There are many challenges associated with characterising and quantifying cells for use in cell- and tissue-based therapies. From a regulatory perspective, these advanced treatments must be not only be safe and effective for their designated indication, but must also be made by high quality manufacturing processes that allow for on-time delivery of viable products. While sterility assays can be adapted from conventional bioprocessing, cell- and tissue-based therapies require more stringent safety assessments, especially in relation to use of animal products, immune reaction and potential instability due to extended times in culture. In addition, cell manufacturers using human embryonic stem cells (hESCs) in their therapies need to be particularly stringent in their final purification steps, due to the unrestricted growth potential of these cells.

This work summarises the current issues in characterisation and quantification for cell- and tissue-based therapies, dividing these challenges into the regulatory themes of safety, efficacy and purity of manufacture. It outlines current assays in use, as well as highlighting the limits of many of these product release tests. Mode of action is also discussed, with particular reference to in vitro surrogate assays that may be used to provide information to correlate with proposed in vivo patient efficacy (Figure 1). Most importantly, we highlight the need for better resources to improve the current scientific knowledge of how these therapies will interact with the body once implanted. Finally, we outline an improved stakeholder negotiation process (Figure 2) to identify the measurement requirements to allow the manufacture of the best possible cell- and tissue-based therapies within the shortest timeframe.

Fig. 1. Dynamic feedback process for determining effective in vitro surrogates for release testing. As the eventual fate of the cell is still unknown, continual feedback will be needed to improve therapy product design from the original bench-based development through to clinical trials and post-marketing surveillance.

Fig. 2. Product development negotiations. Entrepreneurs and public policy actors have different goals, each required to manage risk, reward, and time to market. Management of risk/reward tradeoffs requires both negotiation and consensus on the evidence requirements for product adoption. The science base has a critical role in defining the evidence requirements and collecting necessary data.

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