

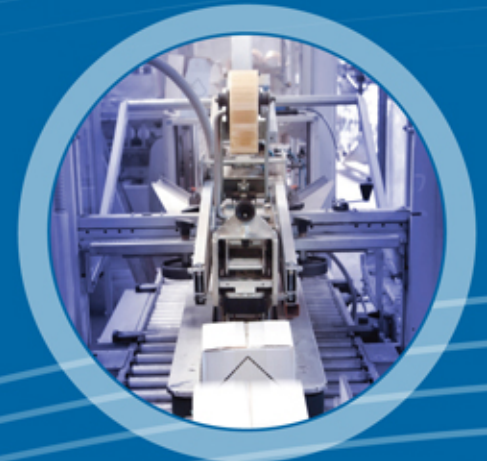


Connecting People, Science and Regulation®

# Trends in Industry for parenteral Fill-finish



**Wenzel Novak**  
Director pharmaceutical  
research and development  
**groninger & co.gmbh**





# Future customers' request in 10 years

## Outcome of discussion yesterday evening

“round table” Pharmaceutical company - supplier

Growing market

- Impact of product
- Impact of material
- Impact of technology
- Impact of new therapies
- Impact of new regulation
- Impact of cost pressure

-> complexity



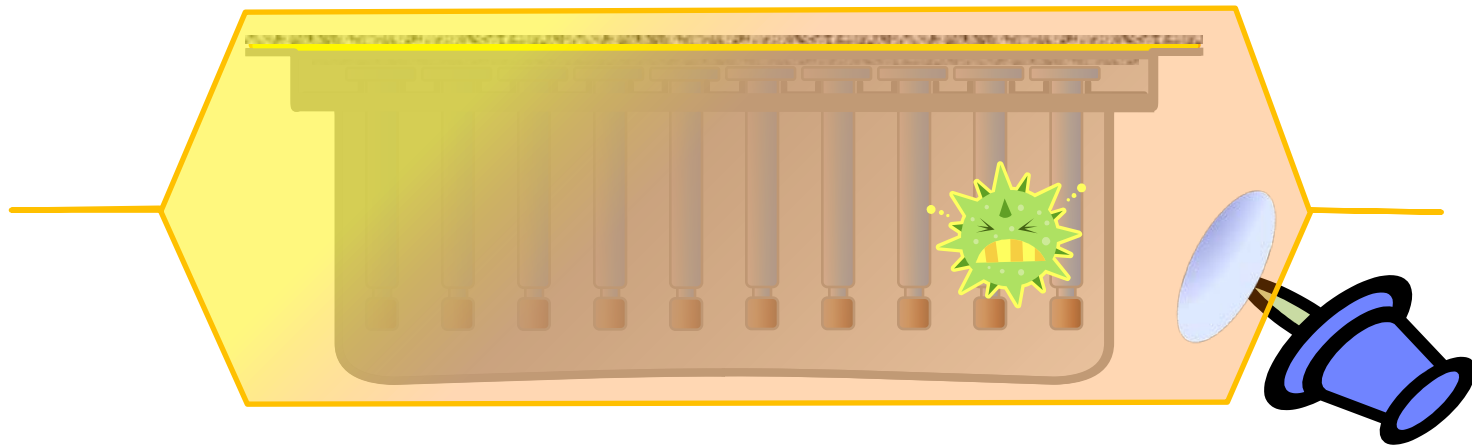
# Decontamination

## Transfer of cfu into sterile container

Inside contaminated due to transport damage (e.g. pinholes)

*Typical material: Tyvek™, HDPE, LDPE*

*(assuming a proper sterilization and packaging closure)*

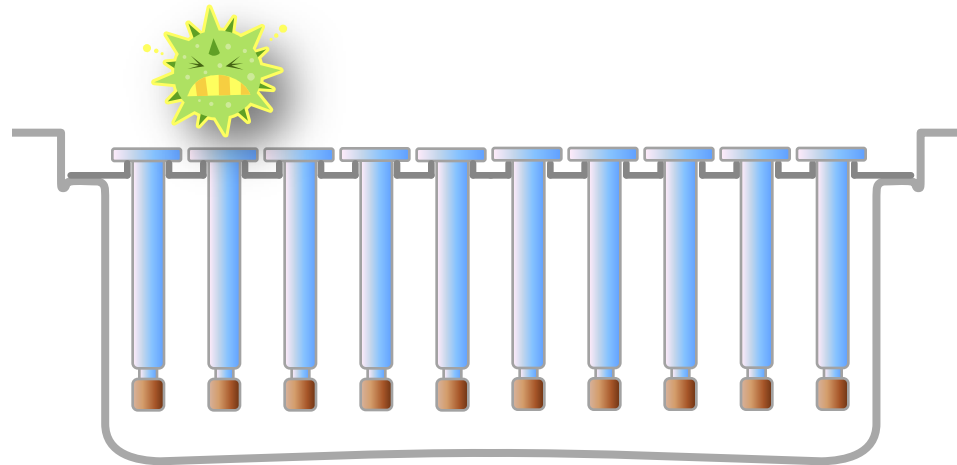




# Decontamination

## Transfer of cfu into sterile container

Contaminant is carried over from the outside into a primary container during opening process



A spore made it into a syringe



# Decontamination

## Regulatory requests by Authorities



### APPENDIX 1: ASEPTIC PROCESSING ISOLATORS

#### *(“Contains Nonbinding Recommendations”)*

...

#### D. Decontamination

...

#### 2. Efficacy

**The decontamination method should** render the inner surfaces of the isolator free of viable microorganisms... Process development and validation studies should include a thorough determination of cycle capability. The characteristics of these agents generally preclude the reliable use of statistical methods (e.g., fraction negative) to determine process lethality (Ref. 13). An appropriate, quantified Biological Indicator (BI) challenge should be placed on various materials<sup>23</sup> and in many locations throughout the isolator, including difficult to reach areas. ... Normally, a four- to six-log reduction can be justified

depending on the application. ... For example, **demonstration of a four-log**

**reduction** should be sufficient for controlled, very low bioburden materials introduced into a transfer isolator, including wrapped sterile supplies that are briefly exposed to the surrounding cleanroom environment.

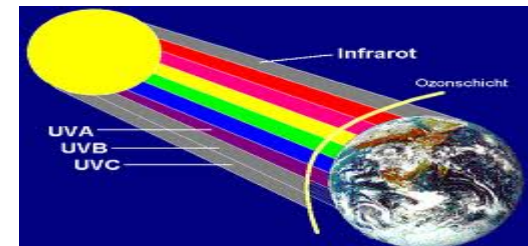
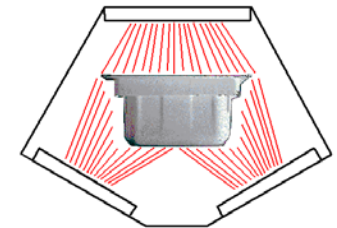
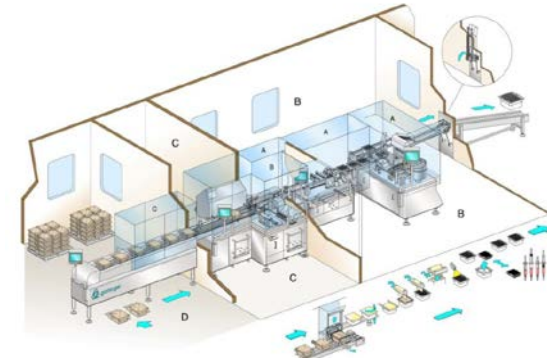
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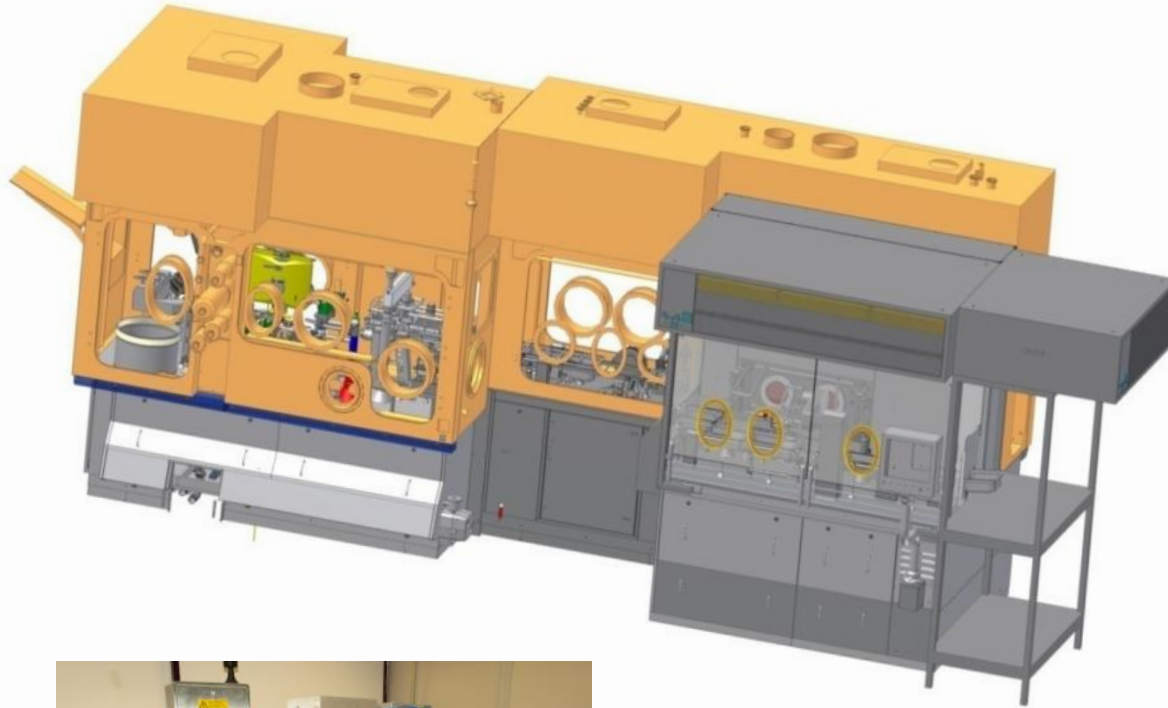
# Decontamination

procedure	note
zone concept	no disinfection
spraying alcohol	not sporicidal; difficult validation; $10^2$ kill
Aerosol (VHP) / wetting by $H_2O_2$	15min - 6h erosion of material residuals (Tyvek)
E-beam	Radicals; oxidation; radiation
UV-light	max. killing rate $10^3$ shadowing effects
Plasma	New technology





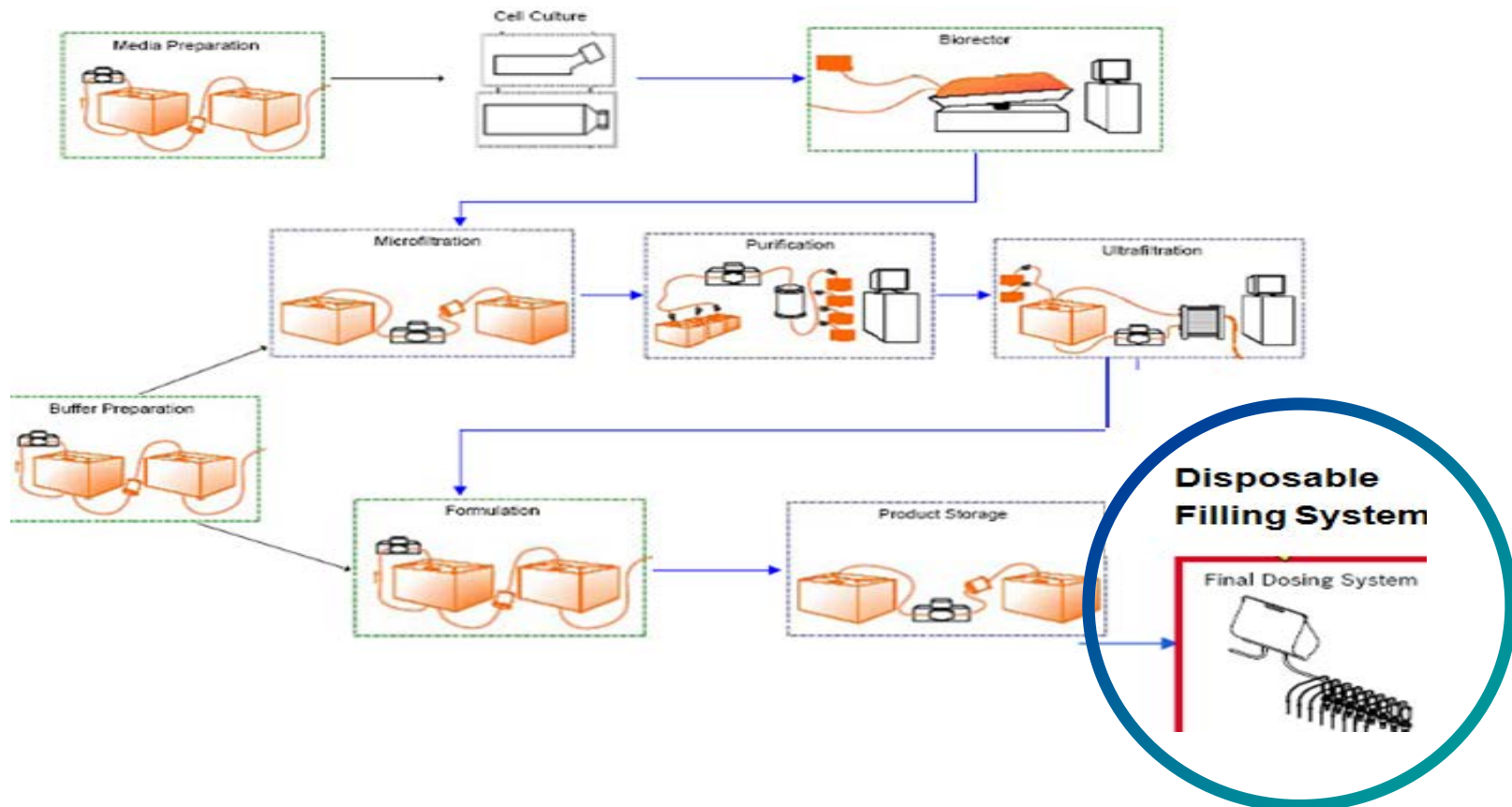
# Plasma Decontamination





# Single-use

## Single-use-systems in (BioTech) - Manufacturing







# Single-use

## Components for disposable systems





# Single-use

## Single-use not available yet

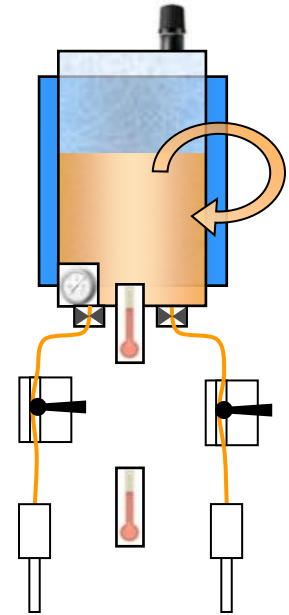
- Mass Flow
- Time Pressure

## Single-use already standard

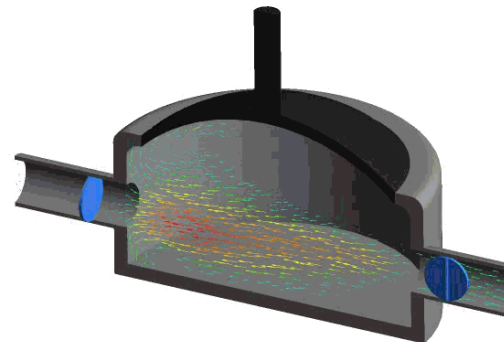
- Peristaltic Pump

## Single-use an option

- Diaphragm Pump
- Rotary Piston Pump  
incl. Filling Needle



ANSYS  
WAVE



By Ryan O'Connor (Ryan O'Connor) [CC-BY-SA-3.0 (<http://creativecommons.org/licenses/by-sa/3.0>) or GFDL (<http://www.gnu.org/copyleft/fdl.html>)], via Wikimedia Commons



# Single-use

## Benefits of single-use fill finish

- Reduce investment costs
- Reduce change over time
- Eliminate CIP / SIP
- Eliminate Cross-Contamination
- Reduce (re)-validation activities
- Reduce qualification activities
- Reduce time to market







# Single-use

Complete single-use product path,  
installed on filling line





# Single-use

## Singel-use vs.traditional approach

<b>CUSTOMER DATA</b>	<b>CIP/SIP</b>	<b>Single Use System</b>
Investment in equipment	\$500,000 (incl. \$200,000 ancillary costs)	-- (even less equipment costs)
Setup (incl. connections)	2 hours	45 minutes
CIP + SIP-cycle	40 + 75 minutes	-- (arrives ready to use)
Cool down cycle	75 minutes	-- (ready to go)
cleanup	1 hour	15 minutes
Post-Use CIP	40 minutes	-- (throw it away)
Summary	~ 7 hours and \$500k (qualification and re-validation efforts are not included)	1 hour and cost of assembly (easy storage)





# Nested objects – Syringes



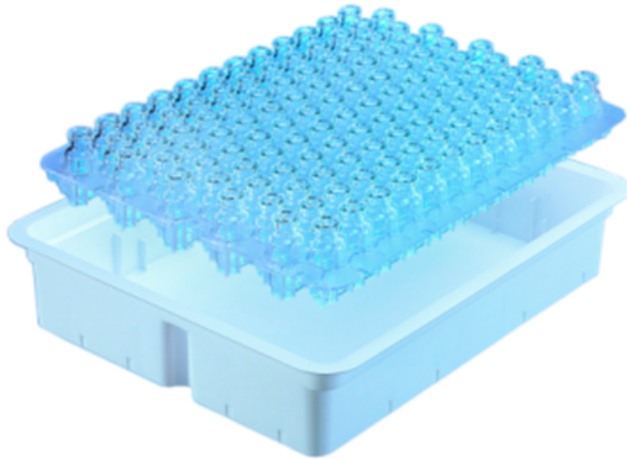
**GERRESHEIMER**

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# Nested objects - Vials

## EZ-fill™ Vial Range: Nest & Tub configuration



Format	dm	h	F	pcs	Nest & Tub
2R	16	35	13	120	Available
4R	16	45	13	120	
6R	22	40	20	32	By Q3 2014
8R	22	45	20	32	
10R	24	45	20	32	
20ml	26,5	63	20	32	To Be Defined
20R					



EZ-fill™ | Courtesy of

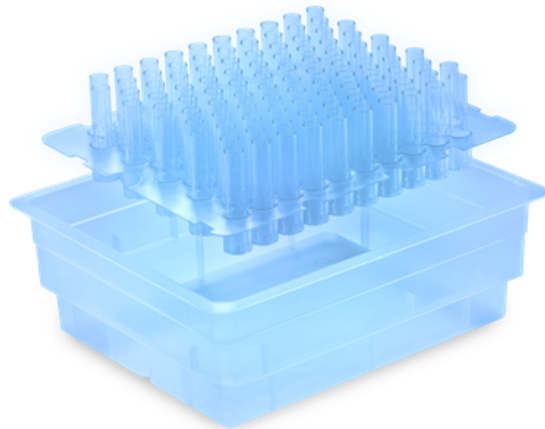


Nuova Ompi  
glass division



# Nested objects - Cartridges

## EZ-fill™ Cartridge Range: Nest&Tub configuration

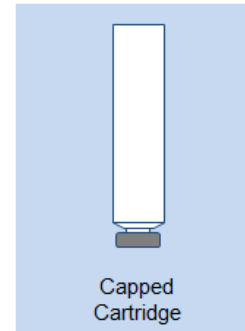


Format	dm	h	F	pcs	Nest & Tub
3ml ISO	11.6	62.3	7	100	By Q2 2014

Cartridge is available in 3 formats:



Only cartridge  
(no components)



Capped  
Cartridge



Cartridge +  
plunger



EZ-fill™ | Courtesy of



Nuova Ompi  
glass division



# Nested objects - Polymers

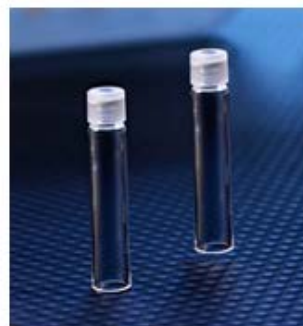
Daikyo Crystal Zenith®



**Vials**  
0.5, 1, 3, 5, 10, 20, 50mL



**Syringes**  
5mL Luer Lock  
1 mL Insert Needle



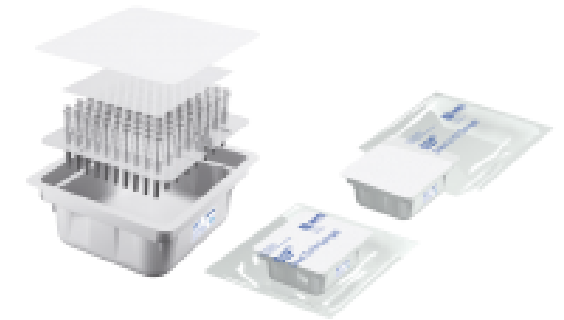
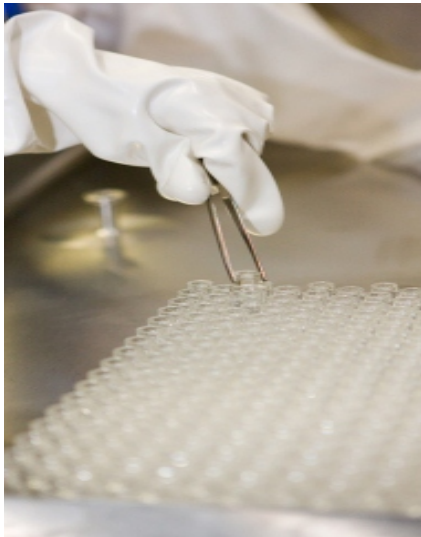
**Cartridges**  
1, 3mL

Available only in EZ-fill N&T format





# Nested objects







# Small batch filling

## Business strategy

Small batch to midsize production

- Clinical trials
- Start-up phase
- New markets & New products
- High margin / low volume production

Flexibility / Easy adaption to changes of:

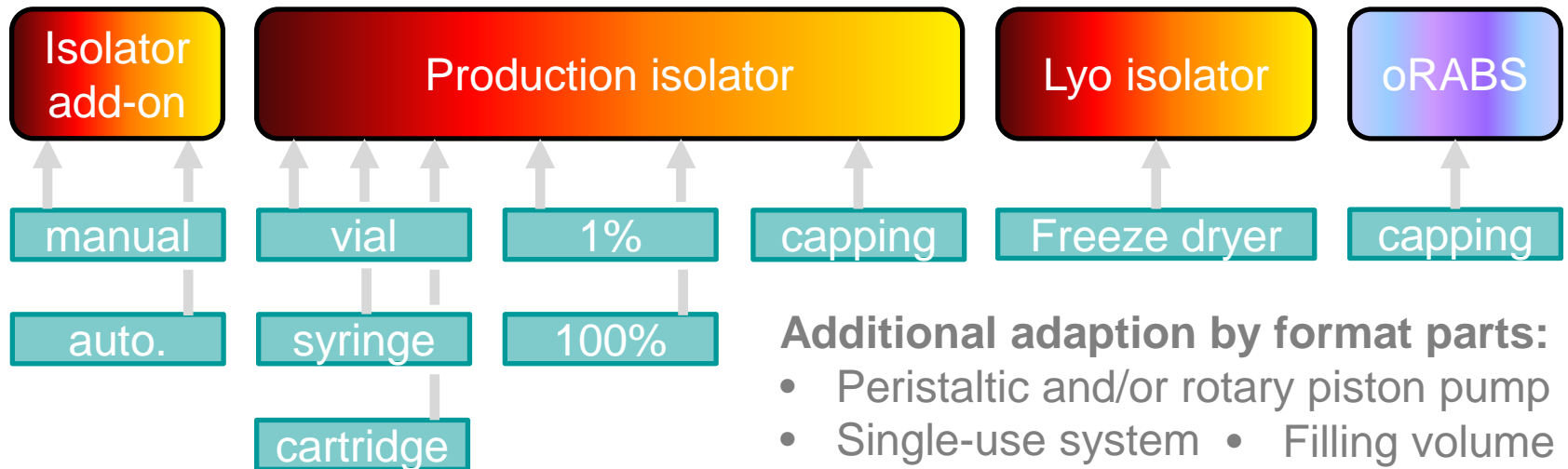
- Containers, Processes, Performance, Layout, Location, Regulatory requirements, ...





# Small batches: modular concept

- 3 standardized isolators
- Modular filling equipment designed for isolator

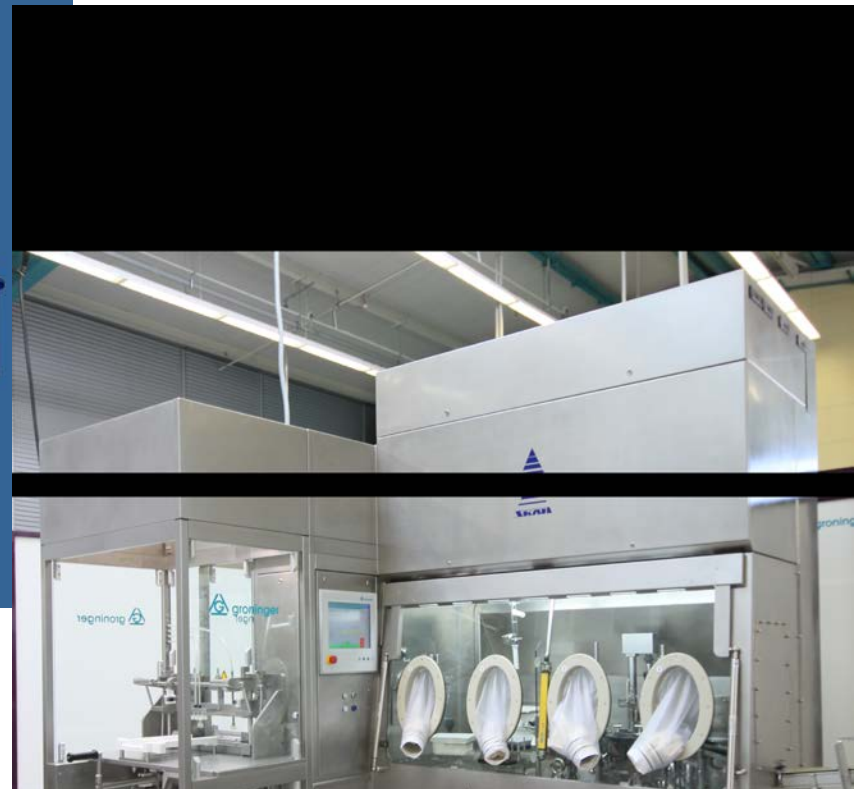
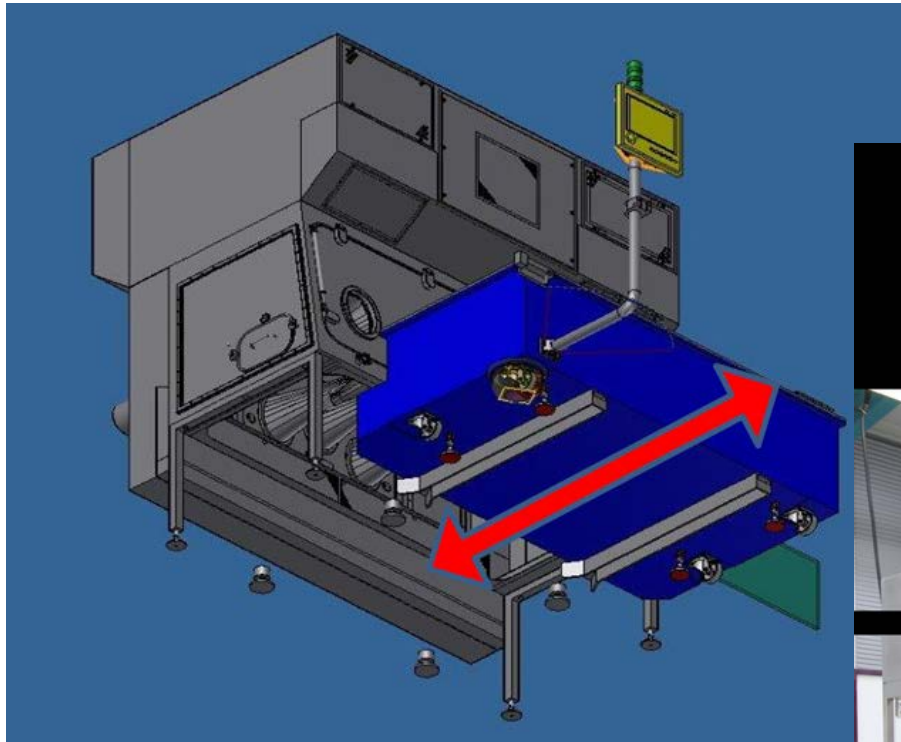


*Sketch not to scale!*

- Additional adaption by format parts:**
- Peristaltic and/or rotary piston pump
  - Single-use system
  - Filling volume
  - Vacuum filling and stoppering
  - Container dimensions made of polymer or glass by several suppliers



# Small batches: modular concept





# Small batches: Requirements



Keep:

- Known processes
- Approved solutions
- Product quality
- Product safety



Reduce:

- Footprint
- Training
- Quali. /  
Vali.
- Investment



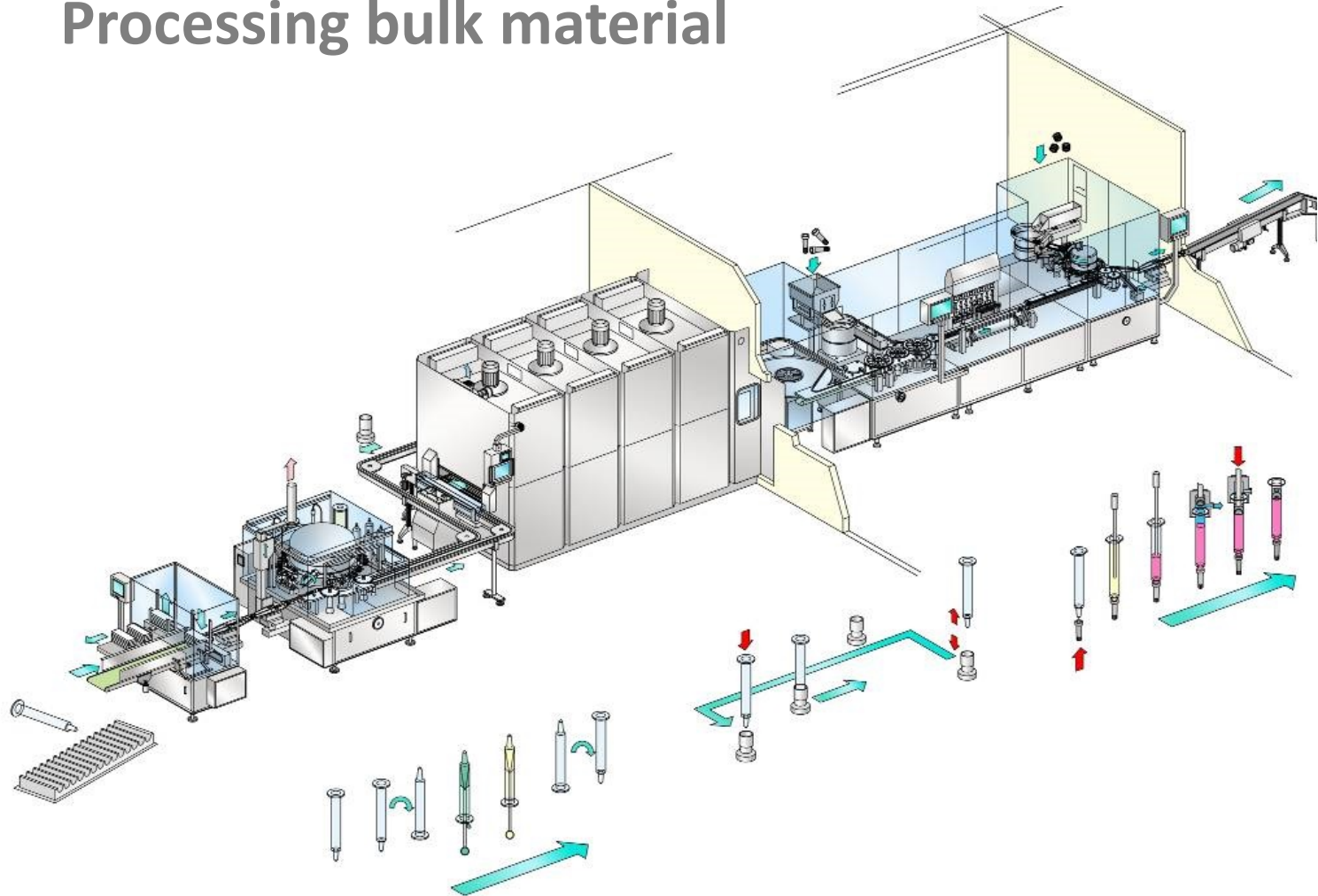
Gain:

- Flexibility
  - on container
  - on location
- Reproducibility
  - on equipment
  - on processes
- Investment safety



# Flexibility & bulk objects

## Processing bulk material

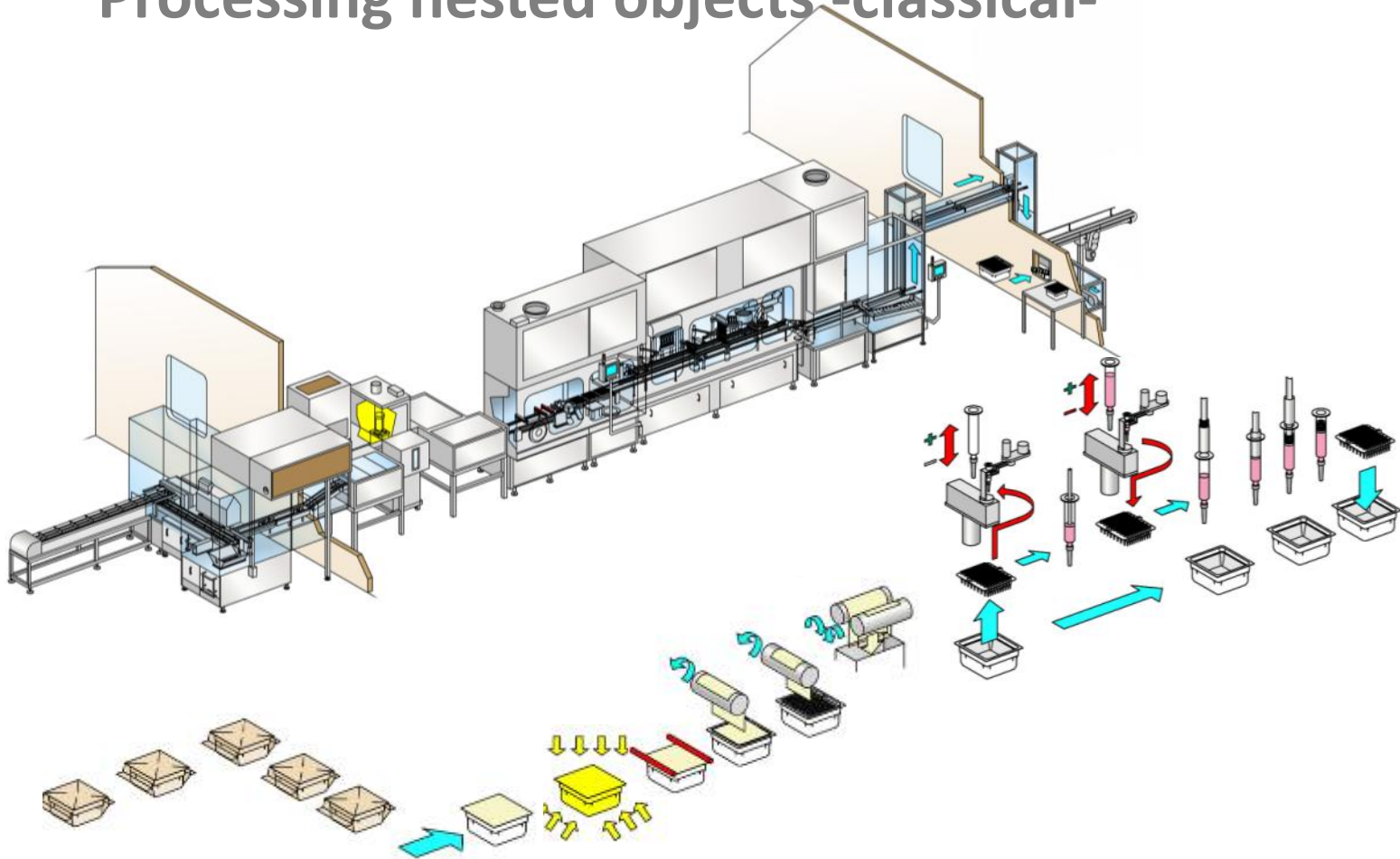






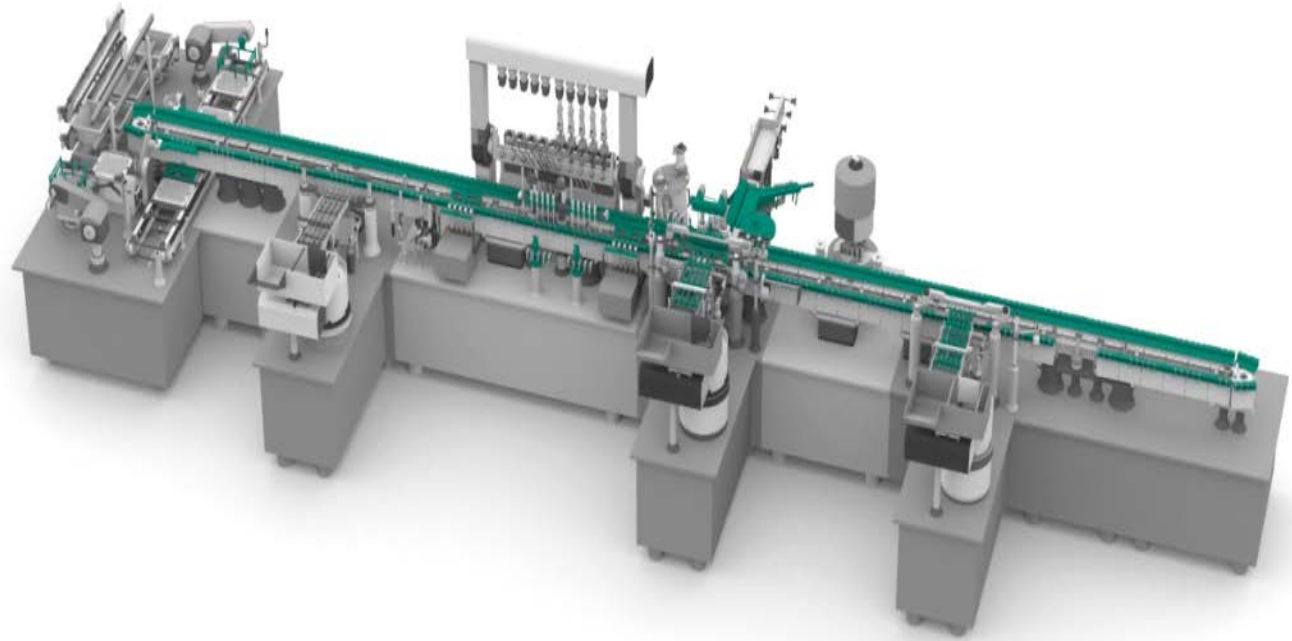
# Flexibility & nested objects

## Processing nested objects -classical-





# Flexibility & nested objects



- All objects (syringes, vials, cartridges)
- Flexible modular concept
- 100% IPC up to 400/min

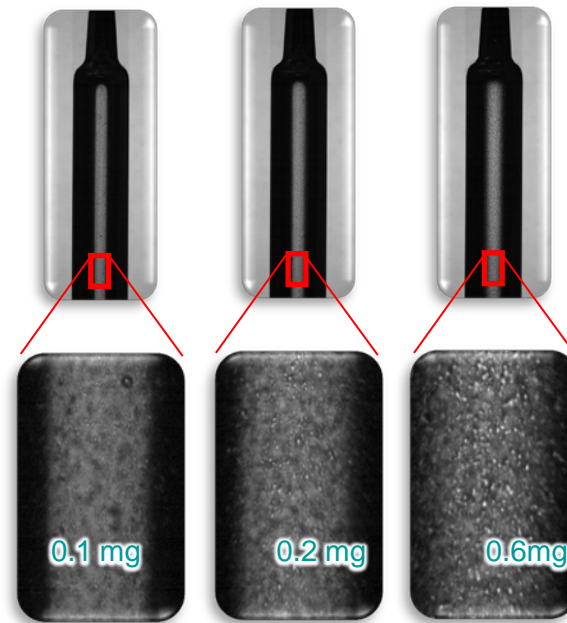
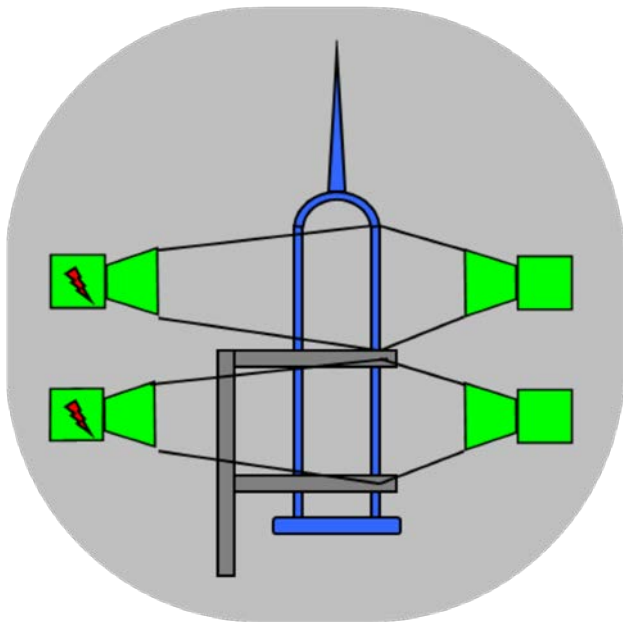


# Future customers' request in 10 years

## Inspection of "all" processes

Parametric release to fulfill future regulations

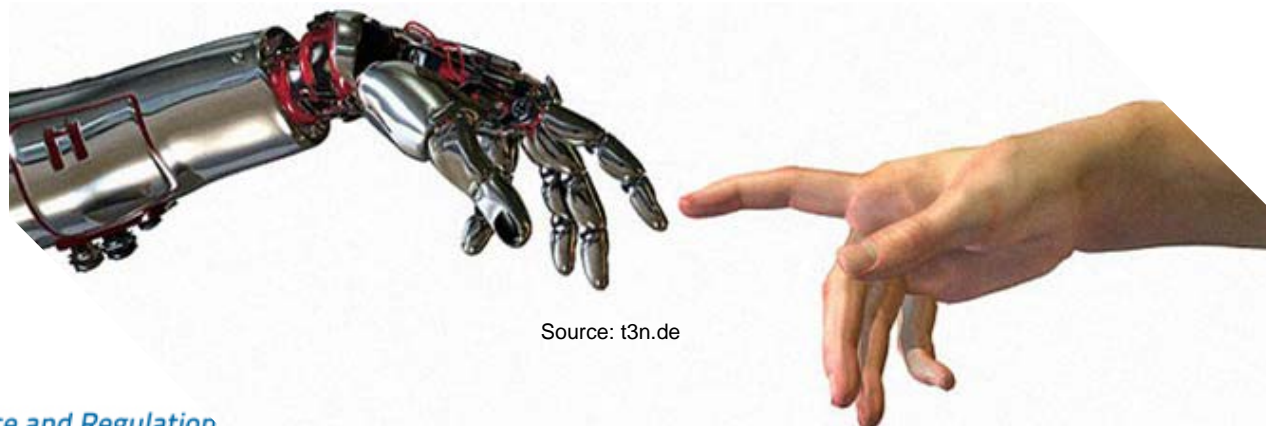
Electronic batch documentation





# Future customers' request in 10 years

## No human intervention



Source: t3n.de

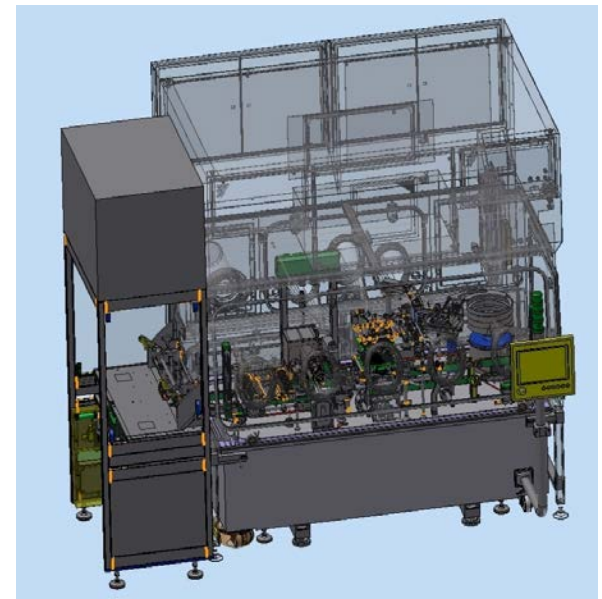
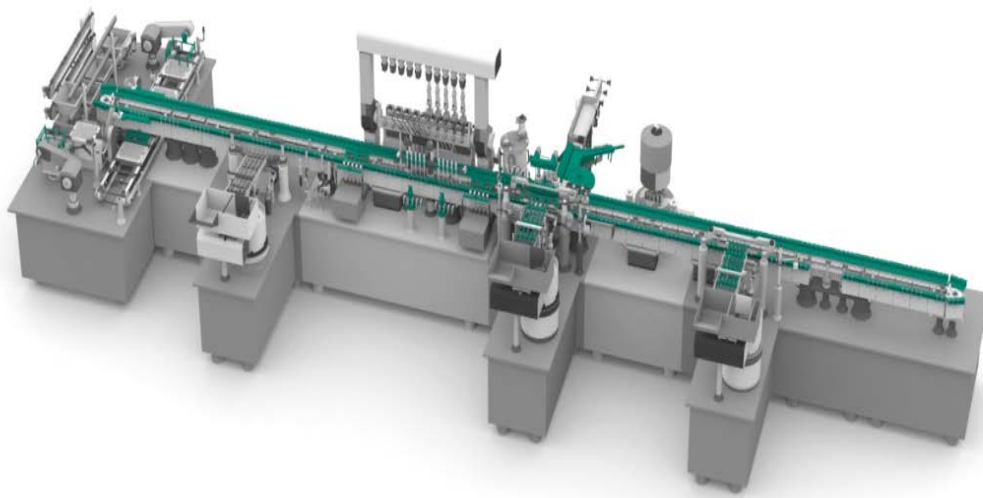




# Future customers' request in 10 years

## Flexibility?

Systems with full flexibility for all kind of containers inside isolators





# Future customers' request in 10 years

## Movable factory?



Source: prozesstechnik-online.de



# Future customers' request in 10 years

Advanced Therapy Medical Products

The next “monoclonal Antibodies” ?



**Advanced Therapy  
Concepts**



# Future customers' request in 10 years

## Outcome of discussion yesterday evening

“round table” Pharmaceutical company - supplier

### Discussed

Impact of product

Impact of material

Impact of technology

Impact of new therapies

Impact of new regulation

Impact of cost pressure

### In progress

Decontamination

Single-use

Nested container

Small batch

Process control

No human intervention

Location

ATMP





=> **Flexibility into the future**

**Thank you very much for your attention!**

We *fill* Visions with Life.



***Wenzel Novak***

Director pharmaceutical  
research and development

**groninger & co.gmbh**