Health Canada Santé Canada

Canada

Regulatory Experiences with Precision Health

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Disclaimer

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Overview

- Precision Medicine
- Regulatory Perspectives
- Review Considerations
- Summary

- **Pharmacogenomics (PGx)**
  - Defined as the study of variations of DNA and RNA characteristics as related to drug response
- **Pharmacogenomic Test**
  - Intended to identify inter-individual variations in whole-genomes or candidate genes, single-nucleotide polymorphisms, haplotype markers, or alterations in gene expression that may be correlated with pharmacological function and therapeutic response
- **Pharmacogenetics (PGt)**
  - A subset of PGx defined as the study of variations in DNA sequence as related to drug response
- **Genomic Biomarker**
  - A measurable DNA and/or RNA characteristic that is an indicator of normal biologic processes, pathogenic processes, and/or response to therapeutic or other interventions

Precision Medicine

- The Genomic Era – Identification of target patient populations
  - Altered efficacy or safety (↑or ↓)
- Benefit/Risk Assessment
  - A better way to develop effective and safe drugs
- BUT need to have validated tests and an established link to clinical outcomes
- Other utilities
  - Surveillance or monitoring of disease-based expression to determine disease stage and whether therapeutic intervention has an effect on disease progression
  - Investigation of genetic basis of adverse drug reactions

Canada’s Legislative Framework

- Canada Health Act
- Food and Drugs Act
  - Drug Regulations
  - Medical Device Regulations
  - Clinical Trial Regulations
- Patent Act
  - Patented Medicines (NOC) Regulations
  - Data protection (Food and Drug Regulations)
- Financial Administration Act
  - Cost-Recovery Fee Regulations
- Controlled Drugs and Substances Act

Personalized Medicine in the Canadian Regulatory Context

- Scope of Food and Drugs Act and Regulations
- Laboratory-developed tests (LDTs)
  - Test not manufactured for sale
  - Genetic tests developed in-house are not regulated by Health Canada
  - Clinical Laboratories are under provincial jurisdiction (varies from province to province
- Labelling implications
- Companion Diagnostic
  - In vitro diagnostic device (IVDD) is Class III
- Medical Device Active Licence Listing (MDALL)
  - www.mdall.ca

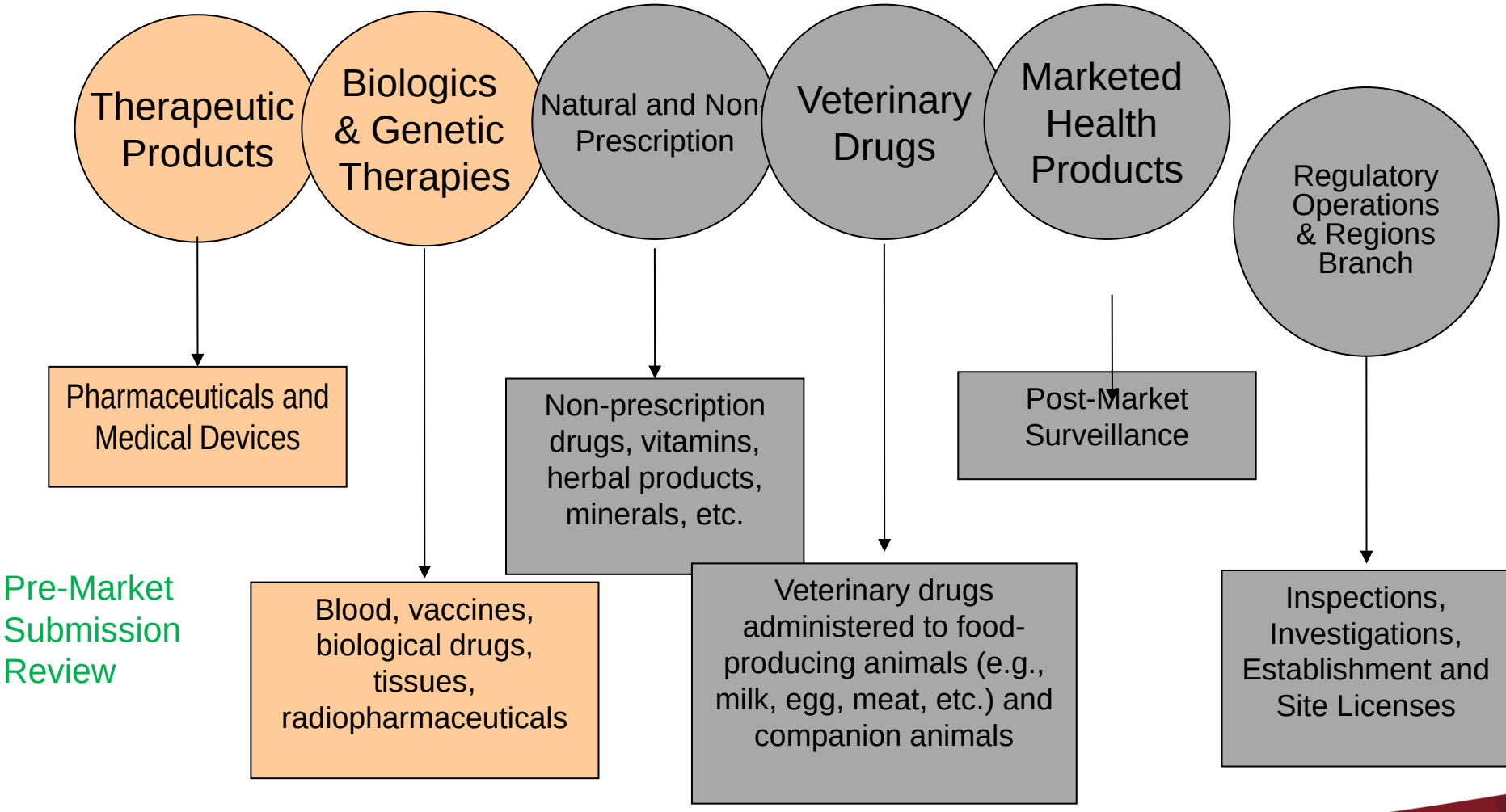
Personalized Medicine in the Canadian Regulatory Context

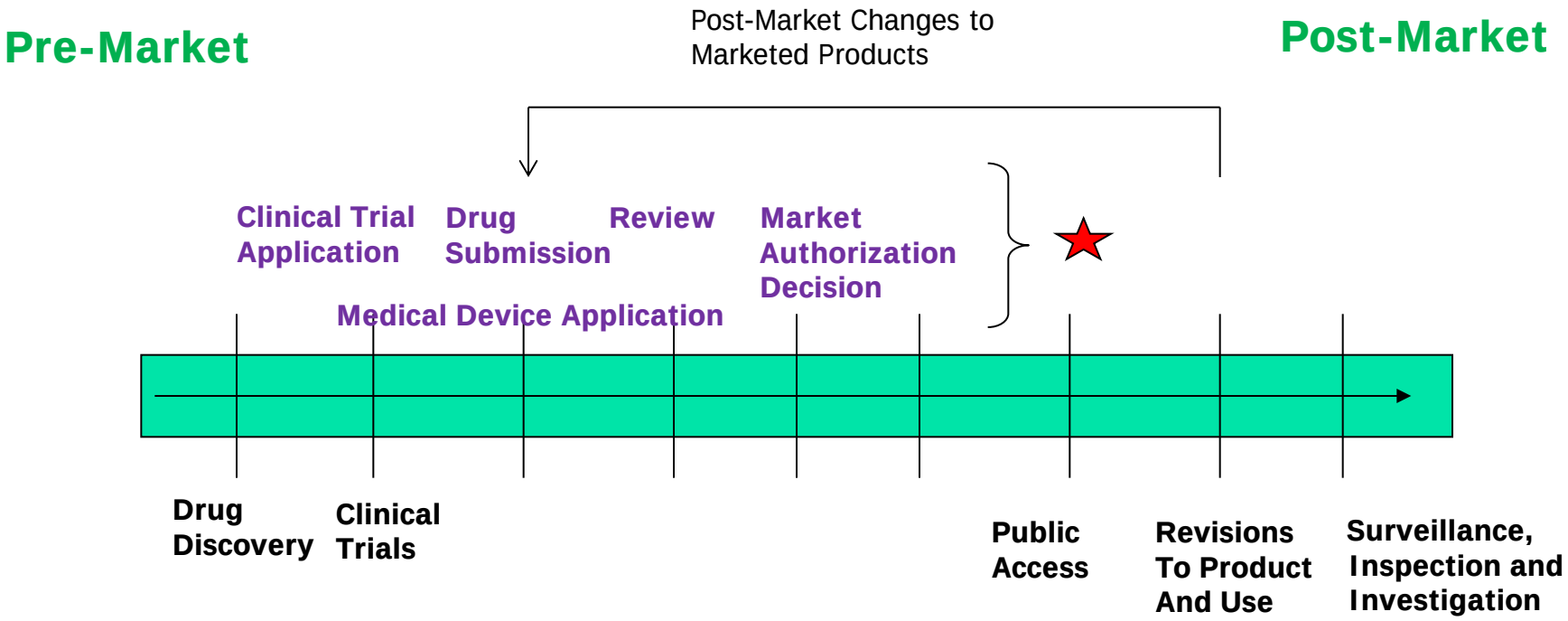
- Biomarkers not defined in the Food and Drugs Act and Regulations but they allow for flexibility in approval
  - Safety, Efficacy, and Quality

- Can rely on guidance within current framework

- Clinical Trial Application, Medical Device Licence, Investigational Testing Application, Special Access Program Request, in a Drug Submission

Health Products and Food Branch





The *Food and Drugs Act* and *Regulations* authorize the Therapeutic Products Directorate to regulate the safety, efficacy and quality of therapeutic products.

Notice of Compliance NOC

- New Drug Submission (NDS) - new therapeutic product
  - New Active Substance (300 calendar days)
  - Priority Review (180 calendar days)
  - NOCc (200 calendar days)

- Supplemental New Drug Submission (SNDS) – new indication
  - Traditional review (300 calendar days)
  - Priority Review (180 calendar days)
  - NOCc (200 calendar days)

- Abbreviated New Drug Submission (ANDS) - generics
  - (180 days calendar review)

Companion Diagnostics - Class III Medical Devices

- All devices intended to be used for pharmacogenomic testing are classified as Class III medical devices
- Pre-market scientific assessment of safety and effectiveness by Medical Devices Bureau
- Requirements
  - Preparation of a Premarket Review Document for Class III and Class IV Device Licence Applications
  - Medical Devices Regulations Section 32
- No “Joint Application” process
  - Medical Device Licence Application
  - New Drug Submission
  - Simultaneous submission; separate review process

NDS, SNDS, or ANDS involving Companion Diagnostic

- Diagnostic test will be used to support a therapeutic decision
  - Patient selection
  - Dosing of the drug
- If a licensed test is not already available for use in Canada
  - Apply for a Medical Device License or, if applicable, for an Investigational Testing Application, as sponsor progresses through their drug development program
- If a licensed test is available, indicate in their submission
  - Name, description, license number of the IVDD that was used

Regulatory Perspectives

- Pharmacogenomics guidance document
  - Provides guidance on how and when to submit pharmacogenomic information to Health Canada
  - http://hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/brgtherap/pharmaco_guid_ld-eng.pdf
  - Consult with Medical Devices Bureau
- ICH E-15 and 16 – adopted guidelines and training staff
- Review time frames allow review of diagnostics in parallel with a drug/biologics submission
- Ongoing policy examination of short and long-term implications of biomarkers and personalized medicines

Regulatory Perspective

- Participation in international collaborations and scientific approaches to analysis and evaluation of regulatory submissions.

- Health Canada does not maintain a list of acceptable biomarkers but has authorized more than 40 active ingredients where a biomarker plays a role in the use of the product.

Review Considerations

- Labelling companion diagnostics
  - Canadian approach to the indication section of the Product Monograph
  - "…A validated test is required to identify XX mutation status. XX mutations were identified in the Phase III and Phase II studies by the Health Canada approved YYY mutation test…"

Review Considerations

- Questions that arise:
  - How valid is validated?
  - Is the test or is a kit readily available in Canada?
  - Should patient access to the medicine be restricted?
  - Where does the information go in the Product Monograph?

Review Considerations – other information

- Consider labelling of additional PGx information when:
  - Subgroups of patients experience higher or lower clinical efficacy
  - Subgroups of patients at higher risk for ADRs
  - Subgroups who require special dosing considerations
  - Testing is recommended to optimize the use of the drug

Review Considerations

- The science is evolving
- Many different players
  - academia; industry; government, HTA, payers, patients
- Regulatory opportunities
  - Internal co-ordination for review of drugs and devices
- Drug submission with validated biomarker data tied to clinical benefit
- Sponsors are encouraged to discuss with Health Canada (MDB/TPD/BGTD)

Summary

- There is value in a Personalized Medicine approach
- Flexibility in approval within existing framework
  - Science is evolving
- Companion diagnostics are regulated by Health Canada
  - LDTs and DTC genetic testing outside the Food and Drugs Act and Regulations (provincial oversight)
- Simultaneous submission not joint review
  - Validated with an established link to clinical outcomes

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- E15: Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories [2008-07-29]
- E16: Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions [2016-01-08]
- Management of Drug Submissions [2013-12-20]
- Guidance Document Product Monograph [2016-12-09]