"QbD-based Cell and Gene Therapy products manufacturing and lifecycle management'

Background and Challenge

For cell and gene therapy (CGT) products, testing the cells as starting materials or analyzing the raw materials is not feasible as biological products. Therefore, the quality of the product can be determined by comprehensive tests called "Verification" just before release to ensure that the product conforms to QC criteria. Since quality of materials and processes by manual is always valuable, it is difficult to define the "permissible" variation. "Verification" is a type of QC that leaves things to chance and does not question the validity of the criteria for release nor contribute to continuous improvement of raw material control, process development or quality of the final product.

Proposed approach

To overcome the stagnant situation in CGT manufacturing, we propose a quality by design (QbD)-based manufacturing approach. In this approach, the product developers must first have a clear image of the CGT product with efficacy substantiated by a robust efficacy assay. Then, they must set up SOPs to manufacture the product properly. Next, establish process parameters (PPs) and acceptable values alongside the PPs to confirm that the product is manufactured "as designed" by verifying that the values measured for each PP are within an "acceptable range" called the design space (DS). These PPs and DS consist of the product's CQAs for manufacturing. Finally, the validity of the predefined PPs and DS is verified by a robust efficacy assay of the product.

Conclusion

This allows us to visualize the CQAs of the product and support the continuous development of the CQA description at each stage of the product's life cycle. This approach accepts for variance in the quality of raw materials, changes in manufacturing scale, and technical development, as long as the manufactured product retains the same efficacy. We believe that a QbD-based approach to manufacturing CGT products would facilitate the seamless development of CGT products.