

Cell and Gene Therapy



Comparability for ATMPs – Challenges and solutions

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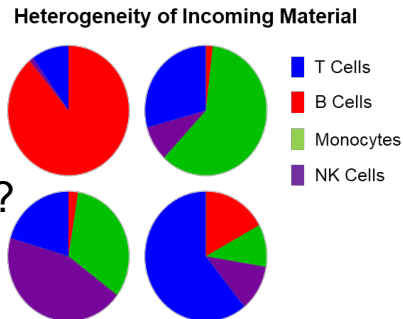
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Comparability challenges

- The product development from PoC to commercialization is rapid due to unmet medical needs
 - The level of process experience is not high and robustness is not fully established
- Hypervariable starting materials (autologous cell therapy)
 - Difficult to compare “healthy donor” and disease affected material
 - How well do “healthy donor” runs describe the process performance?
- Complex process often with many manipulations and open steps



Comparability protocol design considerations: Risk-based approach

- Have an appropriate process risk assessment
- Unit operation vs entire process
 - Do the unit operations compare? Does this impact the final CQAs?
- Same site or multiple sites? What is the scope of change?
- Consider “normal” variance with in the process when setting the acceptance criteria
- Do you utilize multivariate data models?
 - Do these models determine the most appropriate processing pathway prior to execution...
- Are there multiple manufacturing pathways dependent on the starting material?
- At what level is the product characterized – phenotypic profile, CQA's, process yield

Comparability – Solutions

- What is the eventual goal of the exercise?
 - To demonstrate that the process is capable of manufacturing a product with a similar quality to ensure the same safety and efficacy profile
- Leverage follow up data analysis to justify permanent implementation using “real” batches – **Utilize Ongoing Process Verification (Annex 15) effectively**
- Consider working within a design space which has feedback mechanisms to ensure that the final product quality is consistently met
- Statistical tool - Equivalence testing with data driven Equivalence Acceptance Limits (EAL)
- Use of split apheresis (Autologous cell therapy)
- **Use your understanding of biochemical and cellular processes!**