Pharmaceuticals Export Promotion Council of India

(Set up by Ministry of Commerce & Industry, Government of India)

REGULATORY & MARKET PROFILE OF CANADA

Demography

SL. No	Parameter	Description
1	Region	North America
2	Country	Canada
3	Capital	Ottawa
4	Population	35,623,680 (July 2017 est.)
5	Population growth rate (%)	0.73 % (2017 est.)
6	GDP (purchasing power parity)	$ 1.764 trillion (2017 est.)
7	GDP - real growth rate (%)	3% (2017 est.)
8	GDP - per capita (PPP)	$ 48,100 (2015 est.)
9	Epidemiology	Ischemic heart disease, Cancer, Diabetes, Alzheimers disease Cerebrovascular disease, COPD etc
10	Population below poverty line	Canada does not have official poverty line
11	Age structure (%)	0-14 years: 15.44%
		15-24 years: 11.85%
		25-54 years: 39.99 %
		55-64 years: 14.1%
		65 years and over: 18.63%

Source: CIA World Fact Book updated to July 2017(on 6th August 2018)

MARKET REPORT

INTRODUCTION

Canada is a significant manufacturing base for pharmaceutical companies as well as a market in its own right. Canada boasts of one of the best state sponsored Health care systems and is strongly

Pharmaceutical Health Expenditure: In 2017 Canada's Pharma market was of the size USD 20.5 billion and has grown by 5%.(Source: BMI). It is forecasted to grow by 8.4% in 2018 and reach $ 22.3 billion.

Canada's historically high generic prices are now being targeted for downward price revisions. The margin of difference between a generic and patented drug offers virtually no incentive to choose a generic.

Latest Updates

- As of April 2018, member companies of the Canadian Generic Pharmaceutical Association have agreed to reduce prices of Canada's 70 top-selling off-patent drugs by 25% to 40%. The deal sets the prices of these drugs in Canada at either 10% or 18% of the brand-name price.

- Valeant pharma reported FY17 total sales worth USD8,724mn, down by 9.8% compared with the USD9,674mn reported for FY16. Valeant did report a net income of USD2,404mn for FY17, compared to a net loss of USD2,409mn a year earlier; however, the firm noted that the change was mainly attributed to an increase in the benefit from income taxes.

Strengths:

- The Canadian pharmaceutical market is among the top eight leading markets in the world, with high per capita spending.
- Despite an ongoing dispute over pricing and reimbursement regulations, as well as patent law, the regulatory environment in Canada is one of the most advanced and transparent in the world.
- The Canadian economy has emerged relatively unscathed from the global crisis.
- Rising government pharmaceutical procurement.
- Generic segment returns higher revenues as the prices are much higher than in many other nations.

Opportunities:

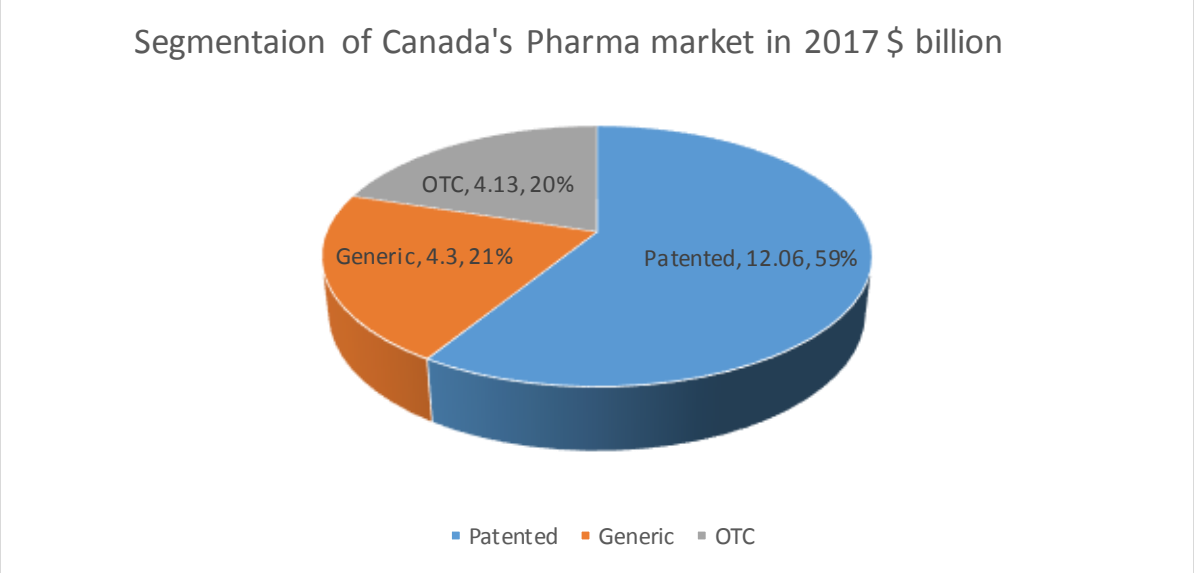
- The growth potential of the Canadian generic drug market is sizeable, with the Government's cost-containment policy

- Despite being a mature market, growth is still solid and per-capita consumption is one of the highest in the world.

Market Overview:

- With Pharmaceutical Per capita sales of USD 559.8, Canada is the 8th largest world market.
- Generic medicines, which are slowly gaining market share, account for 26.3% of prescriptions and 21% of the total sales.
- Non communicable disease account for vast majority of the market and largely seen in the form of diabetes, Cancer, asthma and Cardio vascular disorders.
- The domestic industry comprises about 140 companies, with just over 50 research-based firms. Generic drug manufacturers employ roughly 20% of the industry workforce. Indirect employment totals more than 100,000, which represents a significant proportion of the country's population

Canada's Pharmaceutical sub sector in 2017 in USD billion



Pharmaceutical trade Forecast

Canada's pharma trade during 2017, like most of the countries had negative trade balance as imports exceeded exports by $ 3.07 billion. This is expected to get narrowed by 2022 the negative balance coming down to $ 1.6 billion.

The Canadian Ministry of Industry reports that annual domestic pharmaceutical manufacturing production has experienced a declining CAGR of 2.5% since 2008. Furthermore, employment in the manufacturing portion of the pharmaceutical sector fell by 6.3% in 2014. This is compounded by the fact that total business expenditure on R&D has fallen below CAD1bn since 2011 and industry R&D declined by 29% between 2011 and 2013, lessening the country's offering of necessary medicines.

Epidemiology

Canada has approximately 2 million people with diabetes and most of them have it as uncontrolled. Cancer is another disease significantly affecting people.

Canada has a publicly funded medical system and about 70% of the cost is covered by government funds, while the remainder is covered by private insurance. The greatest proportion goes to hospitals, followed by pharmaceutical expenses and physicians. In Canada's single-payer system, most services are provided by the private sector, with the fee paid for by the government at the same rate.

Generic Market & Forecast:

The Generic market size ws of USD 4.25 billion (in 2015) has negatively grown by 11% and has shrunk to USD 4.16 in 2016. However by 2017 it has come back to 4 4.3 billion. By 2022 Generic market is likely to reach $ 4.63 bn.

Generic drug uptake in Canada is significantly less than patented medicines. This is due to several factors. Firstly, the price of generic drugs is not significantly cheaper than their patented counterparts. Patented drugs have a regulatory approval board which has some influence over pricing; however, there is no equivalent in place for generic products. Drug pricing is generally allocated by province or territory, which can cause further discrepancies between medicines in difference areas. Generic drug prescribing practices are still in need of greater encouragement.

The Pan-Canadian Pharmaceutical Alliance (pCPA) and the Canadian Generic Pharmaceutical Association (CGPA)jointly announced a five-year initiative aimed at providing significant savings on prescription generic drugs for participating public drug plans and employee drug plans. As of April 2018, member companies of CGPA have agreed to reduce prices of Canada's 70 top-selling offpatent drugs by 25% to 40%. The deal sets the prices of these drugs in Canada at either 10% or 18% of the brand-name price.The announcement builds on previous similar initiatives that havesaved over USD1bn for participating drug plans over the past five years. This initiative aims to contribute an additional saving of up to USD3bn over the next five years.

The sales volumes of the generic drug segment will be boosted by patent expirations, cost-containment measures and the improvement of regulatory pathways for biogeneric medicines, in addition to the improvement in the perception of their quality among the population. Future developments in the sector are likely to address existing issues such as the speed of provincial approval of generic drugs; increase flexibility in the new pricing rules so that generic drugs - that are costly to develop and produce remain available; and introduce incentives for generic drugmakers to challenge patents in order to continue bringing new drugs to the market

Statistics:

India's exports:

India's Pharmaceutical exports to CANADA $ Million						
Category	**2015-16**	**2016-17**	**2017-18**	**GR%**	**contbn%**	**Contbn to Region**
BULK DRUGS AND DRUG INTERMEDIATES	56.86	48.52	43.38	-10.59	18.88	10.95
DRUG FORMULATIONS AND BIOLOGICALS	140.56	149.01	181.22	21.61	78.86	3.79
AYUSH	0.62	0.92	0.99	7.20	0.43	6.48
Herbal Products	2.18	2.68	2.82	5.24	1.23	2.61
Surgicals	1.13	1.68	1.39	-17.55	0.60	3.15
Vaccines	0.03	3.78	0.00	-99.88	0.00	0.24
Total	201.38	206.59	229.80	11.23	100.00	4.30

Canada accounted for 1.3 % of India's Pharmaceutical exports during 2017-18 and it was 14th largest exporting partner.

Imports of Canada

Top Ten Importing Partners of Canada $ Million						
Rank	Country	2014	2015	2016	Gr%	Share%
1	USA	4112.11	4251.19	4063.36	-4.42	35.74
2	Switzerland	1572.01	1610.17	1720.61	6.86	15.13
3	Germany	1455.49	1194.24	1457.78	22.07	12.82
4	Ireland	505.80	533.74	605.22	13.39	5.32
5	United Kingdom	664.69	487.29	402.62	-17.38	3.54
6	France	576.31	449.65	365.82	-18.64	3.22
7	Italy	492.29	383.21	353.13	-7.85	3.11
8	Belgium	731.13	260.48	276.82	6.27	2.43
9	Spain	322.13	312.47	258.67	-17.22	2.27
10	Sweden	267.52	279.74	250.21	-10.55	2.20
13	India	141.36	169.21	160.44	-5.18	1.41
	World	12426.07	11353.81	11370.40	0.15	100.00
Source: UN comtrade						

REGULATORY OVERVIEW

The Canadian health ministry (Health Canada)'s Therapeutic Products Directorate is the federal authority that regulates the market for pharmaceutical drugs and medical devices for human use. At a federal level, pharmaceuticals are classified into prescription and non-prescription, with provinces further dividing medicines into general sales and Schedule I to III (I being prescription, II being pharmacist-assistance drugs and III being pharmacy self-selection). Unscheduled medicines can be sold through all retail outlets as general sale items.

Canada's approval process is modelled on the process used by the US Food and Drug Administration (FDA), albeit with only 10% of the resources of its US counterpart.

It can take up to three years for a new biotech product to be approved in Canada - severely shortening the drug's prospects under patentability. This compares with an average of 350 days in the US.

The Canadian Intellectual property council is lobbying for the Canadian government to grant research-based companies an effective right to appeal an adverse court decision on a patent challenge. Currently, only generic manufacturers can appeal an unfavourable court ruling. By granting the same right to innovative drug makers the council believes fairness and equality would be restored.

Canadian Generic Pharmaceutical Association (CGPA) has criticised the proposed changes, saying that they are exactly the same promoted by the European Union as part of the current trade negotiations.

Canada has a Bolar-style provision which allows generic firms to begin producing a generic version of a drug before the patent protecting that drug has expired, but they may not launch the generic until after the patent has expired.

Price Regulation:

Canada's generic medicines sector has no formal body to regulate its prices. Generic prices are higher in comparison to most of the comparable countries. Generic Drug Pricing is not uniform across all the provinces of Canada. As price variances from province to province become more evident, a pressing need for generic drug price regulations will emerge. The Competition Bureau has stated that around CAD600mn a year could be saved if generic drug pricing was made more competitive across all 10 provinces and three territories.

Pharmacovigilance

In Canada, adverse drug reaction reporting is run by the Canada Vigilance Program, which is part of Health Canada. The Program has a network of seven regional offices and maintains an online database of adverse events. Similar to the current US system, adverse reaction reports are submitted by health professionals and consumers on a voluntary basis either directly to Health Canada or via market authorisation holders.

REGISTRATION AND LICENSING REQUIREMENTS

➢	Regulatory Authority	:	**Health Canada**
➢	Website of regulatory Authority	:	http://pharmacyboardkenya.org/
➢	Fees for Drug Registration	:	CAD 49,811 - 176,569
➢	Normal time taken for registration	:	06-24 Months
➢	Registration Requirement [Dossier Format]	:	eCTD
➢	Whether plant inspection is mandatory	:	Yes

Health Canada is the Federal department responsible for helping Canadians maintain and improve their health. It ensures that high-quality health services are accessible, and works to reduce health risks.

Health Canada is engaged in various activities and has numerous responsibilities related to health. Health Canada supports activities that:

- *Preserve and modernize Canada's health care system:* Health Canada manages health care costs by communicating health risks and promoting healthy lifestyles.
- *Enhance and protect the health of Canadians:* Health Canada provides surveillance, prevention, control and research of disease outbreaks across Canada and around the world. The Department also monitors health and safety risks related to the sale and use of drugs, food, chemicals, pesticides, medical devices and certain consumer products across Canada and around the world.
- *Work in partnership with others:* Health Canada partners closely with other federal departments, agencies, provincial/territorial governments and health organizations.
- *Communicate health promotion, disease prevention and safety messaging*.

HPFB (Health Products and Food Branch):

Health Canada's HPFB is the national authority that regulates, evaluates and monitors the safety, efficacy, and quality of

- ✓ Health products (including drugs, medical devices, biologic and genetic therapies, and natural health products)
- ✓ Foods
- ✓ Veterinary drugs (in order to protect the safety of Canada's food supply).

The Therapeutic Products Directorate (TPD) of HPFB is Canada's regulator of prescription drugs and medical devices for human use. Before giving permission to sell a product, the directorate must see scientific evidence of the product's safety, effectiveness, and quality, as required by the Food and Drugs Act and Regulations.

Human Drugs fall under a number of different Schedules of the Food and Drugs Act and the Food and Drug Regulations.

- **Schedule C** (Radiopharmaceuticals excluding radionuclides)
- **Schedule D** drugs (Drugs derived from Human, Animal or microbial sources, such as insulin and blood based products)
- **Schedule F** (Prescription Drugs)
-

A note on how new drugs are authorized for sale in Canada:

New drugs are regulated under Part C, Division 8 of the *Food and Drug Regulations*. Companies are granted market authorization by Health Canada in several ways. Regardless of the method of authorization, a manufacturer receives a Notice of Compliance (NOC) when it has met Health Canada's regulatory requirements for the safety, efficacy and quality of a product. The following provides a brief overview of three of the most common routes by which new drugs are authorized for sale in Canada.

1. **Innovator drugs ("brand name drugs")**: Manufacturers receive authorization to sell these products in Canada by submitting a New Drug Submission (NDS) pursuant to section C.08.002 of the Food and Drugs Regulations.
2. **Subsequent entry drugs ("generic drugs")**: Health Canada often authorizes manufacturers to market these drugs by requiring them to submit an Abbreviated New Drug Submission (ANDS) pursuant to section C.08.002.1 of the Food and Drug Regulations. These products will receive a declaration of bioequivalence to a *Canadian Reference Product* (pursuant to Section C.08.004 (4)), which will be stated on the NOC.

3. **The Health Canada** *Changes in Manufacturer's Name and/or Product Name Policy* outlines another option for manufacturers wishing to receive authorization through an NOC to market brand name and generic drug products. This policy applies to eligible drug submissions submitted to Health Canada for a change in the manufacturer's name and/or product name subsequent to a merger, buy-out or other corporate restructuring or the establishment of a licensing agreement.

Products that receive an NOC according to one of these mechanisms have met Health Canada's regulatory requirements for safety, efficacy and quality.

The type of submission being presented to Health Canada.

1. CTA (Clinical Trial Application)
2. CTA-A (Clinical Trial Application Amendment)
3. NDS (New Drug Submission)
4. SNDS (Supplemental New Drug Submission)
5. ANDS (Abbreviated New Drug Submission)
6. SANDS (Supplemental Abbreviated New Drug Submission)
7. NC (Notifiable Change)
8. DIN (Drug Identification Number submission)
9. PDC (Post-Authorization Division 1 Change)

Clinical Trial Application:

The Canadian CTA dossier is simple and consists of the following documents (exceptions are possible): administrative form, protocol, protocol summary (Health Canada's template), Informed Consent Form, Investigator's Brochure and quality dossier summary (Health Canada's template per study phase).

Health Canada reviews the CTA and notifies the sponsor within 30 calendar days from the date that the application is considered complete. Questions may be issued during the review, and the sponsor will have 2 calendar days to provide the response (exceptions can apply). Note that CTAs are required for phases I to III clinical trials. The authorization (No Objection Letter) is mandatory prior to initiating the trial and importing the investigational product(s) in Canada.

If the HPFB provides authorization, the study can be underway with human subjects that are informed and have given their consent to be administered the drug for their participation. Note that a Canadian Ethic Committee must also approve the study material (protocol, Investigator's Brochure and Informed Consent Form). Tests are conducted in a controlled environment where drug administration procedures and results are closely tracked, monitored and analyzed.

New Drug Submission (NDS):

If results of all the preclinical studies and the clinical trials show that a drug's potential therapeutic benefit outweighs its risks (side effects, toxicity, etc.), and the chemistry and manufacturing dossier is complete, then the sponsor may decide to file an NDS with the appropriate HPFB Directorate in order to be granted authorization to sell the drug in Canada. A sponsor can submit an NDS whether the clinical trials were done in Canada or in other countries. The NDS must include the results of the quality (Chemistry and manufacturing), preclinical and clinical studies, whether done in Canada or in other countries.

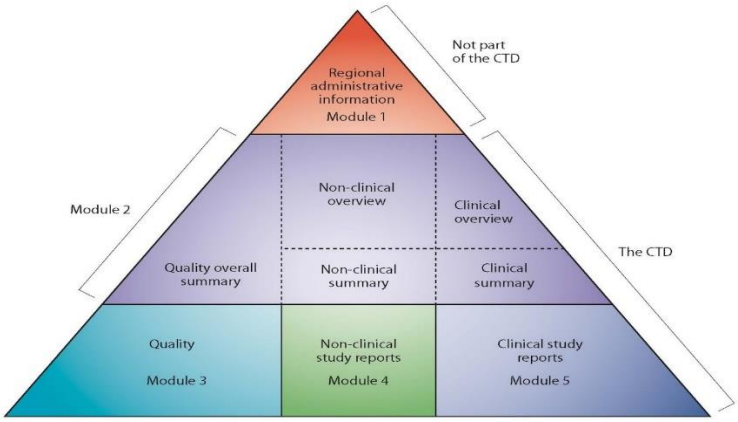
The drug's efficacy and safety data is evaluated and the Risk/Benefit analysis is performed, before reaching a decision.

The information requested as part of an NDS application must be detailed enough that Health Canada can make an assessment on the safety and effectiveness of the new drug. All submissions must be provided to Health Canada in an electronic Common Technical Document (eCTD) format.

The CTD format originates from the International Conference on Harmonization (ICH) initiatives, in their effort to harmonize efficacy, safety and quality (chemistry and manufacturing) requirements globally for the registration of drugs (pharmaceuticals, biologicals, genetic therapies,) for human use. This initiative includes standard information organization for new drug registration applications. The CTD format is divided into five modules: Module 1 contains region-specific information and Modules 2–5 contain common clinical, nonclinical and quality information with some regional variations.

The CTD format is presented below.

CTD Triangle



The CTD triangle. The Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

The Module 1 (regional) includes the following, amongst other information:

- Administrative form
- Product Monograph
- Mock-up of Inner and Outer labels
- Certified Product Information Document
- Brand Name Analysis
- Risk Management Plan etc

Abbreviated New Drug Submission (ANDS)

The ANDS regulation was created to make the approval process for **generic drugs** simpler and more cost effective. Under an ANDS, the manufacturer of a drug has to prove that its product is pharmaceutically equivalent and/and bioequivalent with the innovator's drug. For the purpose of an ANDS the sponsor may need to perform a bioequivalence study or a physico-chemical comparison (parenteral drugs or drugs for which it is not ethical to conduct the study on healthy volunteer).

Steps in the review process for a drug:

1. When a sponsor decides that it would like to market a drug in Canada, it files a "New Drug Submission" with HPFB. This contains information and data about the drug's safety, effectiveness and quality. It includes the results of the preclinical and clinical studies, whether done in Canada or elsewhere, details regarding the production of the drug, packaging and labelling details, and information regarding therapeutic claims and side effects.
2. HPFB performs a thorough review of the submitted information, sometimes using external consultants and advisory committees.
3. HPFB evaluates the safety, efficacy and quality data to assess the potential benefits and risks of the drug.
4. HPFB reviews the information that the sponsor proposes to provide to health care practitioners and consumers about the drug (e.g. the label, product brochure).
5. If, at the completion of the review, the conclusion is that the benefits outweigh the risks and that the risks can be mitigated, the drug is issued a ***Notice of Compliance (NOC)*** *confirming the dossier's compliance with the Food and Drugs Act and its Regulations*, as well as a ***Drug Identification Number (DIN)*** which permits the sponsor to market the drug in Canada and indicates the drug's official approval in Canada.

6. In addition, Health Canada laboratories may test certain biological products before and after authorization to sell in Canada has been issued. This is done through its Lot Release Process, in order to monitor safety, efficacy and quality.

What happens if a Drug receives a Notice of Non-Compliance?

Upon the completion of the review process, if the HPFB finds that there is insufficient evidence to support the safety, efficacy or quality claims of the drug, HPFB will not grant a marketing authorization for that drug. At this point, the sponsor typically has 3 options: to supply additional information to the HPFB, to re-submit a submission at a later date with additional supporting data (without prejudice), or to ask that HPFB to reconsider its decision.

Marketing authorization:

A legal document issued by Health Canada authorizing the sale of a drug or a device based on the health and safety requirements of the *Food and Drugs Act* and its *Regulations*. The marketing authorization may be in the form of a Drug Identification Number (DIN), a device licence for classes II, III and IV medical devices, or a natural health product licence (NPN or DIN-HM).

Drug Identification Number (DIN):

A computer-generated eight digit number assigned by Health Canada to a drug product prior to being marketed in Canada. It uniquely identifies all drug products sold in a dosage form in Canada and is located on the label of prescription and over-the counter drug products that have been evaluated and authorized for sale in Canada. A DIN uniquely identifies the following product characteristics: manufacturer; product name; active ingredient(s); strength(s) of active ingredient(s); pharmaceutical form; and route of administration.

Accelerated Review Process:

For health conditions that are serious, life-threatening or for a severely debilitating disease (such as Alzheimer's disease, cancer, AIDS, or Parkinson's disease), the HPFB can provide faster authorization of a drug as follows:

1. Priority Review (PR): Applies to drugs that shows substantial evidence of clinical effectiveness at the end of the clinical trial phases.

2. Notice of Compliance with conditions (NOC/c): Applies to drugs with promising evidence of clinical effectiveness throughout the clinical trial phases. Approval would be granted to a manufacturer to market and sell that drug in Canada with the condition that the manufacturer execute additional studies to confirm the drug's benefit and safety.

To be considered for PR or NOC/c, the drug must meet the following standards as described by Health Canada; the drug must provide:

- Effective treatment, prevention or diagnosis of a disease or condition for which no drug is presently marketed in Canada; or

- A significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies, preventatives or diagnostic agents for a disease or condition that is not adequately managed by a drug marketed in Canada

Related to the NOC/c, some of the conditions of the Notice of Compliance include a requirement to closely monitor the drug for safety and to provide HPFB with regular updates. Once the conditions are met, the designation of "with condition" is removed from the NOC.

GUIDANCE DOCUMENT Quality (Chemistry and Manufacturing) Guidance: New Drug Submissions (NDSs) and Abbreviated New Drug Submissions (ANDSs) can be identified at https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/chemical-entity-products-quality/guidance-document-quality-chemistry-manufacturing-guidance-new-drug-submissions-ndss-abbreviated-new-drug-submissions.html

Health Canada Consults on Changes to Broaden Access to Generic Drug Equivalence-

Possible Changes to the Food and Drug Regulations: Generic Drug Equivalence and Related Terminology

In July 2017, Health Canada began the consultation process on amendments to the Food and Drug Regulations that will expand which drug products may be approved by way of an ANDS (the equivalent of a US ANDA).

In Canada, generic drug products can be approved via the ANDS pathway by making reference to a Canadian Reference Product (CRP), provided the manufacturer can demonstrate that its product is pharmaceutically equivalent and bioequivalent to the CRP, it has the same route of administration, and the conditions of use fall within those of the CRP. Approval through the ANDS pathway constitutes a declaration of "therapeutic equivalence."

Products with the same medicinal ingredient in the same dosage form are currently considered "pharmaceutical equivalents." The proposed changes would allow drug products with different salts, esters, or complexes of the medicinal ingredient, and/or generic drug products with different but comparable dosage forms to the CRP to be considered "pharmaceutical alternatives." Both pharmaceutical equivalents and pharmaceutical alternatives would be approvable by way of an ANDS and be viewed as therapeutically equivalent, provided bioequivalence with the CRP has been demonstrated and the product has the same route of administration and the same safety and effectiveness.

Use of a Foreign-sourced Reference Product as a Canadian Reference Product:

Health Canada published an updated Guidance document on the Use of a Foreign-sourced Reference product as a Canadian reference Product for the purpose of an ANDS. The guidance provides clarity on the acceptability of foreign reference products for establishing bioequivalence and states that to use a drug product purchased in another country as a CRP, parties should:

- Demonstrate that the drug product is authorised for marketing by a regulatory authority of a country or region with drug assessment criteria comparable to those in Canada;
- Provide evidence that the foreign-sourced reference product is marketed in the country or region of origin by the same innovator company or corporate entity which currently markets the identical amount(s) of the identical medicinal ingredient(s) in the identical dosage form in Canada;
- Provide the product labelling, certificates of analysis, proof of purchase, and sample products of the reference product marketed in Canada and the foreign-sourced reference product; and
- For all comparative in-vitro testing, analyse the foreign-sourced reference product and the innovator product marketed in Canada and provide the results of these analyses.

Furthermore, the guidance document prohibits the use of a foreign-sourced reference product when it contains high risk medicinal ingredients, or for drugs that require patient monitoring in order to avoid the consequences of under or over-treatment.

Human Drug (Pharmaceutical and Biological) Submission and Application Review Fees as of April 1, 2018

Fee Category	**Description**	**Fee as of April 1, 2017**	**Fee as of April 1, 2018**
New Active Substance	Submissions in support of a drug , excluding a disinfectant, that contains a medicinal ingredient not previously approved in a drug in Canada and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate, or polymorph.	$341,770	$348,606
Clinical or Non-Clinical Data and Chemistry & Manufacturing	Submissions based on Clinical or Non-Clinical data and Chemistry & Manufacturing data for a drug that does not include a new active substance.	$173,106	$176,569

Clinical or Non-Clinical Data Only	Submissions based only on Clinical or Non-Clinical data for a drug that does not include a new active substance.	$80,794	$82,410
Comparative Studies	Submissions based on comparative studies (e.g. Clinical or non-clinical data, bioavailability, pharmacokinetic and pharmacodynamic data) with or without Chemistry & Manufacturing data for a drug that does not include a new active substance.	$48,834	$49,811
Chemistry & Manufacturing Data Only	Submissions based only on Chemistry & Manufacturing data for a drug that does not include a new active substance.	$23,089	$23,551
Published Data Only	Submissions based only on published clinical or non-clinical data for a drug that does not include a new active substance.	$19,147	$19,530
Switch status from prescription drug to non-prescription drug	Submissions based only on data that support the modification or removing of a medicinal ingredient listed in Schedule F of the Food and Drug Regulations (i.e. identical claim for existing drug).	$46,491	$47,421
Labelling Only	Submissions of labelling material. (i.e. does not include supporting clinical or non-clinical or Chemistry and Manufacturing data.)	$3,111	$3,174
Administrative Submission	Submissions in support of a manufacturer or product name change.	$324	$331
Disinfectants	Submissions and applications that include data in support of a disinfectant.	$4,305	$4,392
Drug Identification Number application - Labelling Standard	Applications attesting to compliance with a labelling standard or Category IV Monograph for a drug that does not include clinical or non-clinical data or chemistry and manufacturing data.	$1,726	$1,761

Fee structure for various kinds of products like Human drugs, veterinary drugs and medical devices can be identified at https://www.canada.ca/en/health-canada/services/drugs-health-products/funding-fees.html

Post-Notice of Compliance (NOC) Changes:

After a new drug as defined in section C.08.001 of the Food and Drug Regulations has been granted a Notice of Compliance (NOC), it is not uncommon for sponsors to make changes to the drug. A post-NOC change is any change that is made to a new drug that has received a NOC pursuant to section C.08.004 of the Food and Drug Regulations. Many of these changes may be made to improve the quality of the drug product or the efficiency of the manufacturing process, or they could be made for marketing considerations. Changes to the labelling of a drug product could include adding new indications, improving the management of risk for a product by adding warnings, limiting the target population or changing the dosage regime etc.

Level I - Supplements

Level I or Supplements are changes to a new drug that are Asignificantly different@ as it relates to the matters specified in C.08.003 (2) of the Food and Drug Regulations and have the potential to impact the safety, efficacy, quality and/or effective use of the drug. The changes included in this reporting category shall be filed, along with the recommended supporting data, to Health Canada as a Supplement to a New Drug Submission (SNDS) or Supplement to an Abbreviated New Drug Submission (SANDS). The change may not be implemented by the sponsor until a NOC has been issued.

Level II - Notifiable Changes

Level II or Notifiable Changes (NC) are changes to a new drug that have the potential to impact the safety, efficacy, quality and/or effective use of the drug but do not require the issuance of a NOC. The changes included in this reporting category should be filed, along with the recommended supporting data, to Health Canada as a Notifiable Change. All Level II changes should not be implemented by the sponsor until a No Objection Letter (NOL) has been issued.

Multiple Level II (Quality) changes for the same drug product may be filed in a single submission provided those changes are related and/or supported by the same information. If the changes are related, the sponsor should indicate the association between the proposed changes.

Multiple Level II (Safety and Efficacy) changes for the same drug product may be filed in a single submission provided those changes are within the same reporting category (i.e., multiple 90 day NCs in one submission or multiple 120 day NCs in one submission).

If there are too many changes filed within the same submission or major issues are identified with a change which would require extensive time to review, Health Canada may divide the changes into separate submissions.

For submissions that include multiple changes, the sponsor should clearly specify which supporting data supports which change. If the same change is applicable to multiple drugs, a separate submission is required for each drug product but the data may be cross-referenced.

Level III - Annual Notifications

Level III or Annual Notifications are changes to a new drug that have minimal potential to impact the safety, efficacy, quality and/or effective use of the drug. The changes included in this reporting category may be implemented by the sponsor without the prior review by Health Canada of the data supporting such a change.

A Level III change should be submitted at the time the change is implemented, or submitted during the Annual Drug Notification period depending on the type of drug (e.g., pharmaceutical or biologic) and the type of change (Quality or Safety and Efficacy). All Level III changes should be submitted using the Post-Notice of Compliance (NOC) Changes: Level III change form.

For biologics (Schedule D drugs) and radiopharmaceuticals (Schedule C drugs), notification of all Level-III Quality changes that have occurred in the preceding twelve (12) months should be provided annually during the Annual Drug Notification period using the Post-Notice of Compliance (NOC) Changes: Level III change form.

In some instances, after a Level III change has been implemented and Health Canada's awareness of the change is considered necessary, the sponsor may be requested to file an Immediate Notification. A sponsor may also wish to file an immediate Notification for the same reason stated above.

For pharmaceutical drugs for human or veterinary use, Health Canada recommends that Level III Quality changes be filed at the time the change is implemented.

For biologics, radiopharmaceuticals and pharmaceutical drugs for human or veterinary use, Health Canada recommends that Level III Safety & Efficacy changes be filed at the time the change is implemented.

Level IV - Record of Changes

Level IV or Record of Changes (Quality only) are changes to a new drug that are not Level I, Level II or Level III and are not expected to impact the safety, efficacy, quality and/or effective use of the drug. The changes included in this reporting category may be implemented by the sponsor without prior review by Health Canada. The changes should be retained as part of the drug product=s record by either the sponsor or the manufacturer and comply with Good Manufacturing Practices (GMP) requirements of Division 2 of the Food and Drug Regulations.

Guidance document on Post-Notice of Compliance can be identified at
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/post-notice-compliance-changes/framework-document.html

Data Protection under C.08.004.1 of the Food and Drug Regulations:

- The data protection provisions in section C.08.004.1 of the Food and Drug Regulations provide an ***8-year period of market exclusivity for innovative drugs***.

- **Pediatric extension**: In addition to the eight-year period of data protection, an ***additional six-month pediatric extension*** will be applied if an innovative drug manufacturer includes, in its new drug submission, or any supplement to that new drug submission filed within the first five years of the eight-year data protection period, results of clinical trials which were designed and conducted for the purpose of increasing knowledge about the use of the drug in pediatric populations and which will lead to a health benefit for children. To qualify, the drug must be an innovative drug and be eligible for the eight-year period of data protection. This is also applicable for biosimilar drugs.

- **Submissions Comparing to Innovative Drugs: Prevention from filing**
  In accordance with paragraph C.08.004.1(3)(a) of the *Food and Drug Regulations*, a manufacturer seeking an NOC on the basis of a direct or indirect comparison to an innovative drug may not file a submission for six years from the date of issuance of the first NOC for the innovative drug. This language is intended to capture an ANDS or a supplement to ANDS (SANDS), where the innovative drug is the Canadian Reference Product.

- **Prevention from approval**: In accordance with paragraph C.08.004.1(3)(b) of the *Food and Drug Regulations*, a manufacturer seeking an NOC on the basis of a direct or indirect comparison to an innovative drug will not be issued an NOC before the end of the period of eight years after the day on which the first NOC was issued for the innovative drug. The period will be lengthened to eight years and six months where the innovative drug qualifies for the six-month pediatric extension.

- There is also no market exclusivity for the first approved generic drug or biologic drug against subsequent drugs.

International Collaboration

Canada has mutual recognition agreements (MRA) with the European Union, Switzerland, Australia and the European Free Trade Association (EFTA) states, the latter being similar to the EU MRA since EFTA legislation is harmonised with that in the EU.

Implementation of the Comprehensive Economic and Trade Agreement (CETA) and the Right to Supplementary Protection for Patents for Pharmaceutical Drugs:

Canadian and European Union leaders signed the Comprehensive Economic and Trade Agreement (CETA) in October 2016 and it was implemented in September 2017 with resulting reforms to Canadian laws including changes to the Patent Act. These reforms introduce a single-track pharmaceutical patent litigation system under the Patented Medicines (Notice of Compliance) Regulations (PMNOC Regulations) and extended patent-like protection for pharmaceuticals under the Certificate of Supplementary Protection Regulations.

Previously, parties could choose to litigate a patent by way of a summary prohibition proceeding under the PMNOC Regulations, similar to proceedings under the Hatch-Waxman Act in the United States. This often resulted in dual litigation with subsequent infringement actions between the same parties. The new single-track litigation system replaces the summary prohibition proceedings with full actions that determine the infringement and validity of the patent. Actions must be completed within two years and allow for full oral and documentary discovery as well as viva voce trial evidence. Under the previous scheme, innovator companies were often unable to appeal the outcome, however under the new regulations either party may appeal.

Additionally, the legislation provides for Certificates of Supplementary Protection (CSPs). CSPs extend the patent term of eligible pharmaceutical products by up to two years to partially compensate for the additional time required to develop pharmaceuticals in research and the regulatory approval process. A CSP provides "patent-like rights" that take effect after patent expiry and is subject to the "same limitations and exceptions" as the patent.

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Details of importing country embassy in India: http://international.gc.ca/world-monde/india-inde/new_delhi.aspx?lang=eng

Contact details of Indian Embassy abroad: https://www.hciottawa.gov.in/

List of Local Pharma Associations:

- Canadian Generic Pharmaceutical Association: CGPA http://canadiangenerics.ca/
- CAPDM - Canadian Association for Pharmacy Distribution Management https://www.capdm.ca/