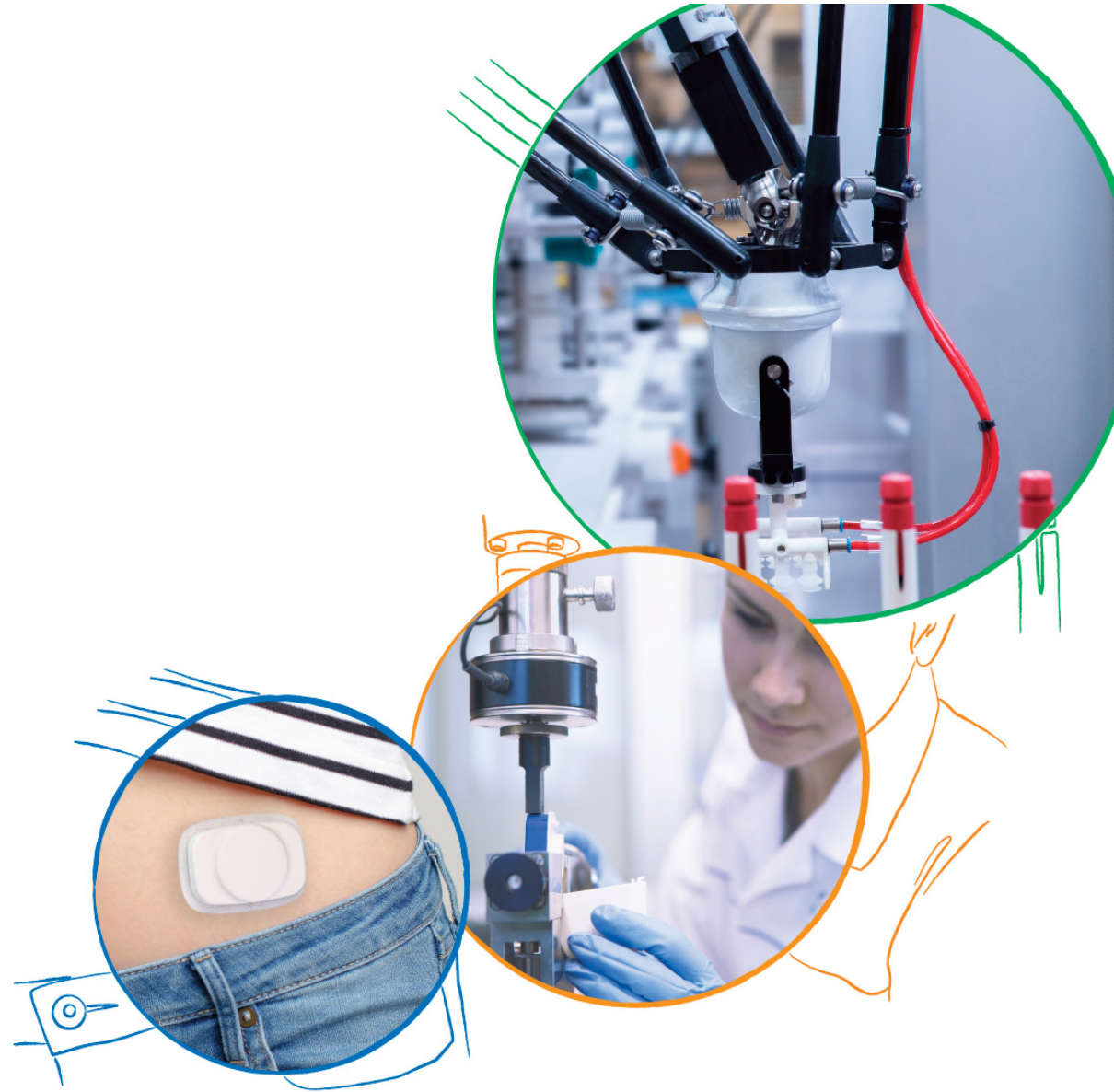


Manufacturing an SVP Drug Containment solutions: quality by design

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Agenda

- Container types, their challenges and critical quality attributes
- Vial Manufacturing Process
- Syringe Manufacturing Process

Which are the main Challenges of Pharmaceutical Glass Packaging?

Global primary packaging market made from glass tubing is worth almost 40 billion containers yearly

	PRE-FILLABLE SYRINGES	PRE-FILLED CARTRIDGES	VIALS	AMPOULES
Volume (B Units 2021, CAGR '21-'25)	 <div>~4_b</div> 	 <div>~4_b</div> 	 <div>~12-13_b</div> 	 <div>~20_b</div> 
Applications	<ul style="list-style-type: none"> • Biologics & GLP-1 • Anti-coagulants • Vaccines (incl. Covid-19) • Cosmetics • Autoinjectors 	<ul style="list-style-type: none"> • Anti-diabetics • Dental anesthetics • Hormones • Emergency Drugs (with AI) 	<ul style="list-style-type: none"> • Biologics • Vaccines (incl. Covid-19) • Drugs for IV infusion • Generics / General Use 	<ul style="list-style-type: none"> • Small molecules • Hospital drugs • Diluents • Generics / General Use
Sealing	<ul style="list-style-type: none"> • Rubber Plunger • Rubber Closure (needle shield or TC) 	<ul style="list-style-type: none"> • Glass + Rubber Lined Cap • Rubber Plunger • Glass + Rubber Stopper + Aluminum Cap (>5mL) 	<ul style="list-style-type: none"> • Glass + Rubber Stopper • Aluminum Cap (crimped) • Plastic Press-Fit Caps 	<ul style="list-style-type: none"> • Glass – hot sealed

Source: Based on data collected by IQVIA, annual reports, internal SG information

Future Volume growth trend (CAGR):



Critical to Quality Attributes

Mechanical

- Mechanical resistance
- Type of glass (Raw Material)
- Treatments

Closure

- CCI
- Rubber type
- Geometry – integration with closure design

Functionality

- Dimensional compatibility (with downstream process)
- Cosmetic quality – False Rejects or glass flaws

Chemical

- Alkali release
- Delamination propensity
- Internal treatments



Critical to Quality Attributes

Functionality

- Silicone quantity
- Coating stability
- Delivered dose
- Dead Volume

Mechanical

- Mechanical resistance
- Functional performance
- Dimensional compatibility

Closure

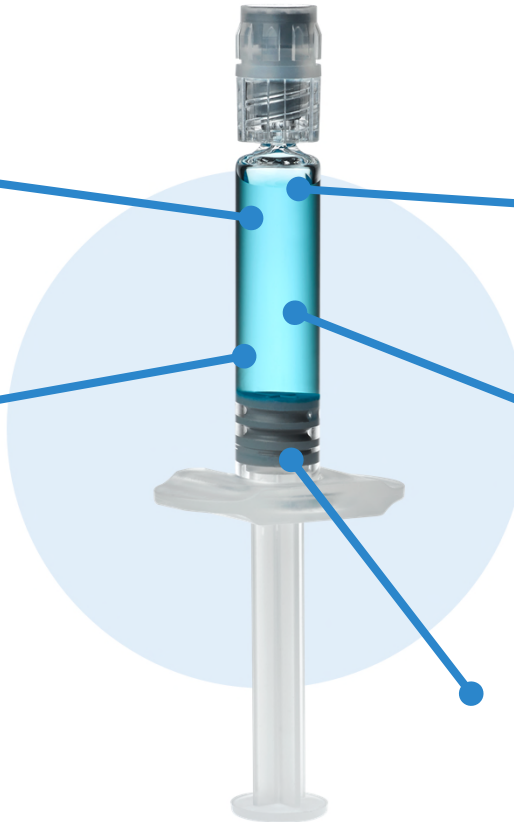
- CCI
- Rubber type
- Geometry – integration to AI
- Pull Off Force

Gliding


- Liquid viscosity
- Silicone distribution

Plunger

- CCI
- Rubber type and geometry
- Airgap
- Rubber/glass interaction
- Plunger displacement



Which are the main Challenges of Pharmaceutical Glass Packaging?

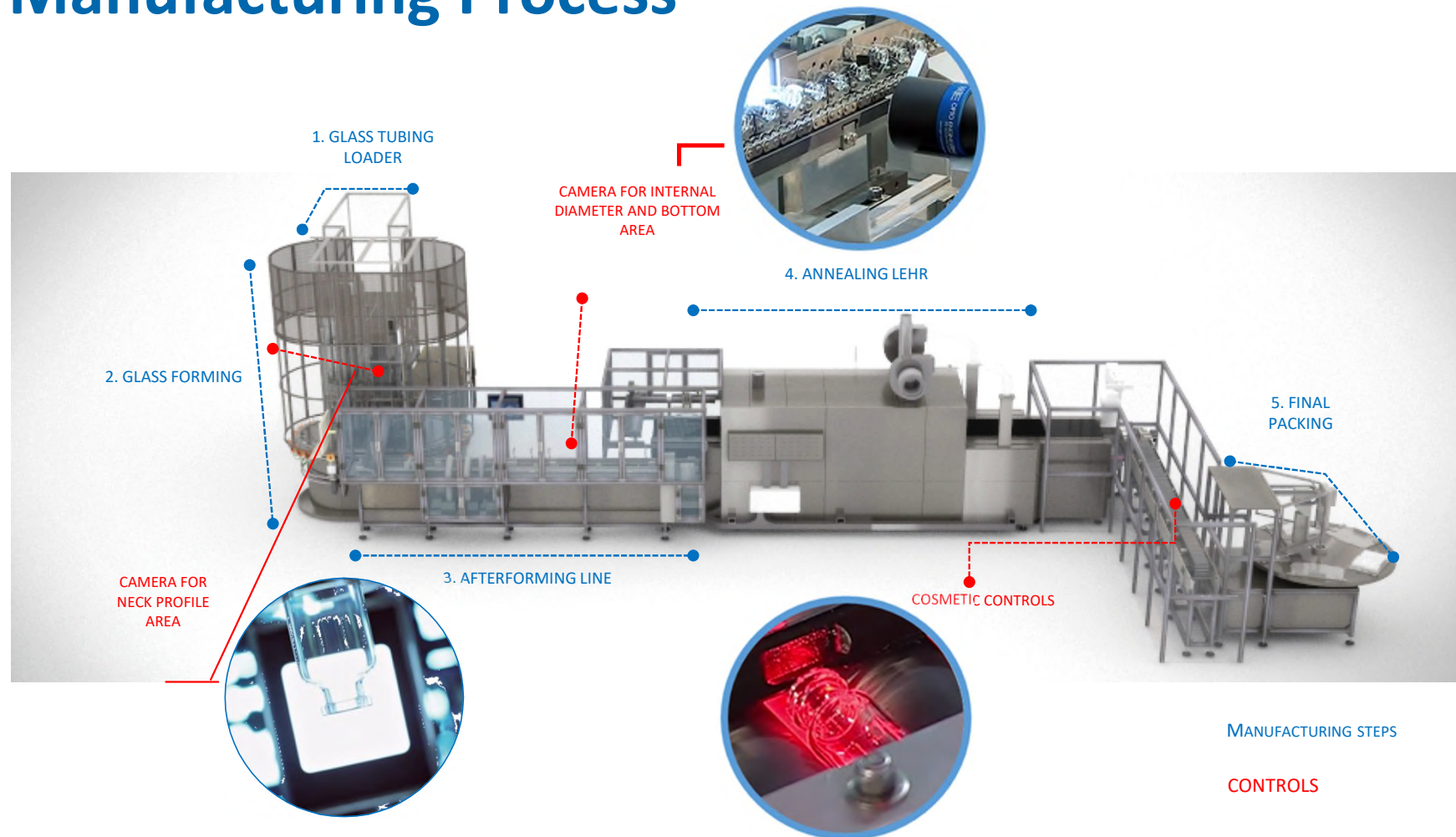


FACTOR	CHALLENGES			
Tungsten residues	<ul style="list-style-type: none"> Oxidation Aggregation Syringe-to-syringe variability of residuals 		•	
Silicone	<ul style="list-style-type: none"> Aggregation Sub-visible and visible particles Functionality challenges 		•	•
Multiple contact materials	<ul style="list-style-type: none"> Organic and inorganic leachable (Rubbers of stopper / RNS, needle glue) Latex allergy Compatibility 	•	•	•
Delamination	<ul style="list-style-type: none"> Particles Glass lamellae 	•		
Lyophilization	<ul style="list-style-type: none"> Risk of breakages Fogging Cake integrity 	•		
Mechanical resistance	<ul style="list-style-type: none"> Risk of breakages Cracks 	•	•	•
High viscosity high volumes	<ul style="list-style-type: none"> Integration with LVWI 			•
Container Closure Integrity	<ul style="list-style-type: none"> Assure integrity under different storage conditions / shipping 	•	•	•

The background image shows a close-up of a glass vial being heated by a flame in a manufacturing setting. A large blue circle is overlaid on the left side of the image.

Vial Manufacturing Process

Vial Manufacturing Process



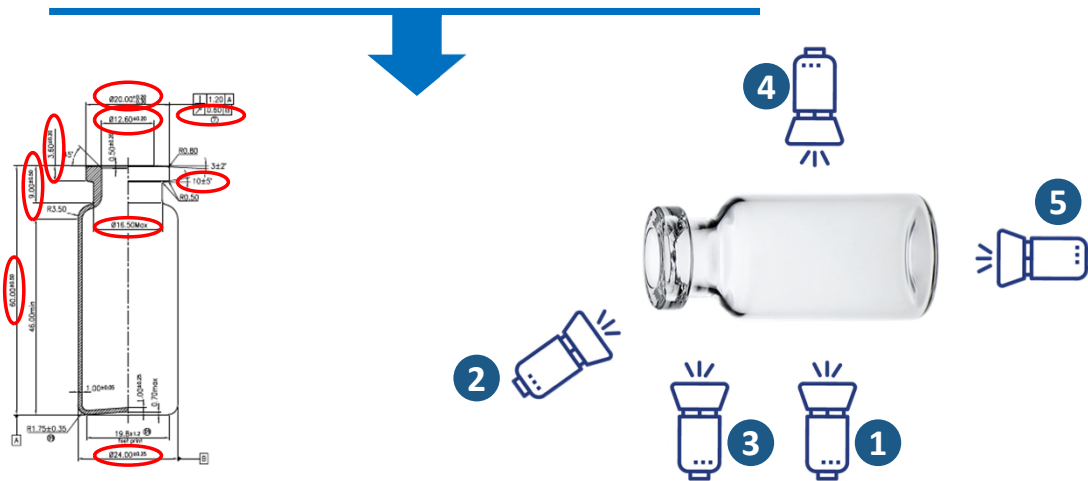
Vial Manufacturing Process



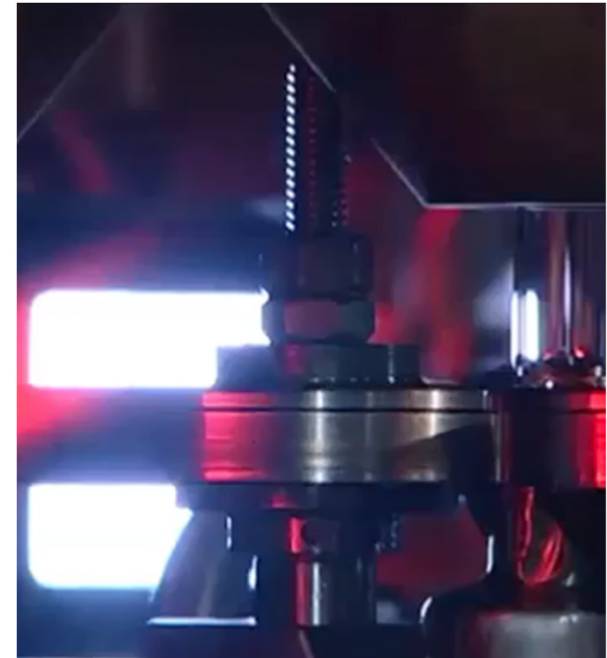
Vials: Camera Controls

100%

Automatic Dimensional & Cosmetic Control



- Automatic rejection of flawed containers
- Real-time feedback on the quality of the batch
- Details of every batch
- Cosmetic Defects: cracks, chips, glass particles, airlines, contamination, scratches, etc...



Dedicated Manufacturing Options

Lyophilization – Container + secondary packaging

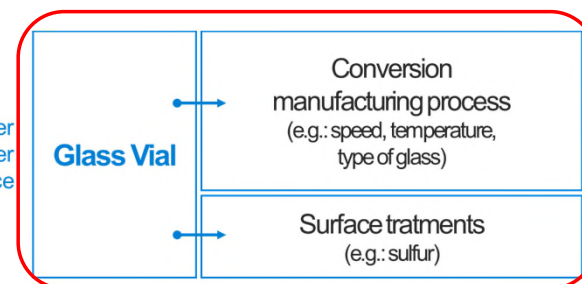


PACKAGING PARAMETER	CRITICAL QUALITY ATTRIBUTES	IMPACT
Bottom shape	Cake Appearance and lower risk of breakage	High
Bottom thickness	Cake Appearance	High
Tube composition	Cake Appearance	Low
Position in the rack	Sublimation Rate	Medium
Inner coating (Silicone)	Cake Appearance /Reconstitution	High
Nest Configuration	Cake Appearance and Process	High
Material (polymer)	Unloading	Low

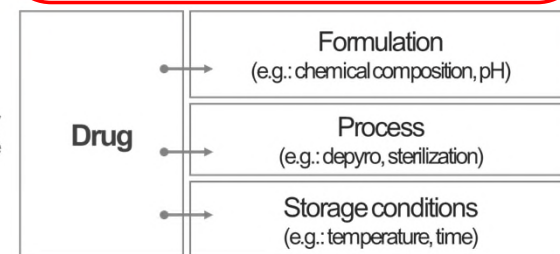
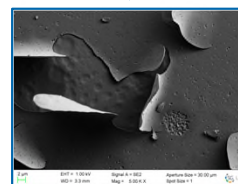
Delamination – Manufacturing and Processing



Container manufacturer direct influence



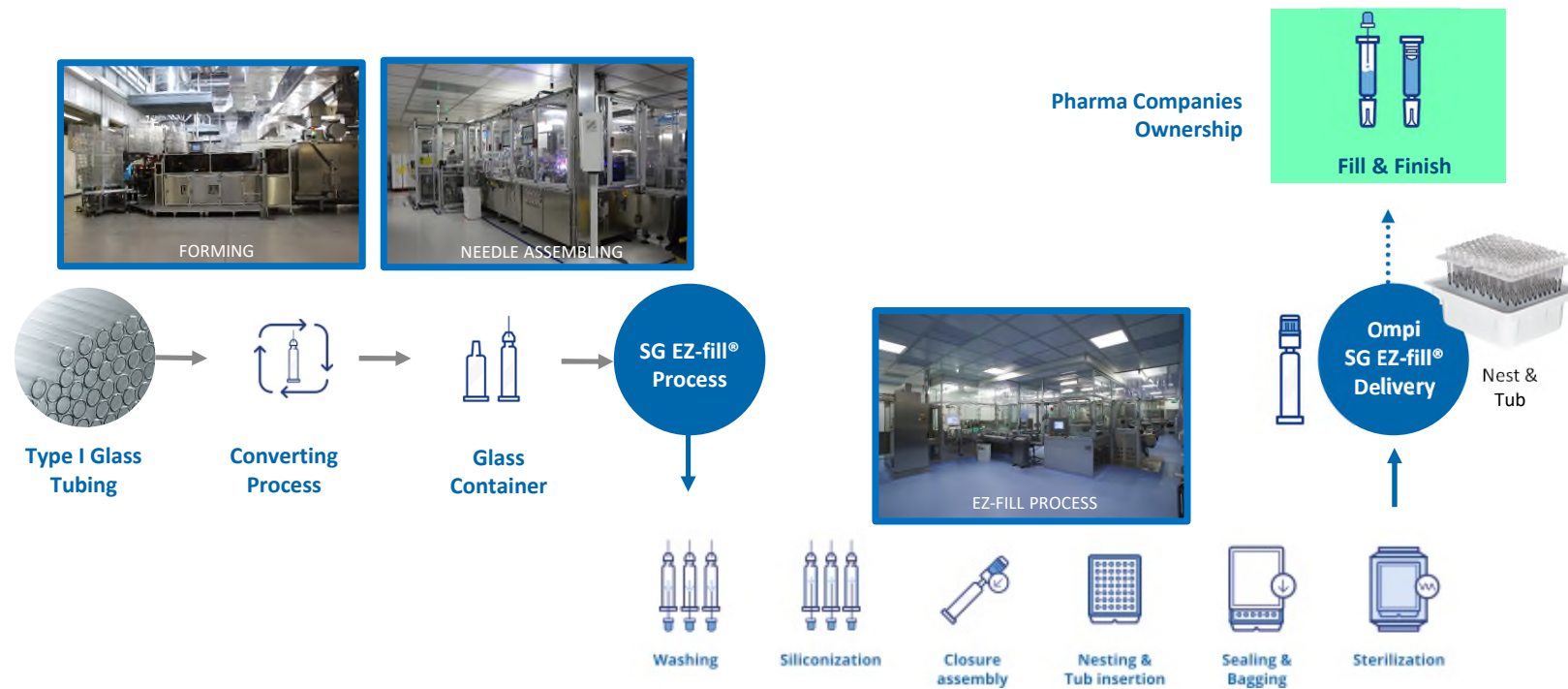
Pharma company direct influence



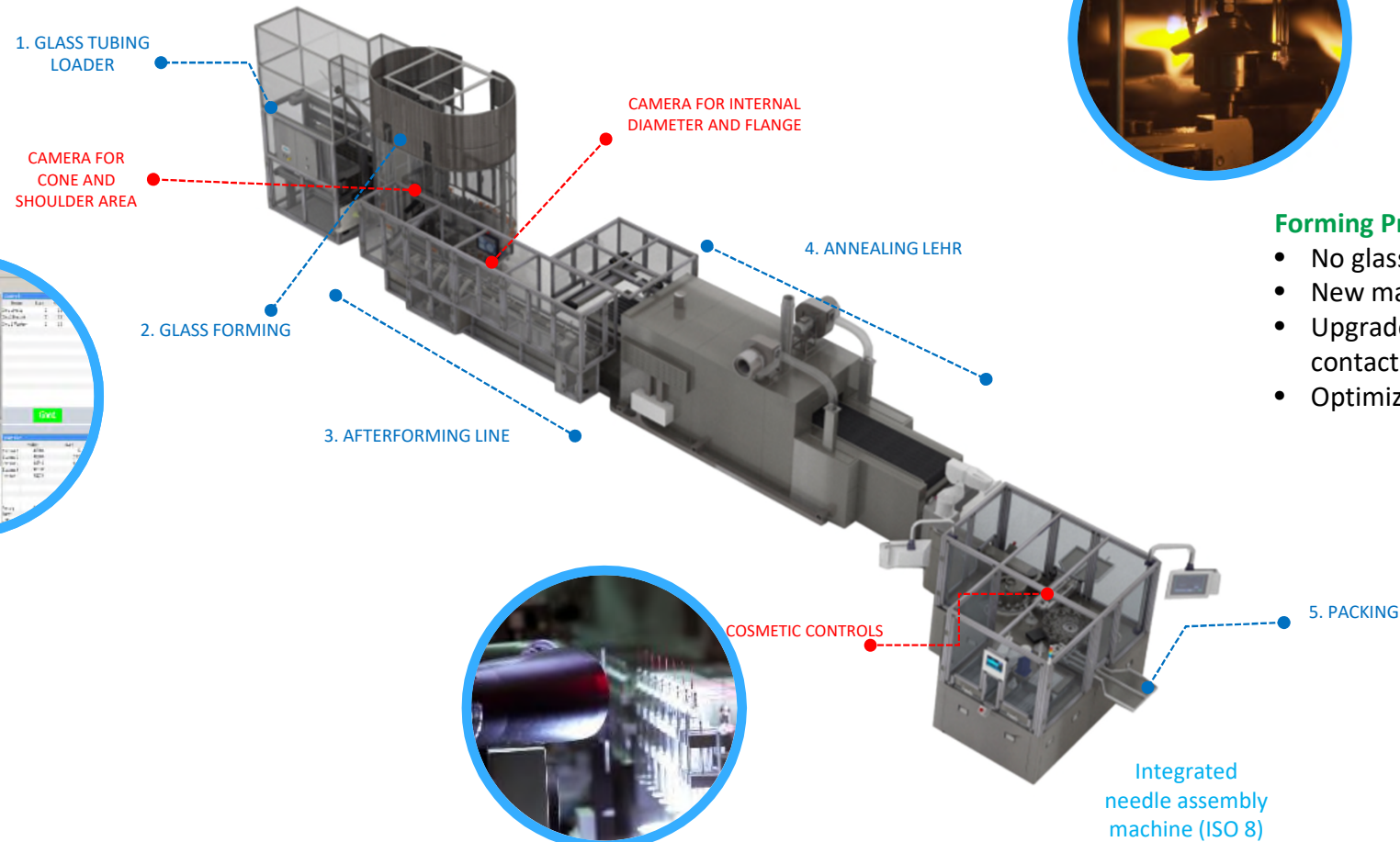
The background image shows a close-up of a syringe manufacturing process. A glass syringe barrel is being heated by a blue flame from a torch. The scene is dimly lit, with warm orange light from the torch and other heat sources in the background. A large, semi-transparent blue circle is overlaid on the left side of the image, containing the text.

Syringe Manufacturing Process

Syringe Manufacturing Process - Overview



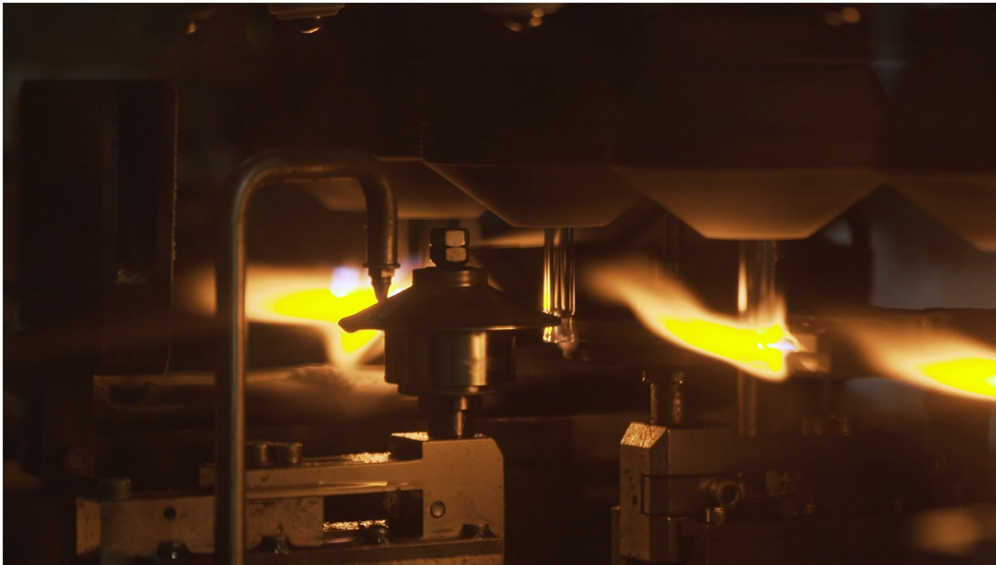
Syringe Manufacturing Process



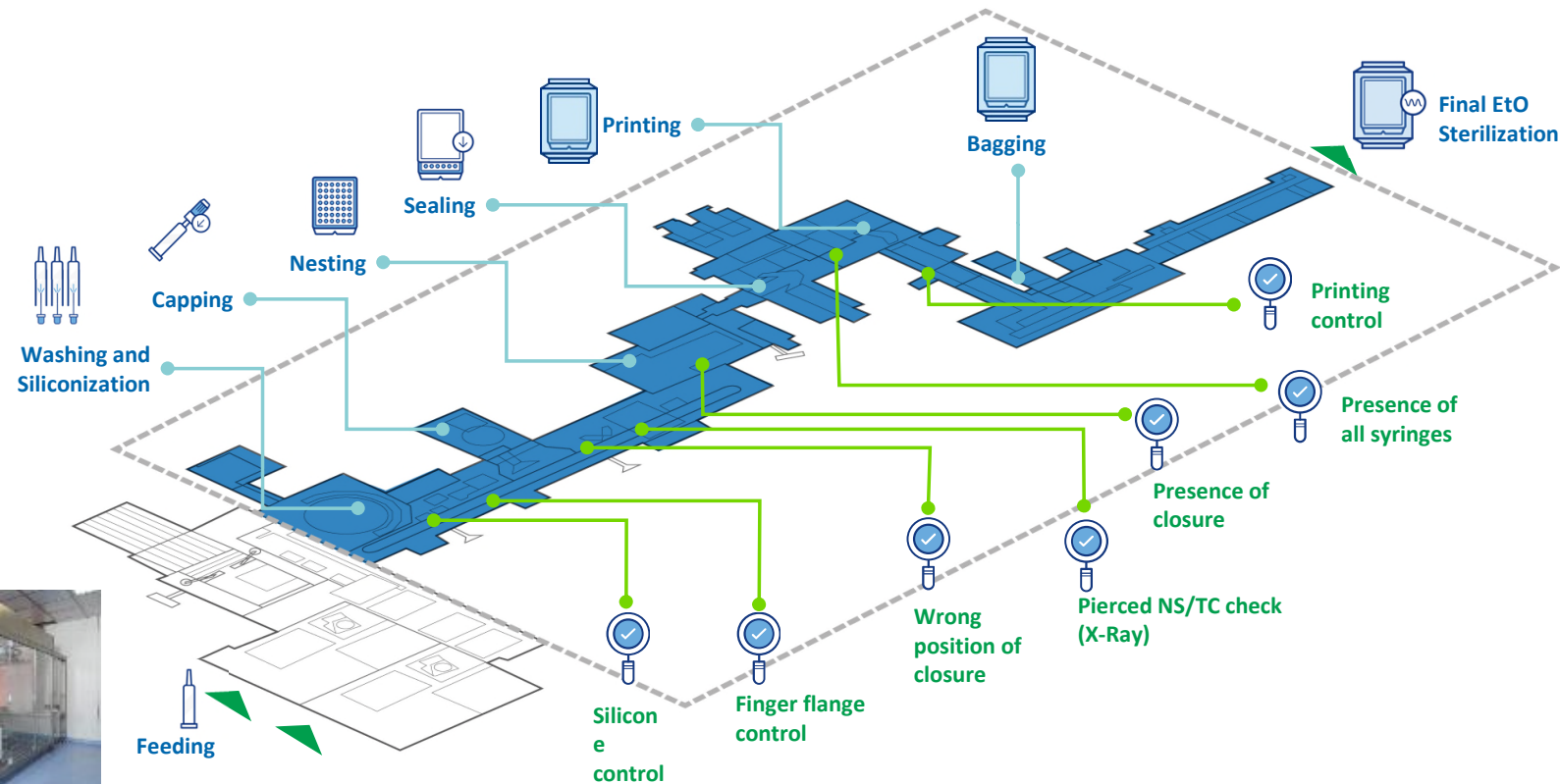
Forming Process

- No glass-to-glass
- New materials to avoid metal-to-glass
- Upgraded forming stations with lower contact forces during forming of glass
- Optimized flame control for bottom forming

Syringe Manufacturing Process



Syringe Manufacturing Process – EZ-fill®



- Process
- Automatic Control

Syringe Manufacturing Process – EZ-fill®



Conclusions

As we saw during this presentation, there are many variables that need to be considered to efficiently develop and pack a drug product. All these variables need to be defined, shared, and discussed together with primary packaging manufacturers to reduce the risk of failure downstream.

Some examples:

- Drug product formulation
- Raw material
- Type of Primary Packaging Container
- Manufacturing of Primary Packaging
- Treatments
- Presentation (Liquid, suspension, Lyo...)
- Processing (F&F)
- Storage conditions
- Route of Administration
- User (self-admin/healthcare personnel)
- Life-cycle Management



Thank You!

For further information please contact me

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or visit www.stevanatogroup.com