**Roundtable Session 1 – Table 4 - Detection of Particulates / Visual Inspection of CGT Products**

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**Abstract:**

Given the nature of manufacturing processes involved, as well as the type of modalities involved in the field of cell and gene therapy field, particulates are common and very likely unavoidable. In addition, there is neither any guidance nor standards specific to either characterizing or computing particulates in these modalities. Given that is the case it is important to discuss and highlight what are the best approaches to detect particulates, and what methods or approaches can be used to assess the risk. In addition, we would like to discuss key metrics that we could use as a first pass as well as fundamental questions that could help as part of the risk assessment to understand the impact to patient safety and product efficacy.

**Roundtable Notes:**

The roundtable on controlling visual particles for CGTs primarily focused on cell-based products. These products present the most challenges because their final formulation can be cloudy, and cells naturally tend to aggregate. Additionally, cells themselves are particles in suspension, which complicates the development of a robust particle control and visual inspection program.

There are currently no methods that can reliably detect all types of particles (inherent, extrinsic, and intrinsic) in cell suspensions. When a visual inspection fails, the characterization testing used to identify the particles is destructive to the product. This is not ideal because these products are highly expensive and available in very limited quantities. In the event of a visual inspection failure for vials, participants indicated that this typically results in the rejection of the batch. Some participants shared that particle-related rejections account for 15-20% of batches.

For cell-based products in bags, it is common to require gentle massaging of the bag post-thaw to de-clump the natural cell aggregation that may occur prior to administration. In cases of allogeneic products, which are typically developed to be administered via vials, massaging to reduce clumping will not be possible. Human serum albumin (HSA) is a common excipient used to prevent or reduce such aggregation. Furthermore, one currently approved cell-based product requires a stainless steel 18-micron filter before administration, as these cells typically range from 10 to 15 microns in size.

Understanding the risks associated with particles requires characterizing cell populations and observing their behavior in suspension, during formulation, and within the body. Identifying

potential risks from process-related particles is crucial for prevention, as current detection methods are not advanced enough to be completely reliable. Single-use materials, as well as other types of plastic, glass, and metal that come into contact with the product, have been problematic in introducing particles.

Participants proposed making visual inspection/particles a topic for next year's conference, noting that there are currently far more questions than answers.

Further reading: https://www.isct-cytotherapy.org/article/S1465-3249(22)00745-9/abstract