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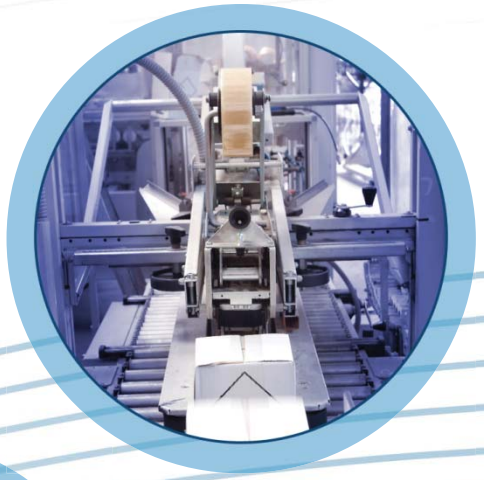
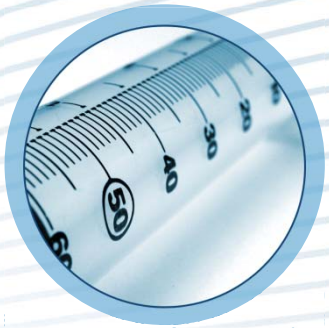
TR-43 Revised: Identification and Classification of Nonconformities in Molded and Tubular Glass Containers, for Pharmaceutical Manufacturers



Roger Asselta,
Genesis Technical Advisors



NE PDA Meeting
November 13, 2013

Introduction

Task Force was charted to develop a guideline that could provide a basis for informed quality decisions on incoming glass container visual inspections resulting in:

- Consistency in terms and specifications
- More uniform approach in meeting regulatory expectations to deliver high-quality products

History

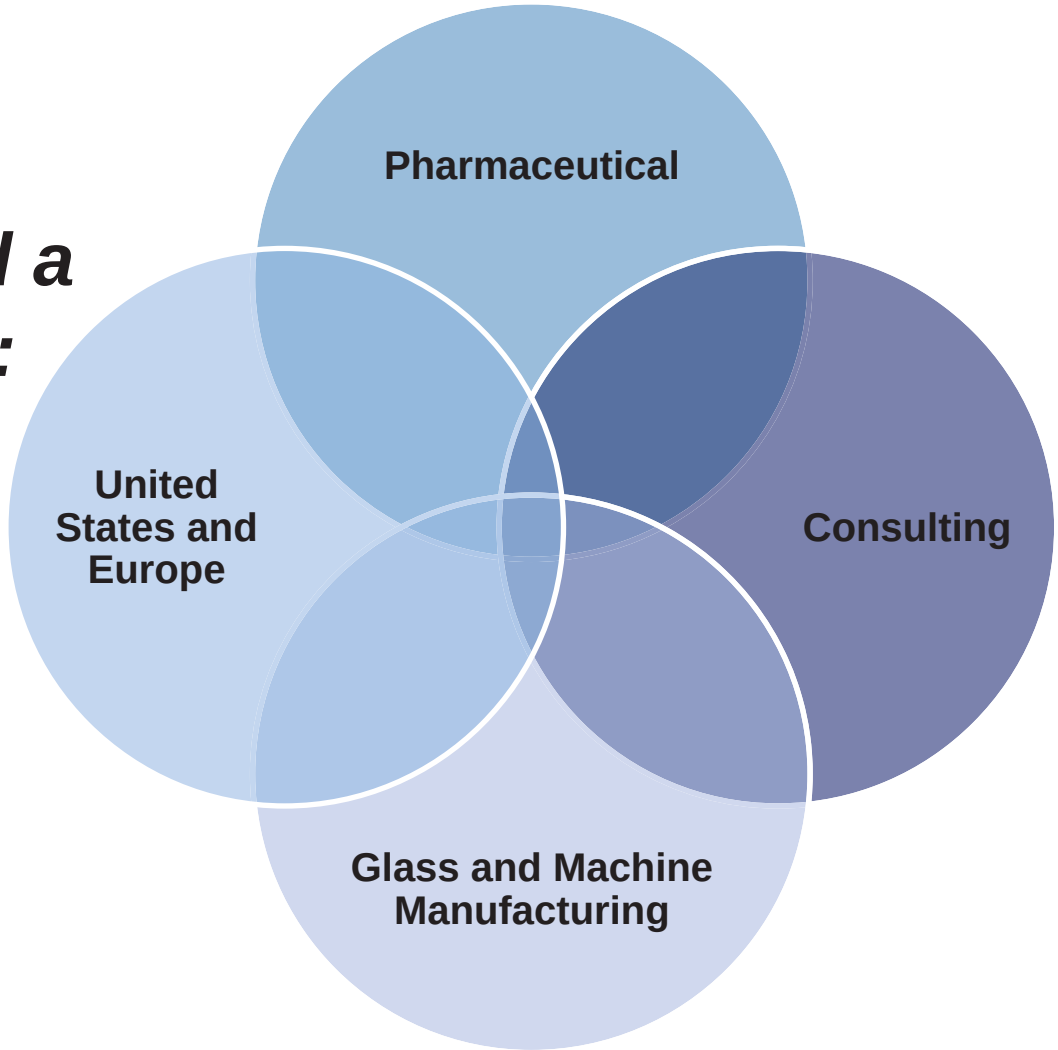
- In the Spring of 2002 the PDA formed its original Glass Task Force
  - Charter
    - To develop guidelines for the identification and classification of visual nonconformities for glass container items.
  - Team Members were cross functional:
    - Pharmaceutical Members
    - Consultants
    - Glass and Machine Manufacturing industries from the United States and Europe.
  - Technical Report-43 was published in the 4th quarter of 2007.

History

- A second Glass Task Force was formed in the 4th quarter of 2007 to compliment and revise TR No. 43.
- Purpose:
  - To enhance TR No. 43 by addressing the identification and classification of visual nonconformities for tubular glass ampoules, cartridges and syringes.
- The new task group is co-chaired by Michael Eakins and Nick DeBello

Task Force

Task Force of 27 members reflected a broad perspective:



Scope

- **In Scope:**
  - Adding Visual Nonconformities for Glass Ampoules, Cartridges and Syringes.
  - Completely Updating Visual Nonconformities for Tubular Vials and Molded Bottles and Vials
- **Out of Scope:**
  - Dimensional Nonconformities
  - Updating Lexicons published in TR No. 43
  - Plastic Syringes and Cartridges

Scope Continued

- **The document was to be:**
  - A consensus based nomenclature
    - Consistent Quality Criteria
    - Standardized Terminology
    - Standardized Classifications
  - A Guideline
  - A listing of most frequently found nonconformities.
- **This document will not:**
  - Be a standard
  - Cover specific equipment
  - Cover product outside of scope
  - Cover topics related to products or lab

Glass Task Group Sub Teams

New Glass Task Group was divided into three sub teams

- Ampoules: Nick DeBello (Chair)
  - Pull Stem
  - Funltop or Funnel Top
  - OPC
  - Closed Top Ampoules
- Cartridges:Mads Espersen (Chair)
  - By-Pass Cartridges
  - Conventional Cartridges
- Syringes: Roger Asselta (Chair)
  - Straight Barrel
  - By- Pass Syringes
  - Luer Tip
  - Luer Lock Tip
  - Staked Needle

- Molded Bottles:- Nick DeBello (Chair)
  - Aluminum Seal
  - Screw Neck
- Tubular Vials: Tony Perry (Chair)
  - Aluminum Seal
  - Screw Thread

Glass Task Group

- Each sub team was chartered to gather information to:
  - Identify the most commonly found defects
  - Reach a consensus on the defect definitions
  - Gather representative photos for the nonconformities
  - Achieve a consensus on the Classification of each nonconformity.
    - Critical
    - Major A and B
    - Minor

Glass Nonconformities Lexicons

- The new lexicons contain the most frequently found glass nonconformities:
  - Molded – 59 slides of imperfections
  - Ampoules – 50 slides of imperfections
  - Cartridges – 40 slides of imperfections
  - Syringes – 43 slides of imperfections
  - Vials – 48 slides of imperfections

Technical Report 43 Revised

- Introduction
- Glossary
- Glass Container Conformance Specification Development Process
  - Glass Container Dimensional Development
  - Glass Container Sampling
    - Definition of Lots
    - Sampling Plans
    - Acceptable Quality Limits

Technical Report 43 Revised Continued

- Glass Nonconformities Lexicons
  - Molded Glass
  - Tubular Glass – Ampoules, Cartridges, Syringes and Vials
  - Re-inspection of Glass Containers
  - Documentation and Training
- Conclusion
- Appendices
- References
- Bibliography

Glass Container Conformance Development Process

Acceptable Quality Limits

Philosophy and goal of zero nonconformities

Requirement of an AQL = 0.0%

Nonconformity Classifications

- Critical
- Major
- Minor

Allows for a distinction based on their potential impact on ***product quality*** and ***patient safety***

Note: *Setting AQL specifications for glass nonconformities requires an agreement between the pharmaceutical and glass manufacturing companies to minimize risk*

Glass Nonconformities Lexicons

Glass Nonconformities

The Glass Task Force reviewed Nonconformities with some degree of rationale based on numerous factors.

Verification of nonconformity classifications may warrant additional testing to establish their rationale.

Quality Criteria

Quality requirements should be aligned with the product and their intended use

Based on:

- Patient safety
- Product process requirements
- Glass manufacturer's production capability

Nonconformity Definitions

Critical: Likely to result in personal injury or potential hazard to the patient.

Nonconformity Definitions

Major A: Leads to serious impairments (e.g., a malfunction making packaging unusable)

Major B: Leads to impairments of a lesser degree (e.g., reduced efficiency in production)

Nonconformity Definitions

Minor: Nonconformities that do not have essential consequences.

N/A: Imperfections considered to be non-applicable or non-defects and therefore acceptable.

Nonconformity Definitions

Limit Sample:

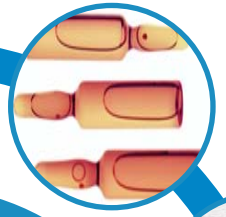
An actual physical unit that is agreed to between the user and the manufacturer that defines the approximate maximum degree of acceptability for a specified non-conformance. Creation of limit samples between the user and the manufacturer is optional.

Nonconformity Lexicons

Visual and descriptive details of glass nonconformities

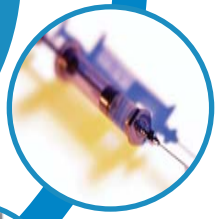
Molded Bottles

Tubular Glass Components



Ampoules

Cartridges



Syringes

Vials

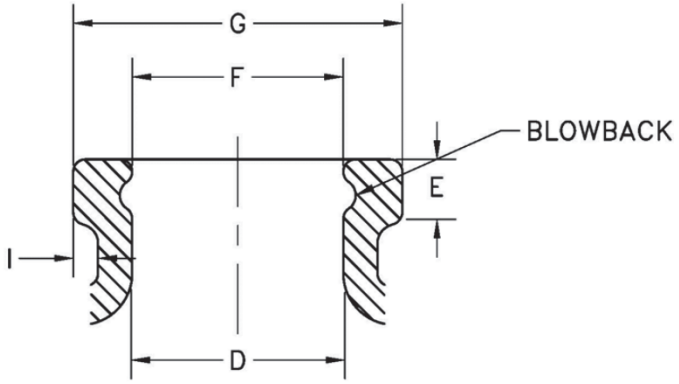
Nonconformity Lexicons

Each Lexicon contains

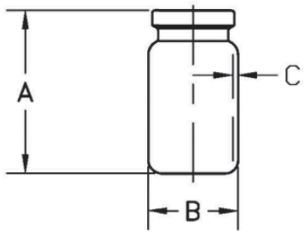
- The Name of the Nonconformity
- Location on the Container
- Classification Of Severity Based On Potential Impact To The Patient
- Definition of the Glass Nonconformity
- Photo or Drawing of the Glass Nonconformity

Tubular Vial Glass Container Lexicon

TUBULAR VIAL – NOMENCLATURE



NECK DETAIL



KEY:
A – OVERALL HEIGHT
B – EXTERNAL BODY DIAMETER
C – BODY WALL THICKNESS
D – CHOKE
E – FLANGE HEIGHT
F – FINISH INSIDE DIAMETER
G – FLANGE OUTSIDE DIAMETER
I – FLANGE PROJECTION

Tubular Vial Lexicon

Crack

Location: General

Class: Critical

Fracture that penetrates completely through the glass wall.

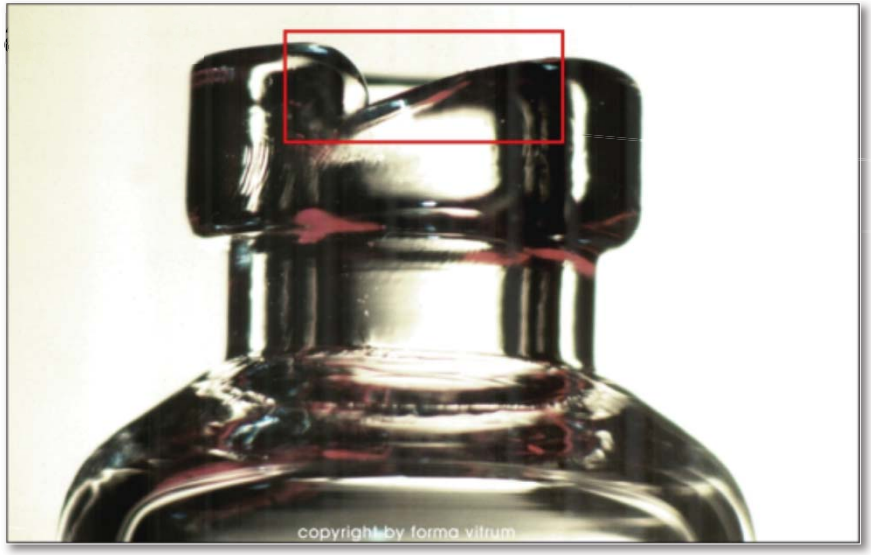
Tubular Vial Lexicon

Malformed

Location: Finish

Class: Critical if seal is compromised; seal is intact.

M



Finish is grossly distorted or deformed.

Tubular Vial Lexicon

Spiticule

Location: General

Class: Critical

Bead or string of glass that is adhered to the inside surface.

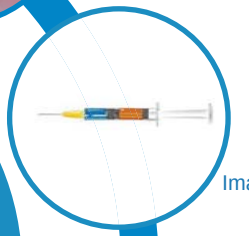
Tubular Syringe Lexicon

Tubular Syringe Lexicon

In Scope:

Visual Nonconformities for all types of pre-fillable glass syringe containers

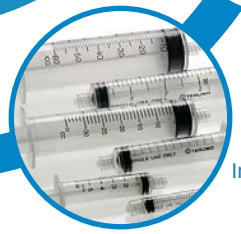
Standard Barrel



By-Pass Syringes

Image courtesy of Debiotech

Luer Tip



Luer Lock Tip

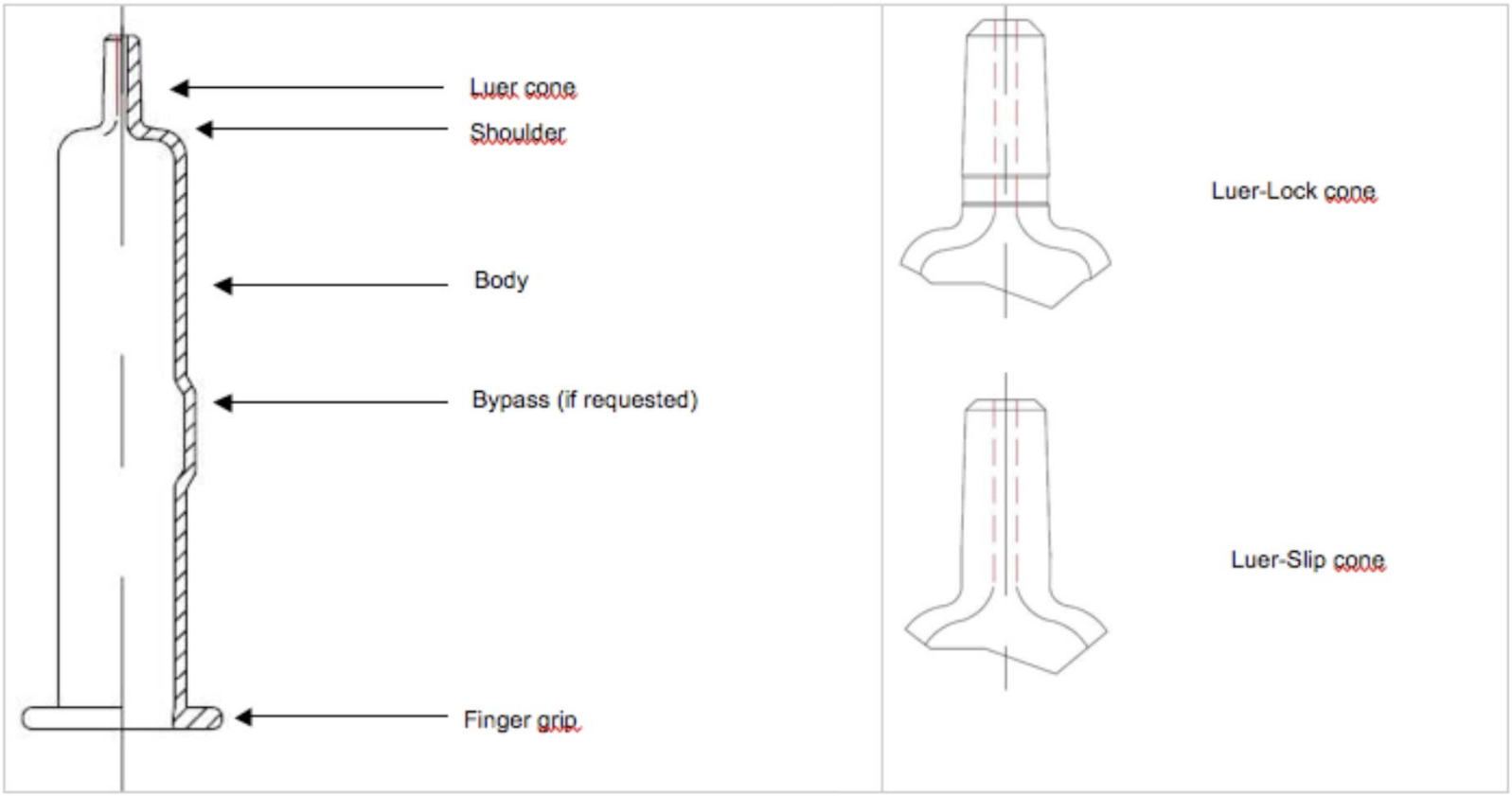
Image courtesy of wolfmed.com

Out of Scope:

- ***Dimensional Nonconformities***
- ***Print Defects***
- ***Siliconization***

Syringe Definition

PREFILLABLE GLASS SYRINGES WITH LUER-SLIP / LUER-LOCK CONE

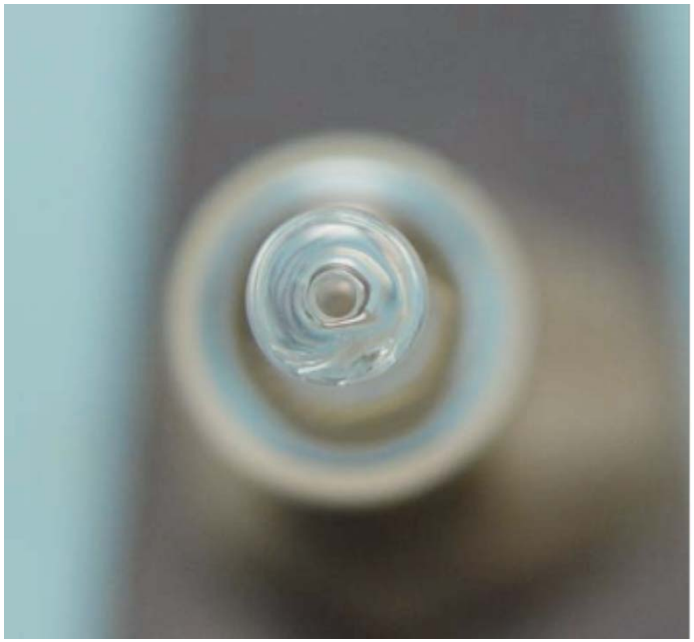


Tubular Syringe Lexicon

Bore, Out of Round

Location: Cone

Class: Major B Luer Tip;
N/A otherwise

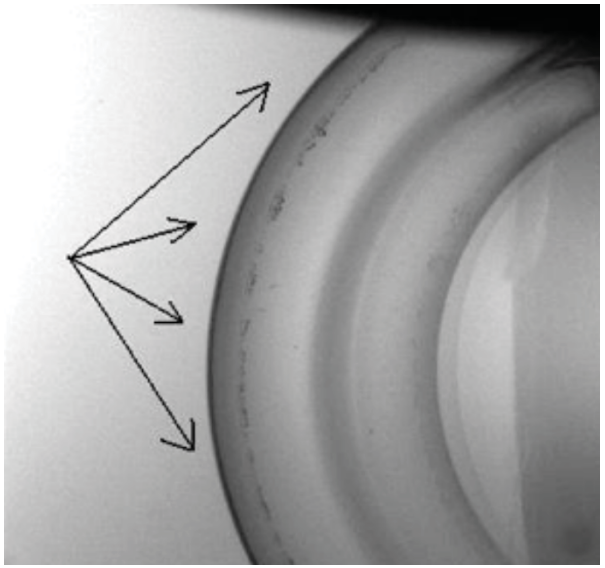


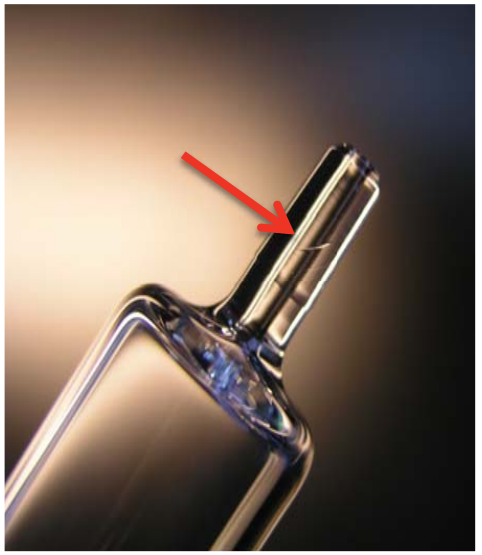
Bore of cone is oval or oblong.

Tubular Syringe Lexicon

Tooling Mark

Location: Cone or Finger Grip **Class: Minor**



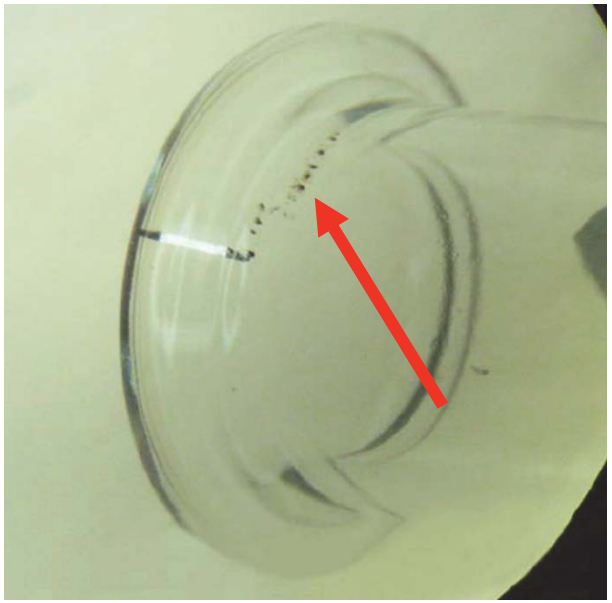


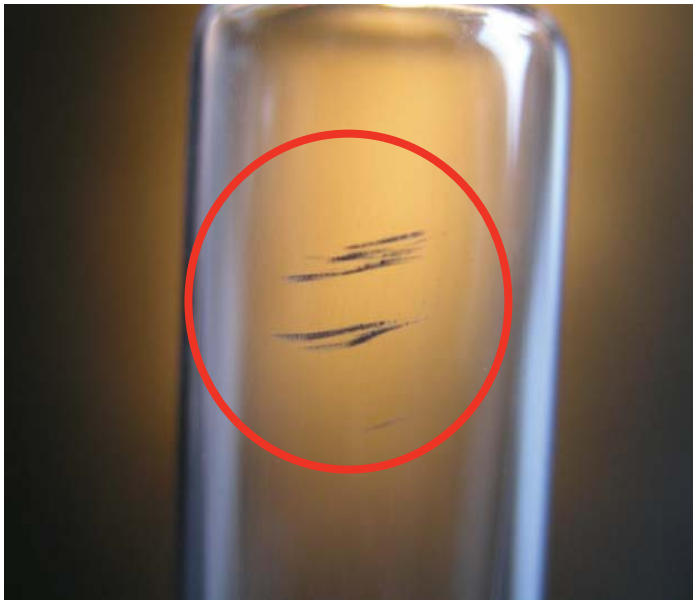
Mark on cone or finger grip by forming tool.

Tubular Syringe Lexicon

Metal Mark

Location: General **Class: Major A if on interior;**
Minor if exterior





Shiny or dark mark on the surface.

Conclusion

- The Task Force believes that the Lexicons provide a guide for most common and current types of nonconformities in molded and tubular glass containers
- Use of lexicons result in the following:
  - Eliminates confusion by establishing a consensus lexicon created by glass and pharmaceutical manufacturers
  - Identification of nonconformity classifications by severity
  - A common nomenclature that can be used throughout the industry for classification of glass container attributes

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Questions? Comments?

Let’s go through some examples in the Technical Report