Drugs and Health Products

Meeting Record

Cell Therapy Stakeholders Group (CTSG) and the Biologics and Genetic Therapies Directorate (BGTD)

February 23, 2016
1:00 pm to 4:00 pm
Tunney's Pasture, Ottawa, ON

Attendance:

Health Canada Participants

Catherine Parker, DGO
Liz Anne Gillham-Eisen, OPIC
Georgette Roy, ORA
Agnes Klein, CERB
Lindsay Elmgren, CBE
Anthony Ridgway, CERB
Francisca Agbanyo, CBE
Patrick Bedford, OPIC
Andrea Bedard, OPIC
Kyle Norrie, OPIC
Jessie Lavoie, CBE
Ariel Arias, CBE
Gina Coleman, CBE
Colin Foster, MDB
Michael Rosu-Myles, CBE
Julie Wallace, ORA
Paul Gustafson (by phone), HPFB-Inspectorate
Kenneth Joly, OPIC

CTSG Participants

Sowmya Viswanathan, CellCAN-Univerty Health Network, ISCT NA LRA
David Courtman, CellCAN- Ottawa Hospital Research Institute
Martin Giroux, CellCAN-Centre d'Excellence en Thérapie Cellulaire-Hôpital Maisonneuve Rosemont
Friederike Pfau (by phone), CellCAN-Laval University/LOEX
Gayle Piat, CellCAN-University of Alberta
Anne-Marie Alarco, CellCAN
Olive Sturtevant , ISCT NA LRA
Deborah Griffin (by phone), ISCT NA LRA
Karen Nichols (by phone), ISCT NA LRA
Michael Mendicino (by phone), ISCT NA LRA
Crystal Ruff (by phone), ISCT NA LRA

Jaysoon Eicholtz (by phone), Nationwide Children's Hospital, Columbus, OH
Tania Bebula, University of Alberta/CellCAN
Erica Cliderman

1.0 Welcome and Introductions

The meeting was co-chaired between BGTD and the CTSG. Liz Anne Gillham-Eisen co-chaired on behalf of BGTD and Sowmya Viswanathan and Olive Sturtevant co-chaired on behalf of CTSG.

C. Parker provided introductory remarks on behalf of BGTD, and identified cell therapies as a Branch priority that has seen significant policy developments since our last meeting.

The agenda was accepted as presented.

2.0 Position Papers to support (1) Autologous Cell Therapies and (2) Banked Material for Future Use

P. Bedford shared two draft position papers that have been developed by BGTD. Health Canada regularly responds to inquiries about the regulatory status of autologous cell therapies and banked human material on a case-by-case basis. An effort has been made to draft clear and concise policy position statements that aim to increase predictability, transparency and consistency in decision making. Two short documents have been provided for early input from the Cell Therapy Stakeholders Group. Initial feedback was requested, and written feedback (detailed comments) in the weeks following the meeting would be appreciated.

S. Viswanathan stated that the cell therapy community will likely find these papers helpful, and then asked whether Health Canada considered the option of expanding the scope of the Safety of Human Cells, Tissues and Organs for Transplantation Regulations to include autologous cell therapies (that are minimally manipulated for homologous use). .

P. Bedford replied that Health Canada has done significant policy work to consider this option, and that it remains a possibility in the longer-term future; however, any potential regulatory amendments must be considered in the context of competing regulatory priorities. The two draft position papers are intended to be a policy solution that interprets existing regulations in the short and medium term. .

D. Griffin asked whether Health Canada has considered accrediting/licensing banks that process and store cells & tissue for use as a starting material or using a third party to do so.

P. Bedford acknowledged this comment, and noted that there may be an opportunity for the Biologics and Genetic Therapies Directorate to work with Health Canada's Inspectorate and Provincial governments to consider a comprehensive list of options for doing this. .

P. Bedford encouraged members to provide any comments they might have on the two position papers. All comments can be sent through Kenneth Joly, BGTD. Comments will be reviewed and then a broader external consultation will be completed.

3.0 Biologic-Device Combination Products

O. Sturtevant presented on the possible need for a review and clarification of regulatory requirements for biologic-device cell-based regenerative medicine combination products and proposals/plans for pathways in the future.

P. Bedford acknowledged that cell therapy researchers face challenges related to (a) determining which set of regulations apply to combination products (i.e. product classification), and (b) determining manufacturing standards (i.e. GMP vs QS). He then described the product classification procedure at HPFB.

Health Canada does not currently have a policy that specifically addresses cell therapy/device combination products; therefore, Health Canada makes case-by-case decisions based on existing terminology in the *Food and Drugs Act* and policies (including the Drug/Device combination policy). The existing regulation and policies allow Health Canada to remain consistent with other national regulatory authorities, and Health Canada has committed to considering US FDA classification decisions in making its own decisions.

Moving forward, BGTD plans to work with MDB to identify and communicate criteria that will help to identify whether devices used to process cell therapies will be considered medical devices (and be regulated under Medical Device Regulations by colleagues in MDB) or whether they can be considered cell therapy manufacturing equipment (see Statement 4 in the *BGTD Position Paper on Autologous Cell Therapy Products*, which was provided to support Agenda Item 2).

In response to a question about whether Health Canada may choose to re-classify a product after it has been regulated as a drug or device (e.g. if it undergoes changes in development), P. Bedford replied that all classification decisions are made based on the best available information at the time. So it remains possible that classification decisions may change if the product changes, or if the understanding of the product changes. For this reason it is in the sponsors best interest to provide the most accurate information about the product, and not (for example) information to obtain the desired classification decision. This will help to avoid the negative impacts of re-classification.

4.0 New Substances Notification Regulations for the Import and Manufacture of Viral Vectors for use in Clinical Trials in Canada

T. Bubela discussed the potential regulatory administrative burden caused by viral vectors for use in human gene therapy, including those that are incapable of replication, and viruses for use as therapeutic agents to treat cancer (oncolytic viruses).

A. Ridgway explained the purposes of the current regulatory requirements and stressed that while the timing of the FDA requirements may be more convenient they are essentially the same as what is required by Canadian regulators. Nevertheless, Health Canada can plan to do more to prepare gene therapy researchers by informing them of these New Substance Notification Regulations and providing appropriate contact information when they come in for pre-submission meetings.

T. Bubela and S. Viswanathan questioned the relevancy of some of the information required in Schedule 1 of the application.

It was suggested that there be communication with the Health Environments and Consumer Safety Branch, who administers the application. BGTD will reach out to federal government colleagues in HECS to determine what may be done to streamline regulatory requirements for gene therapy researchers.

5.0 GMP Facility Requirements for Early Phase Clinical Trials

M. Giroux presented on the potential need for clarification/direction on the licensing needed for an institution submitting a clinical trial. He stated that is room for interpretation in the GMP guidelines and regulations. He also asked: What level of GMP would be advisable for early phase trials?

P. Gustafson discussed the GMP requirements for clinical trials.

6.0 Analytical Assay Requirements and Validation Requirements for Rapid Microbiological Methods

G. Piat and S. Viswanathan presented on the Analytical Assay Requirements and Validation Requirements for Rapid Microbiological Methods. Section 4.2.1 of GUI-001 states that analytical methods must be validated. Section 10 of GUI-0036 refers to the validation status of methods. It is understood why it is important that validated methods are used to release products since as mentioned in GUI-0036, processes may not be standardised or fully validated during a clinical trial and therefore testing takes on more importance in ensuring that each batch meets its specification. What isn't completely clear is whether this testing can be performed by a non-GMP laboratory (e.g. sterility testing conducted by a hospital microbiology laboratory). What kind of qualification or validation is acceptable by Health Canada for early phase clinical trials? For specialized testing requirements (e.g. flow cytometry), is it acceptable to conduct product analysis in an academic laboratory or core facility and if so, what type of documentation and procedures would be necessary to fulfill Health Canada's expectations.

Rapid Microbiological Methods (RMM) for analyzing sterility, endotoxin and mycoplasma are becoming more common place, and accepted by multiple jurisdictions. This is particularly relevant for product release of fresh cells with limited life-span. What

kind of qualification/validation does Health Canada expect for a commercially available, validated kit to support use in early phase trials?

F. Agbanyo responded that Health Canada supports RMM. However, the results must be reliable. There was an FDA guidance in 2008 that has since been withdrawn. Health Canada handles the subject on a case-by-case basis.

7.0 Roundtable

There were no roundtable items.

Meeting Adjourned 4:00 PM.