About OMICS Group

OMICS Group is an amalgamation of Open Access Publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 700+ online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 1000+ International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 700+ open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 1000+ conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Catalent®

addressing the market demands of parenterals through innovation and risk mitigation that drives reliable supply

Bill Hartzel
Director of Strategic Execution
Catalent Pharma Solutions

Warning letters and recalls are still littering the news

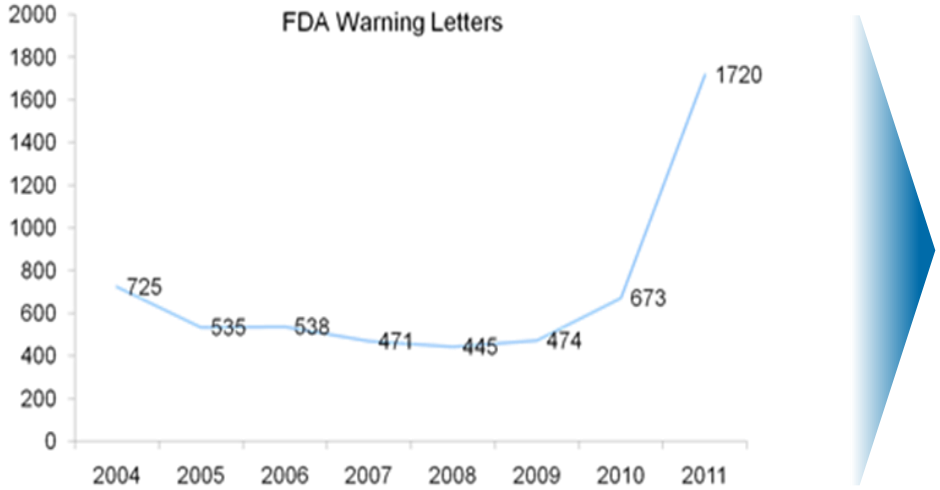
Headlines

"Voluntary Recall Of Two Lots Of IV Solutions Due To The Potential Presence Of Particulate Matter"[1] – 7/17/2015

"Voluntary Nationwide Recall of Select Lots of Fluorouracil Injection, USP 5 G/100 mL (50 mg/mL) Due To Particulate Matter" [1] – 7/24/15

"Recall of ketorolac now close to 40 million vials" [2] – 7/27/2015

"Voluntary Nationwide Recall of One Lot of IV Solution Due to the Potential For Leaking Containers, Particulate Matter and Missing Port Protectors" [1] – 7/30/15



***Source: FDA Fiscal Year 2011 Enforcement Statistics**

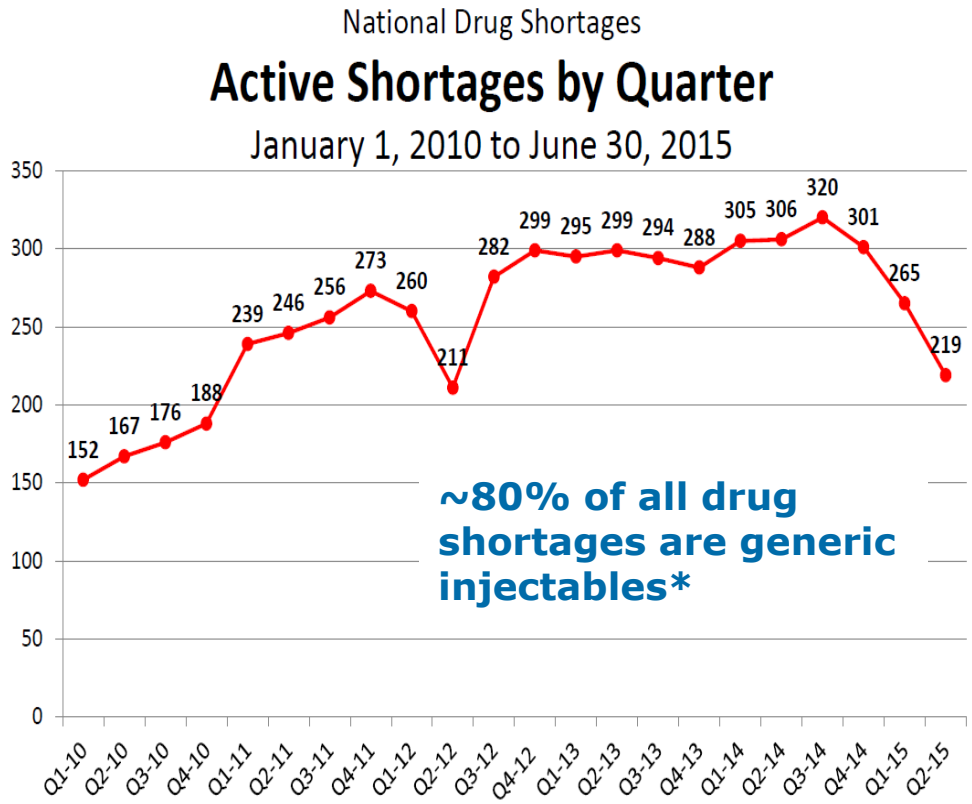
- **Major issues and huge costs to remediate failures in aseptic processing – primarily focused on generic drug manufacturers**
- **Over $1 Billion dollars in remediation activities at just one customer**
- **Closing of sites and businesses driving down capacity**

Even with all the money being spent the challenges are not fully resolved

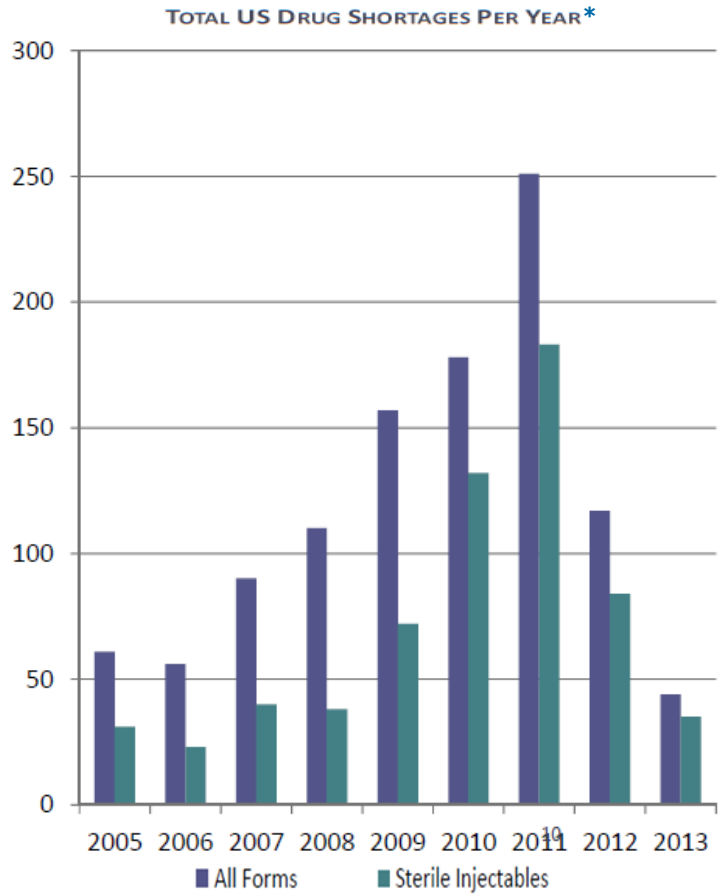
1) http://www.fda.gov/Safety/Recalls/default.htm
2) http://www.fiercepharmamanufacturing.com/story/hospira-recall-ketorolac-now-close-40-million-vials/2015-07-27?utm_medium=nl&utm_source=internal

These issues have put a major strain on supply

Drug shortages are a crisis; even though progress has been made in the prevention of new drug shortages



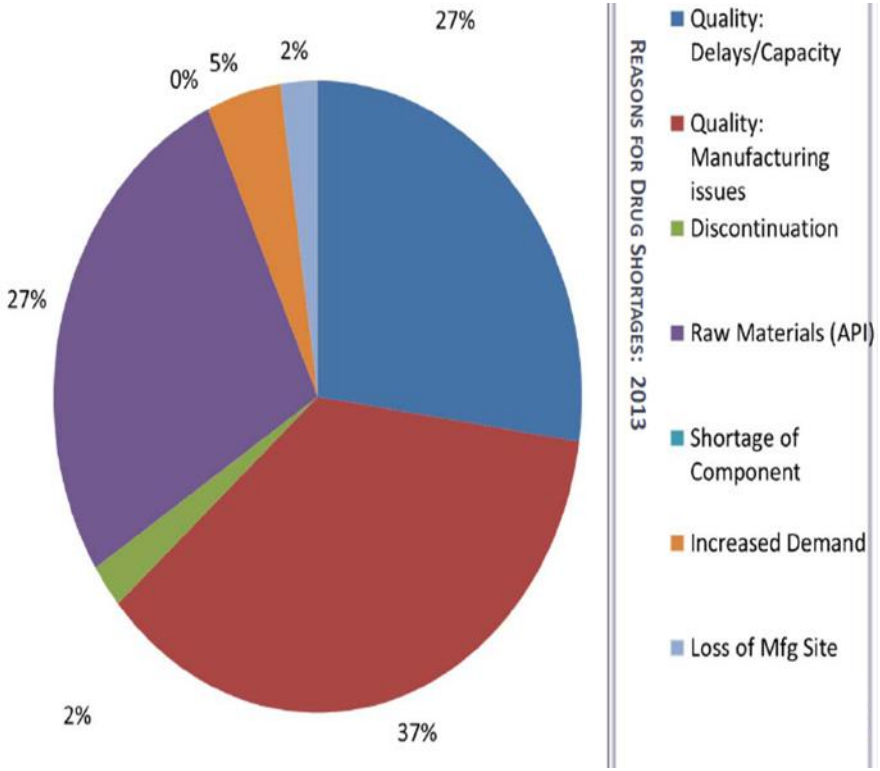
Note: These data represent the count of active shortages on the last day of each quarter, and should not be interpreted as total shortages for that period.



University of Utah Drug Information Service
Contact Erin.Fox@hsc.utah.edu, @foxerinr for more information

*Jensen, Captain Valerie, *FDA Response to Drug Shortages* Washington DC: PDA/FDA Conference on Drug Shortages, Sept. 2014

Where are the drug shortages coming from….



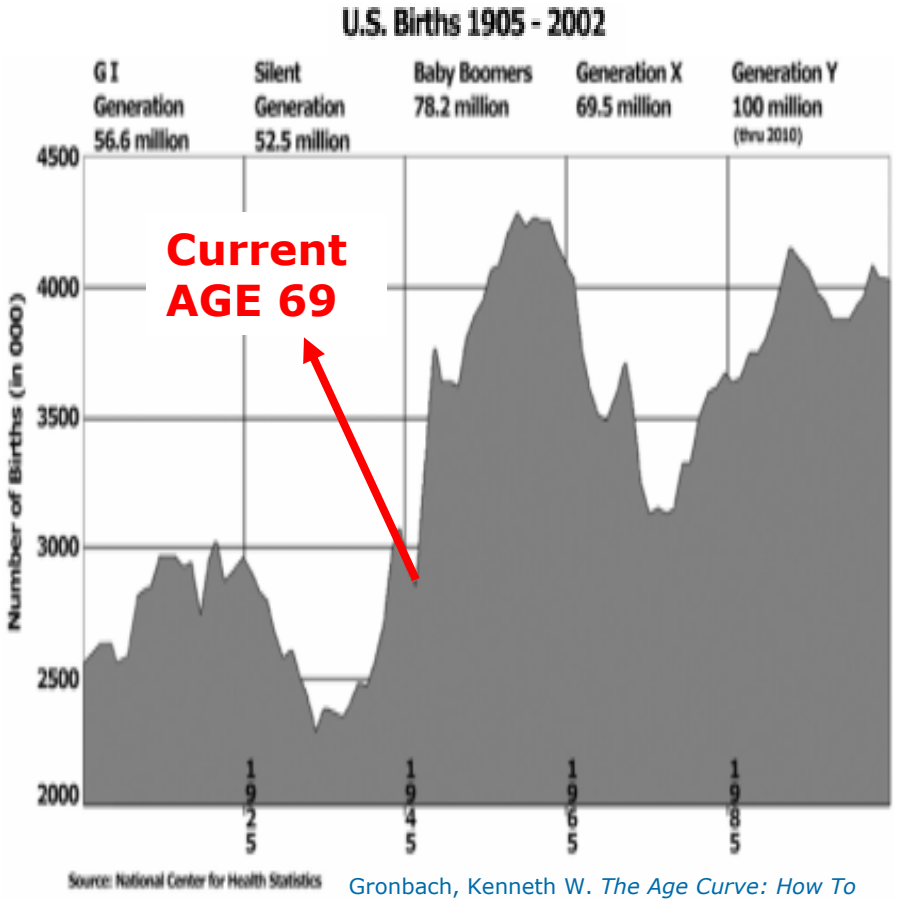
Causes of Shortages: Sterile Injectables

- Quality and manufacturing issues:
  - Sterility: Bacterial and fungal contamination
  - Particulates: Glass, metal or fiber in vials
  - Crystallization: Drug may form crystals
  - Precipitate: Reaction between drug and container or diluent
  - Impurities: Can be toxic (heavy metals)
  - Degradants: Lead to less effective drug product
  - Equipment breakdown
  - Natural Disasters

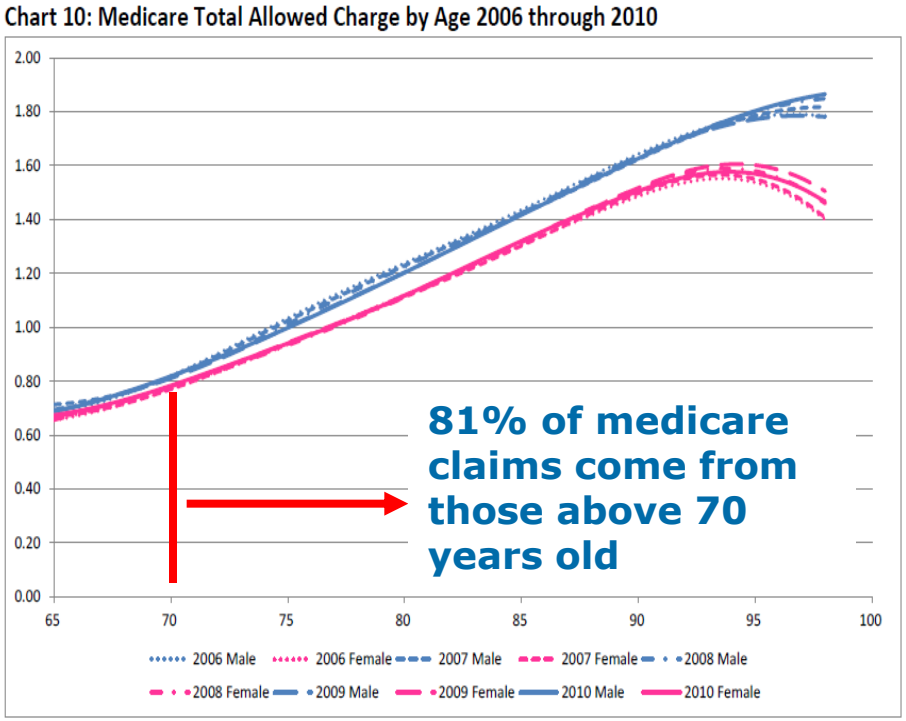
Jensen, Captain Valerie, *FDA Response to Drug Shortages* Washington DC: PDA/FDA Conference on Drug Shortages, Sept. 2014

2015 Recalls to Date for sterile injectable (non-compounders)
19 for Lack of Sterility Assurance & 20 for particulates

The demand for healthcare is going to skyrocket which will put even more pressure on the system



Gronbach, Kenneth W. *The Age Curve: How To Profit From The Coming Demographic Storm.* New York: American Management Association, 2008.



Not to mention the added patients due to the Affordable Care Act

16.4MM more patients now with insurance

http://www.hhs.gov/healthcare/facts/factsheets/2014/10/affordable-care-act-is-working.html

Catalent®

innovation and risk mitigation to help address the challenges

DEVELOPMENT DELIVERY SUPPLY

more products. better treatments. reliably supplied.™

Driving at the root cause of manufacturing issues of aseptic filling by mitigating the risk

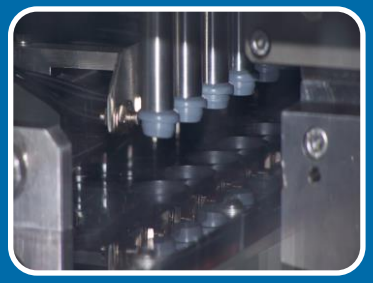
Advanced Aseptic Filling Technology

Why Glass Free?

Quality/Sterility Assurance	**Reduce risk factors for sterility challenges through automation**
Minimizing Particulates	**Elimination of glass particles and delamination with significant reduction in foreign particulates**
Safety/Reduced Product Loss	**Plastic construction reduces risk of breakage and simplifies opening**
Stability/ Compatibility	**Medical grade polypropylene resin for excellent chemical and physical properties**

Reducing Risk with Advanced Aseptic Processing of Blow Fill Seal (BFS) Technology

Engineering controls and automation

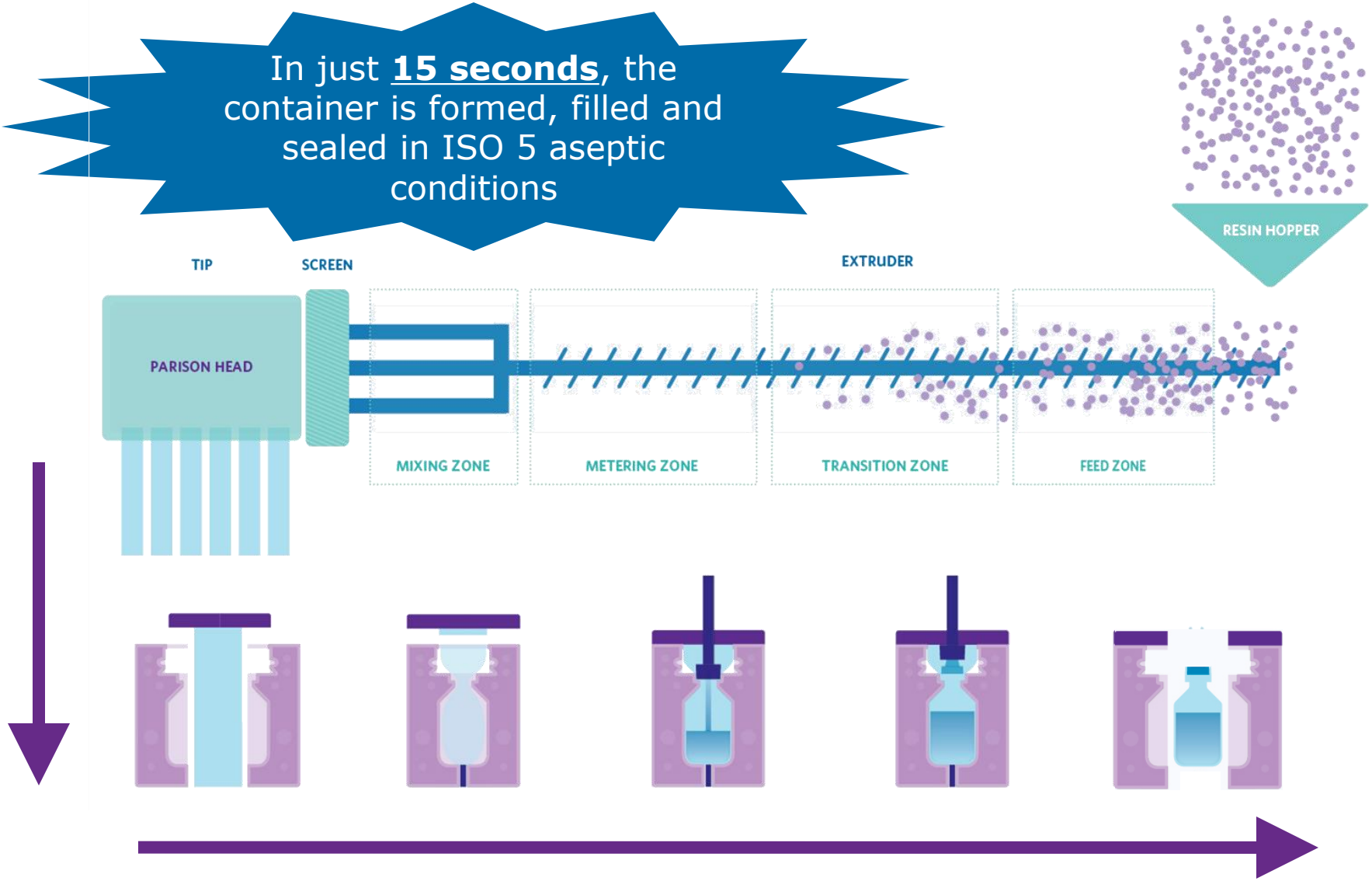


Driving out variables and simplifying the process

Understanding and identifying critical parameters

Minimize Risk: Simplify the Process, Reduce Variables

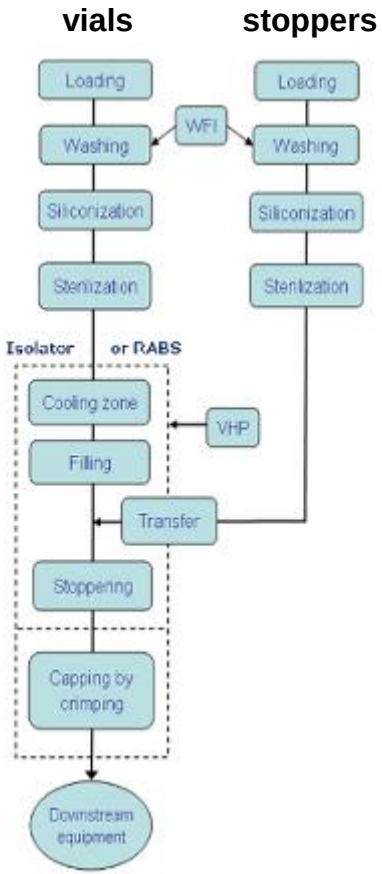
In just **15 seconds**, the container is formed, filled and sealed in ISO 5 aseptic conditions



Minimizing Variables and the Footprint in Aseptic Manufacturing

Utilizing the automated aseptic design of BFS, the technology eliminates traditional manufacturing steps, reduces the required controlled space and decreases the risk of contamination associated with traditional aseptic practices

Glass Vial Filling



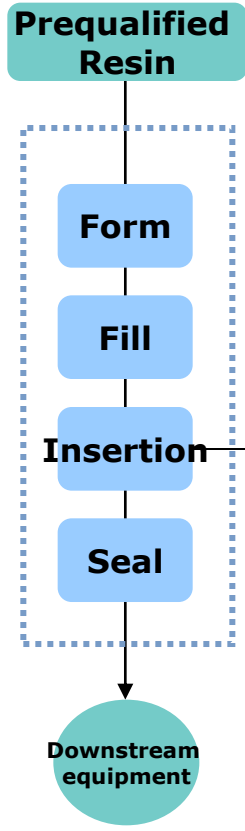
Glass Vial Filling

- **Controlled Space 10,000 sq. ft**
- **Class A Space 1000 sq. ft**

Blow Fill Seal

- **Controlled Space 200 sq. ft**
- **Class A space 10 sq. ft**

Blow/Fill/Seal



Drastic Reduction of Particulates Compared to the Standard and the Industry

Catalent has developed a filling process to reduce particulates to a fraction of the industry average

USP <788>	>10 µm Particles	>25 µm Particles
Specification[1]	6000	600
Industry[2]	219	15
Catalent DOE	5.0	0.89

- **Limits Set by USP General Chapter <788> for Small Volume Parenterals using Light Obscuration Particle Count Test Method**
- **Results from USP <788> particulate matter testing from 295 ANDAs covering 406 lots of drug product**
- **Results obtained from Catalent's Advanced Aseptic Filling Process**
  - Extensive DOE evaluating 32 different processing parameters
  - Average particulate count across all 32 sample sets (385 samples)

References:
1) United States Pharmacopeial Convention. (2014). General Chapter <788>, Particulate Matter in Injections. In USP 37, pp. 398-401.
2) Presenter Shabushnig, John. (November, 2010). *Regulatory and Compendial Considerations for Particles in Parenteral Products.* Presented at AAPS, New Orleans, LA.

Enhancing Sterility Assurance by Challenging the System to Identify the Critical Control Parameters

Catalent was a pioneer in generating data to support the industry in recognizing that BFS is an Advanced Aseptic Filling Process.

Challenging the system was pivotal to understanding the process

Built a self contained area and room to house a commercial BFS machine with separate air handling systems and full EM control

Multiple Microbial Challenge Studies

Room (ISO 7)	Fill Zone (ISO 5)	Resin

Controlling the Critical Parameters

Controlling Critical Factors
Specification of incoming resin
Closed system; sterilized *in situ*
Controlling the critical parameters in fill zone
Elimination of human intervention
Continuous monitoring of air for viable and non-viable particulates in the fill zone
Inspection for container closure integrity

Load equipment in line. Clean and Sterilize in place. Eliminate human intervention into processing points.

Advanced Aseptic Processing with BFS Lowers the Risk of Traditional Glass Vial Filling

Identifying critical parameters

Minimizing variables

Automation and Control

Embracing QbD Principles

Minimizes Risk

This technology forms a glass free container closure system

BFS is Not Just the Filling Process; It also Creates a Container Closure System

Opportunities

- **Glass Free Platform**
- **Lower weight for shipping and disposable**
- **Shatter resistant**
- **Primary container design flexibility**

Considerations

- **Thermal stability due to the heat needed to form the container**
- **Extractables and leachables will be different**
- **Stability will need to be evaluated**

Significant resources have been spent to retire these risks

ADVASEPT® glass free delivery platform

Providing opportunities to break the glass paradigm

ADVASEPT offers unlimited potential with a broad spectrum of possibilities, configurations and combinations for tailored solutions

Potential solutions

Expand device options to enhance delivery to the patient

- Unique shapes
- Multiple ports
- Different insertions

Address molecule interaction issues

- Minimize surface interaction with proteins
- High pH formulations

Providing design freedom of the primary container closure while ADVASEPT technology delivers the aseptic assurance

Catalent's ADVASEPT® Lock
Improved delivery through innovation

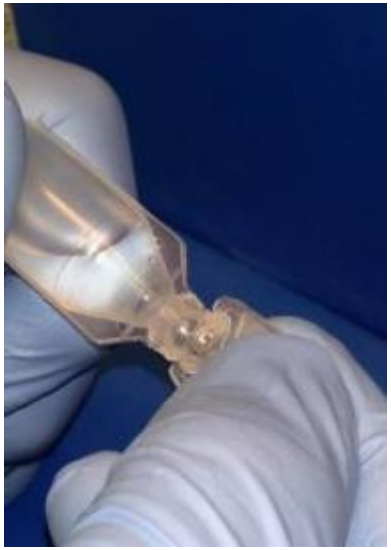
A stopperless glass-free vial that combines advanced aseptic processing with a container closure design that locks to a luer designed syringe

Opportunity

- Cost effective solution compared to glass stoppered vials across a portfolio of products with an optimized design
- Drastically reduced risk profile associated with traditional filling by utilizing advanced aseptic processing

Safety Advantages:

- Reducing the need to use a needle to withdraw a product
- Elimination of glass shards and sharp edges associated with a traditional amp


Catalent's ADVASEPT® Vial Technology

Alternative to traditional aseptic filling of bags & vials for a premix

The advanced aseptic processing of blow/fill/seal technology can drastically reduce particulates and sterility challenges compared to traditional aseptic processing

Opportunity

Premix solutions of molecules that need to be filled aseptically i.e. anti-infectious/anti-bacterial medications

Advantages

- Automated filling process for robust and efficient manufacturing
- Reduces the weight & cost compared to glass vials
- Reduces space in Pyxis® machine compared to bags

*Pyxis is a registered trademark of Carefusion 303, Inc.

Addressing the market challenges…

"When written in Chinese, the word "crisis" is composed of two characters-one represents danger, the other represents opportunity." -John F. Kennedy

We need to challenge our current ways of thinking, embrace innovation, and take advantage of our opportunity to improve the delivery of medications to patients

Let us meet again..

We welcome you all to our future conferences of OMICS International

2nd International Conference and Expo on

Parenterals and Injectables

On

October 24-26, 2016 at **Istanbul, Turkey**

http://parenterals-injectables.pharmaceuticalconferences.com/