Association Bilateral Meeting – Cell Therapy Stakeholders Group - Meeting Minutes - 2018-04-24

Bilateral meeting between the Cell Therapy Stakeholders Group and BGTD-Health Canada

Tuesday, April 24, 2018
1:30 to 4:00pm
100 Eglantine Driveway, Ottawa, Ontario

Attendees

Cell Therapy Stakeholders Group participants
Sowmya Viswanathan (Co-Chair), Friederike Pfau, Sandra Donaldson, Duncan Stewart, Patrick Bedford, Michael Mendicino, David Courtman, Cate Murray, Karen Nichols, Cristina Nostro, Craig Hasilo, Martin Giroux, Erika Fleiderman, Marcelo Pasquini, Rob Burnham, David Hart, Arla Maier, Leigh Turner, Dominic Massimo

Health Canada participants
Catherine Parker (Co-Chair), Georgette Roy, Anthony Ridgway, Agnes Klein, Lindsay Elmgren, Liz Anne Gillham-Eisen, Kyle Norrie, Nadine Kolas, Marie-Noël Deschambeault, Michael Rosu-Myles, Francisca Agbanyo, Robert Pless, Maya Berci,
Joelle Pinsonnault Cooper, Deborah Ashby, Luisa Carter, Julie Chateauvert,
Kenneth Joly, Hocine Abid, Chris Simard, Kathees Anandavel, Jessie Lavoie, Kim Godard, Alicja Kasina, Caroline Gagnon

1. Welcome and Introductions

The meeting was called to order at 1:30.

2. Review of Agenda

The agenda was reviewed and accepted.

3. Terms of Reference

Issue	The Terms of Reference for the Cell Therapy Stakeholders Group is being revised
Respondent	Kenneth Joly, BGTD
Response	BGTD has made comments on the revisions to the CTSG Terms of Reference. The comments will be shared along with the meeting record.
Discussion points	N/A
Decisions/Action Items	BGTD comments on the revised Terms of Reference to be shared along with the meeting record.

4. Update on the NSNR Workshop on March 19, 2018 and next steps

Issue	A Workshop was held March 19 to discuss the *New Substances Notification Regulations (Organisms)*
Presenter	Sowmya Viswanathan, CellCan
Response	S. Viswanathan delivered a report on the NSNR Workshop. She presented that a number of "solutions" were discussed, that stakeholder having access to draft guidance was useful, and discussed next steps.
Discussion points	Health Canada clarified that the *Draft Guidance Document for the Notification and Testing of New Substances: Organisms Used in Gene Therapy and Immunotherapy* can be shared by CTSG to solicit their feedback; however they should not be posted on their websites.
Decisions/Action Items	BGTD to follow-up with BIOTECanada on the draft minutes from the workshop. CTSG to provide comments on the draft guidance document to Health Canada in 3 weeks (by end of May).

5. Proliferation of U.S. Clinics Marketing "Stem Cell Treatments" and the activities of ISCT's Presidential Task Force (PTF) on the Use of Unproven Cellular Therapies

Issue	The unproven cell therapy industry is estimated at up to $2.4 billion and involves 60,000 patients annually paying up to $40,000 per treatment. The proliferation of U.S. businesses advertising unproven cell-based interventions has resulted in FDA warning consumers, taking enforcement steps and the FDA Commissioner releasing a statement regarding the FDA's new policy and procedures to ensure proper oversight of stem cell therapies and regenerative medicine. The activities of ISCT's Presidential Task Force (PTF) on the Use of Unproven Cellular Therapies are closely aligned with the FDA's stance. Initiated in 2010 and formalized in 2013, the PTF has worked to inform the public about the issues surrounding unproven cellular therapies, the proper manufacturing of cellular therapy products and the regulatory frameworks associated with cellular and gene therapy around the world.
Presenter	Massimo Dominici, ISCT
Response	Health Canada is aware of the actions by the US FDA regarding unproven stem cell therapies and continues to communicate its position that all cell therapy products meet the definition of drug under the *Food and Drugs Act*. Furthermore, with limited exceptions the *Food and Drug Regulations* (FDR) authorization requirements apply to stem cell based therapies.
Discussion points	When the question of indication was raised, it was clarified that currently, most of the indications are related to sports medicine and anti-aging.
Decisions/Action Items	N/A

6. Canadian factors to be considered for same surgical procedures / hospital exemption

Issue	Regulatory authorities acknowledge that there is a distinction between

	healthcare products and healthcare procedures. In Canada, the former is regulated by the federal government, while the latter is regulated by provincial governments (and delegated to hospitals & professional colleges). The US FDA, EMA, and TGA have all taken steps to develop official regulatory policies to help people navigate the regulatory intersection of healthcare products and procedures for autologous regenerative medicines that can be prepared at the bedside
Presenter	Patrick Bedford, CCRM
Response	Health Canada continues to communicate its position that all cell therapy products meet the definition of drug under the *Food and Drugs Act* and that, with limited exceptions, the *Food and Drug Regulations* (FDR) authorization requirements apply to stem cell based therapies. A position paper that clarifies the regulation of autologous cell therapies has been developed and is being finalized for web publishing. Health Canada's regulatory framework for drug products does not make separate provisions for therapies prepared "at the bedside". Should a product be proven to be safe and efficacious through authorized clinical trials, Health Canada will take steps where needed to support access for patients in Canada should clear regulatory barriers be identified.
Discussion points	The current discussion is focussed on autologous minimally manipulated therapies, and we are still waiting for proven efficacy. The *Safety of Human Cells, Tissues and Organs for Transplantation Regulations* were just for allogeneic use (where efficacy and safety was shown). The main CTO driver was to minimize the risk of disease transmission (which is not an issue with autologous). There are still plans for Phase II of the CTO regulations. Could the Policy on Manufacturing and Compounding Drug Products in Canada (POL-0051) apply to these products? Health Canada response: There are clear criteria for compounding but the product should be produced from an authorized drug, this is not an exemption from regulation. Health Canada was asked about enforcement of the current cell therapies being done in Canada, and how will they be ended/dealt with? RORB responded that they are aware of and they have some open cases while they gather information and plan their communication strategy. All CTAs need to be approved by Health Canada and interested sponsors should contact the Office of Regulatory Affairs for assistance with filing.
Decisions/Action Items	N/A

7. Safety and quality testing and comparability for ESC to iPSC and between iPSC lines (at the MCB stage)

Issue	Are the standard set of GLP safety tests traditionally applied to hESC-based cell therapies considered adequate for iPSC-based therapies? (tumorigenicity, distribution, basic safety). Once a base iPSC line has satisfied the above GLP safety testing, and if controlled (and in vitro-verified) gene edits have been performed, is in vitro verification adequate to move the edited line into the clinic? What types of comparability studies would Health Canada require for using cell banks such as MSCs or iPSCs for multiple indications?
Presenter	Christina Nostro, RMAC
Response	There is no pre-defined time when a pre-CTA meeting should occur. It is dependent on the question and needs of the sponsor. Some questions are best handled in a face to face meeting; while others can be done as a teleconference. The decision as to which studies require GLP is based on the phase and purpose of the study. As there is a great deal of intra-study variation on the reason, timing and type of the studies, it is not possible to state what are the common information gaps seen in submissions. What needs to be done and when varies based on the type of study being done. At present, there is no consensus among regulators and industry on what the most relevant animal model or if an animal model is deemed to be required. This is decided on a case by case.
Discussion points	N/A
Decisions/Action Items	BGTD will discuss the questions and provide responses when the sponsor comes in for a consultation meeting. *BGTD sent information on June 8.

8. Update on CBMTG's Registry data capture efforts and how it could enable data capture for cell and gene therapies

Issue	An update on the CBMTG's Registry data capture efforts and how it could enable data capture for cell and gene therapies was provided.
Presenter	Marcelo Pasquini, CIBMTR
Response	Canada is looking but not ready. The overall approach is that the data has to be analyzable. Health Canada would be interesting in knowing what kind of data can be gathered from the registry.
Discussion points	A question was asked about funding: funding is provided mainly by the NIH, FCTOD, and the Office of Naval Research. A question was asked about whether Canadian centres use and submit their

	own data, the answer was yes. The consent rate for US sites is >90%
Decisions/Action Items	N/A

9. Roundtable

The meeting adjourned at 4:00 pm.