Advancing the future of therapeutics – **ATMPs**

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When writing this editorial, a wonderfully captivating and entertaining novel came to mind: "Three Men in a Boat". It's a tribute to the fun and much discussion we have had in building this focus issue on advanced therapies for *Regulatory Rapporteur*. Unusually, three consultant editors worked together on this timely edition, given our interest and passion in this field. This issue is one that perhaps has a greater technical and scientific flavour and we hope you enjoy it.

Since the European Medicines Agency (EMA) Committee for Advanced Therapies (CAT) was established in 2009, five applications for marketing authorisation have been approved. Most recently, in February 2015, the first advanced therapy medicinal product (ATMP) containing stem cells, Holoclar, was approved. While the successful registration of ATMPs is encouraging, the number of authorisations is undoubtedly lower than hoped when the ATMP Regulation (1394/2007) was implemented. As the knowledge of this class of therapies rapidly evolves, however, we are now seeing more and more products with encouraging clinical trial results, not least the very promising efficacy findings recently reported with CAR-T cell therapies. In this issue, we explore the major technical issues for ATMPs and strategies for their resolution.

A key challenge for ATMP developers, and an integral component to the acceptability of regulatory filings for marketing approval, is development of orthogonal methods to accurately assess potency. The potency assay is critical to many aspects of development, providing an indication of the intended dose and anticipated clinical effect, but also providing a tool to monitor batch quality at the time of drug release. As sponsors must provide an indication of potency/dose from the commencement of clinical development, when often the mechanism of action of a product is incompletely understood, an incremental approach whereby a simple test is first included and subsequently methods are honed and orthogonal methods added is recommended.

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Our first focus article reviews the current regulatory expectations for potency assay development and key challenges that cell therapy developers face; it also provides an overview of typical issues raised by regulators in relation to assays in regulatory submissions, and outlines a recommended strategy for potency assay development.

Our second focus feature highlights the importance of selection of a suitable analyte, the appropriate quantity and unit of measurement, as well as appropriate reference standards in characterisation of cell therapies in order to monitor manufacturing process drift and therefore changes in product quality over time. While for biotech products it is widely accepted to prepare a "reference batch" for use as a standard for analyses of future batches, our article highlights the need to develop new and creative strategies for selection of a reference standard for cell therapies. This is owing to the typically short shelf life and inherent variability of cell-based therapies, which can result in reference batches of ATMP being inappropriate for use as a reliable standard.

The above-mentioned issues and the wish for the CAT to be collaboratively involved in ATMP development with companies is one of the key messages from our interview with the CAT chair, Paula Salmikangas. Dr Salmikangas provides an overview of the key objectives of the CAT over the coming year.

Our final article on the topic of ATMPs comes in the form of a meeting report covering development pathways for advanced therapies, where a recent workshop organised by the EMA and European Biopharmaceutical Enterprises (EBE) outlined the latest scientific developments and their potential impact on patients.