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Regulatory Update for Cell and Gene Therapies - Health Canada

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CASSS Cell and Gene Therapy Products 2018

YOUR HEALTH AND SAFETY... OUR PRIORITY.

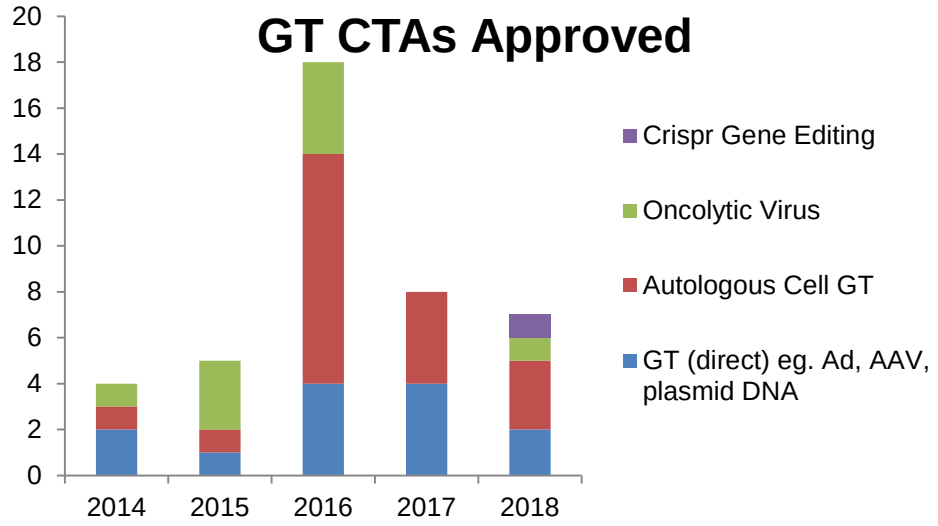
Outline

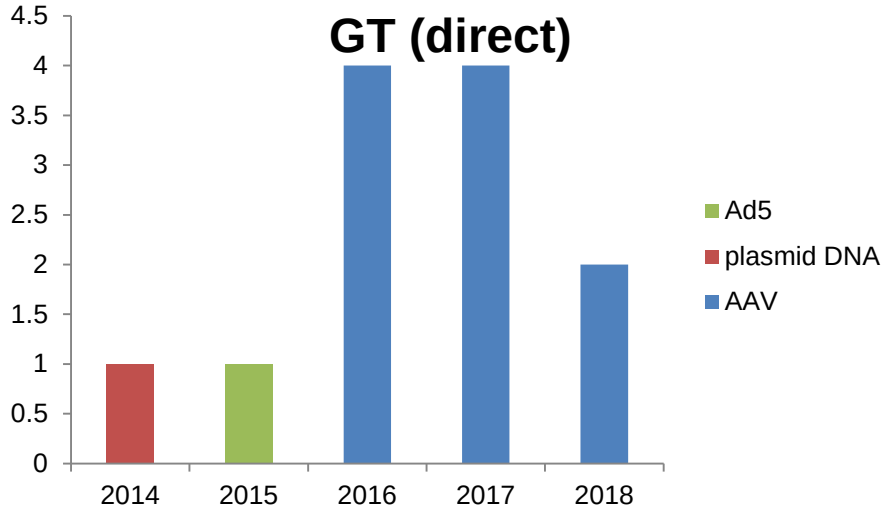
- Submissions update
- Health Canada Expectations

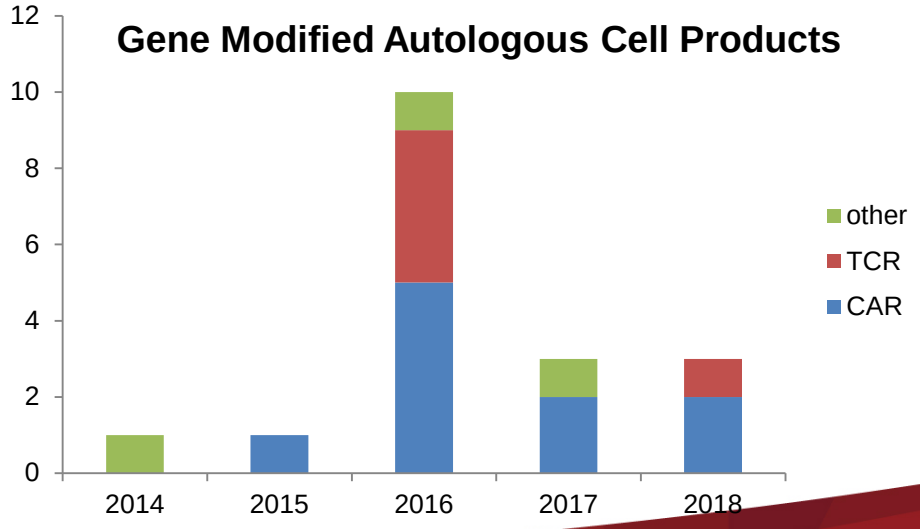
Submissions Update

- 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







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

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Acknowledgements

- Dr. Anthony Ridgway
- Christopher Antonio
- Dr. Dino Petrin
- Dr. Deqi Huang
- Dr. Martin Nemec

THANK YOU!