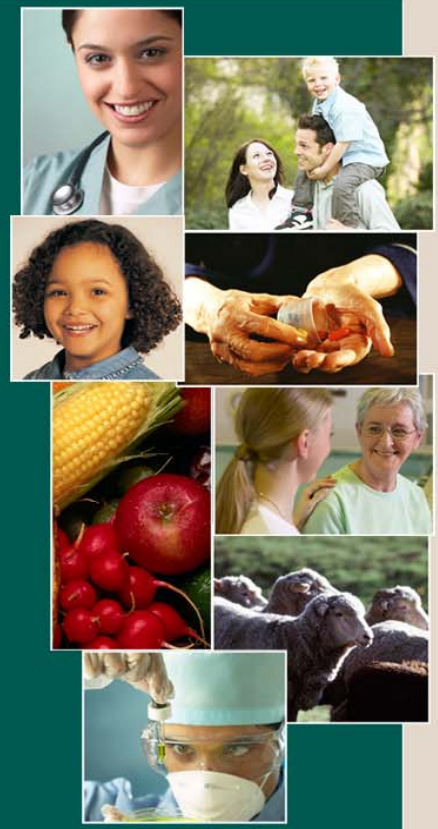
Health Products and Food Branch

Your Health and Safety - Our Priority



Progressive Licensing and the Modernization of the Canadian Regulatory Framework

Workshop on Implementation of ICH Quality Guidelines

Beijing, China 3-5 December, 2008

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DISCLAIMER

- *Disclaimer: the information within*
- *this presentation is based on the*
- *presenter's expertise and*
- *experience, and represents the*
- *views of the presenter for the*
- *purposes of a training workshop*

A Word on Regulation

- Regulators are entrusted to protect and promote public health
- Regulators are also on the drug development/access critical path
- The effectiveness of a regulatory authority in fulfilling its mandate is critical to the achievement of desired public health outcomes
- This in turn depends in large part on the adequacy of the legal framework within which a regulator must operate

A Word on Regulation (2)

- Laws and regulations should:
  - Provide regulators with the necessary authorities and tools to carry out their mandate
  - Define conditions to be met
  - Define prohibitions
  - Provide sufficient flexibility to deal with new or evolving practices and science
  - Take into consideration international norms and best practices

A Word on Regulation (3)

- Laws and regulations should not:
  - Pose unnecessary burden on those regulated
  - Become a barrier to access, innovation and trade

Guidances

- Devil in the details: regulatory expectations for the most part defined at level below laws and regulations, through policies, guidances and procedures
- Laws are regulations define the "what", guidances and procedures the "how" to comply
- Guidances:
  - Not legally binding: alternate approaches may be acceptable if scientifically justified
  - Provide two way flexibility
  - Easier to change than laws and regulations
  - Cannot override or contradict laws and regulations

ICH Product Life Cycle

ICH | **Regulatory Authority**

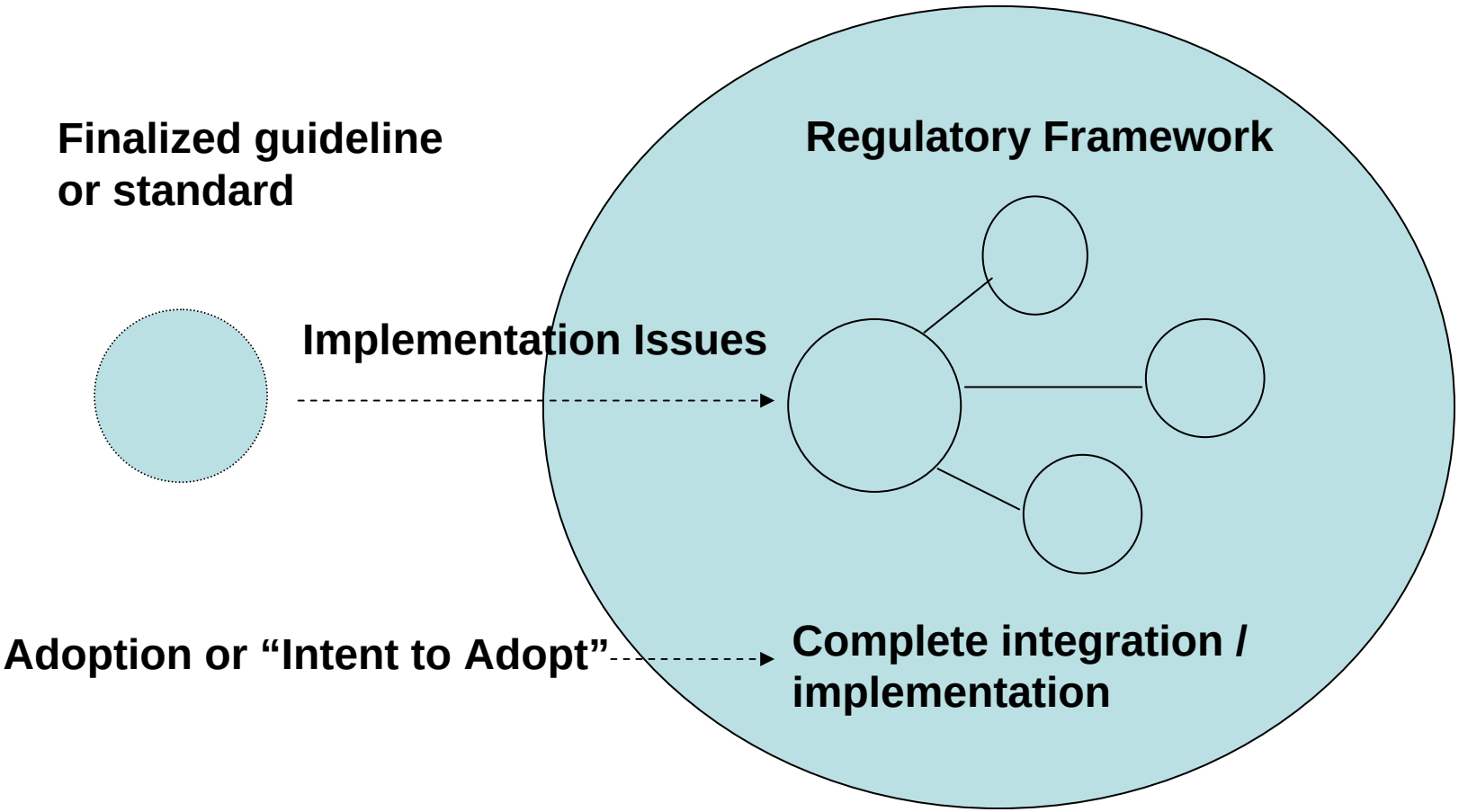
ICH Process:

Steps 1-3 → **Step 4** → **Step 5**

Concept Paper — **Draft for Comment** — **Finalize** — **Adopt** — **Implement**

Implementation Issues

Adoption versus Implementation



Implementation Considerations

- Regulatory implications
- Collateral policy/guidance work
- Scope/phase-in considerations
- Readiness of those regulated
- Training requirements
- Skill sets – right people?
- System/infrastructure requirements
- Organizational/mandate issues
- Inherent complexity of product
- Translation: equivalent terms/concept?
- Resources

….in other words, true, consistent implementation of a guideline represents much more than its publication

Regulating Drugs in Canada: The Need for Change

- Current framework governing regulation of pharmaceuticals over 40 years old
- Represents patchwork of amendments over time, resulting in systems of regulations that do not work well together
- Current framework also reflects outdated approaches and concepts, including "point in time" regulation of products
- Recognition that comprehensive modernisation of legislation was needed to deal with both current and anticipated needs of the regulatory system
- New Bill (C-51) introduced in Parliament in Spring of 2008: proposes sweeping changes to the Canadian *Food and Drugs Act*

Modernization of Food and Drugs Act

- Modernization initiative embodies concepts established under "Progressive Licensing" project
- Three objectives have in turn guided the design of the Progressive Licensing framework:
  - Alignment with the system of health care in Canada to achieve positive health outcomes
  - Ensure new regulatory structure enables Health Canada to implement best international regulatory practices and maintain appropriate oversight without unduly increasing regulatory burden
  - Encourage and make best use of evolutions in the science of drug development and regulation

Good Time to Modernize

- Take advantage of
  - Review of recent and ongoing legislative changes in the EU and US
  - Extensive consultations with stakeholders on Progressive Licensing concepts
  - International developments, notably
    - Evolving science and practices (pharmacogenomics, adaptive trial designs, Benefit/Risk initiatives, etc.)
    - Key ICH guidances and standards that provide tools for newer, more modern approaches to drug development and regulation (such as E2E and Q8,9,10 suite of Quality guidances)
    - Growing number of arrangements with key regulatory counterparts and international organizations

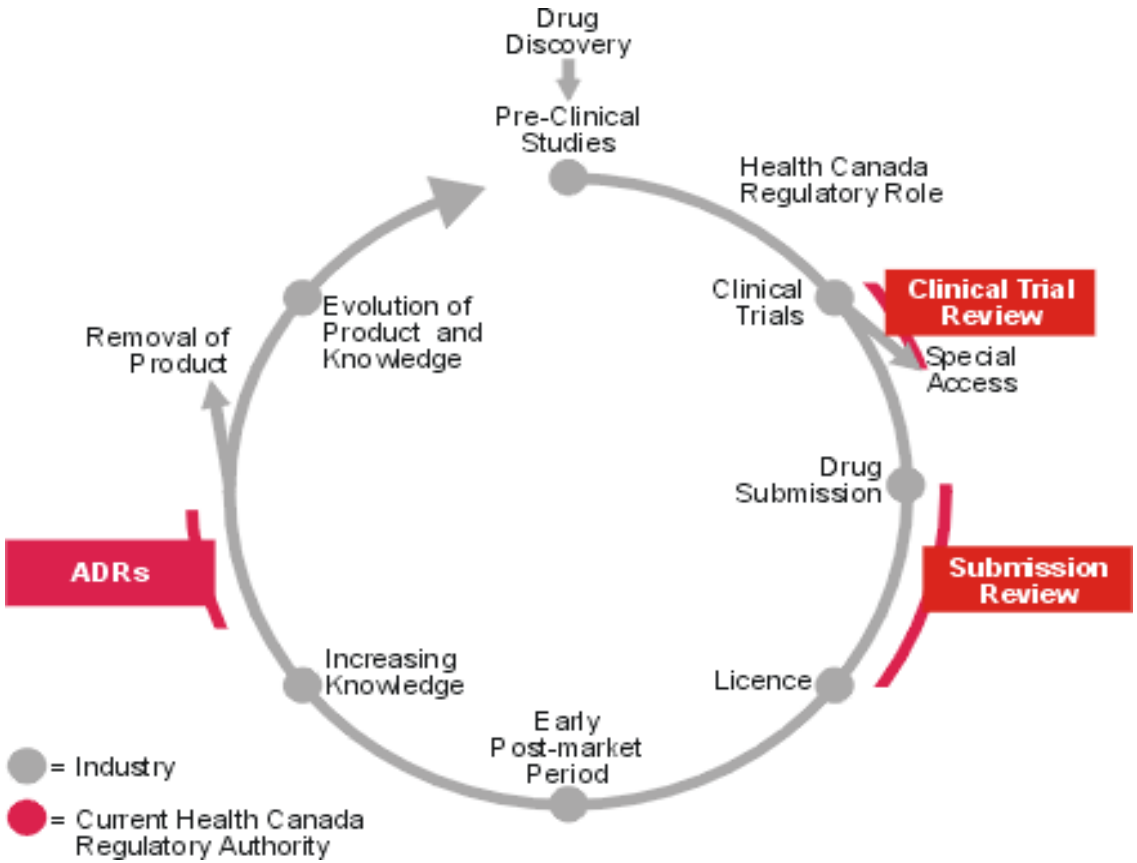
What is "Progressive Licensing"?

- "Progressive" as recognizes that there is an ongoing progression of knowledge about a medicinal product over time, from initial research through development, marketing and eventual product removal
- As a consequence, benefit/risk assessment is not static and should also be assessed throughout product life cycle
- Represents a fundamental shift traditional "point-in time" model
- Progressive Licensing also provides conceptually for alternate licensing models that consider broader B/R factors and Health Care needs

Progressive Licensing – a Vision for the Future

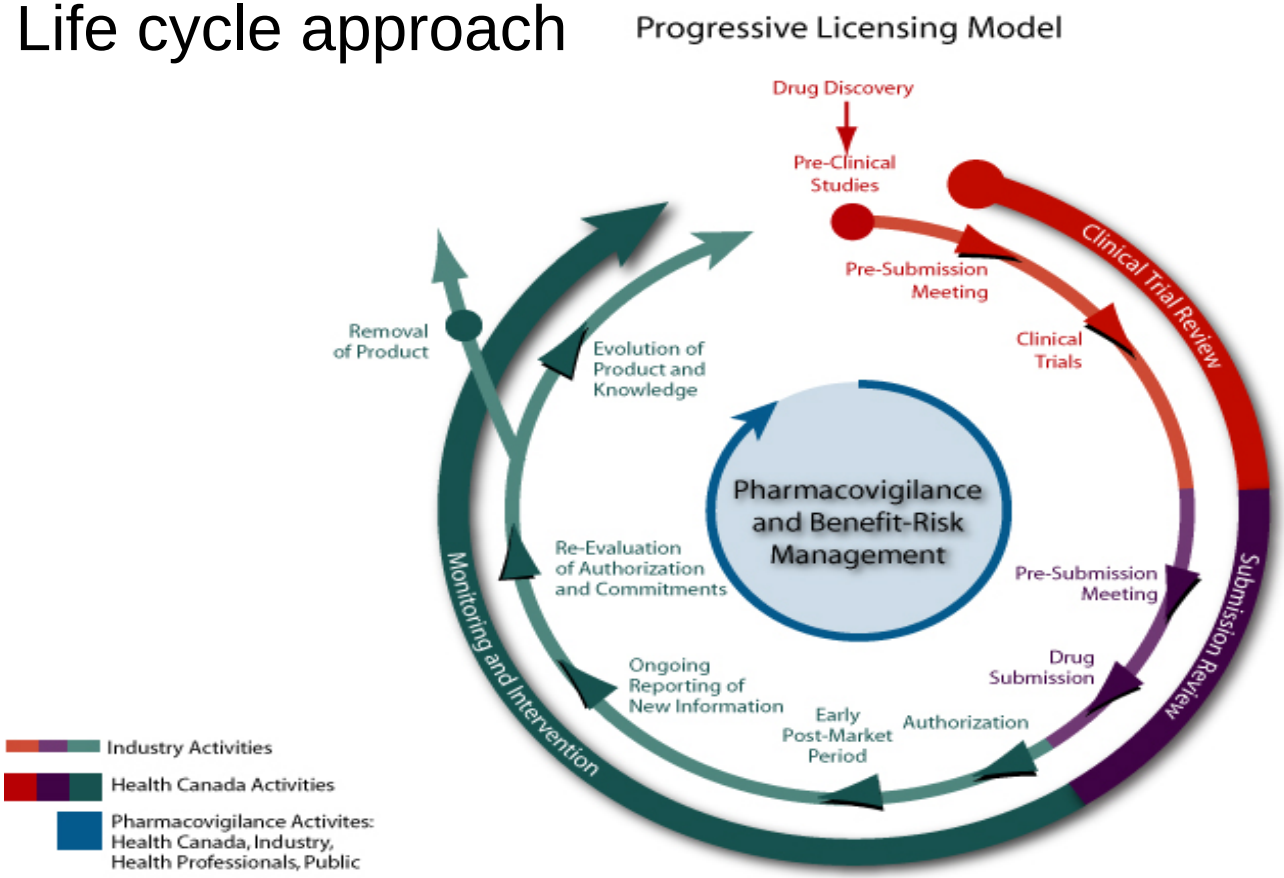
- Key elements of the Progressive Licensing Framework have been tested with stakeholders:
  - Life-cycle approach
  - Evidence-based
  - Good planning
  - Accountability

Current Point-in-Time Process



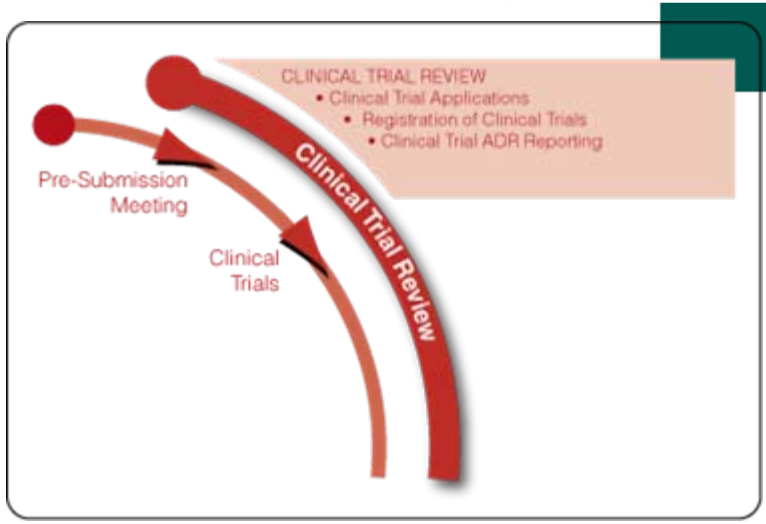
Progressive Licensing Model

Life cycle approach



Highlights

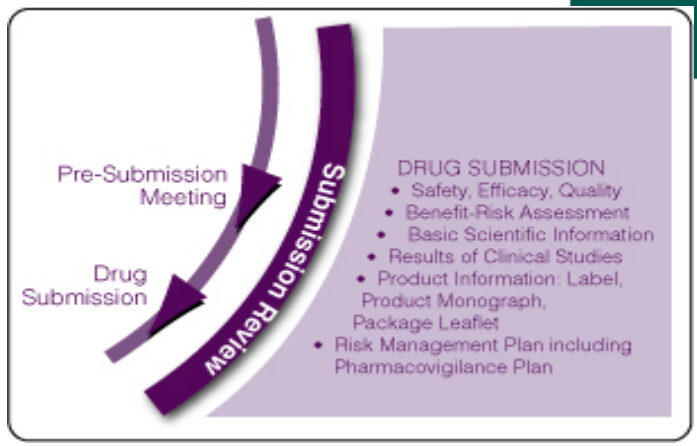
Pre-submission Meetings:



- Not required for every drug
- Could be relied upon subject to amendment only where the science underpinning the advice has demonstrably changed

Highlights

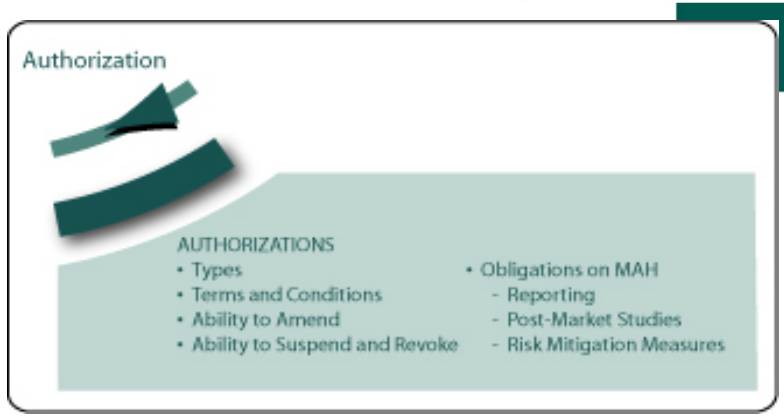
Submission Requirements:



- Will vary across drug lines (eg. Rx, non-Rx)
- Information necessary to establish a favourable benefit-risk profile
- New requirements can include risk management plans, including pharmacovigilance plans
- Also new requirements to publicly register any clinical trial relied upon in a drug submission

Highlights

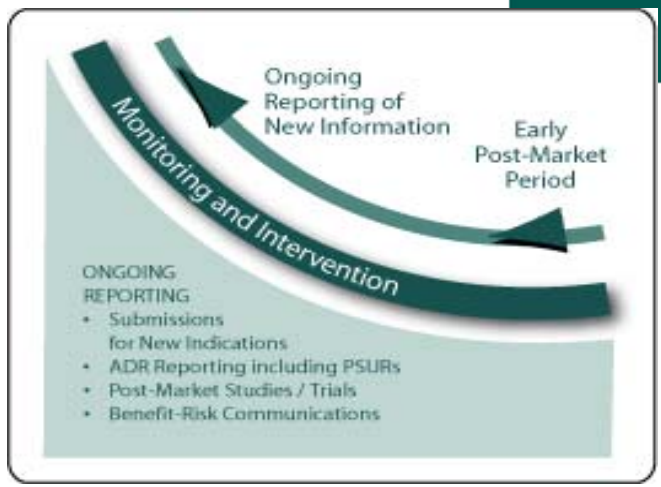
Authorization:



- Demonstration of a favourable benefit-risk profile
- The favourable benefit-risk profile must be maintained throughout the life-cycle of the therapeutic product
- The authorization would be capable of supporting ongoing obligations upon the market authorization holder following the release of the drug into the Canadian market

Highlights

Post-Authorization:



- Obligations for filing of safety reports, active surveillance, post-market studies would be assigned within the authorization.
- Obligations could be amended, depending upon benefit risk profile of the drug.

Highlights

Re-evaluation:

- Not for all drugs only where necessary based upon risk or nature of drug
- Period determined based upon drug, and would be identified as an obligation within the authorization
- Extent of re-assessment would similarly be based upon the drug and specified within the authorization

How Does This Relate to a New Quality Paradigm and Why is Regulatory Oversight Necessary?

- Starting with the second question:
  - Quality equally important to achieving drug's intended effect as the drug's inherent safety and efficacy
  - Case for regulatory oversight: end user cannot independently judge drug's quality, as past tragedies attest
  - Issue is ***how*** best to ensure quality

Link to Progressive Licensing

- Quality an essential element of pharmaceutical regulation and of Progressive Licensing
- Newer ICH Quality concepts align well with Progressive Licensing themes

Life Cycle Management

- Knowledge gained over life-cycle allows for process and product improvement
- Quality by Design (QbD), risk management and quality system important enablers to achieving enhanced confidence in consistent product quality – and regulatory flexibility
- Regulatory flexibility also conditional on knowledge transfer - 'telling the critical story'
- Desired change will also require common understanding and better coordination between reviewers and inspectors

Good Planning

- Planning essential element of QbD:

  "Deliberative design effort from product conception through commercialization" (M. Nasr, FDA, 2007)

- Drug quality considerations form part of proposed life-cycle management plan
- Importance of early communication:
  - Provides regulator with a better understanding of proposed strategy
  - Reduces risk of comments at submission evaluation stage

Accountability

- Responsibility for producing drugs of suitable quality ultimately rests with industry
- Demonstration of enhanced product and process knowledge, combined with implementation of a effective quality management system, makes possible greater shift in 'ownership' of post-approval changes to industry
- ***Not de-regulation*** – same obligation to comply with regulatory requirements

Accountability (2)

- Health Canada also accountable to Canadians by virtue of regulatory mandate
- Accordingly, risk management and quality systems should also be hallmark of a modern regulator, thereby enabling sound decision-making, use of resources and continual improvement

Build upon Best Practices

- Submission review:
  - Long-established request to file pharmaceutical development information
  - Use of QOS as review template; CPID as basis for documenting 'regulatory agreement'
- Leveraging international cooperation:
  - Effective use of MRAs, PIC/S
  - Contribution and adherence to ICH guidances
  - Recent MOU with EDQM
- Risked-based approach to lot release (biologics)

Elements of A Desired State

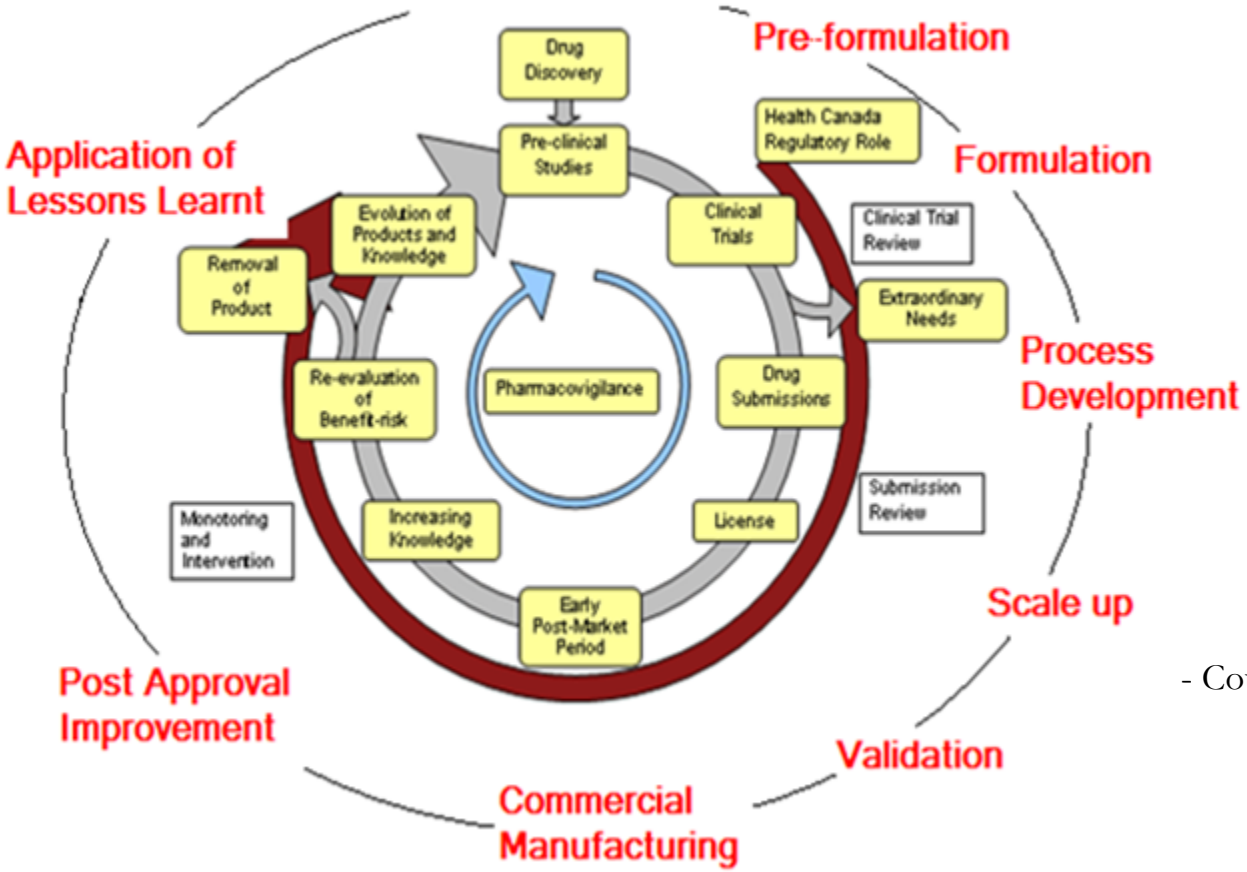
- Manufacturers (and regulators) have extensive knowledge about critical product and process parameters and quality attributes
- Manufacturers strive for continuous improvement
- Regulator's role:
  - initial verification, subsequent audit
  - creating a regulatory environment conducive to innovation, continuous improvement…and ultimately, access to high quality medicines

- adapted from various FDA presentations

Elements of a Desired State (2)

- Regulatory oversight commensurate with risk and product knowledge
- Effective internal, national and international cooperation

Quality Framework within Progressive Licensing



- Courtesy K. Tirunellai

Conclusion

- A well designed, flexible and modern regulatory framework is essential to meeting the current and future regulatory challenges and opportunities
- Progressive Licensing concepts form foundation of Health Canada's legislative and regulatory modernization efforts
- PL concepts aligned with new ICH Quality paradigm and QbD, risk management and continuous improvement principles
- Together, will encourage a more science and risk based approach to the regulation of pharmaceutical quality over the product life cycle

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THANK YOU!