Scaling-up for Commercial Manufacturing of an Allogeneic Product

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Agenda

Aseptic Technologies’ Overview

Position in ATMPs

Requests from users

Scaling up with AT Box
AT Overview

COMPANY

Created in 2002 as a spin-out of GSK Biologicals

Developed and industrialized the concept of a ‘pharmaceutical closed container, filled through the septum, which is resealed by heat’

Since 2011, SKAN A.G. as main share-holder
CONCEPT OF THE CLOSED VIAL TECHNOLOGY

CLOSED VIALS
Produced in ISO5 clean room with the stopper in place and secured
Sterilized by gamma irradiation prior release and delivery

CLOSED VIAL FILLING LINES
Filling performed by a specific needle piercing the stopper
Stopper immediately re-sealed by laser
Capping (snap-fit) inside the barrier
**CLOSED VIAL**

- Vial body made of COC
- Stopper made of TPE
- Hydrophobic material preventing from electrostatic interactions
- Specially designed stopper minimizing loss of residual volume
- Unbreakable vial
- Sizes from 1 to 50 ml

Particularly suitable for:
- Toxic products and high value products
- Very low temperature storage
- Products sensitive to alkali and/or metal ions
**CLOSED VIAL FILLING LINES**

Lean manufacturing eliminates most complex steps of aseptic filling:
- no WFI washing
- no hot-air tunnel
- no siliconization
- no stoppering
- no crimping

Limits risk of batch rejection thanks to lean manufacturing

Secures potent and high-value products

Easily scalable, from manual to fully automated high-speed fillers
Position in ATMPs

ATMP USERS

Connectin People, Science and Regulation
**Position in ATMPs**

**ATMP STORAGE CONTAINERS**

- Opaque materials (no visual inspection)
- Intrinsic particles
- Difficult to scale up (no automation)
- Subject to breakage during handling/transportation
- Important dead volume
Container Closure Integrity

**Past references**

- "Dry ice should not be used in shipping rubber-stoppered vials because the low temperatures can lead to shrinkage of the rubber with subsequent ingress of (unsterile) air and carbon dioxide."
  

- **Effect of Low Temperatures on Parenteral Vial Seal Integrity**
  
Position in ATMPs

ATMP STORAGE CONTAINERS

Container Closure Integrity

Crystal® Closed Vials vs. Stoppered glass vials

No CCI failures in Crystal® Closed Vials during cryo storage

High CCI failures in stoppered glass vials
Position in ATMPs

**ATMP Closed Vial Users**

**Drivers**
- Closed and scalable
- vpLN$_2$ resistant container
- Enables visual inspection
- Cell viability and recovery

**Characteristics**
- Autologous and Allogeneic
- In Phase II or Phase III
Position in ATMPs

**General Requests from Users**

- Solution for bulk product homogenization
- Limited product loss in the process
- Closed system, rapid operations to minimize contact time with DMSO
- Visual inspection (not blood, reach pharma?)
- Track&Trace solution
- Easy to scale-up for allogeneic or deploy (scale-out) for autologus
**SCALING-UP (OUT) WITH AN INTEGRATED PROCESSING EQUIPMENT**

Simple isolator, in positive pressure with HEPA filters

Air from/to the room

<20 min cycles

Catalitic converter to capture $\text{H}_2\text{O}_2$

Robotic L1 equipment for up to 600 Closed Vials per hour

[www.aseptictech.com](http://www.aseptictech.com)
**UPSTREAM INTEGRATION**

The α/β connection system for liquid transfer across the isolator enables to remove the agitation system (wave-induced or mechanical) and pump out of the critical area.

Using smart filling kit allowing in-line measurements

- viability
- morphology
- clusters
- and cell-count
**DOWNSTREAM INTEGRATION**

Using RFID-embedded caps, vials can be individually identified and tracked.

Direct information (product name, batch number, expiry date) and link pointing to any file stored in the cloud.

vpLN$_2$ resistant tag allows tracking and inventory management in the Controlled Rate Freezer, storage dewar and during shipping to the patient.
**Track and Trace from Manufacturing to the Bed Side**

**Secured** data logged in the RFID tag

**Readable any time** thanks to Near Field Communication (NFC) devices

**Real-time indication of use** available at the Point Of Care (POC) during the thawing and injection