Data Protection in Canada:

Strategic Considerations for Protecting Exclusivity of Innovative Drugs

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Agenda

1. Basic Principles
2. Why is data protection important?
3. Data Protection
    a) Background – History
    b) Current laws & cases

Basic Principles

Purpose of Data Protection

- If a manufacturer of an innovative drug (pharmaceutical, biological and radiopharmaceutical) or agricultural product submits undisclosed tests/data as a condition to determine the safety and effectiveness for approval, this data should be protected against unfair commercial use for a reasonable period of time.
- Principles embodied in international agreements and legislation.

Why is Data Protection Relevant to Protecting Exclusivity in Canada?

- Patent life may be near exhaustion by the time NOC issued
- Patent may be invalid
- Biologics:
  - Process patent cannot be listed on Canada's Patent Register.
  - If you wait to sue for patent infringement, left looking for remedy after subsequent manufacturer on market.

Why is Data Protection Relevant to Protecting Exclusivity in Canada?

- US has patent term extension for pediatric studies:
  - No equivalent extension under Canada's *Patent Act.*
  - Use Canada's data protection provisions on pediatric studies for added exclusivity (6 months).

Background to Data Protection:

International Agreements & Legislation

- Data protection first introduced to ensure Canada's compliance with:
  1. **NAFTA**, Articles 1711(5) and (6) – Protection for not less than 5 years.
  2. **TRIPS** Agreement of the WTO, Article 39.

Background to Data Protection

Canada's Data Protection – First Try

- C.08.004.1 *Food and Drug Regulations* ("*FDR*"), enacted June 9, 1995:
  - 5 years from date of first NOC or approval to market.
- *Bayer Inc. v. Canada (Attorney General)* (1998)
  - Protection only triggered when innovator's information directly relied on to approve second-entry product.
  - But HC does not consult original NDS data as part of review, nor implied examination required.
  - No direct reliance = No data protection.

Background to Data Protection: Historical View

Result of *Bayer* Decision

- Prior to the enactment of 2006 *DPR*, only impediment to a generic drug manufacturer was unexpired patent listed on the Patent Register.

Data Protection: Present Laws

- C.08.004.1 amended October 5, 2006 and replaced with new wording.
- Manufacturer introducing a drug containing a new medicinal ingredient not previously approved by HC entitled to 8 year period of exclusivity.

Term of Protection

- 8 year exclusivity has two parts:
  1) Period of "data exclusivity" – Subsequent manufacturer cannot file submission for first 6 years of the 8 year period. Submission on "data protection hold".
  2) Period of "market exclusivity" - Minister cannot issue NOC to a subsequent manufacturer for 8 years.
- 6-month extension for pediatric data
- Period runs from date of first NOC

Constitutionality Challenged

CGPA v. Canada (Min of Health & AG) (2009)

- *DPR* constitutionality challenged by Apotex and the CGPA, with Eli Lilly and Rx&D as intervenors.
  - Result: FC upheld the *DPR*.
  - *DPR* constitutes a valid exercise of the federal trade and commerce power (ss. 91(2) of the *Constitution Act)*.
- Decision appealed to the FCA.
  - Result: FCA (2010) upheld the *DPR*.
  - *DPR* constitutes a valid exercise of the federal criminal law power (ss. 91(27) of the *Constitution Act*).

“Innovative Drug”

What is an “innovative drug” for the purpose of data protection?

- *"a drug that contains a medicinal ingredient not previously approved in a drug by the Minister and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, or polymorph".*

“Innovative Drug”

- Definition excludes variations of a previously approved medicinal ingredient.
- Variations not included in the list (e.g. metabolites or prodrugs) will be assessed on a case-by-case basis.
  - Primary consideration is whether approval is sought primarily on the basis of previously submitted clinical data.
  - A variation supported by pivotal clinic trials will likely be deemed innovative.

“Innovative Drug”

- Variations allowed by the Minister:
  - desvenlafaxine succinate (venlafaxine HCl).
    - A metabolite of venlafaxine.
  - fluticasone furoate (fluticasone propionate).
    - An ester of fluticasone.
  - methylnaltrexone bromide (naltrexone HCl).
    - Methylated naltrexone.
  - methoxy polyethylene gycol epoetin beta (epoetin beta).
    - Pegylated EPO.

"Innovative Drug"

Epicept Corporation v. Canada (Min of Health) (2010)

- EpiCept filed NDS for CEPLENE (histamine dihydrochloride).
- OPML denied request to designate as innovative drug. Reasons:
  - HIST and HIST dihydrochloride previously received DINs and had been approved in several drugs HC.
  - Def'n of "innovative drug" contemplates that medicinal ingredients not previously approved in "any drug" and not just those drugs that receive an NOC.

“Innovative Drug”

- OPML’s reasons (Cont’d):
  - NDS contained new clinical data & use is unrelated to the uses previously approved, but nature or extent of the data only relevant where it is unclear as to whether the drug meets the definition of “innovative drug”.
- EpiCept applied to the FC for judicial review.
- The FC agreed with HC and held that:
  - The *Regulations* are intended to protect NCEs, and not all “new drugs” are NCEs.
  - Court equated an “innovative drug” with a NCE.

“Innovative Drug”

- FC proposed 2-step process for the Minister when assessing eligibility for data protection:

    1. Minister must consider whether the data concerns a “NCE”.

    2. If so, then consider whether the data is undisclosed and if other data is necessary to determine safety and effectiveness.

- Here, the medicinal ingredient was an old ingredient, and CEPLENE was not an NCE.

Combination Drugs

- New combinations of previously approved medicinal ingredients are **not eligible** for an additional data protection period.
- Where at least one of the ingredients is an innovative drug for which a data protection term is still in effect, **data protection provided** for the combination until expiry of original data protection period.

Marketed in Canada

- C.08.004.1(5) – protection only where the innovative drug has received an NOC **and** is marketed in Canada.
- No protection offered to a withdrawn drug.
  - Inactivation of a DIN will be accepted as an indication that the drug is no longer marketed in Canada.
- If re-introduced to market protection is only for the remainder of original data protection term.
- Guidelines suggest leeway will be afforded in certain situations.
  - Notification as per C.01.014.3 of the *Food and Drug Regulations.*
  - Change in manufacturer.

NOC/c

- Will an NOC/c trigger data protection?
- *Lundebeck v. Cobalt, Ratiopharm, and the Minister of Health* (2008)
  - EBIXA (memantine) approved by way of NOC/c
  - Minister accepted ANDSs naming EBIXA as the reference product.
  - Lundbeck challenged the Minister's decision to review the ANDSs and sought a declaration that EBIXA was an "innovative drug".
  - At issue was whether data protection is available for innovative drugs approved by way of NOC/c.

NOC/c

- *Lundebeck,* continued:
  - Court held data protection did not apply because EBIXA was approved before new provisions in place (Oct 5, 2006).
  - Did not rule as to whether data protection applied to drugs approved via NOC/c.
  - Held that an NOC/c is an NOC within the meaning of the *Food and Drug Regulations*.
- Minister has afforded data protection under the new provisions to 11 drugs approved by way of NOC/c.
  - Protection starts when the NOC/c is granted, not when the conditions are met.

Register of Innovative Drugs

- C.08.004.1(9) - Drugs accepted as innovative drugs by the Minister and subject to data protection listed on the Register of Innovative Drugs
- Currently listed:
  - 96 products for human use, 25 with pediatric term extension
  - 13 products for veterinary use

Biologics

- Biologics are afforded the same protection under the *DPR* as small molecules.
  - An NDS for a subsequent entry biologic ("SEB") may have a reduced clinical and non-clinical data package due to a demonstration of similarity to a previously approved reference biologic drug ("RBD").
  - Such submissions make a "comparison" within the meaning of C.08.004.1(3) of the *DPR*.
- SEBs are not "innovative drugs".

Subsequent Entry Biologics – Non-Canadian Proxies

- In some cases, a suitable non-Canadian RBD may be a proxy for the Canadian RBD drug in comparative studies.
- In such cases, submissions containing demonstrations of similarity with a non-Canadian RBD are considered to contain a comparison between the SEB and the Canadian RBD as contemplated by subsection C.08.004.1(3).

Pediatric Extension

- Pediatric extension of 6-months is available.
  - Must submit results of clinical trials designed and conducted to obtain knowledge about use in pediatric populations.
  - May be submitted in the NDS or in a SNDS filed within 5 years of the 8 year data protection period.
- The additional knowledge must be publicly available through additions to the labeling and/or PM.
  - Contraindications and/or other warning statements may be sufficient.

Consents from Innovator

- Consent to File a Submission: Innovator may consent to filing of a submission during the data protection period (C.08.004.1(6)).
- Consent to issuance of NOC: Innovator may consent to issuance of NOC during data protection period (C.08.004.1(8)).

Comparison to Europe

- Exclusivity applies to NCEs.
  - A NCE is a new compound with no prior approval as a drug.
- Exclusivity is the same for small molecules and biologics.
  - 8+2+1 Formula:
    - 8 years of data exclusivity; plus
    - 2 additional years of market exclusivity; plus
    - 1 year extension if a new indication is authorized in the first 8 years for a significant clinical benefit in comparison with existing therapies.

Comparison to the United States

- Exclusivity applies to NCEs.
  - A NCE is a drug that contains an active moiety that has not been approved by the FDA.
  - An active moiety means the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt or other non-covalent derivative.
- Exclusivity differs for small molecules and biologics.

Comparison to the United States

- Small Molecules
  - 5 years data exclusivity
    - Reduced to 4 years if the ANDA contains a Paragraph IV Certification of invalidity or non-infringement.
  - 3 additional years of market exclusivity may be granted for the approval of a new indication.
- Biologics:
  - 4 years of data exclusivity.
  - 12 total years of market exclusivity.

Comparison to the United States

- Other types of exclusivity:
  - Orphan drug (7 years)
  - Pediatric (6 months)
    - Attaches to all existing exclusivities.
  - Generic drug exclusivity (180 days)
    - Period whereby no other generic may be marketed.
  - Biosimilar interchangeable exclusivity (up to 1 year)
    - Period whereby no other generic may be declared interchangeable.

Questions?

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