4th Cell Therapy Conference:
Manufacturing and Testing of Pluripotent Stem Cells

Organized by
The International Alliance for Biological Standardization
IABS

With Support from and in Collaboration with the
California Institute for Regenerative Medicine
CIRM

Los Angeles, California
June 5 - 6, 2018

Scientific Committee

Professor Glyn Stacey	Chair, Scientific Committee International Stem Cell Banking Initiative, United Kingdom
Dr. Abla Creasey	California Institute for Regenerative Medicine (CIRM)
Dr. Stephen Lin	California Institute for Regenerative Medicine (CIRM)
Dr Anthony Lubiniecki	International Alliance for Biological Standardization (IABS), U.S.A.
Dr. Ivana Knezevic	World Health Organisation (WHO), Switzerland
Dr. Yoji Sato	National Institute of Health Sciences, Japan
Professor Jean-Hugues Trouvin	Paris Descartes University, France
Dr. Elwyn Griffiths	International Alliance for Biological Standardization (IABS) United Kingdom
Dr. Kathy Zoon	Emeritus, National Institutes of Health, U.S.A.
Dr. Robert Deans	BlueRock Therapeutics, U.S.A.
Dr. Kathy Francissen	Genentech, U.S.A.
Dr. Thorsten Gorba	IQVIA, U.S.A.
Dr Karin Hoogendoorn	Leiden University Medical Center, The Netherlands
Professor Krishnendu Roy	Marcus Center for Cell-Therapy, Georgia Institute of Technology, U.S.A.

Monday, June 4, 2018

WELCOME RECEPTION

6:00pm – 8:00pm

Hosted by: STEMCELL Technologies

Spotlight on Standards Development

Prof. Glyn Stacey
Introduction and International Stem Cell Banking Initiative.
Consensus standards for hPSCS for clinical application.

Dr. Anthony Ratcliffe, ARM-SCB/ASTM
The ARM-Standard Coordinating Body and ASTM.

Dr. Tatsuo Heki
Industrialisation of regenerative medicine: standards are the key.

Dr. Sheng Lin-Gibson
NIST standardisation programmes

Day 1 – Tuesday, June 5, 2018

8:00 am **Registration & Welcome Coffee**

8:30 am **Welcome**
Dr. Anthony Lubiniecki, International Alliance for Biological Standardization (IABS), U.S.A.
Dr. Abla Creasey, California Institute for Regenerative Medicine (CIRM) San Francisco, California, U.S.A.

8:45 am **Highlights from Cell Therapy 2014 - 2015 - 2016**
Prof. Takao Hayakawa, Kindai University, Tokyo, Japan
Prof. Glyn Stacey, Chair, Scientific Committee; International Stem Cell Banking Initiative, United Kingdom

Session 1 – Learning from the current pluripotent space and the development of international standards

Case studies in the challenges of pluripotent stem cell development
Chairs: **Dr. Thorsten Gorba,** IQVIA Stem Cell Center, San Diego, California, U.S.A
Dr. Kapil Bharti, National Eye Institute (NEI) / National Institutes of Health (NIH), Bethesda, Maryland, U.S.A.

9:00 am Introduction to Session 1, Part 1 by the Chairs

9:05 am Experiences in taking human embryonic stem cells to clinic
Dr. Edward Wirth, Asterias Biotherapeutics, Fremont, California, U.S.A.

9:25 am Taking neural progenitors and iPSC cells to the clinic for ALS and Retinitis Pigmentosa: two case reports
Prof. Clive Svendsen, Cedars-Sinai Medical Center, Los Angeles, California, U.S.A.

9:45 am IND-enabling In vitro and In vivo functional authentication of AMD-patient derived clinical-grade iPSC-RPE tissue
Dr. Kapil Bharti, National Eye Institute (NEI) / National Institutes of Health (NIH), Bethesda, Maryland, U.S.A.

10:05 am **Panel discussion**

Dr. Thorsten Gorba, IQVIA, San Diego, California, U.S.A.
Dr. Edward Wirth, Asterias Biotherapeutics, Fremont, California, U.S.A.
Prof. Clive Svendsen, Cedars-Sinai Medical Center, Los Angeles, California, U.S.A.
Dr. Kapil Bharti, National Institutes of Health / NEI, Bethesda, Maryland, U.S.A.
Dr. Shin Kawamata, Foundation for Biomedical Research and Innovation (FBRI), Kobe, Japan

Topics for discussion

- What challenges have the developers experienced in relation to using pluripotent stem cells as manufacturing cell substrates?
- What experiences can be anticipated in the transition from one cell substrate type to another for the same indication and how can developers best manage the challenge of demonstrating comparability and scale up?
- What have been the major learning outcomes over the last ten years' experience of taking pluripotent stem cells to therapy?
- What are the key differences between developing and standardising autologous versus allogenic cell therapies?

10:45 am **Coffee break**

Learning from international standardisation
Chair: **Dr. Kathryn Zoon,** Emeritus, National Institutes of Health, Bethesda, Maryland, U.S.A.

11:15 am Introduction to Session I – Part 2 by the Chair

11:20 am Historical perspective: the importance of early regulatory guidance for biotherapeutics
Dr. Elwyn Griffiths, International Alliance for Biological Standardization (IABS), United Kingdom

11:40 am WHO standards for cell therapies: key issues in defining quality, safety and efficacy
Dr. Ivana Knezevic, World Health Organization, Geneva, Switzerland

12:00 pm **Panel discussion – International regulatory landscape**

Dr. Kathryn Zoon, Emeritus, National Institutes of Health, Bethesda, Maryland**,** U.S.A.
Dr. Elwyn Griffiths, International Alliance for Biological Standardization (IABS), United Kingdom
Dr. Ivana Knezevic, World Health Organization, Geneva, Switzerland
Dr. Edward Wirth, Asterias Biotherapeutics, Fremont, California, U.S.A.
Prof. Clive Svendsen, Cedars-Sinai Medical Center, Los Angeles, California, U.S.A.
Dr. Thorsten Gorba, IQVIA, San Diego, California, U.S.A.
Dr. Kapil Bharti, National Institutes of Health (NIH) / NEI, Bethesda, Maryland, U.S.A.
Dr. Steven S. Oh, Center for Biologics Evaluation and Research, U.S. FDA, Silver Spring, Maryland
Professor Bao Zhu Yuan, National Institutes for Food and Drug Control, Beijing, China
Dr. Gerald Schumann, Paul-Ehrlich-Institut, Langen, Germany
Dr Francisca Agbanyo, Health Canada, Ottawa, Canada

Questions for each regulator:

- What guidances specific to pluripotent stem cells do you have available?
- What are the challenges in meeting the regulation for pluripotent stem cell based products?
- What need do you perceive for physical standards/reference materials in this area?

General questions:

- Ia there a need for new guidance and standards.
- Are there any special issues relating to off-trial treatments such as Hospital Exemptions/Specials arrangements?
- Any other challenges for the broader scope of cell-based medicines?

12:45 pm **Lunch**

Session II - Bioanalytics and comparability (non-clinical and quality control)

Chairs: **Dr. Kathleen Francissen,** Genentech**,** South San Francisco, U.S.A.
Dr. Steven S. Oh, Center for Biologics Evaluation and Research, U.S. FDA, Silver Spring, Maryland, U.S.A.

1:30 pm Introduction to Session 2 by the Chairs

1:35 pm Cellular product manufacturing and comparability considerations
Dr. Steven S. Oh, Center for Biologics Evaluation and Research, U.S. FDA, Silver Spring, Maryland, U.S.A.

1:55 pm Devising assays and standards for cell therapies
Dr. Orla O'Shea, National Institute for Biological Standards and Control-MHRA, Hertfordshire, United Kingdom

2:15 pm Characterization of CAR T cells- autologous vs allogeneic
Dr. Shirley Bartido, Cellectis, New York, U.S.A.

2:35 pm Is the product the process?
Dr. Stewart Abbot, Fate Therapeutics, La Jolla, California, U.S.A.

2:55 pm **Coffee break**

3:15 pm Developing predictive assays to assess function and purity of dopaminergic progenitors for treatment of Parkinson's Disease
Dr. Agnete Kirkeby, University of Copenhagen, Denmark; University of Lund, Sweden

3:35 pm **Panel discussion - Assay development focusing on characterisation, potency assays and comparability**
Dr. Kathleen Francissen, Genentech**,** South San Francisco, U.S.A.
Dr. Steven S. Oh, Center for Biologics Evaluation and Research, U.S. FDA, Silver Spring, Maryland
Dr. Orla O'Shea, National Institute for Biological Standards and Control-MHRA, Hertfordshire, U.K.
Dr. Shirley Bartido, Cellectis, New York, New York, U.S.A.
Dr. Stewart Abbot, Fate Therapeutics, La Jolla, California, U.S.A.
Dr. Agnete Kirkeby, University of Copenhagen, Denmark; University of Lund, Sweden
Dr. Karin Hoogendoorn, Leiden University Medical Center, The Netherlands

Topics for discussion:

- What approaches can be used to identify key quality attributes of cell therapy products that could be used to demonstrate comparability?
- Do we need to fundamentally re-think approaches to ensuring product quality consistency?
- In the absence of reference standards, how are system suitability standards for analytical tests generally handled?
- Do we have appropriate definitions for potency, purity and identity for cellular therapies and how should they be applied?
- What should a potency assay seek to demonstrate and do we have good examples?

4:20 pm **Presentation to Dr. John Petricciani,** International Alliance for Biological Standardization (IABS), U.S.A.
Dr. Ivana Knezevic, World Health Organization (WHO), Geneva, Switzerland
Dr. Anthony Lubiniecki, International Alliance for Biological Standardization (IABS), U.S.A.
Professor Glyn Stacey, Chair, Scientific Committee; International Stem Cell Banking Initiative, United Kingdom

4:35 pm **End of Day 1**

SPOTLIGHT ON

An Academic Perspective on Cell and Gene Therapy Development

Dr. David L. DiGiusto,
Executive Director, Stem Cells and Cellular Therapeutics Operations, Stanford Healthcare
Senior Research Scientist, Division of Pediatric Stem Cell Transplantation and Regenerative Medicine
Stanford University School of Medicine

Reception

5:00pm – 7:00pm

Hosted by IQVIA Stem Cell Center

Day 2 – Wednesday, June 6, 2018

Session III – Tumorigenicity Testing

***In vivo* and *in vitro* methods, including genetic changes: correlations, issues, the way forward**
Chairs: **Mercedes Serabian**, U.S. Food & Drug Administration (FDA), Silver Spring, Maryland, U.S.A.
Dr. Yoji Sato, National Institute of Health Sciences, Tokyo, Japan

8:30 am Introduction to Session III by the Chairs

8:35 am Regulatory implications of in vivo tumorigenicity testing
Associate Prof. Björn Carlsson, Medical Products Agency, Uppsala, Sweden

8:55 am Tumorigenicity assessment of stem cell-based therapies: FDA/CBER considerations
Mercedes Serabian, U.S. Food & Drug Administration (FDA), Silver Spring, Maryland, U.S.A.

9:15 am Study design considerations for in vivo tumorigenicity assays
Dr. Shawna Jackman, Charles River Laboratories, Horsham, Pennsylvania; U.S.A.

9:35 am Imaging technology and biodistribution studies
Prof. Christopher Goldring, University of Liverpool, United Kingdom

9:55 am Genetic and epigenetic stability of human pluripotent stem cells
Prof. Martin Pera, International Stem Cell Initiative / The Jackson Laboratory, Bar Harbor, Maine, U.S.A.

10:15 am **Coffee break**

10:45 am Design and validation of ESC removal in the manufacturing process
Dr. Jane Lebkowski, Regenerative Patch Technologies, Menlo Park, California, U.S.A.

11:05 am Design of in vivo tumorigenicity assays for iPSC-derived cell product - Lesson from clinical studies in Kobe
Dr. Shin Kawamata, Foundation for Biomedical Research and Innovation (FBRI), Kobe, Japan

11:25 am HESI CT-TRACS: an international platform for discussions on tracking, circulation and safety of cell therapy products
Dr. Yoji Sato, National Institute of Health Sciences, Tokyo, Japan

11:45 am **Panel discussion – Strengths and weaknesses of current standards and discussion of several new methods**

Convener: Dr. Joy Cavagnaro, Access BIO, Boyce, Virginia
Mercedes Serabian, U.S. Food & Drug Administration (FDA), Silver Spring, Maryland, U.S.A.
Dr. Yoji Sato, National Institute of Health Sciences, Tokyo, Japan
Associate Prof. Björn Carlsson, Medical Products Agency, Uppsala, Sweden
Dr. Shawna Jackman, Charles River Laboratories, Horsham, Pennsylvania; U.S.A.
Prof. Christopher Goldring, University of Liverpool, United Kingdom
Prof. Martin Pera, International Stem Cell Initiative / Jackson Laboratories, Bar Harbor, Maine, U.S.A.
Dr. Jane Lebkowski, Regenerative Patch Technologies, Seattle, Washington
Dr. Shin Kawamata, Foundation for Biomedical Research and Innovation (FBRI), Kobe, Japan
Dr. Anthony Ratcliffe, LifeNet Health, Virginia Beach, Virginia

Topics for discussion:

- What are the key pros and cons of the current tumorigenicity assay methods and how relevant are they to development of human disease given the importance of cell microenvironment for tumor development?
- How do we establish and control base lines for genetic stability and tumorigenicity and how can these be related to meaningful assessment of patient safety?

- What impact might the specific cell type have on the development of tumorigenicity assay platforms and the controls used?
- What role will in vitro versus in vivo assays have in evaluating tumorigenicity?
- What should be tested, source cells, cell banks, post-manufacture intermediates production or product?
- How can we begin to utilize current knowledge and gain new information to create improved tumorigenicity evaluation assays?

12:40 pm Lunch

Session IV – Manufacture, Storage and Shipment

Chairs: **Karin Hoogendoorn**, Leiden University Medical Center, The Netherlands
Dr. Ivana Knezevic, World Health Organization (WHO), Geneva, Switzerland

1:30 pm Introduction to Session IV by the Chairs

1:35 pm Developing a global haplobank system for clinical-grade induced pluripotent stem cells
Dr. Stephen Sullivan, GAiT, United Kingdom

1:55 pm The Universal Cells approach to avoiding immune rejection
Dr. Hironobu Kimura, Healios K.K, Tokyo, Japan

2:15 pm Directed differentiation of cGMP compliant human induced pluripotent stem cells into clinically relevant specialized cells from three germ-layers
Dr. Behnam Ahmadian Baghbaderani, Lonza, Walkersville, Maryland, USA

2:35 pm Large scale GMP manufacturing of individualized autologous directly reprogrammed human neural precursor cells for clinical applications
Dr. Jan-Eric Ahlfors, Fortuna Fix, Laval, Canada

2:55 pm Practical considerations in the development of cell therapy manufacturing processes
Dr. Carl Burke, Janssen R&D, Spring House, Pennsylvania.

3:15 pm **Coffee break**

3:45 pm Preservation and cold chain strategies for cellular therapies
Dr. William Shingleton, GE Healthcare, Cambridge, United Kingdom

4:05 pm Enhancing economic reality for cell based medicine through manufacturing optimization
Dr. Benjamin Le Quéré, Saint Gobain, Paris, France

4:25 pm **Panel discussion – Manufacturing standards, preservation and shipment**
Karin Hoogendoorn, Leiden University Medical Center, The Netherlands
Dr. Ivana Knezevic, World Health Organization (WHO), Geneva, Switzerland
Dr. Stephen Sullivan, GAiT, United Kingdom
Dr. Behnam Ahmadian Baghbaderani, Lonza, Walkersville, MD, USA
Dr. Jan-Eric Ahlfors, Fortuna Fix, Laval, Canada
Dr. Carl Burke, Janssen R&D, Spring House, Pennsylvania; U.S.A.
Dr. William Shingleton, GE Healthcare, Cambridge, United Kingdom
Dr. Benjamin Le Quéré, Saint Gobain Performance Plastics, Paris, France.
Dr. Mark Sawicki, Cryoport, Irvine, California, U.S.A.
Dr. Tatsuo Heki, Fujifilm Co., Tokyo, Japan
Dr. Tadaaki Hanatani, CiRA, Kyoto, Japan
Dr. Gary Pigeau, Centre for Commercialization of Regenerative Medicine (CCRM), Ottawa, Canada
Dr. Andrew Gaffney, STEMCELL Technologies, Vancouver, Canada

Topics for discussion:

- What are the new challenges for development of automated cell culture systems?
- What are the optimal approaches to implementing automated processes?
- How can standards contribute to improved bioprocessing?
- What approach should be taken to setting expiration dates for cryopreserved products?
- What does the developer need to understand about the preservation process?

Session V – Conclusions

5:00 pm **Summary of key issues and conclusions**
Prof. Glyn Stacey, IABS, Chair, Scientific Committee
International Stem Cell Banking Initiative, United Kingdom

5:10 pm **End of meeting**