Regulatory Update for Cell and Gene Therapies - Health Canada

Dr. Christopher Storbeck
CASSS Cell and Gene Therapy Products 2018
Outline

- Submissions update
- Health Canada Expectations
Submissions Update

- Currently one CAR T-cell product New Drug Submission (NDS) under review
- Expecting a second CAR T-cell NDS soon
Recent Approved Submissions to Health Canada - CTAs

GT CTAs Approved

- Crispr Gene Editing
- Oncolytic Virus
- Autologous Cell GT
- GT (direct) eg. Ad, AAV, plasmid DNA

GT (direct)

- Ad5
- plasmid DNA
- AAV

Gene Modified Autologous Cell Products

- other
- TCR
- CAR
HC Expectations: Cell and Gene Therapy Product

- CAR T-cell therapy products
- AAV Gene therapy products
- Control strategy
- Potency assays
- eCTD format
- General considerations
CAR T-cell therapy products (autologous)

• Chain of custody
• Chain of identity
• Qualification of apheresis sites
• Manufacturing strategy
  – QTPP
  – CQA/CPP determination
• Lot release
  – Submit multiple lots on a single Fax-back form
  – Include CoA for HSA if used as excipient and not sourced from Canada
CAR T-cell therapy products (autologous) – cont’d

- Strategies for minimizing risk of cross contamination
- A demonstration of understanding of the variability inherent in the process
- Some New Drug Submissions (NDS) are priority review (accelerated time frame) – On site evaluation planning requires manufacturing schedules early in the review period
- Clear explanations of any reprocessing procedures
CAR T-cell therapy products (autologous) – cont’d

• Reference Standard
  – Assay-dependent standards
  – Provide clear rationale for choice of standard
  – Batches from healthy donors

• Failed lots for approved products
  – May proceed depending on risk
  – Separate trial to capture important data
  – Clear communication vital
AAV mediated Gene Therapy Products

- Release specification for empty capsids
- Potency assays
  - Infectivity
  - Presence of transgene
  - Activity of transgene
  - Effect of transgene on biological system
Control Strategy

- Risk based determination of CQAs and CPPs
- Well defined control strategy with adequate in-process monitoring
Potency Assays

• Centred on main mechanism of action
• Develop as product understanding increases
• Matrix approach encouraged
  – Two or more assays addressing complex MOAs giving more complete understanding of released product
Submission format

• Autologous cell therapy products
  – Vector information can be considered as a Drug Substance section
General Considerations

• Clear knowledge of product and process
  – Well characterized
  – QbD approaches
• Provide risk based approach to identification of CQAs and CPPs
• Provide clear justifications for specifications
• Set acceptance criteria for release and stability specifications as early as possible
• Raw materials
  – Provide CoAs for critical raw materials
  – Ensure consistency and supply
Harmonization

• Health Canada embraces harmonization of regulatory approaches with respect to Cell and Gene Therapeutic Products
  – IPRP
    • GTWG
    • CTWG
  – ATMP Cluster
• Contributor to international harmonization efforts through ICH
• Welcome discussion if our position differs significantly from other regulatory authorities
We welcome your questions

- We welcome regulatory questions via pre-CTA meetings or pre-NDS meetings in-person or via teleconference
- Contact Office of Regulatory Affairs

Office of Regulatory Affairs
Biologics and Genetic Therapies Directorate
Health Products and Food Branch
Health Canada
100 Eglantine Driveway, Tunney’s Pasture
Address Locator: 0601C
Tunney’s Pasture,
Ottawa, Ontario, Canada
K1A 0K9
Fax: 613-946-9520, Tel: 613-957-1722

General Enquiries:
Email: BGTD_ORA@hc-sc.gc.ca
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