Overview of the Machine Learning-enabled Medical Devices (MLMD) Guidance

Marc Lamoureux / Ian Glasgow / Dr. Deepak Sharma
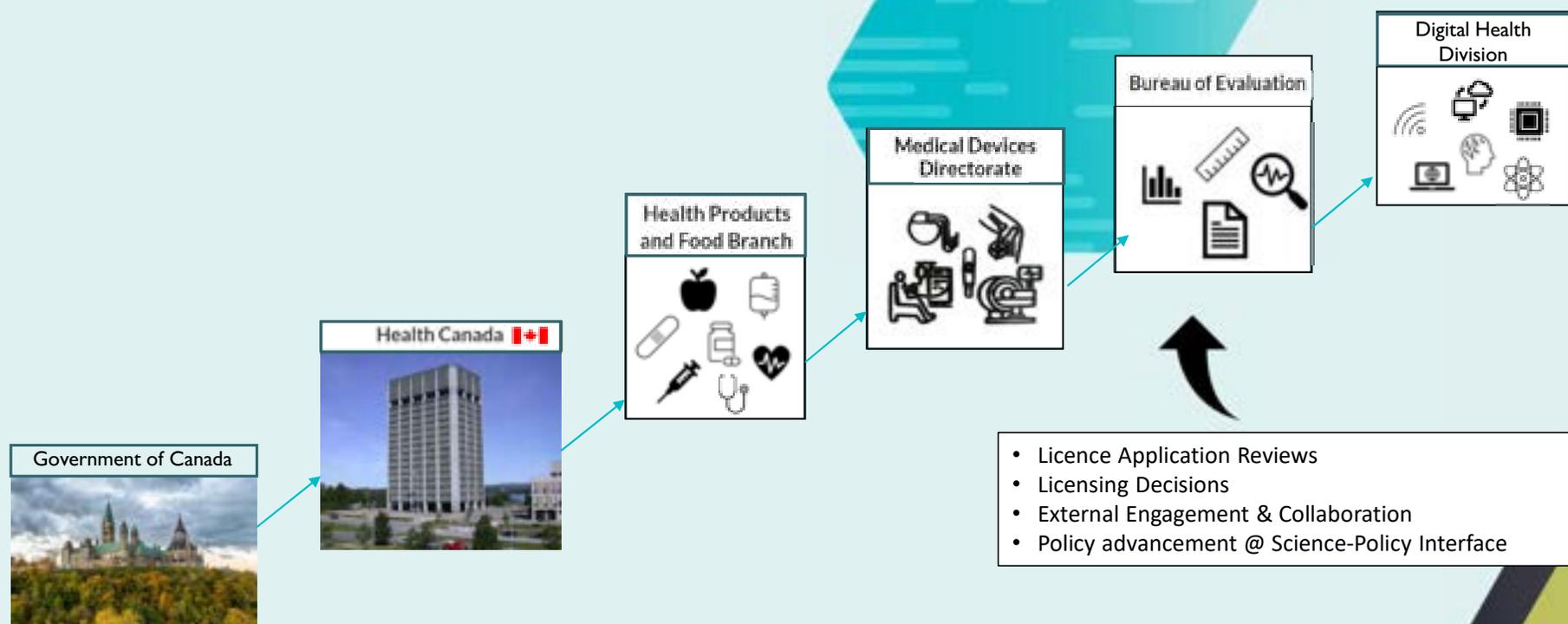
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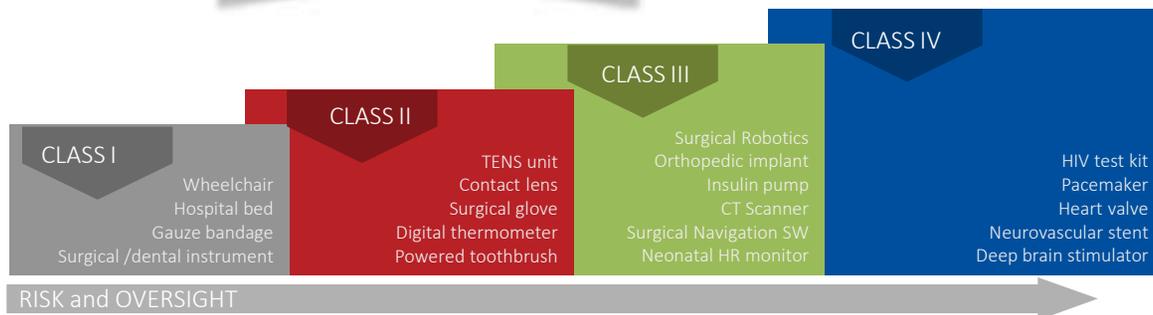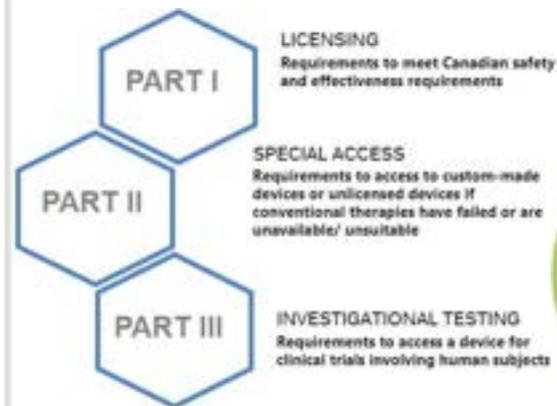
Health Products and Food Branch

Health Canada

Health Canada / Santé Canada

Canada

Who We Are: The Federal Regulator of Medical Devices

Digital Health Division

Bureau of Evaluation

Medical Devices Directorate

Health Products and Food Branch

Health Canada

Government of Canada

- Licence Application Reviews
- Licensing Decisions
- External Engagement & Collaboration
- Policy advancement @ Science-Policy Interface
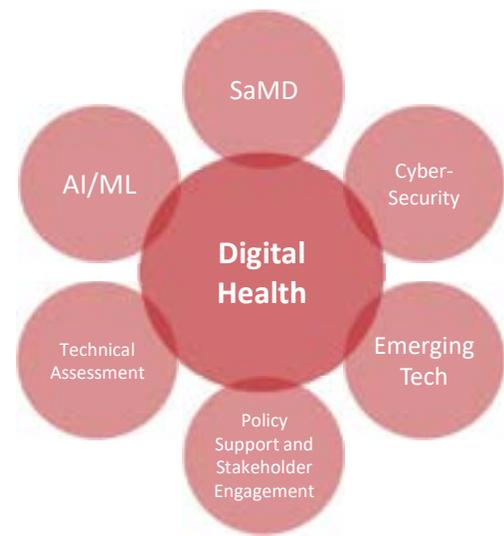
Health Canada   Santé Canada

Canada

Regulation of Medical Devices in Canada

Medical Device: a [THING] that is manufactured, sold or represented for use in diagnosing, treating, mitigating or preventing a disease, disorder or abnormal physical state, or any of their symptoms, in human beings […]

Medical Devices Regulations / Règlement sur les instruments médicaux

PART I — LICENSING
Requirements to meet Canadian safety and effectiveness requirements

PART II — SPECIAL ACCESS
Requirements to access to custom-made devices or unlicensed devices if conventional therapies have failed or are unavailable/ unsuitable

PART III — INVESTIGATIONAL TESTING
Requirements to access a device for clinical trials involving human subjects

Pre-market Authorization

Post-Market Risk Detection and Management

Executive, Policy, Operations, etc.

Compliance and Enforcement

CLASS I	CLASS II	CLASS III	CLASS IV
Wheelchair	TENS unit	Surgical Robotics	HIV test kit
Hospital bed	Contact lens	Orthopedic implant	Pacemaker
Gauze bandage	Surgical glove	Insulin pump	Heart valve
Surgical /dental instrument	Digital thermometer	CT Scanner	Neurovascular stent
	Powered toothbrush	Surgical Navigation SW	Deep brain stimulator
		Neonatal HR monitor	

RISK and OVERSIGHT →

What is Digital Health for Medical Devices @ Health Canada?

...To advance and adapt regulatory approaches to respond to emerging technologies, facilitating their market entrance while maintaining safe, effective, high quality medical devices in Canada...
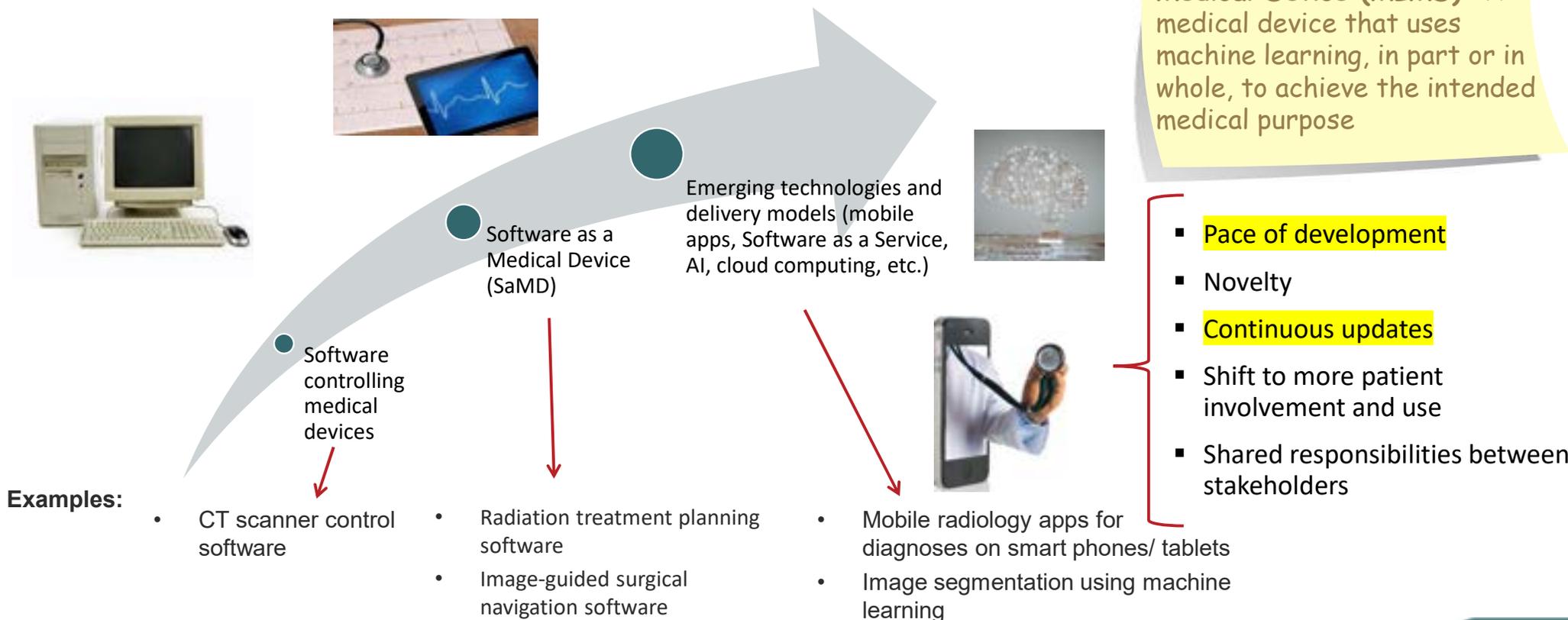

Make health products more accessible

Improve and facilitate more timely diagnoses

Increased access to devices for patients at home, at other health care facilities, and in rural and remote communities

Digital Health

SaMD

Cyber-Security

Emerging Tech

Policy Support and Stakeholder Engagement

Technical Assessment

AI/ML

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Ongoing work in Digital Health Division @ Health Canada

- Medical device safety reviews of Digital Health & Radiation Emitting Technologies

- Policy Advancement at the Science-Policy Interface

- Scientific Advisory Committee on Digital Health Technologies

- External work and collaborations:

Medical Device Software's Evolving Regulatory Landscape

Software controlling medical devices

Software as a Medical Device (SaMD)

Emerging technologies and delivery models (mobile apps, Software as a Service, AI, cloud computing, etc.)

Machine Learning-enabled Medical Device (MLMD): *A medical device that uses machine learning, in part or in whole, to achieve the intended medical purpose*

- Pace of development
- Novelty
- Continuous updates
- Shift to more patient involvement and use
- Shared responsibilities between stakeholders

Examples:

- CT scanner control software

- Radiation treatment planning software
- Image-guided surgical navigation software

- Mobile radiology apps for diagnoses on smart phones/ tablets
- Image segmentation using machine learning

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SaMD Guidance and Examples

- Health Canada's 2019 Guidance, *Software as a Medical Device (SaMD): Definition and Classification* is intended to:

  1. Clarify what software products **are and are not** considered medical devices

  2. If the software is a medical device, provides information to **determine the risk class**

  3. Provide **examples**:

Software Product Example	Determination
A risk calculator based on well-established, publicly available models to generate a score for obese individuals at risk of developing heart disease	Not a medical device
Picture Archiving and Communication System (PACS)	Not a medical device
Software that classifies screening mammography images into BI-RADS density categories to aid in the evaluation of individual breast cancer risk and decisions about any additional screening	Class 2 medical device
Software that performs image analysis for the detection of intracranial hemorrhage	Class 3 medical device

Types of ML-enabled Medical Devices Authorized
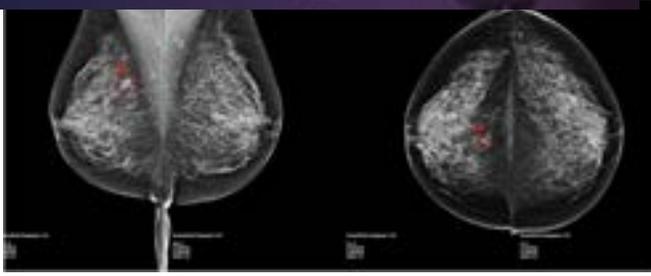
Pre-market guidance for machine learning-enabled medical devices

Provides information for consideration in supporting the safety & effectiveness of an MLMD
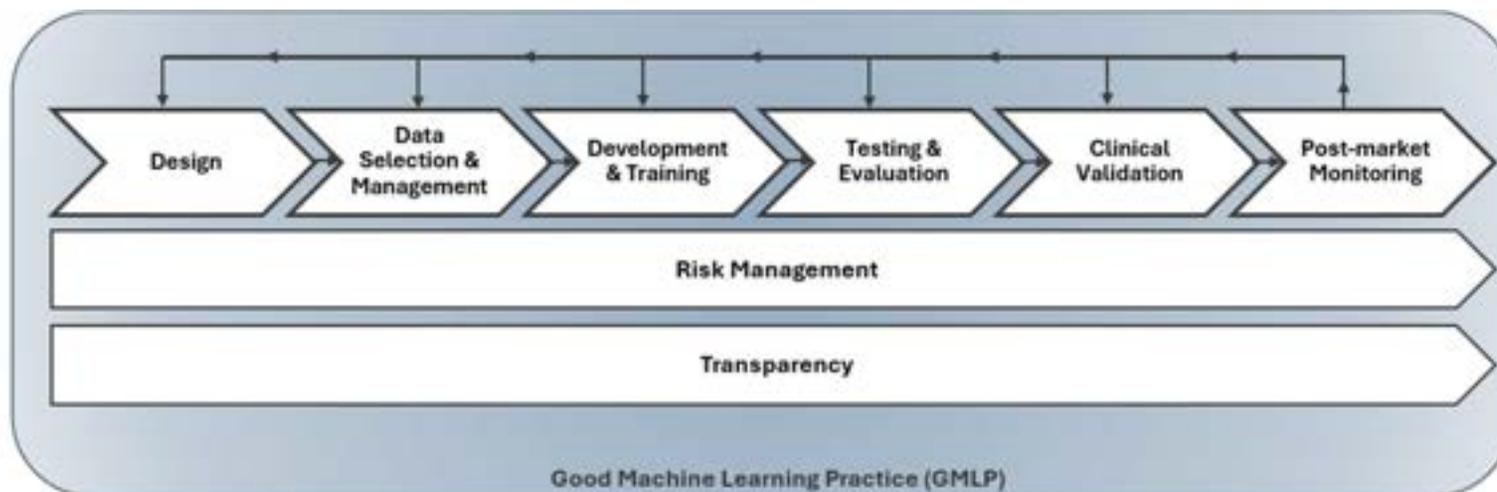
Highlights the potential for licence **terms and conditions (T&Cs)** to ensure ongoing safety and effectiveness.

Structured according to the iterative, non-mutually exclusive components of the MLMD lifecycle (below)

Introduces the concept of a **pre-determined change control plan (PCCP)** in the design of the MLMD

Design → Data Selection & Management → Development & Training → Testing & Evaluation → Clinical Validation → Post-market Monitoring

Risk Management

Transparency

Good Machine Learning Practice (GMLP)

Pre-market guidance for machine learning-enabled medical devices (2025)

- Provides industry with guidance on what should be considered when submitting a medical device licence application to Health Canada for a machine learning-enabled medical device

- Structured according to the iterative, non-mutually exclusive components of the MLMD lifecycle (below)

Lifecycle Component	Expected Considerations related to Machine Learning
Design	Intended use, ML methods, input parameters, output, compatible devices, etc.
Risk Analysis and Management	**Bias**, impact of false negatives/positives, overfitting, under fitting, **model drift**, automation bias, etc.
Data Management and Selection	Descriptions of **training, tuning and test sets**, data augmentation, data exclusion, annotation, etc.
Development and Training	Input parameters, reference standard, etc.
Testing and Evaluation	Performance metrics, ROC operating points, **subgroup analysis**, robustness testing, etc.
Clinical Validation	Representativeness of the intended population, **independence of training data**, etc.
Transparency	Inputs, compatibility, **description of training and test sets, performance metrics, model limitations,** etc.
Post-market Performance Monitoring	Processes and risk mitigations in place to ensure **ongoing performance** and inter-compatibility, etc.

Good machine learning practice (GMLP)

- GMLP Guiding Principles were co-published in 2021 by the UK MHRA, US FDA and Health Canada.
- These principles apply to designing, developing, evaluating, deploying, and maintaining an MLMD

Good Machine Learning Practice for Medical Device Development: Guiding Principles

Multi-Disciplinary Expertise Is Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices Are Implemented
Clinical Study Participants and Data Sets Are Representative of the Intended Patient Population	Training Data Sets Are Independent of Test Sets
Selected Reference Datasets Are Based Upon Best Available Methods	Model Design Is Tailored to the Available Data and Reflects the Intended Use of the Device
Focus Is Placed on the Performance of the Human-AI Team	Testing Demonstrates Device Performance During Clinically Relevant Conditions
Users Are Provided Clear, Essential Information	Deployed Models Are Monitored for Performance and Re-training Risks are Managed

Machine Learning in Medical Devices:
Some Considerations Prior to Authorization

Bias

Mission: Investigate sources of bias and address them.

Performance

Mission: Ensure the AI tool has been appropriately tested.

Device Characterization

Mission: Promote clear intended use statements for regulatory decision-making and safe integration into the clinical environment without unintended consequences.

Innovation

Mission: Balance safety and effectiveness while facilitating access to innovative products.

Important Consideration: Model Drift

- **What is Model Drift?**
  - The degradation of a model's prediction power due to changes in the environment

- **How can Model Drift happen?**
  - **Data drift:** Change in data distributions. The model performs worse on unknown data.
  - **Concept drift:** Change in relationships. The relationship between the input data and the target variable changes

"An important threat to [machine learning solution] performance is data-set shift, where temporal changes in clinical practice or the distribution of patient characteristics result in a data set that differs from that which was originally used to train the algorithm"

Evaluation of machine learning solutions in medicine, Canadian   Medical Association Journal, September 2021

https://evidentlyai.com/blog/machine-learning-monitoring-data-and-concept-drift
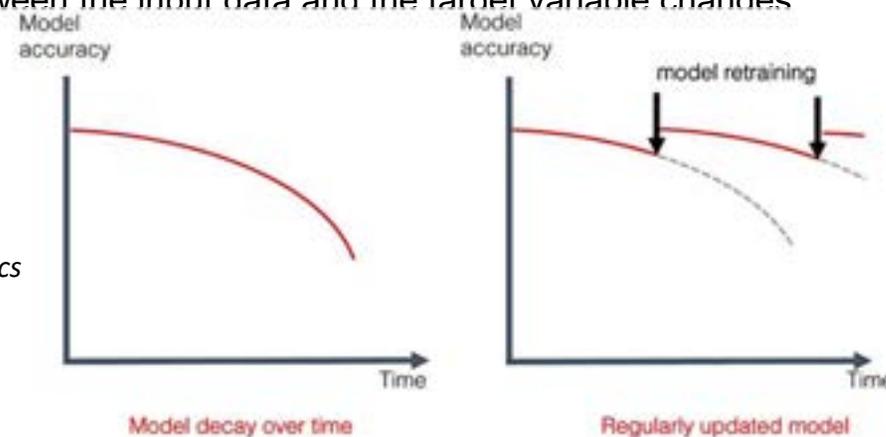
How to regulate MLMD with the known risk of model drift?

Licence T&Cs

Terms and conditions

Device PCCPs

Pre-determined change control plans

MLMD with Licence Terms and Conditions (T&Cs)

Issuance

36 (1) If the Minister determines that a medical device in respect of which an application is submitted meets the applicable requirements of sections 10 to 20, the Minister shall

(a) issue to the manufacturer of the device a medical device licence, in the case of an application for a medical device licence; or

(b) amend the medical device licence, in the case of an application for a medical device licence amendment.

(2) The Minister may set out in a medical device licence terms and conditions respecting

(a) the tests to be performed on a device to ensure that it continues to meet the applicable requirements of sections 10 to 20; and

(b) the requirement to submit the results and protocols of any tests performed.

(3) The Minister may amend the terms and conditions of the medical device licence to take into account any new development with respect to the device.

(4) The holder of the medical device licence shall comply with the terms and conditions of the licence.

SOR/2015-193, s. 7.

For example, *to manage uncertainties surrounding post-market performance degradation/drift over time (e.g. due to input changes relative to the training data) the provision of periodic (e.g., annual) comprehensive summaries can be required that outline performance analyses and usability testing on selected Canadian reference sites.*

Pre-determined Change Control Plans (PCCPs)

- Health Canada guidance introduces the concept of a **predetermined change control plan (PCCP)**.

- A PCCP provides a mechanism for **pre-authorization of planned changes** to address a known risk.
  - E.g. Maintenance or improvement of performance to address the risk of model performance degradation over time

- PCCP is documentation that describes:
  - The 'What': Specific, planned modifications to the device
  - The 'How': The protocol for implementing those modifications
  - The 'Impact': The assessment of the impact of those modifications

- Health Canada and FDA co-chair the International Medical Device Regulators Forum's (IMDRF) Software as a Medical Device (SaMD) Working Group, working to harmonize this PCCP concept across member jurisdictions.

✔ Promote faster **Access for Patients**

✔ Promote **Innovation**

✔ **International Alignment**

FDA Pmda

IMDRF International Medical Device Regulators Forum

MLMD with Pre-determined Change Control Plans (PCCPs)

1. **GMLP**

2. **Baseline Product Safety & Effectiveness**

3. **PCCP:**
   - Change description (changes & performance envelope)
   - Change protocol
   - Impact assessment

4. **Terms & Conditions (T&Cs)**

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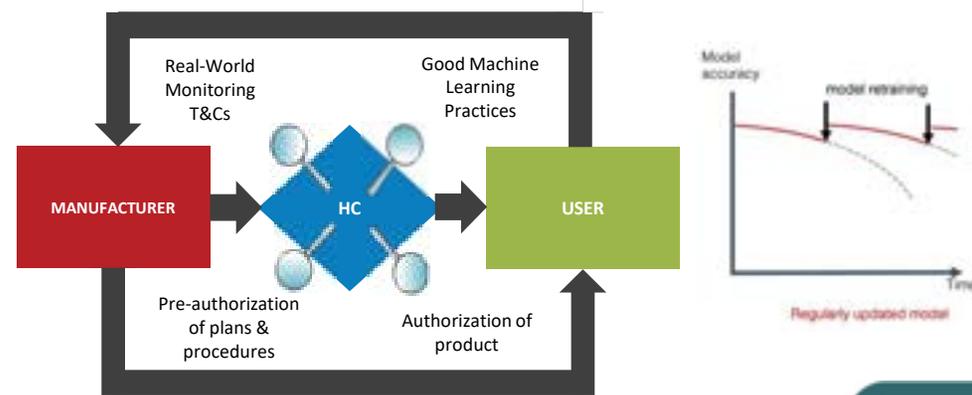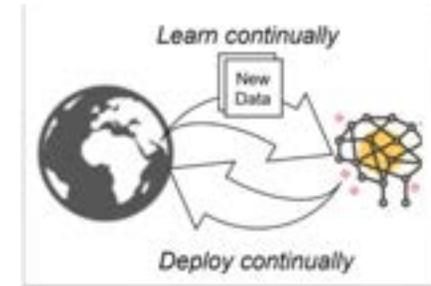
Joint Statements

- Longstanding collaboration in Digital Health with the US FDA and UK MHRA, leading to multiple joint postings:
  - *Good Machine Learning Practice for Medical Device Development: Guiding Principles (2021)*
  - *Transparency for machine learning-enabled medical devices: Guiding principles (2024)*
  - *Pre-determined change control plans for machine learning-enabled medical devices: Guiding principles (2024)*

Perspectives on MLMD Regulation

- **Reflections:**
  - Health Canada has been regulating MLMD that remains in a locked state for many years
  - We recognized the benefits associated with enabling access to adaptive MLMD
  - Regulatory barriers were identified in Canada

- **Current Initiatives**
  - We continue to gain insights from external stakeholders and national and international experts
  - Health Canada has adopted the PCCP concept via policy to authorize adaptive MLMD
  - T&Cs are being leveraged to address uncertainties and ensure maintained MLMD performance

- **Expectations**
  - Pre-market expectations around GMLP, PCCPs and T&Cs will enable robust regulation of these novel products and in turn patient access to beneficial devices
  - The benefits can be realized and the risk minimized through this multi-disciplinary effort including regulators, innovators, users, healthcare providers, and beyond.

Questions ?