An Overview of the New Drug Submission and Approval Process for Canada

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Abstract: Health Canada is a 9th largest growing pharmaceutical market in the world. The Health Canada is the regulatory Authority of Canada that works under department of Minister of Health. Health Canada is responsible to approve the New Pharmaceutical Drug in Canada under the Food and Drug Branch with applicable Food and Drug Act and its Regulations. The health Canada is also responsible for approval or rejection of the various types of applications related to drug in Canada. There are Various submission types are there in Health Canada i.e., NDA, SNDA, ANDA, SANDA. In the present review article, we will discuss about the New Drug Submission and approval process in Canada.

Keywords: NDS, Canada Drug approval Process, Health Canada, Regulatory Body, New drug Submission and Approval Process, Pharmaceutical market

1.INTRODUCTION

The health Canada is a federal department responsible for helping Canadians, Preserving Canada's health care system, Enhancing the health of Canadians, partnering with others, and communicating with Canadians while respecting individual choices and circumstances. Health Canada along with various other Food and Drug Related Branches comes under minister of health. (1) [accessed on: 18.08.2022]

Health Canada is involved in various activities and have more responsibilities regarding health. (2) [accessed on: 18.08.2022]

The New Drug Submission for the Health Canada is the process which provide the clear information of "How New Drug approved and reviewed in Canada" and based on the regulatory guidance's provide the information Regarding the how Drug Product aligned with canada's guidelines. The food and drug act and its regulation provide clear cut information of the product approval in Canada.

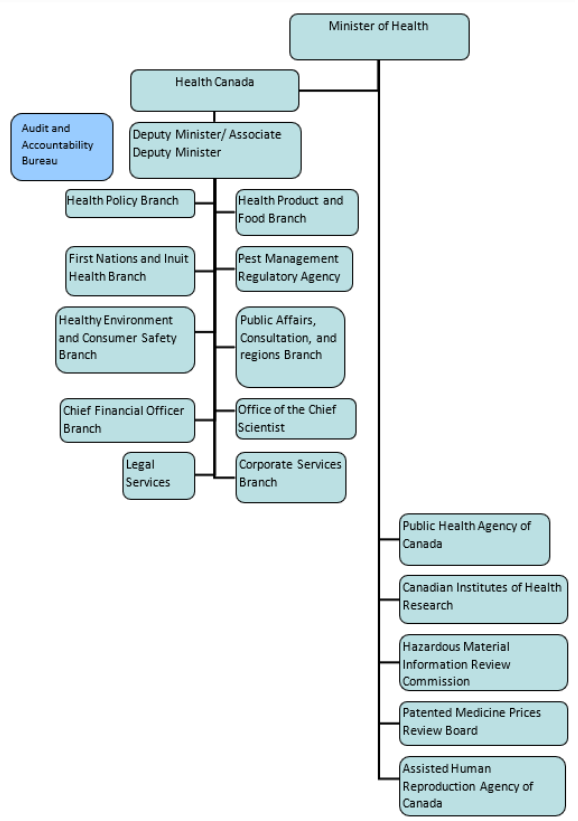


Fig.No.:1-Health Canada's Organisational Structure

There are several Branches, offices, and bureaus in Health Canada which mainly includes- (3) [accessed on: 21.08.2022]

1. The office of Audit and Evaluation: The mandate of the Office of Audit and Evaluation (OAE) is to provide independent and objective advice and assurance to the Deputy Minister, on the effectiveness of risk management, controls, and governance processes.
2. Chief Financial Officer Branch: The Chief Financial Officer Branch is the departmental focal point of accountability to ensure rigorous stewardship of resources, manage for results and provide integrated financial services.

The Branch provides the necessary enabling frameworks, policies, systems, and best practices and tools to support program management and operations.

3. Communication and Public Affairs Branch: The Branch plays a key role in delivering Health Canada's commitment to transparency. Through CPAB, Health Canada will continue to improve communications and the flow of information to and from stakeholders, clients, partners, media, and the Canadian public.
4. Controlled Substances and Cannabis Branch: The Controlled Substances and Cannabis Branch's (CSCB) mandate is to reduce or prevent the harms associated with the use of substances in Canada.
5. Corporate Services Branch,
6. Departmental Secretariat,
7. Health Product and Food Branch: HPFB work to protect and promote the health and safety of Canadians by being a trusted scientific and regulatory authority for health products and food in Canada and internationally.
8. Healthy Environments and Consumer Safety Branch mission is to protect the health of Canadians through leading research, active prevention, targeted oversight, and timely response by leading research, regulating, and managing chemicals, products of biotechnology, radiation, environmental contaminants, workplace hazardous products, consumer products, and cosmetics.
9. Legal Services: The departmental Legal Services Unit provides legal services to the Department of Health and the Public Health Agency. These include legal policy advice, opinions, development of legislative proposals, litigation support and assistance to the Minister, Deputy Minister and to senior managers as well as to working level managers and officers.
10. Opioid Response Team: The mandate of the Opioid Response Team (ORT) is to help protect the health of Canadians and promote healthy choices by:
    - coordinating the federal response to the opioid crisis
    - providing leadership for Canada's drug policy
    - regulating drugs and substances
11. Pest Management Regulatory Agency: It is responsible for pesticide regulation in Canada. Created in 1995, this branch of Health Canada consolidates the resources and responsibilities for pest management regulation.
12. Regulatory Operations and Enforcement Branch: The primary function of the Regulatory Operations and Enforcement Branch of Health Canada is compliance and enforcement.
13. Strategic Policy Branch: The Strategic Policy Branch (SPB) plays a lead role in health policy, communications, and consultations.

2.LEGISLATION AND GUIDELINES

Health Canada administers several parts of legislation and develops and implements regulations that directly affect the health and safety of Canadians. The Department consults with the Canadian public, industry, non-Governmental organisations (NGOs) and other interested parties in the development of these laws. Health Canada also produces guidelines to help and interpret legislation and regulation.

Legislation is making and enforcing laws by local, state, or national legislatures. Regulation usually means the control of activity or process through rules. Guidelines are departmental documents used to interpret legislation and/or regulation respectively. Health Canada is responsible for administering certain federal acts and regulations. (4) [accessed on: 01.09.2022]

The Act: After the Creation of the Federal Department of Health in 1919, the Food and Drug Act introduced in 1920. Also, Rules and Regulations developed under the Act and established the requirements for licensing and creating of drugs in Canada. The law empowered the health minister to revoke or suspend the license of companies that did not comply with the requirements. (5) [accessed on: 23.11.2022]

According to the Food and Drug Act, "a drug includes any substance or mixture of substances manufactured, sold, or represented as being used for: Diagnosis, treatment, relief, or prevention. Prevent disease, disorder, abnormal physical condition, or symptoms thereof, in humans or animals; Restore, correct, or alter organic functions in humans or animals; or Disinfect in a facility where food is produced, processed, or stored."

The Food and Drugs Act (the Act) (formal title An Act respecting food, drugs, cosmetics and therapeutic devices) is an act of the Parliament of Canada regarding the production, import, export, transport across provinces and sale of food, drugs, contraceptive devices and cosmetics. (6) [accessed on: 17.09.2022]

3.FOOD AND DRUG REGULATION IN CANADA FOR DRUG

The drug in Canada is regulated by Food and drugs regulations under part A to part J, in that the Several Part are Eliminated like part F, H, I.

The part A which includes the Administration. Part B is for Food, Part C is for Drug, Part D is for vitamins, minerals & amino acids, Part E is for cyclomate & saccharin sweeteners, Part G is for Controlled drugs and the art J is for Restricted drugs.

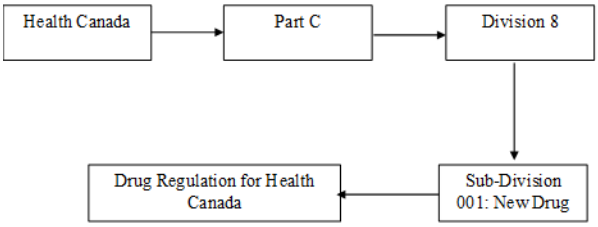


Figure No.:2-Food Drug Regulation

The food and drug Act was not significantly changed until 1947, when the foundation of today's market was laid. In 1951, drug manufacturers were required to submit a dossier for each new drug before marketing their product. However, in the early 1960s, the drug thalidomide, which was approved to enter the market, resulted in thousands of infant deaths and severe birth defects in others when women took the drug during pregnancy. Because of the problems caused by the thalidomide drug, The Act was revised and strengthened by Health Canada. The revised version places new requirements for manufacturers to provide evidence of efficiency in obtaining a Notice of Compliance, which must be obtained before any drug is sold. The Food and Drug Regulations set out requirements for the manufacture, packaging, labelling, storage, importation, distribution and sale of food and prescription and over-the-counter medicines in Canada. (7) [Accessed on: 10.10.2022]

The Guidance Document for Management of Drug Submissions and Applications (MDSA) gives sponsors and Health Canada staff from the Pharmaceutical Drugs Directorate (PDD) (11) [accessed on: 12.10.2022] , the Biologic and Radiopharmaceutical Drugs Directorate (BRDD), the Medical Device Directorate (MDD), the Non-Prescription Drug Evaluation Division (NDED) of the Natural and Non-Prescription Health Products Directorate (NNHPD), the Office of Submissions and Intellectual Property (OSIP) within the Resource Management and Operations Directorate (RMOD), and the Marketed Health Products Directorate (MHPD) operational direction and guidance when managing information submitted in accordance with the Food and Drugs Act and its Regulations.

Submission Type for New Drug for Human use

The following submission types are listed in Accordance with the Health Canada database:

New Drug Submission (NDS): This is followed for submitting an application for new molecule which has never been marketed earlier.

Supplement to a New Drug Submission (SNDS): After Issuance of Notice to Compliance for NDS then the SNDS file for to notify the changes that have substantial potential to have an adverse effect on the Identity, Strength, Quality, Purity, or Potency of a drug Product.

Abbreviated New Drug Submission (ANDS): it is generic version of new drug which is already Present in market, When the New drug or Innovators Product Patent Was Expired then the Manufacturer can file the Abbreviated New Drug Submission (ANDS) and Supplement Abbreviated New Drug Submission (SANDS): Supplement to an Abbreviated New drug Submission.

In this article an attempt has been made to explain the submission and approval process of NDS under Food and Drugs Act and its Regulations as per Health Canada.

1) NDS:

Health Canada's New Drug Submission (NDS) is the process by which new drugs are approved and reviewed before they enter the Canadian market. In Canada, new drugs are regulated under Part C, Division 8 of the Food and Drug Regulations. Applicant obtains approval to market the new drug in Canada by submitting the NDS

under Section C.08.002 of the Food and Drug Regulations. (10) [accessed on: 09.10.2022] The Part C is for DRUG which mainly have 9 Divisions like Division 1 is for General, Division 1A is for Establishment Licences, Division B for Good Manufacturing Practices, Division 3 is for Schedule C drug, Division 4 is for Schedule D drug, Division 5 for Drugs for Clinical Trials Involving Human Subjects, Division 6 is for Canadian standard drug, Division 7 is for Sale of Drugs for the Purposes of Implementing the General Council Decision and the Division 8 is for New Drugs, Division 9 is for Non-prescription drugs. (12) [Accessed on: 02.11.2022]

Submission Requirements (e-CTD): The CTD format arose from the International Conference on Harmonization (ICH) initiative to harmonize efficacy, safety, and quality requirements (chemical and manufacturing) globally for the registration of medicinal products (pharmaceutical, biological, gene therapy, etc.). for human use. (The CDT guidance are provided in ICH M4 guideline) This initiative includes a standard information organization for new drug applications. The CTD format is divided into five modules. Module 1 contains regional information and Modules 2-5 contains general clinical, non-clinical and quality information, with some regional differences. The TOC is only called for in the paper version of the CTD; there is no entry needed for the eCTD (A TOC is not applicable for eCTD).

Generally, the 5 modules which needs to attach in Dossier are as follows, (8) [accessed on: 23.08.2022]
Module 1 is not Part of CTD which mainly Includes Administrative Information and Prescribing Information

1.1 Table of Contents of the Submission Including Module 1
1.2 Documents Specific to Each Region (for example, application forms, prescribing information).
Module 2: CTD Summaries
2.1 CTD Table of Content
2.2 CTD Introduction
2.3 Quality Overall Summaries
2.3.S Drug Substances (Name, Manufacturer)
2.3.P Drug Product (Name, Dosage Form)
2.3.A Appendices (Facilities and Equipment)
2.3.R Regional Information
2.4 Non-Clinical Overview
2.5 Clinical Overview
2.6 Non-Clinical Written and Tabulated Summaries

- Pharmacology
- Pharmacokinetics
- Toxicology

2.7 Clinical Summary

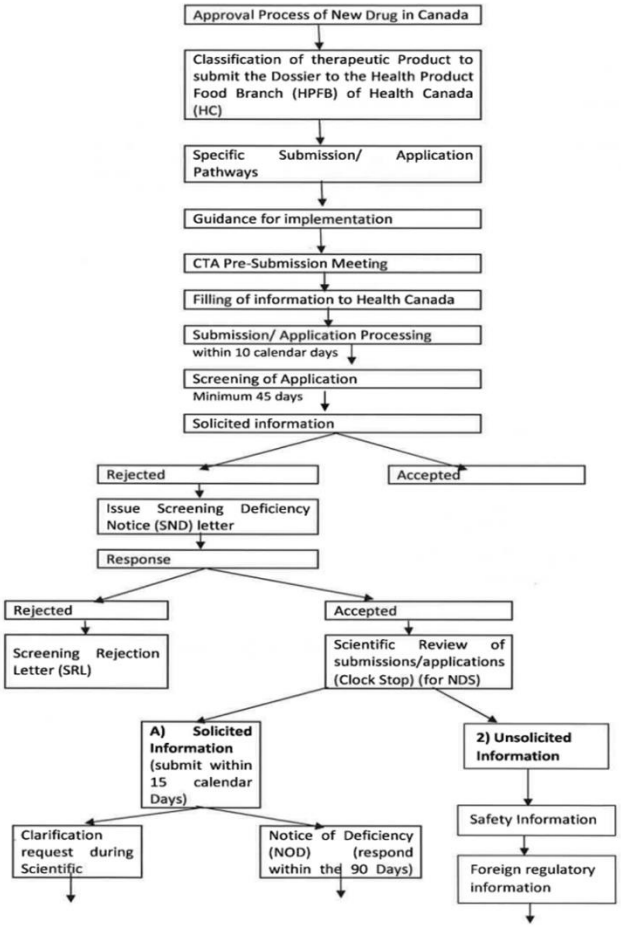
- Biopharmaceutic Studies and Associated Analytical Methods
- Clinical Pharmacology Studies
- Clinical Efficacy
- Clinical Safety
- Literature References
- Synopses of Individual Studies

Module 3: Quality
3.1 TOC of Module 3
3.2 Body of Data
3.3 Literature References
Module 4: Non-Clinical Study Reports
4.1 TOC of module 4
4.2 Study Reports
4.3 Literature References
Module 5: Clinical Study Reports
5.1 Table of Contents of Module 5
5.2 Tabular Listing of All Clinical Studies
5.3 Clinical Study Reports
5.4 Literature References

4.APPROVAL PROCESS OF NDS IN DETAIL

Sponsors can submit NDSs regardless of whether the clinical trial was conducted in Canada or another country. The NDS should include the results of quality (chemical and manufacturing), preclinical and clinical studies, whether conducted in Canada or elsewhere. Currently, Health Canada accepts submissions/applications in the electronic common technical document (eCTD) electronic-only format and in the non-eCTD electronic-only format. Paper documents are no longer accepted by Health Canada for any type of submission/application.
Depending on the product type, the appropriate branch or agency of Health Canada will review the NDS to ensure compliance with current regulatory requirements. Sponsors are required to file submissions electronically to Health Canada in either Electronic Common Technical Document (eCTD) format or non-eCTD format, depending on the regulatory activity type.

The general approval process for new drug by Health Canada is depicted below:



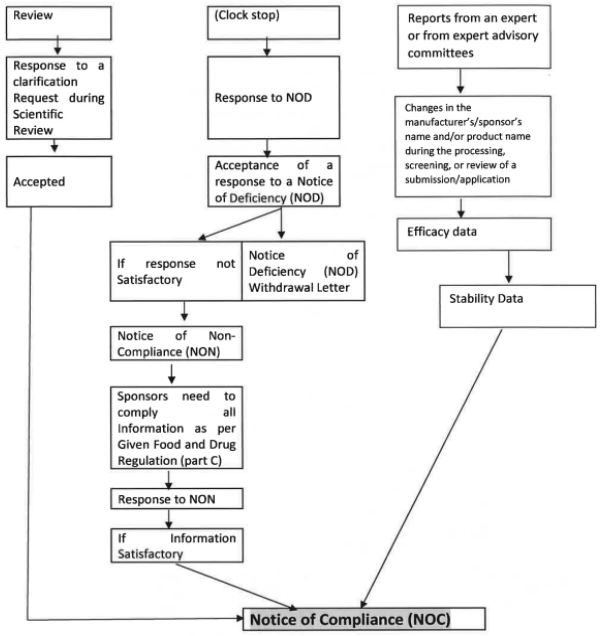


Figure No.3: Approval Process of New Drug in Canada

Once the quality, safety, and efficacy aspects of the new drug have been satisfactorily verified, The Authority will issue a Notice of Compliance (**NOC**) allowing sponsors to move on to the next step to market.

Figure No. 4 Approval Process with Conditions (9)
[accessed on: 24.12.2022]

5.CONCLUSION

Health Canada is the federal agency that regulates the drug approval process under the Food and Drug Act (FDA) and Regulation (FDR), related policies and guidelines. Before a drug can be distributed and sold in Canada, the manufacturer of the drug must receive a Notice of Compliance (NOC) from Health Canada and the drug must be assigned a Drug Identification Number (DIN). In Canada. New drugs must also go through extensive testing before being granted AC certification.

Health Canada may take six months to two years to review information about a drug's safety and efficacy before deciding to approve a NOC. Once approved, it means that the drug meets the standards required by the Food and Drug Administration and its use in humans. Drug safety monitoring continues even after the drug reaches the end consumer.

ABBREVIATIONS:

a) NDS: New Drug Submission
b) NOC: Notice of Compliance
c) NOD: Notice of Deficiency
d) DIN: Drug Identification Number
e) NON: Notice of Non-Compliance
f) SRL: Screening Rejection Letter
g) SDN: Screening Deficiency Notice
h) NGO: non-Governmental organisations.

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