COMPLEX BRIDGING AND COMPARABILITY STRATEGIES TO IMPLEMENT GENE THERAPY DESIGN MODIFICATIONS

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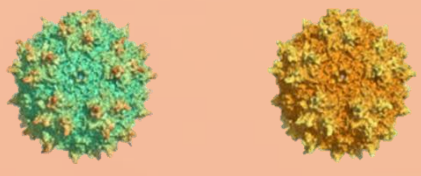
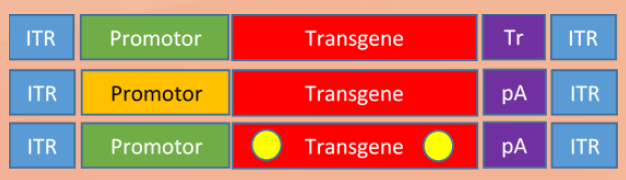
EXAMPLES OF CHANGES TO PRODUCT AND PROCESS INTRODUCED DURING DEVELOPMENT

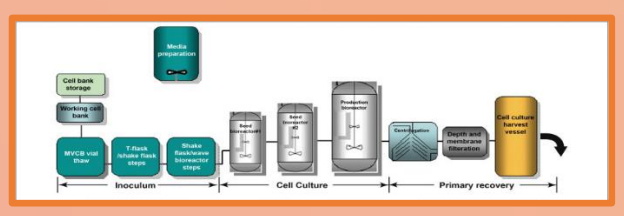
Vector capsid changes



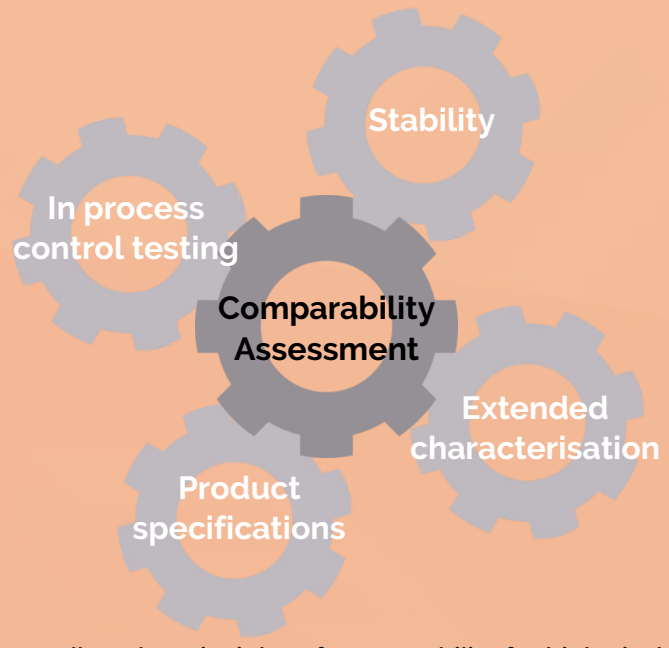
Vector genome changes



Process changes



WHEN CHANGES ARE MADE: COMPARABILITY SHOULD BE DEMONSTRATED



Follow the principles of comparability for biological medicinal products (ICH Q5E)

COMPARABILITY AND BEYOND…

Reflection paper on design modifications of gene therapy medicinal products during development

"in order to maximise the efficacy/safety profile of a gene therapy medicinal product (GTMP), changes to its design in order to obtain new improved product characteristics could be required during its development.

The consequences of these changes in terms of regulatory compliance are somewhat complicated

It can be difficult to fully predict the impact of the modification on the safety/efficacy profile established with the previous product "

EUROPEAN MEDICINES AGENCY
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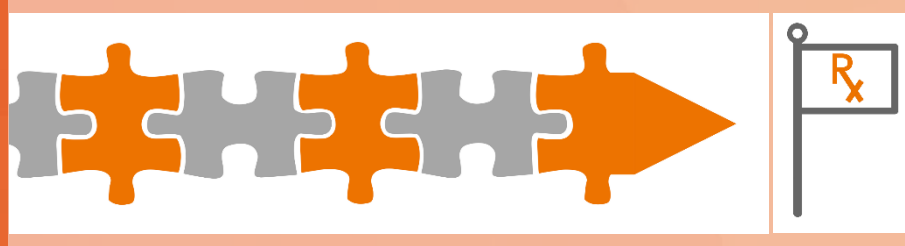
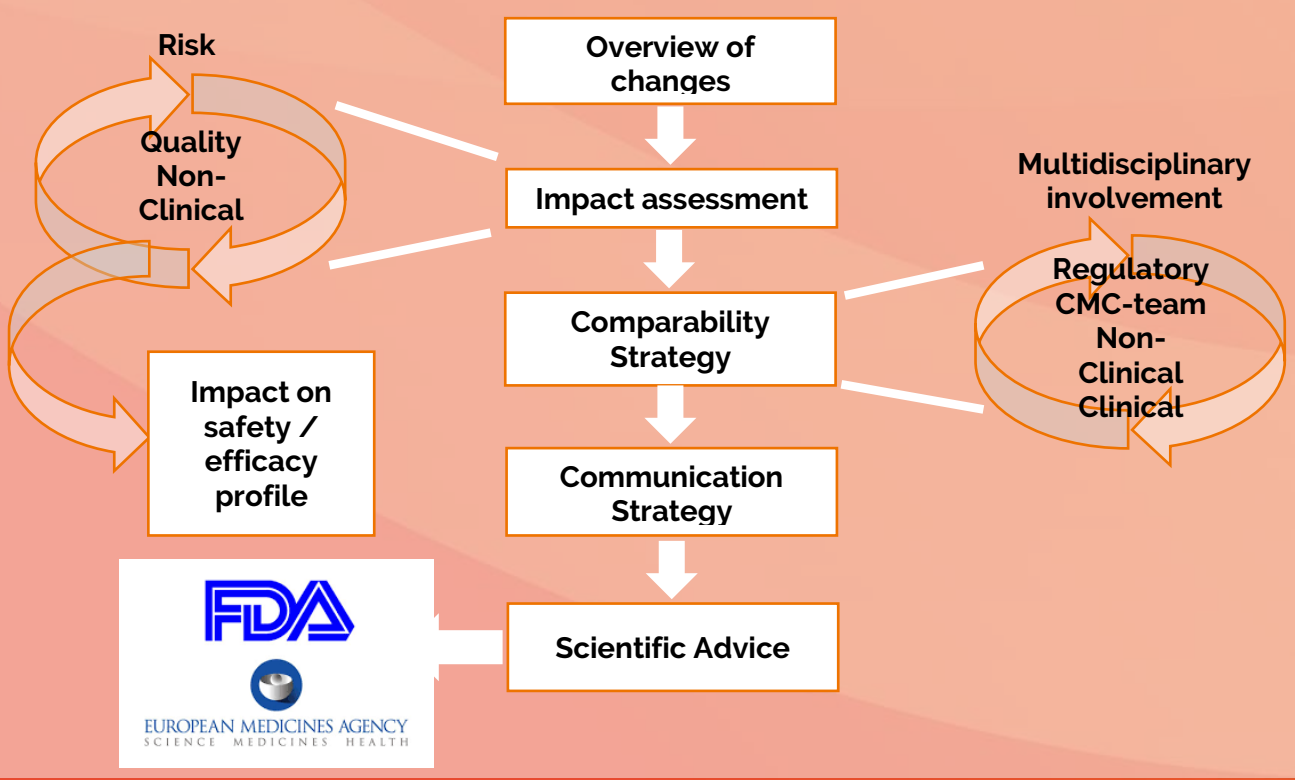
BRIDGING IS KEY…

- When design modifications are introduced a regular comparability approach is not sufficient
- In these cases bridging strategies should be developed which may need to be expanded to non-clinical studies required before further clinical trials

- **FOLLOW A RISK BASED APPROACH**



STEPWISE APPROACH



CMC FOCUS THROUGHOUT DEVELOPMENT

- A regulatory strategy is a reversed engineered document
- Start with the end in mind
- Developing a bridging / comparability strategy requires involvement of a multidiciplinary team
- Apply Risk Based Approach
- Develop a solid communication plan
- Ensure regional alignement
- Seek early health agengy advice and feedback on your bridiging / comparability strategies