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Particle Control For Cell Therapy Products

Roman Mathaes[1], Filip Fedorowicz[1], Andreas Zerr[1], Atanas Koulov[1]

Executive Summary

Health authority inspection focus

➢ Agencies started to enforce VI and particle guidelines for CGT products

Challenges for particle control

➢ Manual manufacturing process, no sterile filtration, single use components with high particle load, unconventional container closure systems, impaired analytical methods because of cell therapy product characteristics

Solution to the challenge

➢ Holistic particle control strategy, process simulations, use of cell strainers, adequate container closure systems, product specific analytical methods

Background

From R&D to larger scale commercialization

➢ *Cell therapies remain a fairly new pharmaceutical modality with CMC processes derived from R&D labs, the pharmaceutical ecosystem currently adopts to the new needs of a scaling cell therapy market*

Health authority paradigm shift

➢ Cell therapies were frequently granted waivers for particle control
➢ Recent FDA warning letters and IND/BLA holds indicate a shift in regulatory expectations, with HA's prioritizing robust particle control

Five Challenges

Manufacturing process

- Low degree of automation with manual operations
- Often in a safety workbench, no isolator containments

Purification process

- No sterile filtration process (cells cannot pass a 0.22 µm filter)
- Only cell strainers are available for particle reduction

Single use manufacturing components

- SUS components adopted from R&D labs
- Focus on ensuring sterility, not optimized for low particle shedding

Container closure systems

- Unconventional primary packaging (e.g. polymer I.V. bags)
- High particle load / particle shedding upon mechanical stress/freezing

Analytical methodologies

- Product characteristics strongly impact performance of the conventional visual inspection methodologies
- Primary packaging (e.g. bags) challenging to inspect with conventional VI instrumentation and pharmacopoeial VI inspection procedures

Solution to the Challenge

Holistic particle control strategy

- QRM based on product and process knowhow
- Controlling all stages of the particle lifecycle

Process simulations / operational excellence

- Particle characterization studies using e.g. water runs/ media fills
- Eliminating sources introducing particles into the product/ process

Implementation of cell strainers

- Optimize the use of cell strainers beyond reduction of cell clumps
- Systematic assessment of cell flow vs particle retention

Container closure systems

- Use of traditional primary packaging e.g. glass vials, polymer vials
- Control strategy for primary packaging components e.g. pre-inspection, components with reduced particle shedding, etc..

Analytical methodologies

- Validate a product specific visual inspection method beyond pharmacopoeial procedures (instrumentation, inspection time, light intensity, etc..)
- Product specific VI test sets for VI operator training / qualification
- Consider supplemental destructive testing when appropriate

*CONTACT: roman.mathaes@clearsolutions-labs.com

Scan and request the "Particle Control For Cell Therapies" white paper →