Roundtable Session 1 – Table 2 – Donor Selection Criteria Across ICH Regions for Cells Used as Starting Material for ATMP Manufacture

Facilitator: Andrew Weiskopf, S*ana Biotechnology*

Scribe: Kerin Ablashi, *Biologics Consulting*

Abstract:

This roundtable will explore the global landscape of donor selection criteria and qualification requirements for human cells used in the manufacture of cell therapy products. While the foundational goals—ensuring donor safety and minimizing the risk of disease transmission—are consistent across regulatory jurisdictions, the specific approaches to donor eligibility, testing, and documentation can vary significantly. Participants will discuss key regulatory frameworks from global health authorities, highlighting areas of convergence as well as notable differences in requirements related to donor screening, infectious disease testing, and traceability. The discussion will also address the implications of these differences for international development, clinical trial design, and product manufacturing strategies. By sharing experiences, identifying common challenges, and seeking potential opportunities for harmonization, this roundtable aims to inform more globally coherent practices in cell therapy product development.

Discussion Questions:

1. Where do current regulatory requirements for donor eligibility and testing align across the US, EU, Japan, and other regions? Where do they diverge most significantly?

2. What are the challenges faced by global sponsors in meeting divergent donor qualification standards when manufacturing for multinational clinical trials or commercial distribution?

3. To what extent is regulatory convergence or harmonization feasible, and what role might international bodies (e.g., ICH, WHO) play in facilitating it?

4. How should emerging technologies (e.g., induced pluripotent stem cells, gene-edited products) influence the evolution of donor selection criteria and associated regulations? Does the end-use matter?

Notes:

Globally, regulations are variable: each country has its own committee for cells of human origin. This variability includes:

- Required donor testing – what must be tested and when
- Amounts of material required for testing and retains (and duration of sample retention)
- Requirements for donor histories – information that must be collected and when the information may be collected (e.g. can missing information be provided after materials have been collected, and if so, for how long afterwards?). In some countries, donors may be located after the fact to provide donor history information.
- Differences in the actual tests to be performed (e.g. HIV testing)
- Intended use for donor materials (e.g. apheresis, GMP starting material, medicinal product) dictates the required testing
- US requires CLIA – compliant collection / testing; materials collected ex-US are not CLIA-compliant

Potential strategies to address the global variability in requirements:

- In the EU, perform testing per requirements for France and Belgium, which are the most comprehensive. This may be sufficient for other EU countries.
- Perform risk assessment to determine which testing requirements to follow in each specific case – due to limited materials and costs, it may not be possible to perform testing compliant with all major regulatory body requirements.
- Collect additional blood / material in case more testing is needed later.
- For allogenic donations, could have donors from a wide variety of sources for global studies.
- Discuss testing plans with FDA – ask for exemptions for testing. FDA may allow this for clinical trials but it's unlikely that they will agree that this exemption will carry over through marketing – they will want to see the data and then assess. This makes it hard to perform risk assessment.
- Establish cell lines from the starting material – in some regions the bank can be tested to provide information that is missing from the donor history. Note that in this case, if changes are made to a stem cell MCB, or the resulting material will become a different product.

Challenges with sampling/testing include:

- Differences in the testing kits based on the test kit origin (e.g. transfusion, apheresis), expectations of local authorities.
- Blood and cells are tested under the transplantation not ATMP. Requirements are regional; ICH has no oversight.
- Cord blood, stored frozen – all must be used or discarded once thawed so no additional testing can be performed even if needed (e.g. testing error). (Fresh must be used soon after collection, limiting additional testing.)
- Testing costs (performing testing that complies with multiple regional requirements is expensive – who pays?)
- CDMO that manufactures the DP controls the testing they require for incoming material – companies need to ensure that the donor site performs the required testing

Other considerations:

- Reimbursement to donors and testing centers generally makes a difference in the testing performed – sites are paid for clinical trial collection & testing but not for other uses.
- Costs to train staff and perform testing go into the profit margin
- Authorized Treatment Centers are not considered to be part of manufacturing, and are controlled by their own SOPs. Difficult for companies using their services to affect their procedures.
- Collection centers are not all the same – Centers collection allogenic materials are more centralized with more harmonized practices. Not necessarily the same for autologous. Cord blood is collected at hospitals and maternity centers which have widely variable quality.
- To reach commercial scale, quality starting materials are needed. Global variability in requirements makes industry success more challenging.