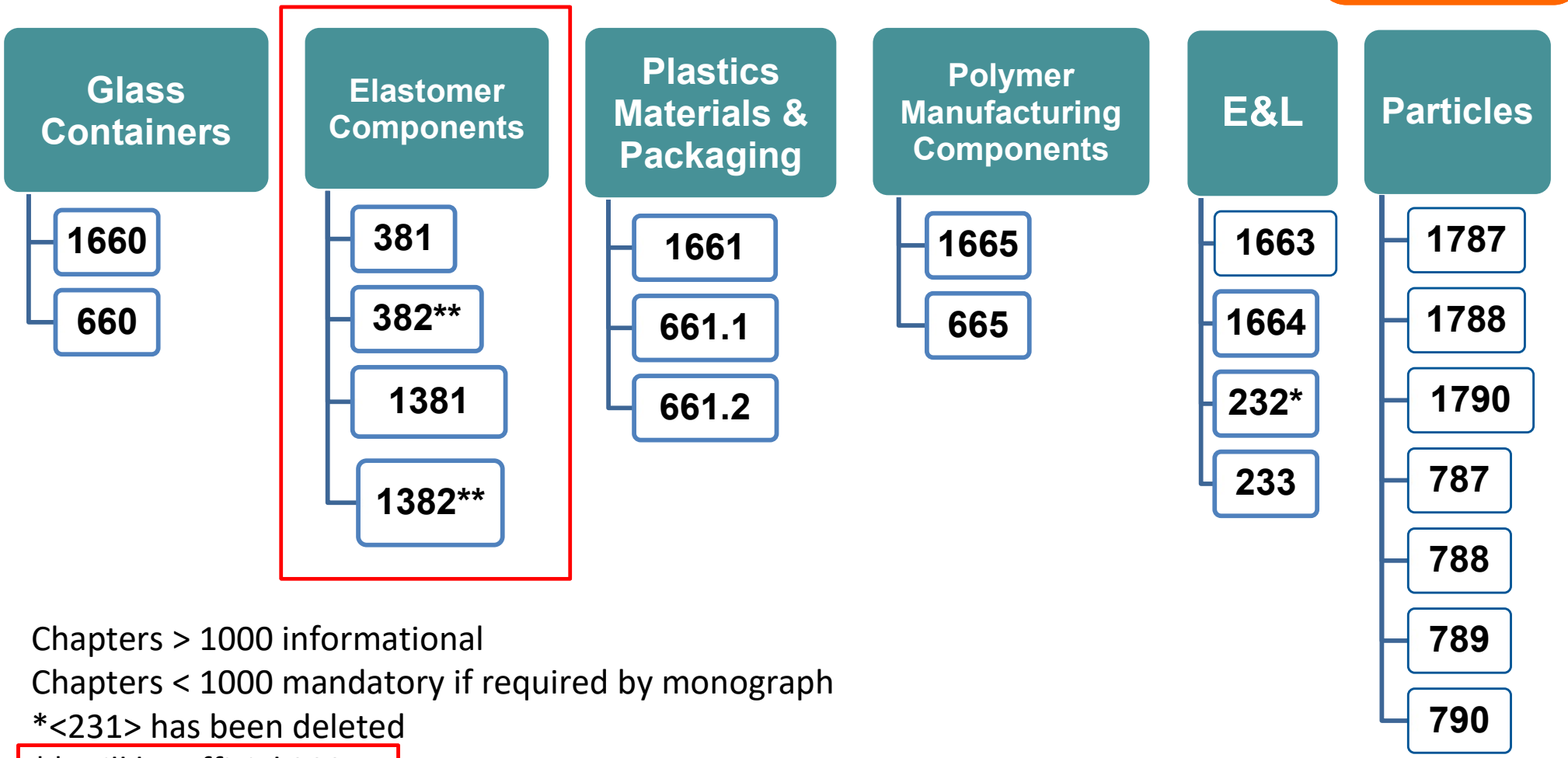
functionality tests are moving to USP 382 starting from 2025

Global comparison of elastomer chapters

usp U.S. Pharmacopeia	European Pharmacopeia 10th Edition	JP Japanese Pharmacopeia	PHARMACOPOEIA OF THE PEOPLE's REPUBLIC OF CHINA
• Development of a new chapter addressing functionality tests USP <382> • Including E&L	• Revision of Heavy Metals / Elemental Impurities and methods • Plastics materials & additives	• Deletion of pyrogen and hemolysis test • Addition of cytotoxicity test	• Ongoing revisions in all topics with a strong attention to the global revision process and discussion

Overview of relevant USP chapters

usp U.S. Pharmacopeia



Chapters > 1000 informational
Chapters < 1000 mandatory if required by monograph
*<231> has been deleted
** will be official 2025

Introduction to USP <1382> and <382>

<1382> Assessment of Elastomeric Component Functional Suitability in Parenteral Product Packaging/Delivery Systems

- Assist in the functional suitability assessment of elastomeric components as part of packaging / delivery systems
- ISO references
- Sampling plan guidance

<382> Elastomeric Component Functional Suitability in Parenteral Product Packaging/Delivery Systems

- Fitness for intended use functional suitability tests and requirements

Released December 2020 with 5-year implementation grace period

Current <381> versus <382>

From: USP <381>

Elastomeric Closures for Injections

- Functionality Tests
  - Penetrability
  - Fragmentation
  - Self-Sealing Capacity

Container Closures for Vials and Bottles

To: USP <382>

Elastomeric Component Functional Suitability in Parenteral Product Packaging and Delivery Systems

- Package/Delivery System Integrity Tests
- Needle and Spike Access Functionality Tests
  - Fragmentation
  - Penetration Force
  - Needle Self-Sealing Capacity
  - Spike Retention and Sealability Capacity
- Plunger Functional Suitability Tests
  - Plunger Break Force and Plunger Glide Force
  - Plunger Seal Integrity
- Tip Cap and Needle Shield Functionality Tests

System Closures for Vials, Bottles, Blow Fill Seal Containers, Plastics, Cartridges and Syringes

Thank you very much for your attention!

Any Thoughts?
Any Questions?

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