THE NATIONAL FOOD LAB

Recent Developments in Microbial Validation of Aseptic Packaging Systems: An US Process Authority Perspective

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Presentation Outline

- Objective
- The NFL
- Overview and Latest Developments Aseptic Rotary Aseptic Fillers (RAF)
- Validation for RAF using PAA as Sterilant
  - Application of Food Safety Objective
  - Application of Performance Criteria
- Conclusion

Today's Objective

To provide a general overview of a pathway for the FDA filing and microbial evaluation of new sterilization technologies intended for high-speed, low-acid aseptic bottle fillers.

The National Food Laboratory, Inc.

The NFL is the wholly owned subsidiary of the Grocery Manufacturers Association formerly:

NCA, NFPA and FPA.

The NFL may change to…

GMA
The Association of Food, Beverage and Consumer Products Companies

MAJOR LEAGUE BASEBALL

NBA

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Check out our new digs….

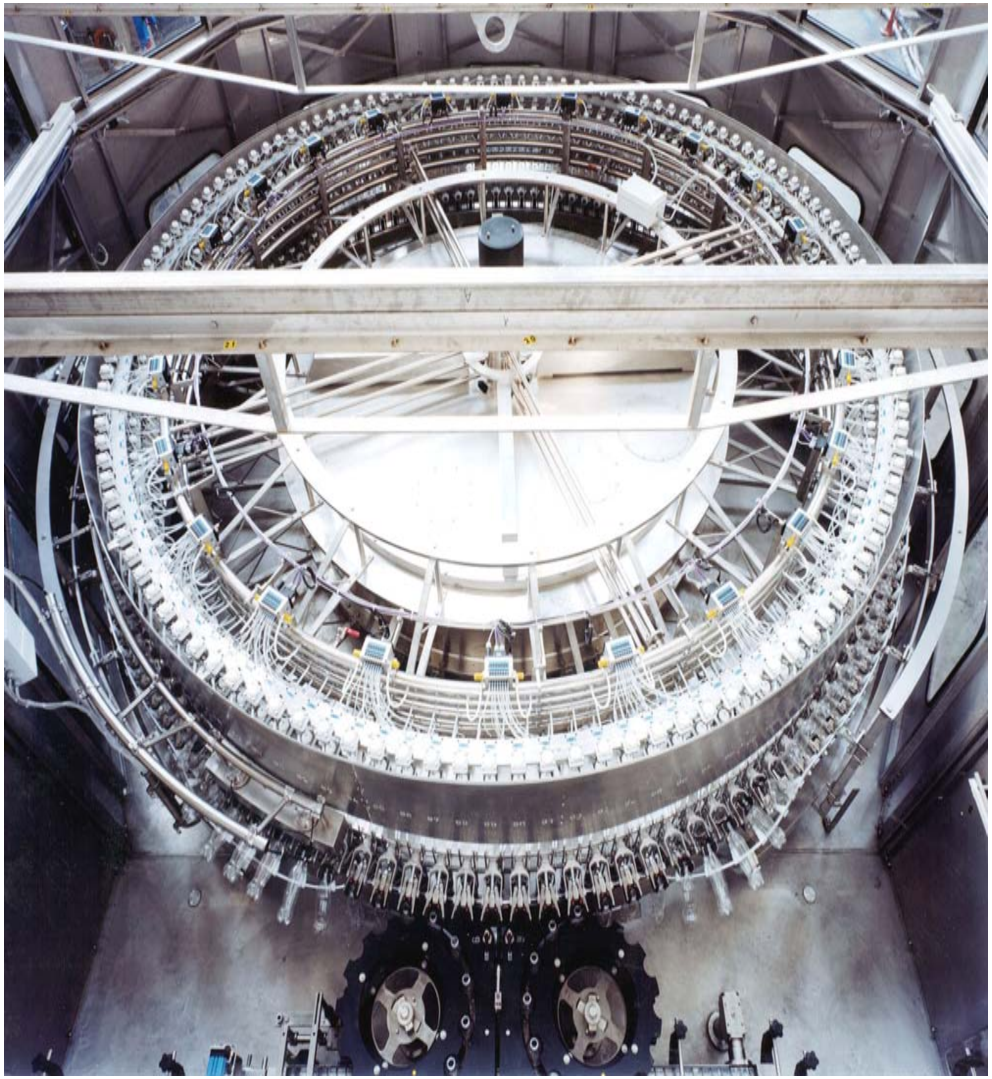
- The National Food Lab
  Innovation Center:
  365 North Canyons Parkway
  Suite 201
  Livermore, CA 94551

  Technology Center:
  2441 Constitution Drive
  Livermore, CA 94551

High-speed Rotary Fillers

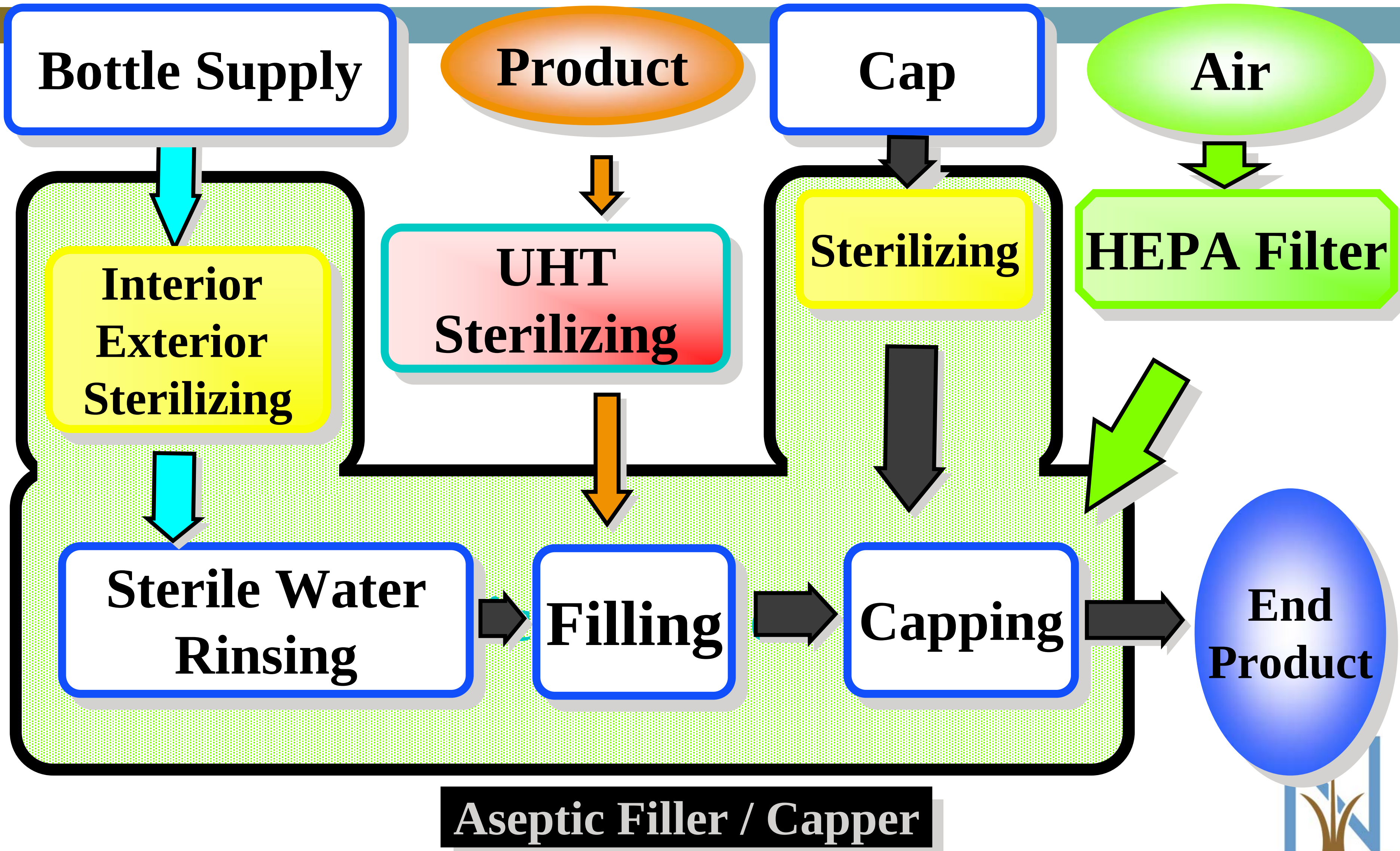
Overview and Latest Developments

Aseptic Rotary Bottle Fillers



- High Speed
- Flexible Bottle Shape
- PET or HDPE
- PAA or H_2O_2
- No foil seal
- More Complex
- Large Aseptic Zones
- Numerous Critical Factors

PET Bottle Aseptic Filling



Latest Developments – USA Firsts

- 2002 – Shibuya/Mott's: 1st FDA "LONO" for high-speed aseptic bottling system (H_2O_2)
- 2005 – Shibuya/HP Hood: 1st FDA filing for high-speed bottling system (H_2O_2)
- 2008 – Procomac/Ecolab/Aseptic Solutions: 1st FDA "LONO" for PAA (two-phase) sterilized high-speed system

Latest Developments – USA Firsts

- 2008 – KHS Filler @ Gehl's (H202vapor)
- 2009 – Procomac/Ecolab/Nestle: 2nd FDA "LONO" for PAA sterilized high-speed system
- 2009 – Toyo/FMC/Nikkako: 1st FDA "LONO" for single-phase PAA sterilant
- 2009 – Procomac/Ecolab/Nestle: 5 Additional Lines are currently under validation/filing process

Shibuya Aseptic Bottle Filler

Shibuya Aseptic Bottle Fillers

	Shibuya @ Mott's, Aspers, PA	Shibuya @ HP Hood, Winchester, VA
FDA Status	LONO - 2002	Filed Process - 2005
Product	NA	Various Milk-Based
Sterilant	35% H_2O_2	35% H_2O_2
Plastic/Size	PET / 32 oz	HDPE / 14-oz
Speed/Size	322 BPM	600 BPM

Steps to FDA Filing – Shibuya Filler

1. **Worked with The NFL prior to design phase**

↓

2. **Prepared FDA compliant design**

↓

3. **Presented design/concept to FDA**

↓

4. **Preliminary prototype sterilization testing**

↓

5. **Identified 1st Food Processor partner and installed system**

Steps to FDA Filing – Shibuya Filler cont.

7. Invited regulators to observe system as installed

↓

8. Shibuya conducted preliminary validation tests

↓

9. Adjusted sterilization parameters as needed

↓

10. The NFL conducted final validation tests

↓

11. Presented data package to FDA and obtained letter of non-objection

Steps to FDA Filing – Shibuya Filler cont.

12. Identified 2nd Food Processor (HP Hood)

↓

13. Invited regulators to observe system

↓

14. Repeated steps 8-10

↓

15. Presented filing package to FDA and successfully filed processes for low-acid beverages

Procomac Fillers

	Procomac @ Aseptic Soln's, Corona, CA	**Procomac @ Nestle, Inc., Anderson, IN**
FDA Status	LONO - 2008	LONO - 2009
Bottle Sterilant	PAA @ 4000 ppm Ecolab Envirosan™ + ES 1000 penetrant	PAA @ 4000 ppm Ecolab Envirosan + ES 1000 penetrant
Cap Steriliz	Pre-irradiated	PAA or Pre-irradiated
Plastic	PET 16 oz	PET 16 oz
Speed/Size	250 BPM	720 BPM

Toyo Aseptic Bottle Fillers

	Toyo @ Nikkako; Yamaguchi, Japan
FDA Status	LONO - 2009
Product	NA – (Tea and Coffee-based)
Sterilant	PAA, 4000 ppm (single phase) FMC, Clarity™
Plastic/Size	PET – 500 ml
Speed/Size	350 BPM

Case Study

FDA Filing of Procomac Filler Using PAA as a Sterilant

Pertinent Regulations

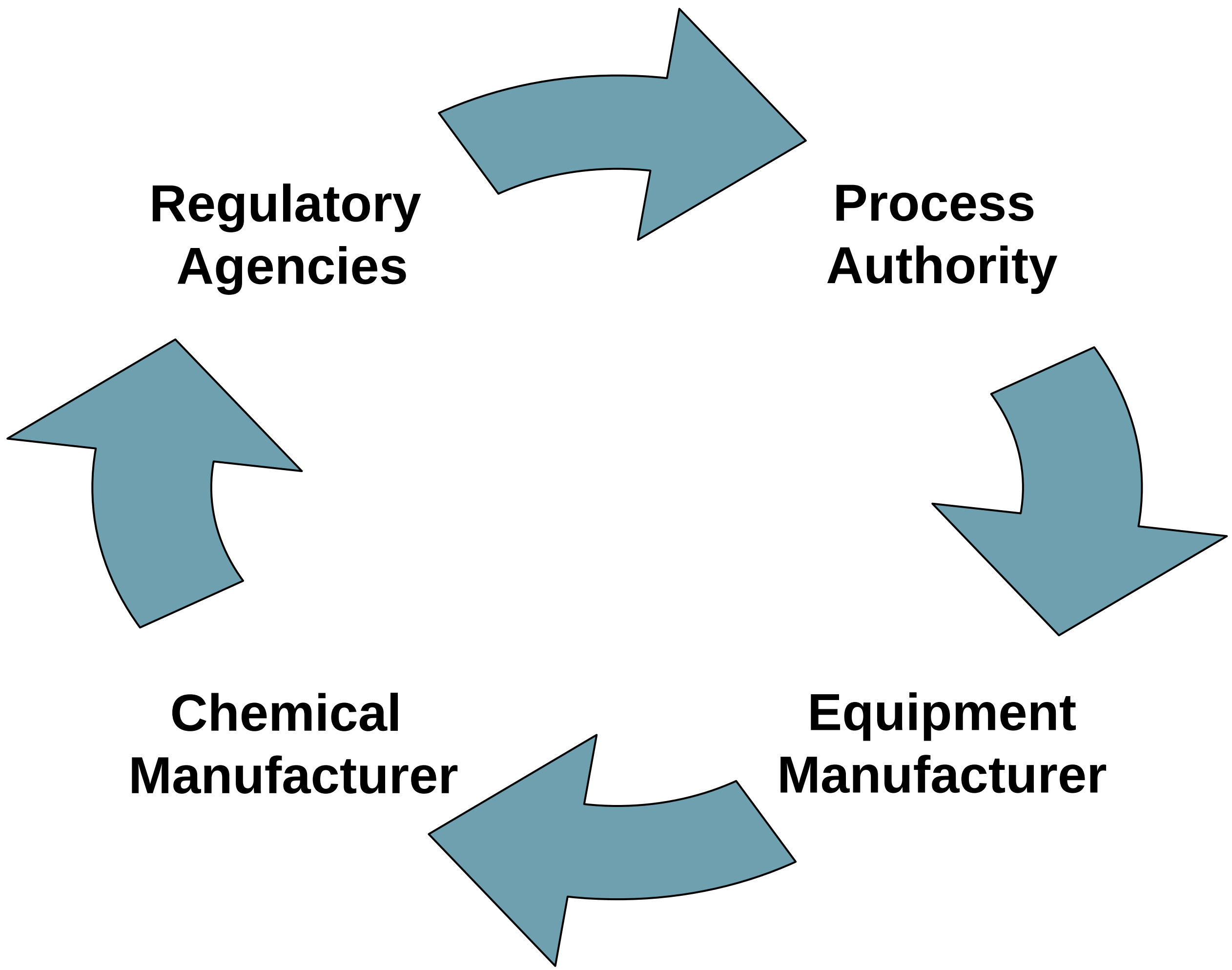
- **Food and Drug Administration (FDA) – Low-acid canned foods:**
  21 CFR 108
  21 CFR 113.40.g

- **FDA – Food Additive Petition**

- **Environmental Protection Agency (EPA)**
  New chemical sterilants for low-acid applications must be registered with US EPA

1.Team Work

Essential to Success



2. Parallel Efforts

Minimize time to filing

System Design → **Validation Testing**

New Sterilant Work → **Validation Testing**

Validation Testing → **FDA Submission**

3.System Design

Work with PA from Beginning

- **Define Aseptic Zone**
- **Optimize Sterilization Cycles (aseptic zone, bottles, closures)**
- **Identify Critical Factors**
- **Define Critical Limits**
- **Monitor, Alarm, Record Critical Factors**

4. Define Performance Criteria
Relation to FSO Principles

- **Sterilization Criteria or <u>Performance Criteria</u> (PC) was established for bottle, cap and machine sterilization.**

- **Performance Criteria (PC) was based on an appropriate <u>Food Safety Objective</u> (FSO) which was in turn based on an acceptable probability of producing a non-sterile unit (PNSU).**

- **Performance Criteria (PC) was expressed as a log reduction for the most resistant microorganism.**

4. Define Performance Criteria cont.
The 12 D Concept

For most low acid foods target organism is *C. botulinum* spores:

- **FSO = PNSU of 10^{-9}**
- **Performance Criteria = 12 log reduction of C bot**
- **12D is based in providing a PNSU of 10^{-9} when the initial contamination level is expected to be equal or less than 10^{3} *C. botulinum spores* per unit.**

4. Define Performance Criteria cont.

The 12D Concept - Calculations

Calculating a target lethality (Y):

$$Y = \log N_o - \log N_F$$

Where:

N_o = Initial spore load; and N_F = number of survivors

If a PNSU of 10^{-9} is desired and a maximum initial load of 10^{3} spores per unit is expected, then:

$$Y = \log 10^{3} - \log 10^{-9}$$

$$Y = 3 – (-9) = 12$$

4. Define Performance Criteria cont.
The 12D Concept

For *C. botulinum* in low-acid foods using heat sterilization:

FSO = 1 NSU in 10^9 total units

PC = 12 log reduction (assuming $N_o = 10^3$ spores/unit)

This FSO and PC is tremendously excessive for PAA sterilization of plastic bottles, caps and machine sterilization.

4. Define Performance Criteria cont.
Applying FSO Principles to PAA

- Establish resistance of pathogenic organisms
- Establish desired FSO and PC based on most resistant pathogen
- Select an appropriate test surrogate to validate sterilization
- Conduct microbial challenge testing

Resistance of Pathogens

1. **Screen multiple pathogens**

   C. botulinum **– 12 strains were studied**

   B. cereus **– 10 strains were studied**

C. botulinum Screening Results

Organism	D value
C. botulinum	
56A (proteolytic)	<1.42
62A (proteolytic)	<2.24
69A (proteolytic)	<2.39
77A (proteolytic)	<2.48
90A (proteolytic)	<2.07
4B (proteolytic)	<1.44
53B (proteolytic)	<2.33
113B (proteolytic)	<2.20
213B (proteolytic)	<2.09
Lamanna B (proteolytic)	<2.16
Kapchunka B (nonproteolytic)	<2.44
2129B (nonproteolytic)	<2.14

- PAA - 4100 ppm
- Adjuvant – 1,200 ppm
- Temperature 58°C
- Inoculum level 10^6

B. cereus Screening Results

Organism	D value
B. cereus	
N1127	**4.82**
N1051	2.32
N1009*	2.26
N1012	2.13
N1028	2.11
N2101	1.47
ATCC 10876	<2.19
ATCC 14579	<2.06
N2103	<2.00
N2100	<1.31

*Most resistant strain in Blackistone paper.

Temperature 58°C (136.4°F)

PAA Sterilant: 4,100 ppm

Adjuvant: 1,200 ppm

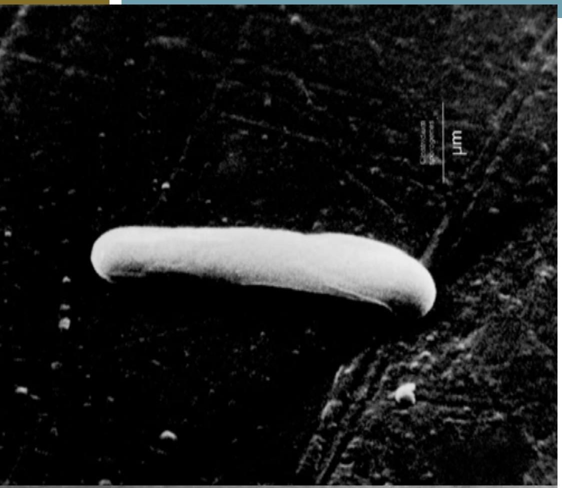
Resistance of Pathogens cont.

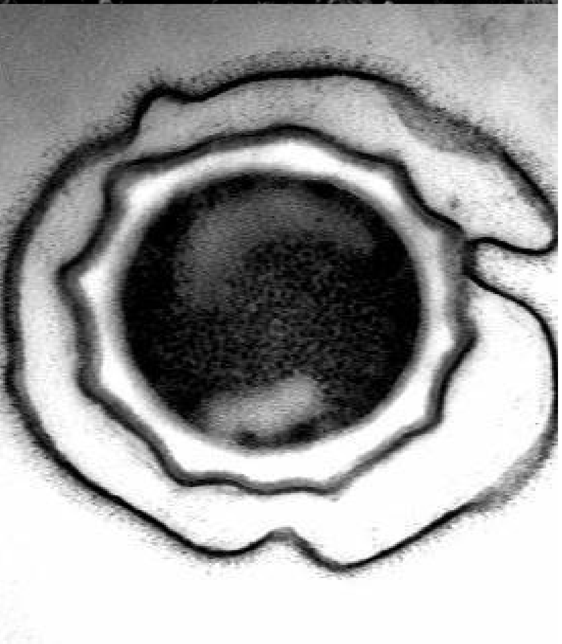
B. cereus **Strain N1127 was selected as most resistant strain for subsequent work**

PAA + Adjuvant, D_{58C} = 4.82 seconds

PAA w/o Adjuvant, D_{58C} = 8 seconds

4. Define Performance Criteria cont.
Applying FSO Principles to PAA





FSO for Bottle, Cap and Machine Sterilization using PAA:

- **Achieve PNSU = 1 x 10^{-6} for *B. cereus* N1127**
- **Equates to a PNSU > 1 x 10^{-9} for *C. botulinum* and vegetative pathogens**

4. Define Performance Criteria cont.
Justification for FSO

- **FSO of 1 PNSU in 10^6 units is widely used in pharmaceutical applications**
- **Severity of illness presented by *B.cereus* is much lower that *C. botulinum***
- **Target strain displayed unusually high resistance as compared to other tested strains**

4. Define Performance Criteria cont.
Establishing PC based on FSO

- **Bio-burden survey of empty bottles showed that incidence of spores is less than 1 in 500**

- **Conservative assumption: 1 BC spore/100 bottles or 1×10^{-2} / bottle.**

Thus, $Y = \log N_o - \log N_F$

$Y = \log (1 \times 10^{-2}) - \log (1 \times 10^{-6})$

$Y = -2 - (-6) =$ <u>4</u>

- **Therefore, the <u>log reduction</u> needed to achieve a 10^{-6} PNSU = 4 = <u>Performance Criteria</u>**

5.Validating Delivery of the PC

Selecting a Surrogate

- **Twenty-seven non-pathogenic spore crops were screened for resistance against PAA**
- **One showed resistance nearly identical to N1127 while all others were much more sensitive to the sterilant**
- **Thus, N1127 is an appropriate target for both commercial sterility and public health**
- **Full microbial destruction kinetics were performed to define D and z values and establish correlation with target organism**

5.Validating Delivery of the PC

Ideal Surrogate Found

- Non-pathogenic
- Not a common spoilage organism
- Nearly identical resistant as compare to target
- Can be prepared as stable suspensions (i.e., spore crops) that can be transported to test site
- Possesses distinct metabolic and morphological characteristics.
- Can be appropriately calibrated prior to use for validation.

6. Validation Tests Successfully Conducted

- **Filler Pre-sterilization Tests :**
  -Isolator Chambers (PAA)
  -Product lines, air filters, filler bowl (steam)
- **Cap Bags and Chamber Sterilization Tests (H_2O_2)**
- **Internal Bottle Surface Tests**
- **External Bottle Sterilization Tests**
- **Filler Sterility Maintenance “Smoke Tests”**

Conclusion

✓**High-speed rotary fillers are a viable option for aseptic bottling in the USA**

✓**PAA based sterilants (single or multi-phased) can be effectively used for this application**

✓**B. cereus has been established as most resistant and appropriate surrogates have been developed**

✓**Appropriate FSO and PC should be established based on scientific understanding of the resistance of target and surrogate organisms and expected bioburden**

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THANK YOU!

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