International Alliance for Biological Standardization

Glyn N. Stacey, Ph.D.
Chair of the Conference Scientific Committee

Session 6: Shipment and preservation, K Hoogendoorn and G Stacey

- What are the key challenges in preservation and shipment?
- What types of initiatives might support their resolution?

Session 7: Summary

3rd IABS Conference on Cell Therapy Manufacturing and Testing, London, 2-3 November 2016

Session 1: Regulation and Registries

- Products derived from stem cells need support as well as somatic cell therapies
- Regulatory terms and definitions vary between jurisdictions and this needs careful explanation
- Many regulations for cell therapy but manufacturers moving to multiple jurisdictions and developing countries need support to manage this.
- Coordination on cell data/ontogeny standards would valuable.

Session 2: Raw and Starting Materials

- Coordinated discussion needed on establishing acceptable raw, ancillary and starting materials for use in international products and in developing countries.
- Need to reconsider risk assessment approaches: avoid making assumptions about safety (e.g., “human origin materials are safer than animal”, “origin in non-mammalian sources cannot cause human infection”)

Session 3: Autologous and Allogeneic Products

- Development and use of Potency assays ("layering" : animal model>3D cell culture> markers, may be a useful approach) with careful validation of routine surrogate markers against other layers
- Effective training of both hospital and operations staff is crucial.
- Autologous and allogeneic therapies may require different approaches.
- Semi-automation can be crucial for improving reproducibility and reliability in manufacture
- Comparability is a big challenge for cell therapies (key markers/assays may not yet be known).
- Coordinated discussion needed on assessment of process change, use of alternate raw and starting materials, use of cell panels for single products.

Session 4: Manufacture

- Ongoing staff training in SOPs and its refreshment is important but it is also vital to provide training/education in scientific issues to enable staff to understand impact of changes/unplanned deviations
- Consider training the innovators through academic-industry interface. An independent safe harbour model led by a neutral organisation might facilitate this whilst protecting industry IP)
- Other areas would benefit from training systems to addressing regulatory issues and process and enable researchers to be ready for translation.
- Models for manufacturing and development established for biologicals have significant value for cell-based medicines
- Be prepared for unexpected challenges e.g., cell responses to leachates from processing materials
- Characterisation of cells and product: will change through phases from cell line selection, cell banking, intermediates and final product
- Very difficult to change a products significantly in response to a rapidly developing science but this may become more feasible when cell therapy manufacturing platforms are established

Session 5: Standardisation and Testing

- QbD can add value for aspects of process and analytical method optimisation
- Lack of international consensus on performance, relevance and control of tumorigencity assays
- Value of genetic data not yet clear: need to understand it and coordination of experiences will be important
- International standardisation is crucial to industrialisation of cell therapies to ensure common understanding
- Establishing new standards: need to identify the real needs for industry and coordination of standards organisations and stakeholders will be crucial
- MSC-based therapies are in need of better markers and functional assay related to clinical outcome

Session 6: Preservation and Shipment

- Cell therapy developers are challenged by the need to transport cells over long distances to point of use which limits the rate at which therapies can be made more broadly available.
- Lack of solutions for successful preservation is one of the most fundamental challenges in the cell therapy field lack of which impacts on our ability to assure provision of a safety tested and stable live cell products.
- Preservation is a complex process with many significant variables are poorly understood and therefore difficult to control
- Life scientists in general do not have a good appreciation of the scientific principles involved in preservation processes and this inhibits efficient technical progress. Training and education in the science and technology of preservation is an urgent requirement in the field.
- The substatial losses of cells are known to occur in thawed
- Viability is a Standard cryoprotectants can cause adverse effects in patients and alternatives may be needed to optimise the risk benefit ratio of therapies thawed and used at bedside
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Ongoing Activity

- Compile a meeting report to submit to Bilogicals (2017)
  - Speakers annotated abstracts annotated with key issues/messages
  - Speaker sections and summaries of discussion, plus a summary of conclusions/recommendations
  - Scientific Committee to help finalise draft
- Disseminate via WHO and others – N.B. let us know of other opportunities/organisation
- Further IABS Cell Therapy meeting under consideration

Thanks!

- IABS Committee: T Hayakawa and J Petricciani
- Conference Scientific Committee: S Bauer, K Hoogendoorn, M Kibbey, I Knezevic, **A Lubiniecki**, N Medcalf, Y Sato, G Schumann, J-H Trouvin, J Vandeputte, B-Z Yuan.
- All speakers for such a great meeting!
- Supporters: **Catapult - Cell & Gene Therapy; German Stem Cell Network (GSCN); Medical Research Council (MRC); TiGenix; UK Stem Cell Bank/NIBSC-MHRA**
- You, the delegates - Regulators manufacturers and academic groups from at least 15 countries
- **IABS/NIBSC secretariat: Abbie Charlet and Gill Cathro**