Current Issues with Nanomedicines in Canada

1st INTERNATIONAL WORKSHOP ON NANOMEDICINES
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Overview

- Regulatory Framework for Approval of Therapeutic Products
- Policy Initiatives for Nanotechnology
- Current Status

Regulatory Framework

Food and Drugs Act

"Drug" includes any substance or mixture of substances manufactured, sold or represented for use in:

- The diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms in human beings or animals
- Restoring, correcting or modifying organic functions in human beings or animals or
- Disinfection in premises in which food is manufactured, prepared or kept

Food and Drugs Act

Authority to make regulations respecting:

- The sale or the conditions of sale of any food, drug, cosmetic or device
- The use of any substance as an ingredient in any food, drug, cosmetic or device

To prevent the purchaser or consumer thereof from being deceived or misled in respect to the design, construction, performance, intended use, quantity, character, value, composition, merit or safety thereof, or to prevent injury to the health of the purchaser or consumer

Food and Drug Regulations

New Drugs:

Manufacturer must provide sufficient information and material to enable the Minister to assess the safety and effectiveness, including:

- Details of the method of manufacture and the controls to be used in the manufacture, preparation and packaging of the new drug
- Details of the tests to be applied to control the potency, purity, stability and safety of the new drug
- Detailed reports of the tests made to establish the safety of the new drug for the purpose and under the conditions of use recommended
- Substantial evidence of the clinical effectiveness of the new drug for the purpose and under the conditions of use recommended

Clinical Trials

Sponsor must submit the following information:

- The physical, chemical and pharmaceutical properties of the drug
- The pharmacological aspects of the drug, including its metabolites in all animal species tested
- The pharmacokinetics of the drug and the drug metabolism, including the biological transformation of the drug in all animal species tested
- Any toxicological effects in any animal species tested under a single dose study, a repeated dose study or a special study in respect of the drug
- Any results of carcinogenicity studies in any animal species tested in respect to the drug
- Any results of clinical pharmacokinetic studies of the drug
- Any information regarding drug safety, pharmacodynamics, efficacy and dose responses to the drug that were obtained from previous clinical trials in humans
- **The chemistry and manufacturing information in respect of the drug**

Clinical Trials may be refused if:

- The information and documents in respect of the application:
    - are insufficient to enable the Minister to assess the safety and risks of the drug or the clinical trial, or

- Based on an assessment of the application, and under section C.05.009 or a review of any other information, the Minister has reasonable grounds to believe that:
    - the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person
    - the clinical trial is contrary to the best interests of a clinical trial subject, or
    - the objectives of the clinical trial will not be achieved

The Canadian Environmental Protection Act

- Mandates the government to:
  - Exercise its powers in a manner that protects the environment and human health
  - Assess whether existing substances or those new to Canada are toxic or capable of becoming toxic and assess the risk that such substances pose to the environment and human life and health
- Applies to substances manufactured or imported in amounts >1000 kg per year

Policy Initiatives for Nanotechnology

- *Health Portfolio Nanotechnology Working Group:*
  - Representation from all groups within Health Canada regulating products containing nanomaterials

- *Participation in:*
  - Organisation for Economic Co-operation and Development (OECD) Working Party on Manufactured Nanomaterials (WPMN)
  - International Organization for Standardization (ISO) Technical Committee (TC) 229 on Nanotechnologies
  - Tri-National Workshop on Standards for Nanotechnology
  - Canadian Standards Association Working Group on Nanomaterials

- *Interim Policy Statement on Health Canada's Working Definition for Nanomaterials* released for comment February 11, 2010

  (http://www.hc-sc.gc.ca/sr-sr/consult/_2010/nanomater/index-eng.php)

- Center of Expertise (Science, Policy and Research Initiative on Nanotechnology (SPRINT)) launched March 31, 2010

Working Definition of Nanomaterials

Health Canada considers any manufactured product, material, substance, ingredient, device, system or structure to be nanomaterial if:

- It is at, or within, the nanoscale in at least one spatial dimension, or
- It is smaller or larger than the nanoscale in all spatial dimensions and exhibits one or more nanoscale phenomena

For the purposes of this definition:

- The term “nanoscale” means 1 to 100 nanometres, inclusive
- The term “nanoscale phenomena” means properties of the product, material, substance, ingredient, device, system or structure which are attributable to its size and distinguishable from the chemical or physical properties of individual atoms, individual molecules and bulk material
- The term “manufactured” includes engineering processes and control of matter and processes at the nanoscale

Current Status (2010)

10 medicines approved that may contain nanomaterials:

- 2 liposomal encapsulated drugs (*Myocet, Caelyx*)
- 5 albumin/polyethyleneglycol (PEG) bound drugs (*Abraxane*/*Pegasys, Unitron PEG, Neulasta, Somavert*)
- 3 milled products (*Megace, Rapamune, Emend*)

Indications:

- 4 oncology (*Myocet, Caelyx, Abraxane, Emend*)
- 1 immunostimulant (*Neulasta*)
- 1 immunosuppressive (*Rapamune*)
- 2 anti-infective (*Pegasys, Unitron PEG*)
- 1 anorexia (*Megace*)
- 1 growth hormone (*Somavert*)

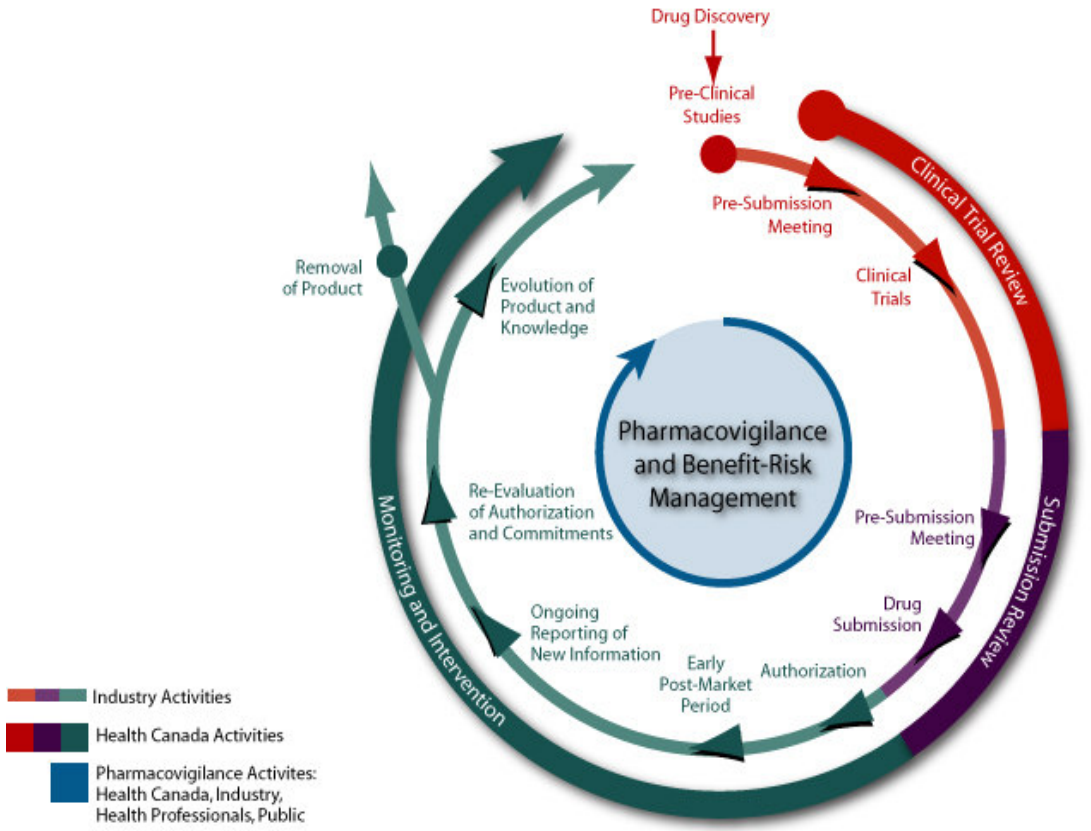
- Currently, approved products and those in clinical trials are nanosize formulations of existing products:
  - most formulations are biodegradable
  - approved within existing regulatory framework

- Requirement for disclosure of nanomaterials on drug submissions, including clinical trial applications (April, 2010)

Challenges

- Limited experience with novel nanotechnology based medicines
- Based on current information, concerns regarding potential toxicity and lack of efficacy
  - heavy metal toxicity of uncoated quantum dots; chronic inflammatory response to carbon tubes
  - poor clearance of coated quantum dots (potential toxicity and potentially limited efficacy as diagnostic agents)
- Limitations for post-market surveillance within the current regulatory framework

Limitations for post-market surveillance being addressed through product life-cycle approach



- Elements of Improved Post-market Surveillance
  - Strengthened labelling requirements
  - Improved adverse reaction reporting
  - Use of strategies to manage and mitigate risk

- Applicable to all therapeutic products