MITIGATING THE RISKS OF ADVENTITIOUS AGENTS IN SERUM: ELIMINATION OR VIRAL INACTIVATION

Kelly O'Neill, Celgene, USA
keoneill@celgene.com
Erik Trinkle, Celgene, USA
David Hsiung, Celgene, USA
Seth Jones, Celgene, USA

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Human AB serum (hABs) is used in culture medium for some cell therapies, such as chimeric antigen receptor T cell (CAR T) or engineered T cell receptor therapies, to provide the necessary growth factors and nutrients for cell proliferation. While hABs has been demonstrated to effectively sustain primary cell cultures, hABs has several drawbacks including lot-to-lot variability, supply constraints, and, above all, the risk associated with adventitious agents. hABs is derived from either whole blood or plasma donations that are subject to stringent sourcing controls such as viral screening on individual donations. The addition of a viral clearance step can further mitigate the risk associated with potential adventitious agents. Celgene is exploring two strategies to mitigate the risk associated with adventitious agents: γ–irradiation of hABs to inactivate viruses and serum-free medium (SFM) formulations to eliminate the use of complex animal-derived materials.

γ-irradiation has been proven to be an effective viral reduction method in animal sera, but its application to human serum is currently limited. γ-irradiation is known to impact serum composition, thus risking potential changes to process performance and critical product quality attributes. Additionally, there is a limited number of hABs vendors with γ-irradiation experience, ultimately requiring close collaboration between company and vendor to establish a robust supply chain.

Adoption of a SFM formulation can eliminate some of the challenges associated with serum. SFM formulations are commercially available, well defined, and can serve to replace hABs entirely. Implementation of a new SFM formulation in an existing process risks changes to critical quality attributes of the cell product and may require significant development efforts to achieve comparability. In addition, many commercially available SFM formulations still contain human- or animal-derived materials, such as human serum albumin or transferrin, which also can present viral disease transmission risk and must undergo appropriate viral reduction treatments.

Celgene's strategy is to evaluate both γ-irradiated hABs and SFM for cell therapy applications. Both media containing γ-irradiated hABs and SFM support T cell expansion, though differences have been observed when compared with typical hABs containing media. Moreover, both γ-irradiated hABs and serum-free alternatives may result in differences in CAR T cell quality attributes, such as phenotype and activity. Investment in development and comparability is critical when planning to incorporate γ-irradiated hABs or SFM in cell therapies in order to reduce the risk associated with adventitious agents. Careful selection of media formulation for future programs should also be a consideration given the challenges of changing media formulations for an existing product.