Health Canada Santé Canada

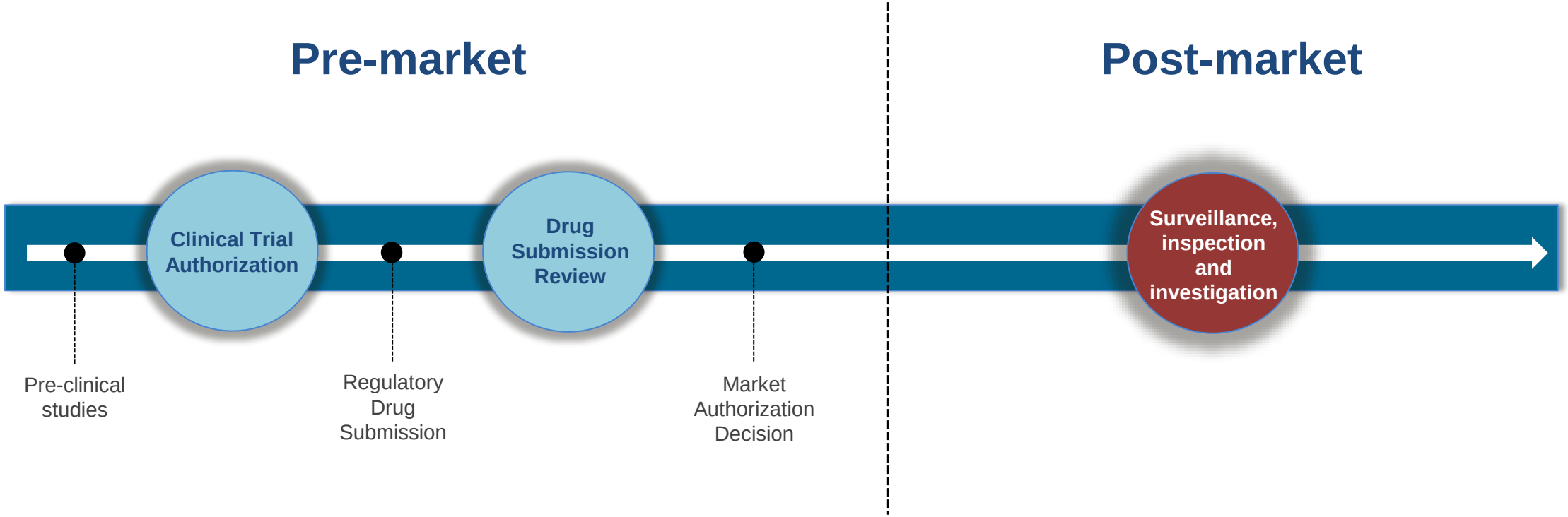
Canada

Advanced manufacturing and other trends supporting access to medicines for patients

Hugo Hamel, M.Sc., MBA
Biologics and Radiopharmaceuticals Drugs Directorate
Health Canada

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Modernization Harmonisation in Pharmaceutical Science and Manufacturing

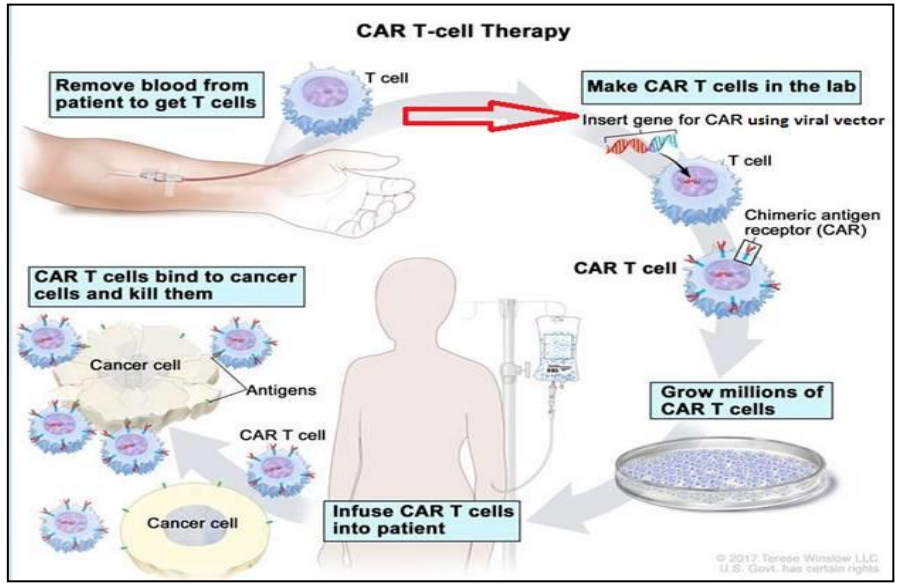


Regulations and guidance
Increased communication and Transparency
Leveraging international partnerships and consortiums
Public Health Emergency Drug and Agile regulations

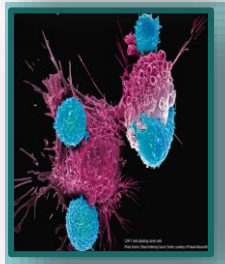
Good Manufacturing Practices
Drug Establishment Licences
Partnership and international collaboration
Supply chain surveillance and drug shortages
Supporting innovation and life & biosciences

TRENDS SHOW A CLEAR GROWTH OF COMPLEX AND PERSONALIZED PRODUCTS SEEKING APPROVAL FROM HEALTH CANADA

- In 2022, 44 “New Active Substances” were approved, an increase from 2021.
- Half of drugs approved by Health Canada in 2022 were for rare diseases.
- Over the past 6 years, over 40% of new active substances (NAS) authorized in Canada are classified as orphan drugs in Europe or the United States.
- In the next 3 years, 60% of cancer drug submissions anticipated to be for rare diseases
- Pediatric drugs for rare disease are increasing, but gaps remain (80% drugs for children are prescribed “off label”)
- Health Canada has also approved a number of innovative cell and gene therapies, such as:
  - **CAR-T cell therapies** where a patient's own T cells are altered in a laboratory and then re-infused to attack specific cancer cells
  - **Targeted gene therapies** such as one to treat spinal muscular atrophy, a rare disease and a leading genetic cause of infant mortality



SOME PRODUCTS ARE SO COMPLEX, THEY CANNOT BE REGULATED WITHIN TODAY'S SYSTEM, CREATING BARRIERS TO ACCESS

 **Adaptive Machine Learning-Enabled Devices**	AI-driven technologies have the potential to revolutionize the health care system. But some advancements – such as adaptive algorithms that learn from new datasets and frequently update to improve performance – fundamentally challenge global regulatory systems, creating access barriers for cutting edge technologies.
 **Fecal Microbiota Therapy**	Fecal Microbiota Therapy is important in the fight against antimicrobial resistance, such as treating recurrent C. difficile infections. However, clinical use of the therapy is limited due to current regulatory restrictions.
 **Products manufactured at point of care**	Cell therapies or 3D bio-printed tissues produced in a hospital or doctor's office, rather than a manufacturing plant, are challenging traditional oversight models. For example, applying quality regulations (that were originally designed for large scale drug facilities) to a hospital is not feasible.

STAKEHOLDERS HAVE BEEN CLEAR THAT MORE REGULATORY AGILITY IS NEEDED TO ADDRESS THESE TRENDS, LEADING TO HEALTH CANADA'S MODERNIZATION PLAN FOR INNOVATION

Design Agile Regulations

By adopting international best practices, eliminating duplication across jurisdictions and decreasing review times

- In 2018, the Government of Canada's **Health and Bio-Sciences Economic Strategy Table** and **Advisory Council on Economic Growth** highlighted opportunities to enhance regulatory agility in support of innovation and economic growth
- **Targeted Regulatory Review** of the health and bio-sciences sector also highlighted the need for modernization to address issues and bottlenecks.
- In 2019, Health Canada began implementing a **regulatory modernization plan** to enhance Canada's position as a destination of choice for product submissions through a more modern, agile and internationally-aligned system
- Our multi-year plan (2019-2024), approved by the Treasury Board Secretariat, received the necessary legislative powers and time-limited funding to develop policy and regulatory modernization initiatives

THESE INITIATIVES OFFER CONCRETE WAYS TO ENSURE CANADIANS GET ACCESS TO NOVEL AND SAFE INNOVATIONS

Modernizing clinical trial regulations

- Increased agility to oversee patient safety in innovative trial designs with an expanded compliance and enforcement program
- Improved ability to monitor risk, and collect data, and manage uncertainties in complex or higher risk trials
- Enable trials (e.g., decentralized) that support recruitment of more diverse patient populations
- Better access and transparency on information about trials

Enabling Advanced Therapeutic Products

- Creation of tailored pathways based on unique product characteristics using modernized inspector powers
- A collaborative approach working with stakeholders to define the evidence standards for regulatory approval
- Leveraging regulatory approaches from international jurisdictions
- Concierge service to provide guidance and assistance to innovators

Agile licensing for drugs

- Allow risk-based approval and oversight of products throughout their lifecycle
- Provide more agile regulatory tools to optimize oversight (e.g., Terms and Conditions)
- Support the use of decisions from trusted foreign regulators in specific situations
- Modernizing compliance and enforcement to align with current realities and international jurisdictions

Agile licensing for medical devices

- Facilitating market access of emerging innovations through agile solutions (e.g., exploring use of foreign reviews/decisions)
- Strengthening monitoring of medical devices (e.g., Unique Device Identifier tracking system)
- Modernizing application requirements for Medical Device Establishment Licences, and improve international alignment

• THE COVID-19 REGULATORY RESPONSE REINFORCED THE NEED FOR AGILITY, AND WILL INFORM FUTURE MODERNIZATION

- The public health crisis posed by COVID-19 created an urgent need for products such as testing devices, disinfectants, treatments, and vaccines
- An agile and collaborative regulatory response required:

temporary legislative, regulatory and policy measures (e.g. 'rolling' scientific review processes to help expedite review and applying terms and conditions to manage risks and uncertainties, flexible measures to help address critical supply issues)

partnerships and networks with companies and various levels of government to bring products to market quickly

international collaboration to ensure alignment in approach, work together on certain submission reviews, and share emerging safety and supply chain information

easily accessible guidance and timely product information

adapted approaches to conducting regulatory oversight using virtual/remote tools, and onsite inspections, where possible

These measures, along with funding for surge capacity, positioned Health Canada as a competitive regulator that was among the first in the world to approve COVID-19 vaccines

International Collaboration: Efficient Access to Medicine for Patient

Health Canada continues to work closely with international partners on a coordinated and aligned approach to respond to the COVID-19 pandemic

Multi-national fora – coordinated international strategy and guidance

- **International Coalition for Medicines Regulatory Authorities (ICMRA)** as an executive committee member and plays a leadership role in aligning policy approaches and regulatory agility (Joint statements: COVID-19; Clinical Trials; Drugs and Vaccines)
- **World Health Organization's** research and development (R&D) blueprint vaccines plan to develop a COVID-19 vaccine (Joint statement: Improved global regulatory alignment)
- **Pan American Health Organization** as a member of its COVID-19 task group

Bilaterally – to align and coordinate product specific regulatory work

- **Parallel reviews and information sharing -** to maximize the use of global expertise
  - European Medicines Agency
  - Access consortium – Singapore, UK, Switzerland, Canada and Australia
  - US Food and Drug Administration
- **Post-market monitoring** to share international data on potential safety issues
  - Ongoing regular information-sharing and rapid communication regarding potential safety issues

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

Pharmaceutical Inspection Cooperation Scheme (PIC/S)

Publications

Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management: Q12

Continuous Manufacturing of Drug Substances and Drug Products: Q13

Concept Paper on the revision of EU-PIC/S GMP Annex 11 (Computerised Systems)

The revised Annex 1 on “sterile manufacturing of the PIC/S GMP Guide

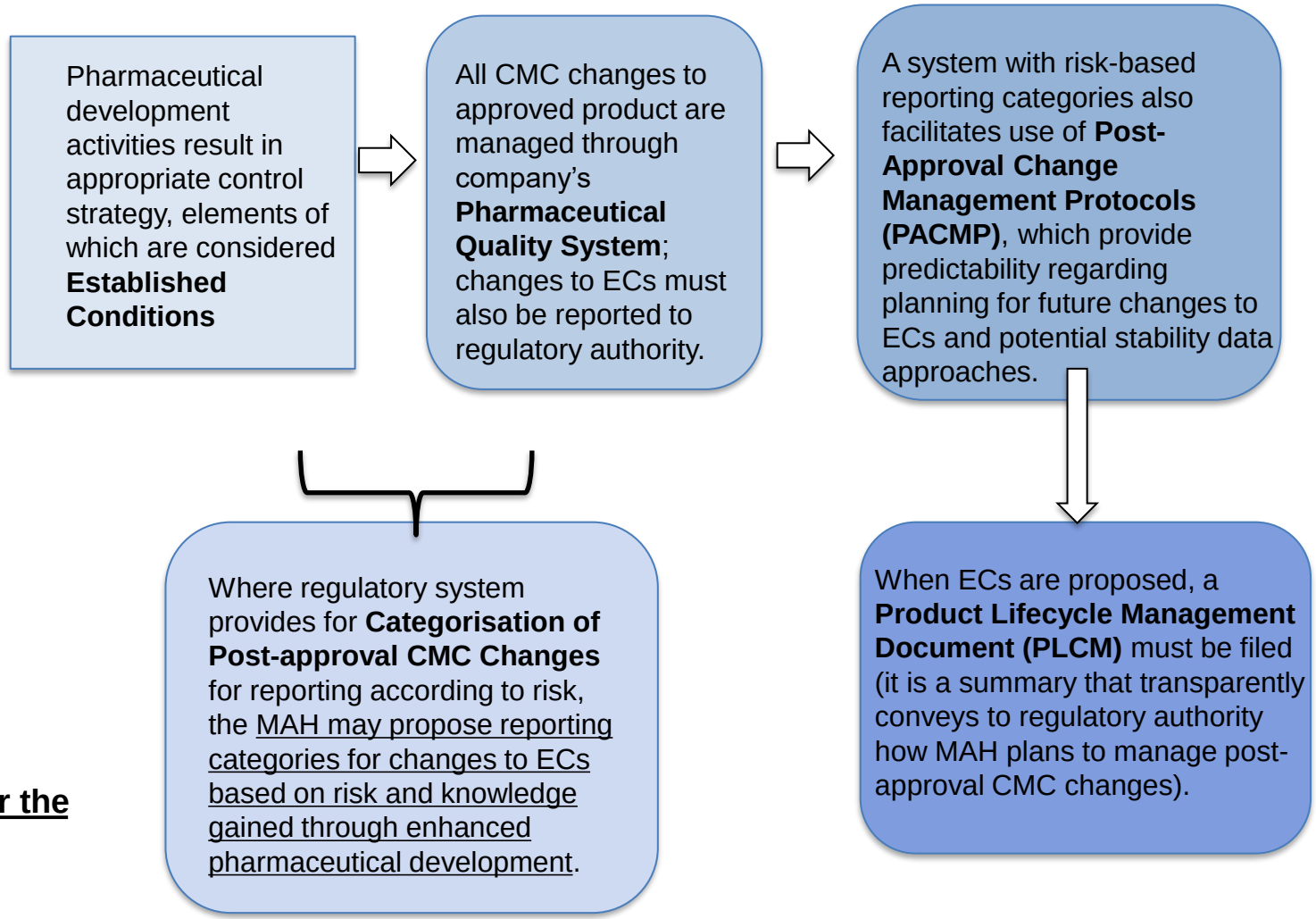
LIFE CYCLE APPROACH TO QUALITY MANAGEMENT WITH ICH Q12

Implementation Benefits

Harmonised approach regarding technical and regulatory considerations for lifecycle management will benefit patients, industry, and regulatory authorities by:

- promoting innovation
- promoting continual improvement in the pharmaceutical sector
- strengthening quality assurance
- improving supply of medicinal products

Health Canada has established a working group for the application of the Q12 principles.

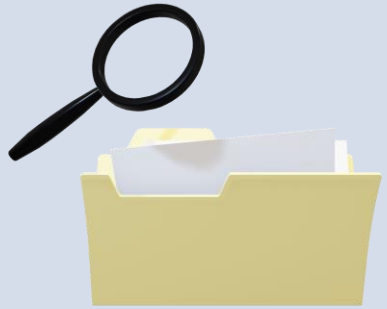


Implementation timelines in Canada

- The Post-NOC Changes guidance document has been updated to incorporate the ICH Q12 tools and concepts (i.e., ***Established Conditions***, ***Post-Approval Change Management Protocol***, ***Product Life Cycle Management*** document), including the addition of the ***"Immediate Notification"*** reporting category

  - **August 2021:** External consultation with stakeholders (120 days)
  - **January 2022:** **Training sessions** for the reviewers
  - **March 2022:** Launch of the **pilot program** (on ECs and PACMPs)
  - **February 2023:** End of the pilot program on ECs and PACMPs
  - **February/March 2023:** Finalization of the PNOCC guidance document
  - **2024:** Projected partial Implementation of ICH Q12 in Canada (Step 5)

• ICH Q13: Continuous Manufacturing of Drug Substances and Drug Products



Purpose of the ICH Q13 guideline

- Provides harmonized regulatory guidance and a framework to facilitate assessment, implementation and lifecycle management specific to Continuous Manufacturing (CM)

Key Principles of the ICH Q13 guideline

- Continuous manufacturing (CM)
- Provides clarification on CM concepts, describes scientific approaches, and presents regulatory considerations specific to CM of drug substances and drug products

Objective of the ICH Q13 guideline

- Capture key scientific and regulatory considerations
- Provide guidance to industry and regulatory agencies
- Describe fundamental aspects of CM within the main guideline
- Annexes to augment the main guideline by providing illustrative examples and scientific and regulatory considerations specific to certain modalities

Health Canada is actively adopting Q13 and supports its purpose, principals and objectives.

PROJECT ORBIS: HEALTH CANADA

- Health Canada has been a partner in Project Orbis since its inception in May 2019. Health Canada worked with the FDA and TGA on the first Project Orbis submission. This led to Health Canada's timely approval of a treatment for women with advanced endometrial cancer in September 2019
- Regulatory review service standards do not change with Project Orbis submissions. However, under Project Orbis, we may review some submissions and make decisions faster than our service standard.
- Sponsors can select the number of partners included in a Project Orbis submission. Health Canada has flexible approach to determine the submission Type with respect to:
    a) filing date compared to the US
    b) resource capacity.

NDS & SNDS

Health Canada review of new oncology products exceeded the review target.

11 NDS in 2021
10 NDS in 2022

9 SNDS in 2021
14 SNDS in 2022

PROJECT ORBIS - APPROVED NDS & SNDS BY PO TYPE

Submissions reviewed and cleared since Project Orbis initiative began – 54 submissions:

NDS

YEAR	TYPE A	TYPE B	TYPE C	TOTAL
2019	0	0	0	0
2020	3	0	0	3
2021	3	3	5	11
2022	2	2	6	10
Total	8	5	11	**24**

SNDS

YEAR	TYPE A	TYPE B	TYPE C	TOTAL
2019	3	0	0	3
2020	3	0	1	4
2021	4	5	0	9
2022	4	6	4	14
Total	14	11	5	**30**

Types of completed Submissions

Health Canada completed 5 NDS, 9 NDS Priority, 10 NOC/c, 18 SNDS & 13 SNDS Priority submissions from 2019 to 2022.

ACCESS WORK-SHARING INITIATIVES

ACCESS CONSORTIUM
AUSTRALIA
CANADA
SINGAPORE
SWITZERLAND
UNITED KINGDOM

Access work-sharing initiatives are designed to:

- facilitate simultaneous market access in all submitted jurisdictions
- promote interagency regulatory convergence
- distribute work across different jurisdictions
- incentivize earlier filing

Strategic Plan 2021-2024

Strengthening Access work-sharing initiatives

Making Access a competitive and efficient submission pathway of choice for industry, supported by regulators

Expanding lifecycle approach

Maximizing collaboration throughout the health product lifecycle

Regulatory innovation that integrates a healthcare systems approach

Increasing regulatory capacity while collaborating with key national healthcare system partners to facilitate uptake of innovative health products

Generic Medicines Work Sharing Initiative (GMWSI)

- Innovative work-sharing model for the coordinated assessment of generic applications filed with multiple Access agencies
- Launched as a trial in 2016

New Active Substances Work Sharing Initiative (NASWSI)

- Launched in 2017 building on experience gained from the GMWSI
- Focus on work sharing of new active substances
  - New drugs and new indications
  - Standard and priority review are considered

Biosimilars Work Sharing

- In 2021 Access started accepting new drug submissions filed with 2 or more Access regulators for a new biosimilar

ACCESS - Collaboration and harmonization

- The Access Consortium is committed to maximizing collaboration by aligning regulatory and policy approaches and reducing duplication. As a member of Access, Health Canada is working to optimize work-sharing through greater alignment of our regulatory approaches and technical and scientific requirements.

- Health Canada recognizes that there are country specific requirements that may make this process less harmonized and that all of the different countries experience this. We are always looking for ways we can harmonize, recognizing that each of the agencies unique regulations may not permit total harmonization.

- Health Canada aims to further harmonize with a perspective informed by an increased understanding of the various requirements and constraints of others as well as learning from their processes and scientific views.

SUBMISSION PATHWAYS COMMON BENEFITS

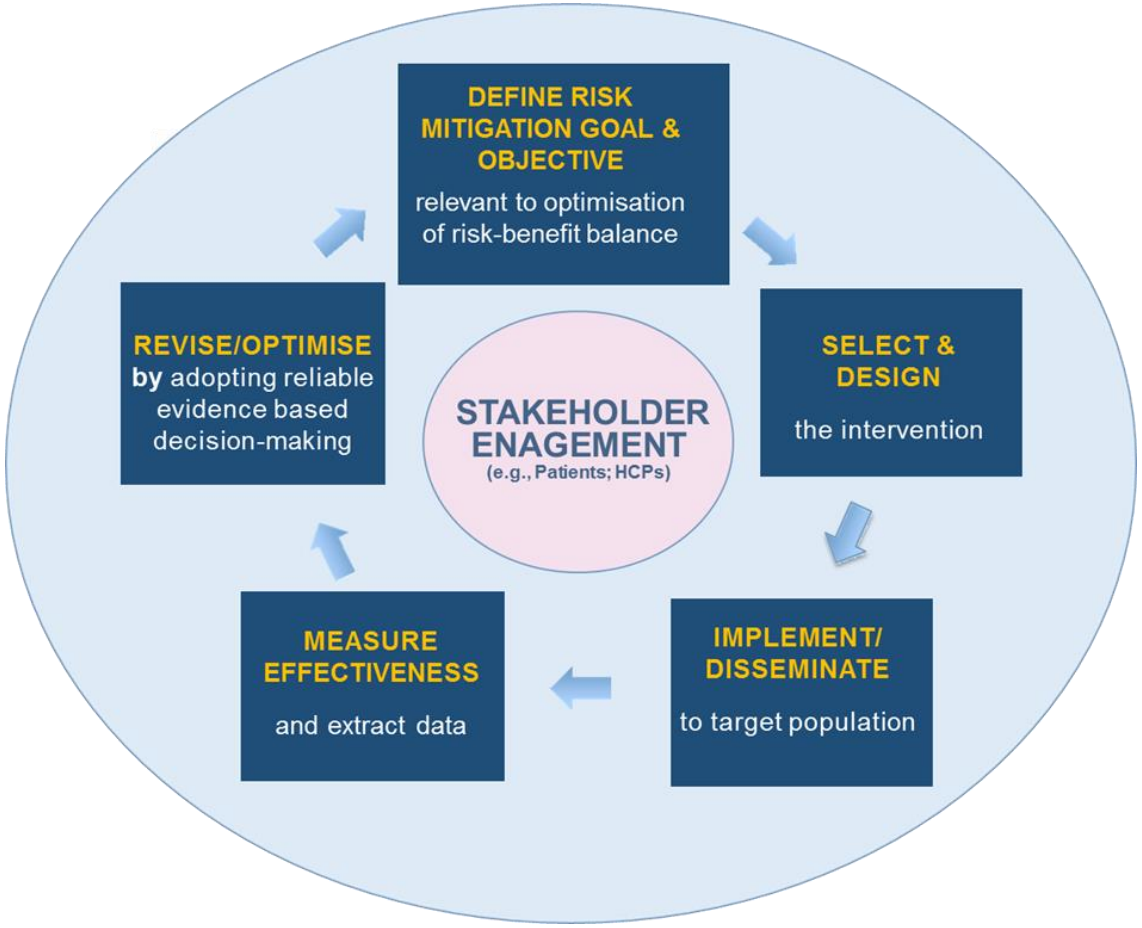
REGULATOR BENEFITS

- Maintain sovereign and robust regulatory decisions
- Strengthen interagency relationships for cooperation and collaboration
- Leverage expertise, real-time information and submission updates, exposure to emerging global trends and innovations
- Open up space for novel collaboration areas, understanding of partner's evaluation approaches, alignment of submission requirements to agency for review
- Learn from partner experiences and best practices to refine our own regulatory procedures and policies
- Multi-disciplinary assessment aid/partner review reports available for information share, where applicable

SPONSOR BENEFITS

- Earlier access and or near simultaneous approval of novel, safe, and effective products to multiple markets of choice.
- Reduced regulatory efforts due to increased submission alignments and decreased duplicative questions
- Open to and encourage sponsor pipeline meetings

Excellence in manufacturing practice reduces risk of drug shortages and contributes to Continuous learning & Improvement Risk Management Plans



Health Canada takes a leadership role in coordinating and implementing a consistent approach to conduct post-market surveillance, monitoring, assessing and intervening on all regulated marketed health product types

The MHPD does post-market surveillance of drug products

Mouchantaf R, et al. Risk Management for the 21st Century: Current Status and Future Needs (June 2021 Drug Safety).

Artificial Intelligence Projects within Marketed Pharmaceuticals Bureau

- Council for International Organizations of Medical Sciences (CIOMS) Working Group XIV Artificial Intelligence in Pharmacovigilance
  - The objective of Working Group XIV is to establish and promote principles and guidance for use of artificial intelligence or intelligent augmentation in the field of pharmacovigilance.
  - Due to the increasing volume of data (e.g. adverse reaction case reports), as evident during the COVID-19 pandemic, and advancements in technology, there is significant interest to leverage artificial intelligence or intelligent augmentation.
  - Health Canada is one of the representatives on Working Group XIV which is comprised of regulatory authorities, pharmaceutical companies, academia and WHO.
  - Currently, the Working Group is drafting the consensus report.

Innovation across Life Cycle Management of Products

Ongoing Engagement with Domestic Stakeholders and Provinces and Territories

Manufacturers:

Required to monitor ongoing manufacturing process after issuance of market authorisation

Expedited Timelines for Quality Management System updates and Q8 principles.

International Collaborations:

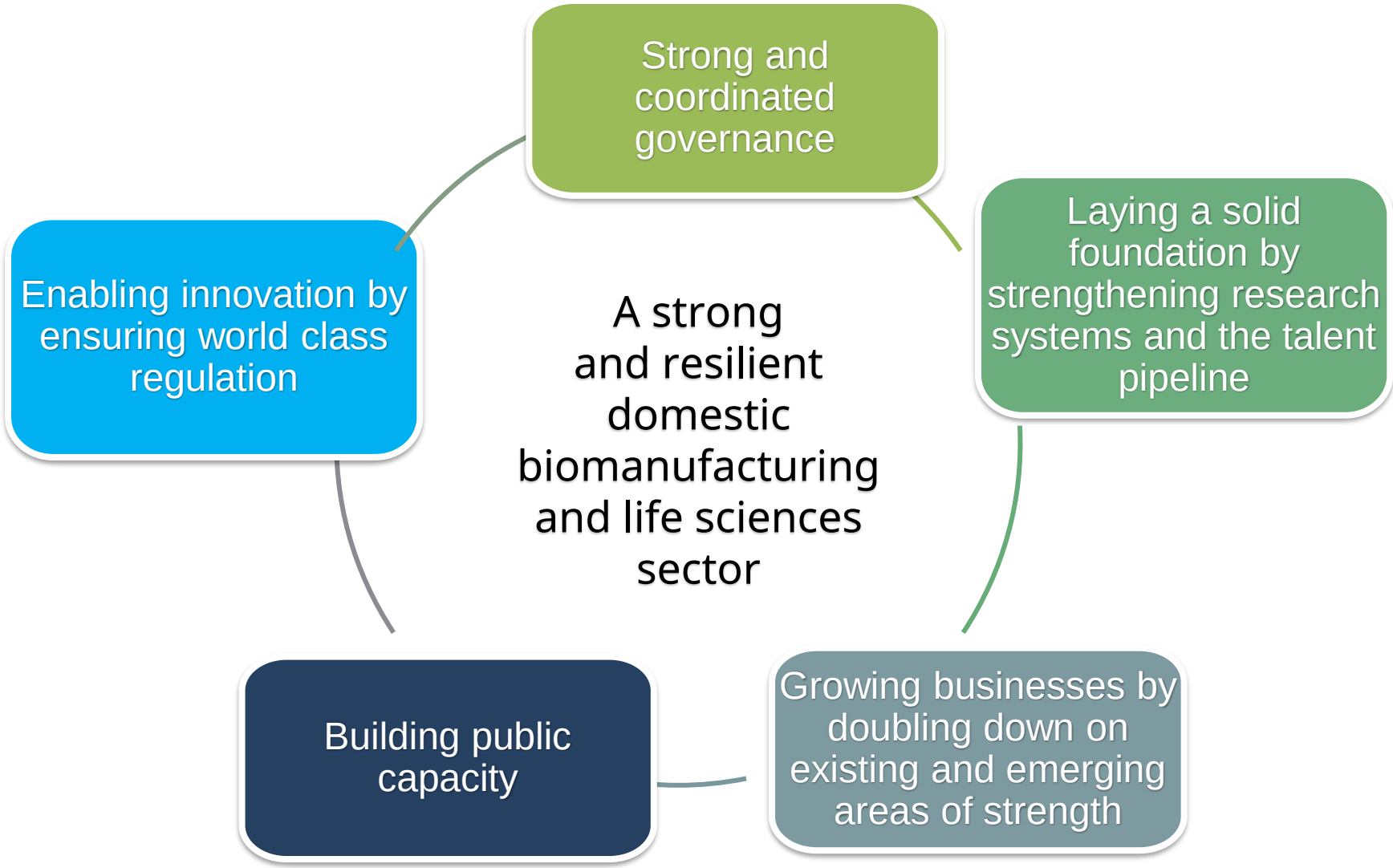
Active collaboration with International partners via multiple forums: ICH, PICS, ICMRA, ACCESS, Ad-hoc Meetings with key partners

Active collaboration with sponsors during evolving clinical trial stages

Regulators and Collaborative approaches:

- Enhanced monitoring of domestic and international manufacturing sites
- Enhanced adoption best manufacturing approaches
- Scanning actions from Regulatory agencies

Canada's Biomanufacturing and Life Sciences Strategy



WHAT'S NEXT FOR ADVANCED MANUFACTURING?

- Reaching out to or encouraging industry, where applicable, to arrange pipeline meetings
- Continuing to build strong interagency collaborations by aligning regulatory and policy approaches, where possible reducing duplication, taking into consideration each agency's national requirements and policies expanding the scope of work and information sharing to more area/products types
- Build upon, apply, and refine the learnings and best practices of our experiences and current procedures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