# Bill C-51

- Impact on Pharmaceutical Industry in Canada

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# Approach to the Food and Drugs Act

- The Progressive Licensing Framework (PLF)
  - was developed as a strategy for the modernization of the existing framework for the regulation of drugs, the bulk of which is set out in the Food and Drug Regulations
- It was decided that the Food and Drugs Act would be modernized before the Food and Drug Regulations
  - with an understanding that the great majority of the PLF would be implemented through the Food and Drug Regulations.
- It is necessary to modernize the Food and Drugs Act to accommodate changes to the Food and Drug Regulations that will be required to implement the PLF.

# Title

- Food and Drugs Act becomes “An Act Respecting Foods, Therapeutic Products and Cosmetics”

# Definitions

- Contraceptive device folded under definition of device
- “Lease” is added to the concept of sell
- Disinfectants remains in the definition of drugs
  - Now would have been the time to remove it to be consistent with international standards.
- Clinical trial is added to the Act
  - Was formerly regulated at the level of Regulation
- Definition of “Confidential Business Information” is added
- Concept of a “Controlled Activity” and “Designated Therapeutic Product” has been added
- Definition of “Therapeutic Product” has been added

# Definitions

- Amend the definition of “device” by removing the words “but does not include a drug”
- The purpose of this amendment was to ensure that the definition of the term “device” does not exclude drugs, thus allowing for the possibility of regulating drug-device combination products mainly as devices under the Medical Devices Regulations or mainly as drugs under the Food and Drug Regulations.

# Definitions - Labels

- Product Monographs
  - 2.1 indicates that for the purposes of the Act, product monographs are considered to be a label.

# Definition – Therapeutic Product

- 1953 – Food and Drugs Act defined Foods, Drugs, Cosmetics and Devices
- 2004 – Natural Health Products were defined as Drugs under the Act and Natural Health Product Regulations set up to cover.
- 2004 – Safety of Human Cells, Tissues and Organs for Transplantation Regulations issued. These products were defined as drugs.

# Definition – Therapeutic Product

- What do you call a cardiac valve from a pig transplanted into a human? A drug? A device?
- What do you call a product administered to human cells outside the body and then have the modified cells readministered to the patient?
- What do you call a solution in which a kidney is pefused before being transplanted?

- The language of 1953 is not applicable to the needs and technology of 2008.

# Definition – Therapeutic Product

- Regulatory agencies in general are moving toward the use of the term “therapeutic product”.
  - Australia – Therapeutic Goods Agency
  - US – many guidelines refer to “therapeutic products”
  - TPD – Therapeutic Products Directorate

# Definition – Therapeutic Products

- Therapeutic product means
  - A drug
  - A device
  - Cells, tissues or organs that are distributed 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, or
    - Restoring, correcting or modifying the body structure of human beings or animals or the functioning of parts of the bodies of human beings or animals, or
  - A combination of two or more of the [the above]

# Therapeutic Product - Definition

- What does this mean for industry?
  - NHPs are clearly defined as therapeutic products.
    - They have always been drugs.
      - They are still regulated by the NHP Regulations.
      - They are still handled by the NHPD.
    - Now is the appropriate time to request a separate designation for Natural Health Products.
  - Medical Devices and Drugs remain therapeutic products
  - Cells, organs and tissues are clearly determined to be therapeutic products and are subject to this Act.
    - They are still regulated by the CTO Regulations
    - The pathway is opened for broader regulation of these products.

# Therapeutic Product

- Schedule D that defines a biologic is retracted.
- How will companies or regulators know what a biologic is?
- Is the intent to not have separate requirements for biologics?

# Designated Therapeutic Products

- The intent is that designated therapeutic products would include products that do not require a market authorization (i.e., cells, tissues and organs)
- These products may have to be distributed by organizations that hold an Establishment License.

# Definition – Clinical Trials

- Clinical trials were never defined in the Food and Drugs Act before.
- They are now very clearly defined, including bioavailability or bioequivalence studies.
  - There is an indication that these trials have to be done under a Clinical Trial Authorization
    - The Regulations (Drug, Medical Device, NHP, or CTO) would then define what that Authorization was and the process for getting it.

# Definition – Clinical Trial

- Clinical Trial means
  - An investigation in respect of a therapeutic product for use in human beings that involves human subjects and that is intended to discover or verify the therapeutic product's clinical, pharmacological or pharmacodynamic effects, to identify adverse events in respect of the therapeutic product, to study the absorption, distribution, metabolism or excretion of the therapeutic product or to ascertain its safety or efficacy.
  - An investigation in respect of a drug for use in animals that produce food, that are intended for consumption as food or in which the use of the drug could affect human health.

# Controlled Activity

- "Controlled activity" means
  - In relation to a therapeutic product – manufacturing, collecting, processing, preserving, labelling, packaging, importing for sale, distributing, wholesaling or testing, and
  - In relation to a designated therapeutic product – manufacturing, collecting, processing, preserving, labelling, packaging, importing, distributing or testing.
- 13 – no person shall conduct a controlled activity unless they are authorized by an establishment licence to do so.
  - The controlled activities described above for clinical trials will require an Establishment Licence. This is far broader than the current number of companies who require an Establishment Licence.

# Controlled Activity and Clinical Trials

- ELs are not currently required for clinical trials, but it is necessary to do most of these activities for clinical trials.
- Currently clinical trial material can be sent from the US into Canada with the investigator serving as the importer.
- If this change is made, only companies with an EL will be able to import clinical trial material.
- Companies who are not yet at the stage of marketing will need to procure an EL.
- This is not necessary and will be detrimental to the number of clinical trials done in Canada, particularly those at Phase I and II.

# Importation of Clinical Trial Materials

- 12(2)(a) states that clinical trial material can be imported if the importation is for the purpose of a clinical trial **to which the authorization relates.**
- This means that a company cannot import clinical trial material until they have the authorization for the clinical trial.
- Clinical trial materials are complex to package and label.
- Having to do this after the authorization adds 60-90 days to the trial.
- This regulation is forcing this activity to be done outside of Canada and is not in the interest of Canadians.

# Importation of Therapeutic Products

- 12(1) states that no person shall advertise, sell or **import for sale** a therapeutic product that does not have a market authorization.
- When preparing to launch a product, it is frequently necessary to import a drug for packaging and release prior to the NOC issuing.
- It is unclear what “import for sale” means.
- It should be clear that importing for the purpose of preparing the product for sale is allowable.
- Recommendation: 12.(2) be re-written as: “A person does not contravene subsection (1) if they import the drug in preparation for the launch of a product after the marketing authorization has been granted.

# Prohibitions

- General
  - False or misleading information [Section 3]
  - Tampering [Section 3.1(1)]
  - Hoaxes (scare tactics about a product) [Section 3.2]

# Prohibitions

- Therapeutic Products
  - Adulterated products [Section 8]
  - Unsanitary conditions [Section 9]
  - No clinical trial without authorization [Section 10]
  - No clinical trial contrary to regulations [Section 11]
  - Selling, advertising and importing without a marketing authorization [Section 12]
  - Conducting controlled activity without an Establishment License [Section 13]
  - Deception, etc [Section 14]
  - Counterfeiting [Section 15]
  - Sale of prescription therapeutic products to non-authorized individuals [Section 15.1]
  - **Samples of drugs only to practitioners [Section 15.2]**

# Prohibitions - Samples

- Under the new Act, samples of drugs could only be distributed to practitioners.
  - Nonprescription drugs and natural health products should be able to be sampled to potential users.
    - Toothpaste with fluoride
    - Two cough lozenges
- Recommendation: no person shall distribute or cause to be distributed a **prescription** drug as a sample.

# Authorizations and Licences

- Purpose
  - To provide a mechanism through which Health Canada can regulate a range of therapeutic products with the ability to tailor the appropriate amount of continued regulatory oversight to the nature and risk of the product
  - The authorization is the primary vehicle for achieving and maintaining the integration and flexibility which underlies the PLF.

# Clinical Trial Authorizations
## Sections 18.2, 18.3, 18.4, 18.5, 18.6

- A clinical trial authorization would be required for the investigational use of therapeutic products that have not been marketed in Canada.
- Clinical trial authorizations could be amended, suspended or revoked for therapeutic products.
- Terms and conditions could be imposed on such authorizations, e.g., CT registration
- Holders or former holders of clinical trial authorizations would be required to continue to report information about a therapeutic product to Health Canada following the discontinuance or concellation of a clinical trial.

# Market Authorizations
## Sections 18.7, 18.8, 18.9, 19, 19.1

- A market authorization (note not NOC) would be required to sell, advertise or import a therapeutic product.
- Market authorizations would be issued on the basis of a favourable benefit-risk profile, and could be subject to specific terms and conditions.
- Market authorizations could be amended, suspended or revoked.
- Market authorization holders could be required to conduct a reassessment of the therapeutic product to which the authorization relates.
- Holders could be required to compile information, conduct studies and monitor experience in relation to therapeutic products and to report information, the results of tests or studies, and monitoring to Health Canada.

# Establishment Licenses
## Sections 19.2, 19.3, 19.4, 19.5, 19.6, 19.7

- An establishment licence would be required to manufacture, package, label, store, wholesale or import for sale a therapeutic product.
- It would be prohibited to sell a therapeutic product that was manufactured, packaged, labelled, stored, wholesaled or imported for sale in an unsanitary or unsafe manner.
- ELs could be amended, suspended or revoked.
- Terms and conditions could be imposed on such licences
- Specific information regarding establishment would be included in a registry.

# Powers of the Minister

- Power to require information [Section 19.8]
- Power to require tests or studies, etc [Section 19.9]
- Power to require information after discontinuance or revocation of clinical trials authorization [Section 20]
- Power to require labels to be revised [Section 20.1]
- Power to require reassessment [Section 20.2]
- Power to disclose risk information [Section 20.3]

# Information

- Required information – serious risk [Section 20.5]
- Required Information – Health Care Institutions [Section 20.7]
  - Prescribed health care institutions would be required to report to Health Canada adverse reactions associated with therapeutic products of individuals who receive medical treatment from them.
  - Mandatory ADR reporting on institutions only.
- Register [Section 20.8]
  - A publicly available register would be created that will contain information about therapeutic products, such as market authorizations and product labels. (DPD-like list]

# Mandatory ADR Reporting for Institutions

- It is not necessary for all adverse reactions to therapeutic products to be reported.
  - The requirement, if enacted, should be restricted to serious, unexpected and possibly related adverse reactions.

# Example of What PLF Might Mean

- For drugs labelled for use in pregnancy a more structured approach to the provision of data throughout the life-cycle of the drug could be undertaking
  - Post marketing commitments
  - Pharmacovigilance and risk management plans to determine whether the benefits of the drug continue to outweigh its risks as more knowledge is gained about the drug in real world use.

# Example of What PLF Might Mean

- Should drugs authorized for use in pregnancy be submitted to a re-evaluation process at a specified period of time? If so, what specifications do you suggest and why?
- Should Health Canada draw from a committee of external experts in matters of pregnancy in order to develop regulatory guidances in this area?

# What PLF Could Mean

- Enhanced **post-market surveillance** for drugs used in pregnancy, with re-evaluation at a defined point in time.
- **Pharmacovigilance plans and risk management plans** to be submitted by manufacturers for drugs intended for use in pregnancy.
- **Post marketing surveillance programs** (i.e., prospective with control group) at time of approval
  - Monitor for pregnancy outcomes and teratology (minor and major and behavioural and cognitive outcomes).
  - Follow-up period could start from birth and extend for an appropriate period.
- Establishment of **pregnancy registries**.

# What PLF Could Mean

- Should Health Canada consider adopting a system of pregnancy registries? Would this result in better risk management, in earlier detection of signals, and in a reduction of preventable birth defects? How could this system not only help detect maternal adverse side effects but also measure fetal outcomes?
- How might manufacturers and other stakeholders be encouraged to work together, as well as with health professionals and their organizations, patient groups, and medical societies to endorse and assist in the conduct of pregnancy exposure registries, thereby facilitating patient recruitment?

# What PLF Could Mean

- What would be some of the challenges of implementation? How can issues pertaining to privacy and ethics best be addressed in pregnancy exposure registries?
- Should Health Canada have the authority to request and enforce pregnancy registries and post-marketing studies from drug manufacturers for prescription drugs labelled for use in pregnancy?
- Should post-marketing programs be mandatory for all prescription drugs authorized for use in pregnancy?

# Summary

- Life cycle management of pharmaceutical products, natural health products and devices is coming.
- Bill C51 is an attempt to set the platform for changing the regulations.
- The regulations will be modified bit by bit.
- Separate regulations for drugs, devices, natural health products and Cells/Organs/Tissues will continue.
- The cost to market products in Canada will be higher.
- Payers are likely to be involved in the decision making process about what post-marketing studies should be required and when products should be approved.