International Cooperation Among Regulators

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Canada

Outline

- Departmental and Health Products and Food Branch General Perspective on International Engagement
- Health Products and Food Branch International Regulatory Cooperation (IRC) Approach:
  - Drivers, Benefits, Enablers, Challenges, Trends and Priorities
- HPFB's IRC Experiences and Approach: Lessons Learned
- Use of Foreign Regulatory Information




Health Canada and Health Products and Food Branch International Engagement




General Perspective on International Engagement

- Health Canada and Health Products and Food Branch have a long history of cooperation with foreign counterparts and international organizations (ranging from informal information exchange to multilateral harmonization initiatives)

- Canada is increasingly affected and challenged by health issues beyond its borders. This means that the Government must be active internationally to help protect and enhance the health of Canadians.

- Active international cooperation ensures that Health Canada is aware of new and emerging policies and issues that may affect the health of Canadians and contributes to strengthening our domestic capacity. It also permits the Department to share information on Canadian health issues with the rest of the world and to contribute/influence international processes.




Departmental International Health Strategy

(includes other part of Health Portfolio including CIHR, PHAC)

Strategic priorities

1. Preventing, preparing and responding to global health threats
2. Food, health and consumer product safety
3. Health and environment
4. Health systems and capacity
5. Health promotion and disease prevention

Goals for 2008-2011

1. Improve and protect the health of Canadians
2. Enhance global health security
3. Support global health efforts

collective action




Health Products and Food Branch (HPFB) Mandate

- Minimize health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food

- Promote information and conditions that enable Canadians to make healthy choices and informed decisions about their health.

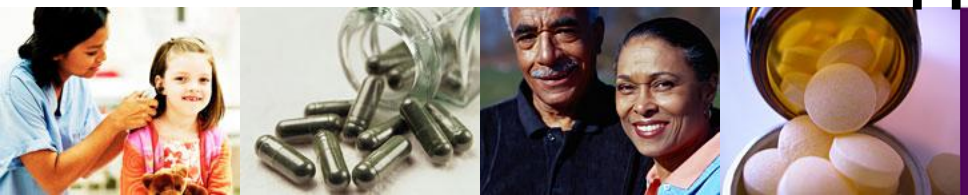
- HPFB's Scope of Responsibilities
  - Therapeutic Products for Human Use
    - Pharmaceuticals; Medical Devices; Biologics -including vaccines; blood; cells/tissues/organs
  - Veterinary Drugs
  - Natural Health Products
  - Food




HPFB International Strategic Engagement …

- Develop and strengthen international relations with key regulatory counterparts and other organizations (bilateral, regional, multilateral);
  - Eg. Heads of Agency-Annual Summits; Quadrilateral (HPFB, HSA Singapore, TGA Australia, Swissmedic); Bilateral MOUs
- Active and transparent collaboration in international standards setting, equivalency and “harmonization” initiatives
  - Eg. ICH/VICH; GHTF; PANDRH; ICCR; APEC; PIC/S; ISO/IEC/HL7; WHO (CIOMS, IRCH, Vaccines, Blood, Codex Alimentarius)
- Strategic engagement with countries that have lesser resourced regulatory systems
  - Eg. Collaboration with WHO re: India NRA Vaccine Regulation; HPFB International Regulatory Forum

… in support of Branch Mandate



HPFB International Engagement and Activities Must ….

- Collaborative bilateral and multilateral efforts must be practical, relevant, flexible, align with the mandate and support the scientific and regulatory capacity of the Branch.
- Cooperative regulatory efforts should, whenever possible, be directed towards multilateral networks and fora as a means of maximizing investment and impact.
- “Strengthening others helps strengthen all” – engage with developing regulatory authorities through existing networks by promoting synergies/avoiding duplication of effort




International Regulatory Cooperation (IRC)




Drivers of IRC

- Globalization of industry has led to a desire for common standards and reduction of unnecessary regulatory burden
- Global dimension of issues confronting regulators, including pandemics, counterfeits and other product safety issues
- Growing gap between domestic capacity and workload and challenges
- Increasing complexity of new technologies and pace of change
- Expectations of well-informed public to use best science and information to mitigate risks in timely fashion
- Growing realization that in this dynamic, inter-related environment no single regulatory authority has a monopoly on good science/approaches nor can ‘do it alone.’




HPFB International Cooperation Focus

- Developing regulatory arrangements with regulatory counterparts and multilateral/international organizations
- Targeting worksharing activities that enhance the quality and efficiency of domestic regulatory decision making
- Participating in development and implementing harmonized guidelines and standards
- Approaching technical assistance and capacity-building initiatives through cost effective channels
- Integrating international best practices in modernizing the regulatory system



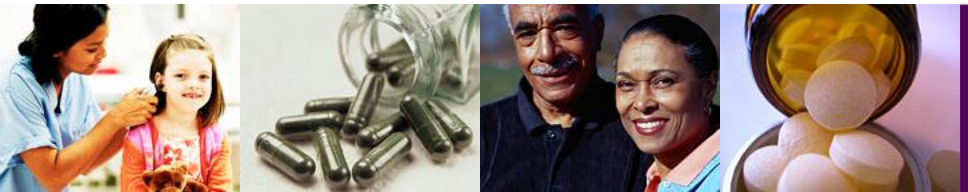

Three Major Clusters of Engagement

Harmonization	Regulatory Cooperation	Capacity Building
Continue the active involvement on the development international standards and guidelines including therapeutic products and food, but be strategic (be selective and strategic) (ICH, ECBS-WHO, CODEX, GHTF, PIC/s, VICH and IRCH, including OECD)	- Focus the collaboration with regulatory authorities relevant to each product line such as, Europe and FDA for human and veterinary drugs and food, and Australia -Maintain and enhance activities with EMA and leverage the expertise of EMA and FDA to expedite access to new therapies -Moving toward more multilateral collaboration	- Training and knowledge transfer activities such as, the IRF when resources can be leveraged with partners - Continue to support WHO in strengthening regulatory capacity of developing NRAs through training and provision of expertise(e.g. Vaccines) -Work multilaterally with the FDA, TGA, EMA and WHO on the African Medicines Registration Harmonization Initiative. Engage with regional bodies such as, APEC, and PANDRH



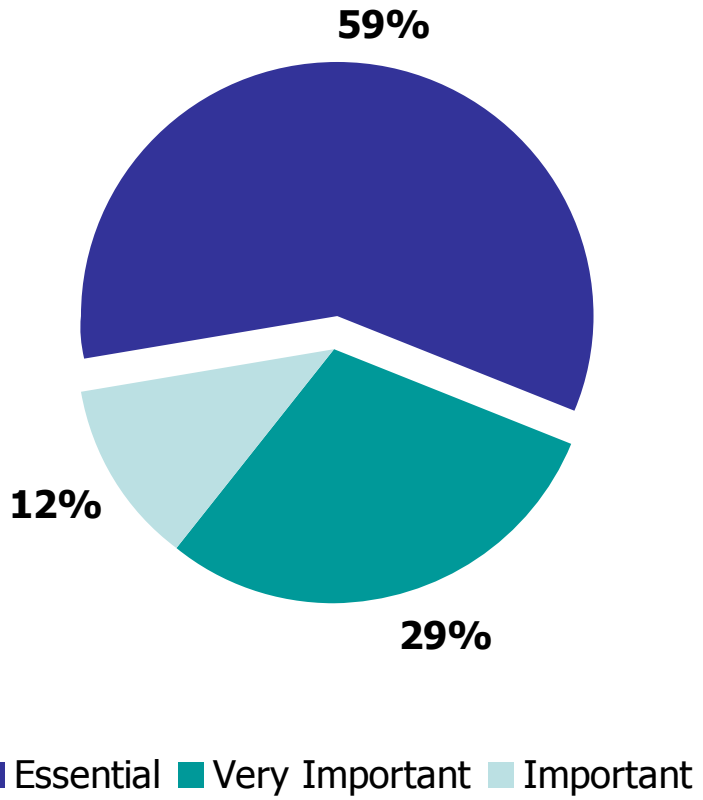

Benefits of Effective and Sustainable IRC

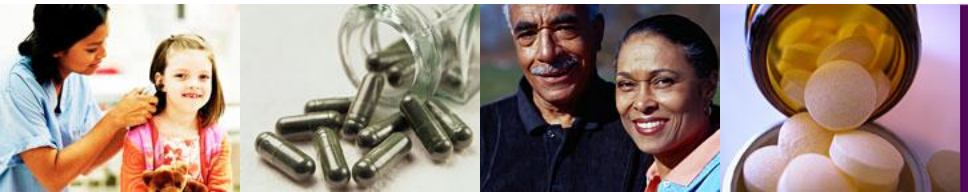
- IRC contributes to public health and innovation by strengthening efficiency and effectiveness of regulatory authorities through:
  - More informed, timely decisions
  - Coordinated actions
  - Better use/leveraging of resources and knowledge
  - Adoption of best practices, including risk based approaches
  - Increased harmonization of processes and practices



HPFB International Activities Distribution in Relation to Mandate

- Essential:
  - Engaging with Europe/EMA, the USFDA and WHO on regulatory issues
  - Engaging with ICH, WHO, PAHO, USP, EU Pharmacopia, GHTF and CODEX, to contribute to international standard setting and guidelines (harmonization)
  - Engaging with WHO on capacity building (such as, the PQP for vaccines regulation)
- Very Important:
  - Collaboration with other regulatory authorities, such as Australia
  - Engaging with IRCH, VICH, APEC on harmonization
- Important:
  - Harmonization activities with PANDRH
  - Capacity building through the IRF





Enablers of Effective and Sustainable IRC

- Common standards and approaches
- Political and institutional will
- Investment of resources
- Trust
- Virtual networks and secure IT platforms
- Transparency and public availability of information
- Practical, relevant, incremental and flexible approaches that result in tangible benefits
- Strategy and business case – national, regional, international level



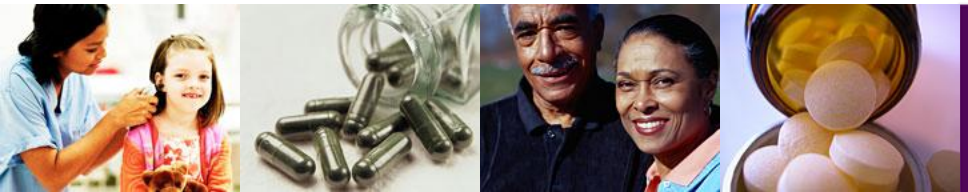

Enablers of Effective and Sustainable IRC

- Appropriate instruments that define nature of cooperation and allow for information exchange:
  - Legally binding agreements
    - e.g. Mutual Recognition Agreements (MRAs)
  - Non-legally binding arrangements
    - e.g. Memoranda of Understanding (MOUs)
    - Confidentiality Arrangements




HPFB's MRAs with 32 Countries

		Signed	Evaluation	Operational
European Union		1998	1998-2003/ 2005- …	Feb. 2003 On-going
Switzerland		1998	1998-2000 2003-2005	June 2000
EEA-EFTA (Norway, Iceland, Liechtenstein)		2000	2001-2002	Nov. 2002
Australia		2005	2001-2002	Jan. 2006



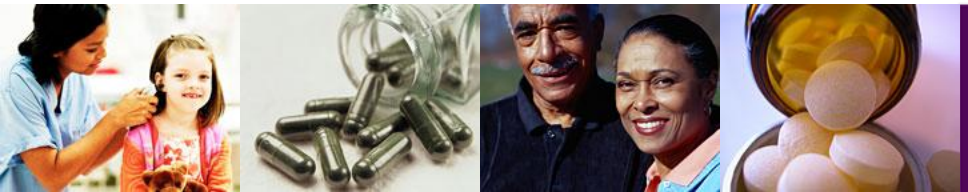
HPFB's Bilateral Arrangements (MOUs etc.)

- SFDA (September 1999)
- FDA (November 2003)
- TGA (April 2004)
- HSA (September 2006)
- Swissmedic (October 2006)
- EU (EC/EMA, December 2007)
- ANVISA (October 2009)
- New Zealand - NZFSA (March 2009), MEDSAFE (August 2009)
- MHRA (October 2009)
- MHLW/PMDA (October 2009)
- IMB (October 2010)
- Distinct but complementary to
  - Other more focused arrangements (eg. EDQM, DoH HK)



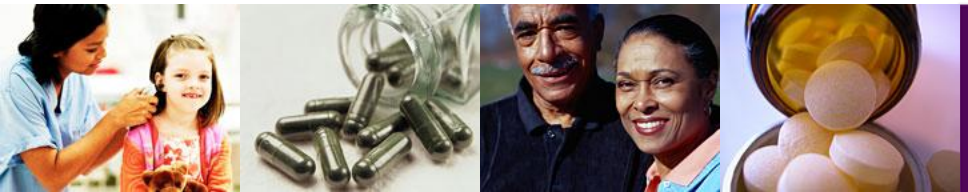

IRC Trends and Priorities

- Growing number of regulatory networks
- Expansion and linkages between harmonization initiatives
- Pooling of resources/capacity:
  - Worksharing and supranational arrangements
  - Mutual/unilateral recognition
- Increasing focus on multilateral initiatives
- Inspection and post-market surveillance activities



Challenges to Effective and Sustainable IRC

- Time scale required to realize desired outcomes
- Diversity in capacity
- Sovereignty considerations
- Legislation
- Overlap and duplication of effort
- Growing burden of managing cooperative efforts
- Financial and Human Resources



HPFB's IRC Experiences and Approach: Lessons Learned



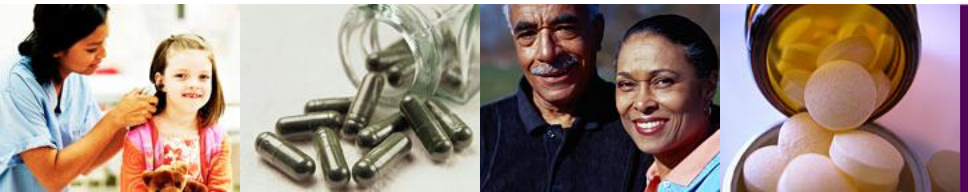

Observations (1)

- Bilateral arrangements and recent genesis of regulatory networks and fora establish important mechanisms through which participants may leverage expertise, knowledge and capacity to address common challenges
- At same time, ongoing management and coordination of growing number of bilateral arrangements proving to be challenging

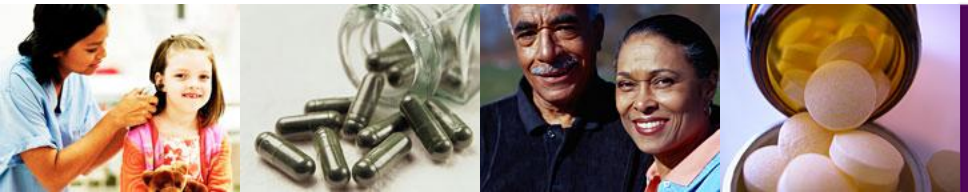



Observations (2)

- Apparent that overlap exists in activities originally foreseen under bilateral arrangements and new/contemplated multilateral interactions
- Further complicating the picture: fact that growing number of multilateral regulatory fora have been formed without collective thought as to respective roles and potential synergies/gaps

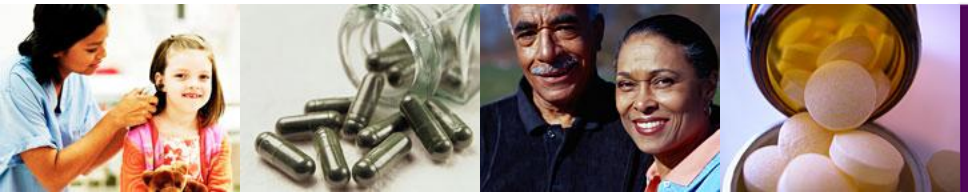


Opportune time to give further thought to a more strategic and coordinated approach to international regulatory efforts



HPFB Examples of More Strategic Approach

- (Annual) International Regulatory Forum
- APEC Life Sciences Innovation Forum (LSIF)
- Enhanced and optimal use of foreign regulatory information



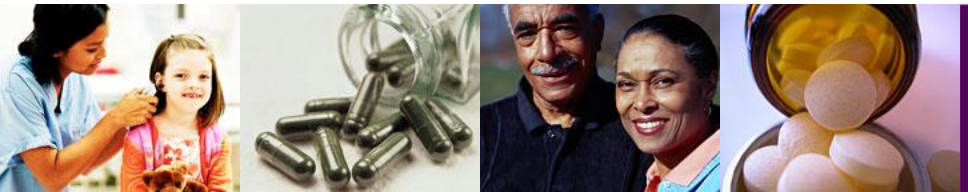
International Regulatory Forum

- Multi-directorate forum in high interest areas
- Aims to respond more effectively to growing number of visit requests from regulatory authorities
- Inspired by and complementary to FDA Forums
- Links with bilateral efforts
- Complements harmonization and other international capacity-building work
- Ability to address French (and for 2011-Spanish) speaking nations
- Program content/focus evolve based on feedback



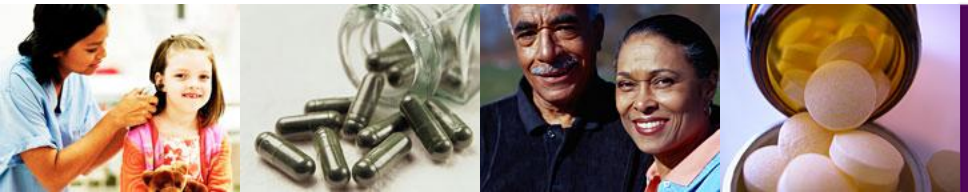

APEC LSIF

- APEC leaders endorsed creation of annual forum in 2002 to promote innovation in life sciences
- Tripartite structure: government, industry, academia
- LSIF serves as an ***enabler*** of harmonization:
  - Unique RHI in that doesn't *produce* harmonized guidances; rather, promotes use of *existing* international guidances
  - Voluntary basis for engagement: ensures participation of those economies interested and committed to cooperation
  - APEC region "hotbed" of harmonization; confirmed interest from China



Training: a Key Focus

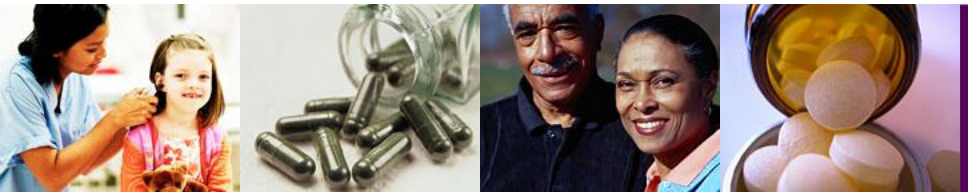
- LSIF has sponsored successful series of workshops on anti-counterfeiting, clinical trial evaluation and GCP inspection, supply chain, biosimilars, ICH quality guidances and harmonization of medical device regulatory approaches based on GHTF
- Good model:
  - Delivered to group of countries, including some outside APEC region: a desired approach
  - Workshops on CTA assessment and inspection have moved training beyond understanding of ICH guidelines to their application from a regulatory perspective



Outcomes of Strategic Discussions Lima, Peru 2008

Series of recommendations, including two of strategic importance:

- Support for the establishment of the APEC Harmonization Center (AHC)
- Creation of a Regulatory Harmonization Steering Committee (RHSC)



APEC Harmonization Center (AHC)

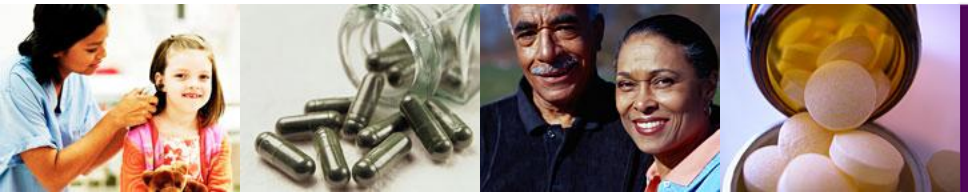
- APEC-wide resource to enhance and sustain harmonized and capacity building efforts by:
  - conducting research and surveys
  - providing educational programs
  - publishing and web posting
  - establishing networks and exchanges among participants and other international institutions
- Operate under the authority of LSIF, with direction from RHSC and an international advisory board




RHSC Mandate and Goals

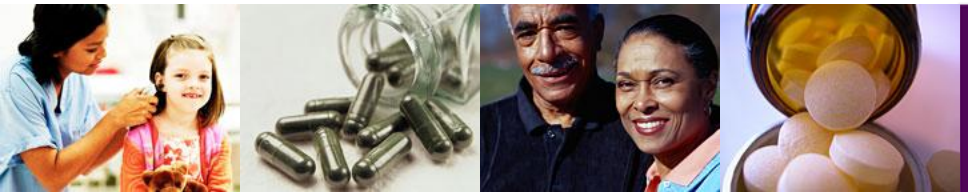
To promote a more ***strategic***, ***effective*** and ***sustainable*** approach to harmonization by:

- ***Proactively*** identifying and prioritizing projects seen to be of greatest value
- In partnership with AHC, establish or strengthen linkages with harmonization initiatives, training organizations and other key players in efforts to promote ***complementary*** actions and most effective use of resources
- Products within remit of SC: *medical products,* notably drugs and devices



Training

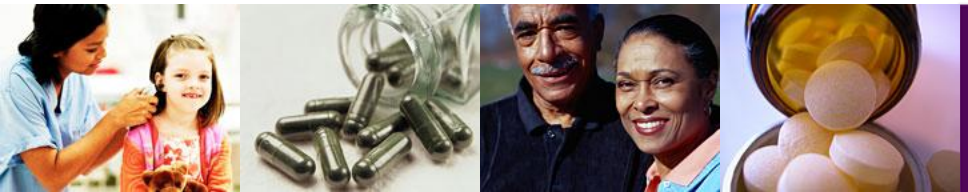
- Develop training strategy and overall plan with goal to promote regulatory harmonization and capacity building efforts in the APEC region
- Approach
  - Workshop as diagnostics
  - Act upon recommendations from workshop
  - Use regional approach vs. individual country
  - Capture information for future use and by those unable to attend in person



Moving into Formal Implementation of the Use of Foreign Regulatory Information in HPFB

Three year Master Plan to develop the approaches and mechanisms for the consistent and systematic integration and use of foreign regulatory information into marketing authorization review processes

- Optimize the use of foreign regulatory information in marketing authorization review processes
- Provide HPFB with consistent, transparent and predictable approaches and procedures



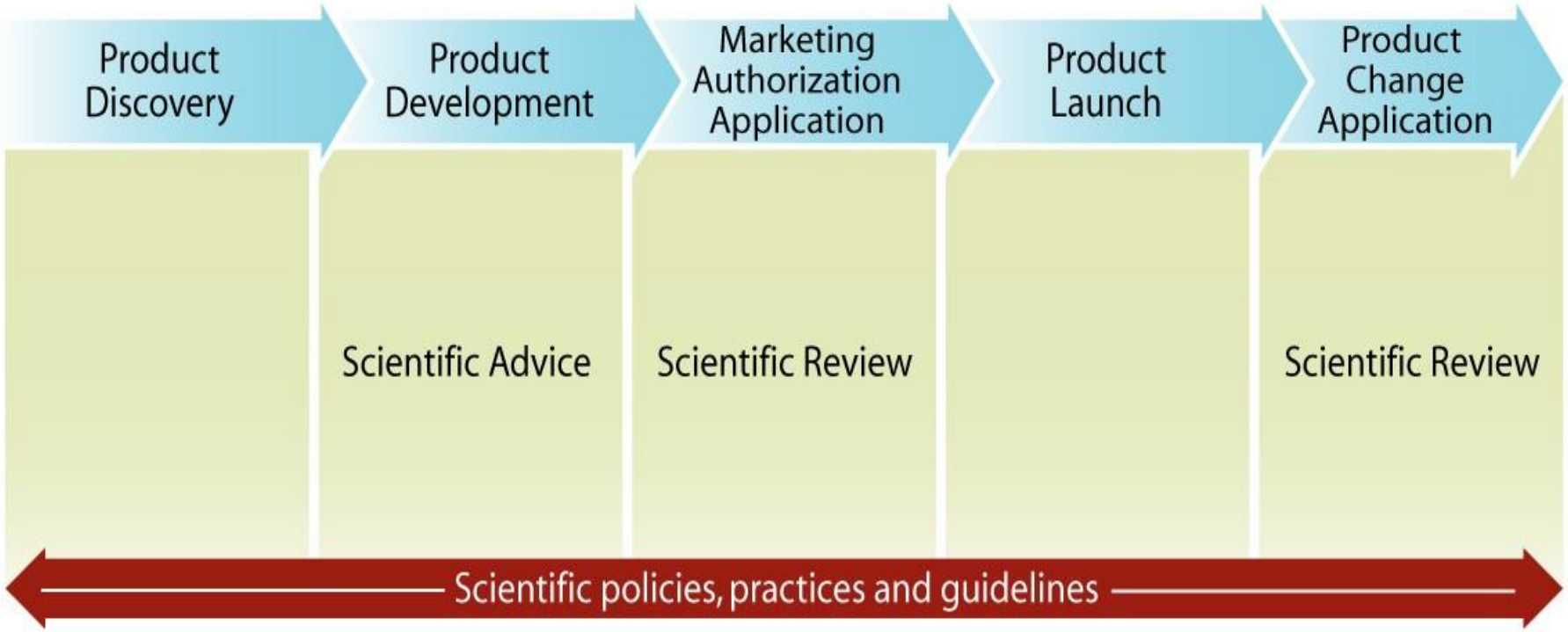
HPFB's Objective

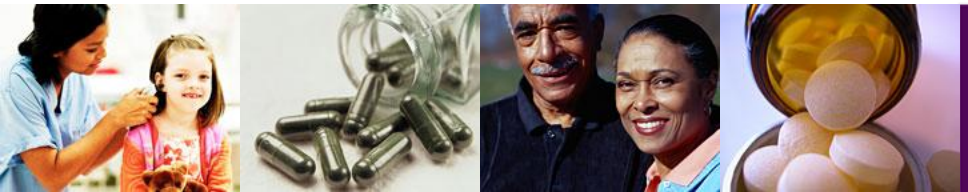
To enhance:

- the robustness of HPFB regulatory assessment
- the efficiency of the review process
- the strategic use of HPFB available resources
- Canadians' timely access to safe, efficacious and high quality health products




Inclusive Scope: Throughout Product Life-Cycle

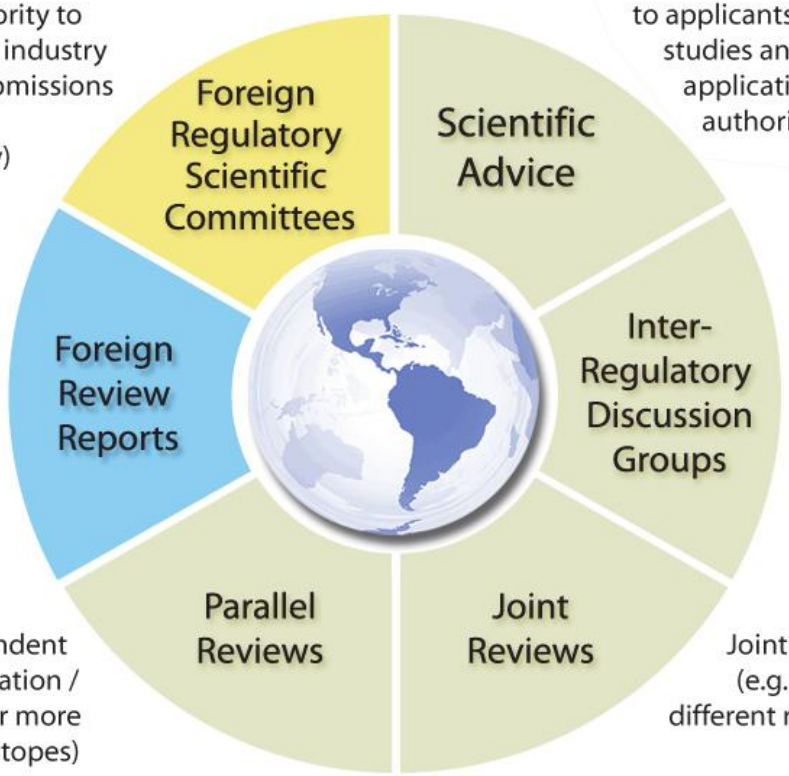




Six Mechanisms to Optimize Access to Foreign Regulatory Information

Foreign Regulatory Scientific Committees are run solely by another regulatory authority to form policies, practices, and guidance for industry on broad issues related applications / submissions for marketing authorization. (e.g. EMA's Vaccine Working Party)

Scientific Advice is regulatory authority assistance to applicants / sponsors regarding the conduct of studies and the proposed content of specific applications or submissions for marketing authorization. (e.g. Protocol Assistance)

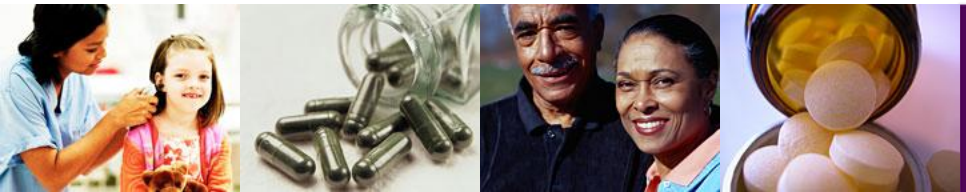


Foreign Reviews are scientific safety, efficacy, and quality reports prepared by foreign regulatory authorities, upon which the decision on marketing authorization are based.

Inter-Regulatory Discussion groups are expert panels run jointly by two or more regulatory authorities. (e.g., HPFB – European Medicines Agency Oncology Panel, H1N1)

Parallel Reviews are separate, independent review conducted on the same application / submission at the same time by two or more regulatory authorities (e.g. Medical Isotopes)

Joint Reviews consist of review sections (e.g. preclinical, clinical) conducted by different regulatory authorities and consolidated at the end of the process.



MOU Confidentially Arrangements

Work Sharing

MRA

Information Sharing

Real-time Scientific Regulatory Discussions

Parallel Reviews

Joint Reviews

Sharing of Safety Information

Harmonization

Joint Inspections

Mutual Acceptance of GMP Certificates

Standard Setting (CODEX, ISO)

Development of Technical requirements (ICH,VICH,GHTF)

Use of Foreign Reviews

No use of FR

Review supplemented by FR

Review based principally on FR

Decision based on FR

Methods

Approach to the Use of Foreign Reviews – in a nutshell

- Applies to all health products regulated by HPFB (except NHPs)
- Final regulatory decisions to grant or refuse to grant market authorization must be made by the Minister of Health
- Extent of use will vary: foreign review may be used for the review of the entire Canadian application / submission or for (a) component (s) of the application / submission
- 4 methods for the use of foreign review are being proposed. Different methods may be used for different components of the Canadian application / submission.
- Extent to which a foreign review may be used should be guided by the an estimation of benefit and the risk of using a foreign review




Use of Foreign Reviews: Key Challenges

- Availability and suitability of foreign review reports
- Potential delays in review process
- Industry willingness to provide foreign review reports
- Differences between products reviewed by foreign regulatory authorities and the products proposed for the Canadian market
- Manage high expectations concerning efficiency gains and reduction in submission review times
- Public perceptions
- Staff buy-in; cultural change management




In Conclusion

- International regulatory cooperation has become an essential part of dealing effectively with the challenges of an increasingly complex and global environment
- Cooperation should lead to tangible, meaningful results
- Despite challenges, some encouraging developments and trends taking place
- Maximum benefit will come from more strategic discussions, planning and action