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
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.
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 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

Pharmaceutical Company and Glass Manufacturer develop a glass container quality specification

- Dimensional Design
- Definition of Lots
- Acceptable Quality Limits
- Sampling Plans
- Classification and Disposition of Non-Conformances
- Re-inspection Plan
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

Tubular Glass Components

- Ampoules
- Cartridges
- Syringes
- Vials

Molded Bottles
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
Crack

Location: General
Class: Critical

Fracture that penetrates completely through the glass wall.
**Malformed**

**Location:** Finish

**Class:** Critical if seal is compromised; Major B if seal is intact.

Finish is grossly distorted or deformed.
Spiticule

Location: General
Class: Critical

Bead or string of glass that is adhered to the inside surface.
Tubular Syringe Lexicon
In Scope:

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

Out of Scope:

- Dimensional Nonconformities
- Print Defects
- Siliconization
Syringe Definition

PREFILLABLE GLASS SYRINGES WITH Luer-Slip / Luer-Lock Cone

- Luer cone
- Shoulder
- Body
- Bypass (if requested)
- Finger grip
- Luer-Lock cone
- Luer-Slip cone
Bore, Out of Round

Location: Cone

Class: Major B Luer Tip; N/A otherwise

Bore of cone is oval or oblong.
Tooling Mark

Location: Cone or Finger Grip

Class: Minor

Mark on cone or finger grip by forming tool.
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
Contact Information:

Roger Asselta,
Senior Advisor and Vice President
Genesis Technical Advisors
400 Eagleview Boulevard, Suite 100
Exton, PA 19341 USA

Rasselta@gen-techno.com
610 458 4928
Questions? Comments?

Let’s go through some examples in the Technical Report