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GENERIC DRUGS (ANDS) APPROVAL PROCESS IN CANADA: A REVIEW

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ABSTRACT

A regulatory requirement for generic drug development has the impact on launching the drug into the market. The regulatory documents which are going to submitted to the regulatory agencies should be carefully reviewed by the skilled professional to minimize the queries raised by the regulatory agencies and speed up the approval process. In CANADA. The literature work, difference in generic drug approval requirements has been studied and explained in detailed in this work, which gives the clear over view of the role of generics in the world market and where Canada lies in its generic drug approval process, generic market and the challenges that Canadian regulatory authority has to overcome in the near future.

KEYWORDS: ANDA, CANADA, REGULATORY REQUIREMENTS, GENERICS, HEALTH CANADA.

INTRODUCTION

In Canada, a ‘new drug’ has been defined in section C.08.001 of the Food and Drug Regulations as a drug which contains a substance which has not been sold in Canada for a sufficient time and in sufficient quality to establish its safety and efficacy. Thus, ‘new drug’ includes both novel products as well as drug that are not novel but are ‘new’ in the sense that the particular version of the drug has not been previously marketed (as in case of a competing or a generic version of a drug that has the same property). Under Canada’s Food & Drugs Act, the therapeutic products program (TPP) of the federal department of Health (Health Canada) is responsible to ensure that “new drug” meet health and safety requirements.

Both generic as well as patented products are treated as ‘new drugs’ by the Food and Drug Regulations because generic is equivalent, and not identical, to the patented product it replicates. The major difference between submission for a patented and a generic product is the data required to establish the safety of new drug and its clinical efficacy. For a generic drug comparative studies to establish pharmaceutical and bioequivalence with another, usually innovator’s product, i.e., “Canadian Reference Product” identified in section C.08.001.1 of the Regulations is required while extensive pre-clinical, toxicity studies in animals, clinical studies and pharmacokinetic studies to establish safety and efficacy of new drug is must. The generic drug must be demonstrated to deliver the same amount of active ingredient at the same rate as the original.

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 DrugAdministration (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.

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:

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

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.

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.

Aim

The aim of this study explains about complication of dossiers of generic drugs (ANDS) in Canada.

Objectives

1) The main objective is to have regulatory requirements for compilation of generic drugs (ANDS) for Canada by following guidelines and regulations of Health Canada and proceeding of ANDS by considering CTD along with ICH guidelines.
2) To get the knowledge of documents required for that ANDS filing and the process of review.
3) Preparation, development and the review of QOS & quality of ANDS for Submission in Canada.
4) To explore brief discussion regarding exclusivities offered by the Health Canada.

To show the brief information regarding market share of generic drugs in Health Canada

METHODOLOGY

ANDS Eligibility

Subsection C.08.002.1 (1) of the Food and Drug Regulations defines the eligibility criteria for an ANDS as follows:

1) "A manufacturer of a new drug may file an abbreviated new drug submission for the new drug where, in comparison with a Canadian reference product,
2) The new drug is the pharmaceutical equivalent of the Canadian reference product;
3) The new drug is bio equivalent with the Canadian reference product, based on the pharmaceutical and, where the minister considers it necessary, bioavailability characteristics;

4) The route of administration of the new drug is the same as that of the Canadian reference product; and
5) The conditions of use for the new drug fall within the conditions of use for the Canadian reference products".
6) Generally, subsequent market entry products which satisfy the above criteria would be eligible for filing as an ANDS.

Pharmaceutical Equivalence

As stated in the section C.08.001.1 of the "Food and Dug Regulations", pharmaceutical equivalent means "a new drug that, in comparison with another drug, contains identical amounts of the identical medicinal ingredients, in comparable dosage forms, but that does not necessarily contain the same non-medicinal ingredients".

Declaration of Equivalence

As stated in the subsection C.08.004 (4) of the Food and Drug Regulations, "a notice of compliance is issued in respect of a new drug on the basis of information and material contained in a submission filed pursuant to section C.08.002.1 shall state the name of the Canadian reference product referred to in the submission and shall constitute a declaration of equivalence for that new drug."

Bioequivalence

Bioequivalence is defined in the TPD guidance "conduct and analysis of Bioavailability and Bioequivalence Studies –Part A" as "a high degree of similarity in the bio availabilities of two pharmaceutical products (of the same galenic form) from the same molar dose, that are unlikely to produce clinically relevant differences in therapeutic effects, or adverse reactions, or both."

In using the CTD format for ANDSs, the dossier should be organized similarly to a NDS, although certain CTD modules will not normally need to be submitted.

The majority of ANDSs are supported by one or more pivotal comparative bioavailability studies.

When filing an ANDS in the CTD format, it is anticipated that only the following relevant modules will normally be required.

2 Outline of CTD modules

Module 1: Administrative Information and Prescribing Information

1.1 Table of contents (Modules 1-5)

1.2Application Information

1.3 Product Labelling

1.4 Health Canada Summaries

1.5 Environmental Assessment Statement

1.6 Electronic Review Documents

Module 2: Common Technical Document Summaries

2.1 Overall CTD Table of Contents (Modules 2-5)

2.2 Introduction

2.3 Quality Overall Summary (QOS)

Module 3: Quality

Module 4: safety (do not required for Abbreviated Submissions)

Module 5: Clinical study Reports

Review Process of a new drug in Canada

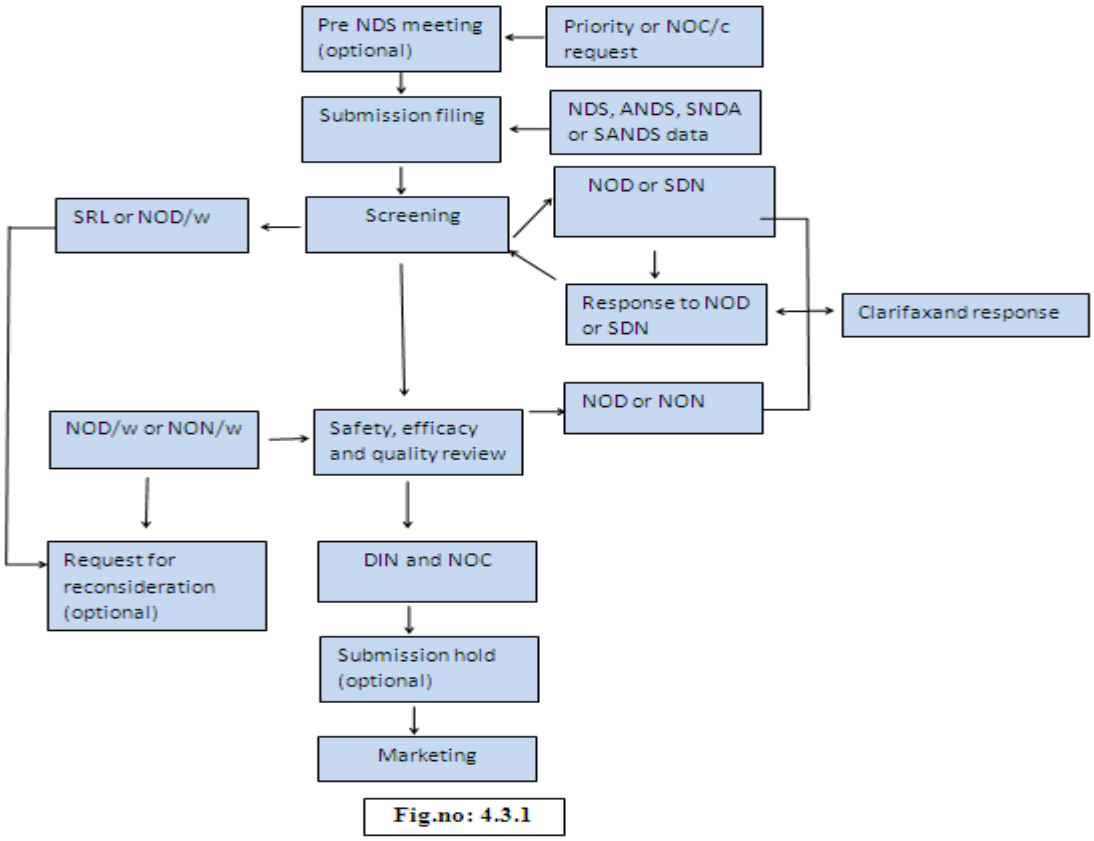

Fig.no: 4.3.1

It includes the following steps:

NOC: Notice of Compliance

NOD: Notice of Deficiency--sponsor has 90days to respond

NON: Notice of Non-compliance--sponsor has 90days to respond

NOD/w: Notice of Deficiency/withdrawal letter

NON/w: Notice of Non-compliance/withdrawal letter

SDN: Screening Deficiency Notice--sponsor has 45days to respond

SRL: Screening Rejection letter

NOC/c: Notice of compliance--with conditions

Clarifax--can be issued at any point during review and sponsor has 15days to respond

Submission filling

A sponsor files duplicate copies of its submission to the TPD, at which point it undergoes a screening procedure. Sponsors seeking a priority review or review under the NOC/c (Notice of compliance with conditions) regulations should submit a request in advance of filing the NDS/ANDS. For a priority review request, a response from the TPD should be received within 30 calender days. A response for a review under the NOC/c guidelines should be received 10days working after the finalization of the meeting minutes from the Pre-submission meeting. Sponsors are then required to submit the ANDS for either a priority drug or NOC/c application within 60days.

Screening

Upon receipt of the NDS/ANDS, the TPD will undertake a screening process to ensure it is complete and in the appropriate format. This is an administrative review and does not include any technical review of the information. The TPD targets 45 calender days to complete the screening of an NDS/ANDS. Priority submissions and those accepted for advance consideration under the NOC/c policy have a 25 day screening target. Once the screening is complete and accepted, the submission enters the queue for technical review.

If the screening process identifies deficiencies in the NDS/ANDS, the sponsor will receive a screening deficiency notice, and has 45 calender days to respond and resolve any identified deficiencies. The TPD notes that submission containing interim analysis of pivotal data or safety studies will be considered deficient. If a sponsor's response to a screening deficiency notice contains unsolicited information, the the TPD will reject the submission (i.e., this is

not an opportunity to add further information to a file). Upon re-submission, a new screening period of 45 calender days starts.

Evaluation of submissions: Safety, efficacy and quality review

Only quality and efficacy data should be analysed by following the check list of Canada. If TPD is not able to commence the review of a submission prior to its performance target date, the sponsor will receive an Update Notice, which provides an opportunity for the sponsor to update the file with additional information. The sponsor has 30days to decide and then notify the TPD if it will submit additional information. The sponsor then has a further 60days to update its submission. During the review of a submission, a sponsor can receive a variety of different types of letters requesting additional information.

In the updated screening process, sponsors will confirm through the attestation form if DMFs and requisite Letters of Authorization have been provided. Should the DMF not be in order (fees paid, accessible), a screening Deficiency Notice (SDN) will be issued. The "closed" portion of the DMFs will be no longer be verified at screening.

Clarifax (clarification request)

A Clarifax is a request to expand, clarify or re-analyze existing data. Clarifaxes do not contain requests for additional data. A sponsor has 15 calender days to respond to a Clarifax. If the sponsor is able to meet the timeframe for response, the review will continue uninterrupted. The TPD has no limit on the number of Clarifaxes that it may issue in relation to a submission.

Notice of Deficiency (NOD)

If there are significant deficiencies or omission that preclude the continuation of the review, the TPD will send an NOD. The NOD will list all deficiencies in the file that has been reviewed to date. Note that the review of all aspects of the submission may not necessarily be complete when the NOD is issued. For example, the clinical review may be complete but the chemistry, manufacturing and controls (CMC) review may not have started. Only one NOD will be issued per submission. Review of the submission stops on issuance of an NOD. The sponsor has 90days to respond to the matters identified in the NOD. The response goes through the screening procedure and, if found acceptable, it re-enters the review queue.

When the response to an NOD is reviewed, if it is still found to be deficient, the TPD will issue a Notice of Deficiency--Withdrawal (NOC/w). The sponsor is required to withdraw the file from review but can re-file at a later date without prejudice.

If a sponsor disagrees with TPD's decision, it can submit a Request for Reconsideration.

Notice of Non-compliance (NON)

After the review of a submission is complete, the TPD may issue an NON. This letter indicates that the submission is deficient or incomplete. The NON lists deficiencies from all parts of a submission (e.g., clinical, pre-clinical, CMC). Only one NON is issued per submission, and the review stops on issuance of the NON. A sponsor has 90days to respond.

A response to an NON will enter a new screening process and, if accepted for review, it will re-enter the queue. If a response to an NON contains unsolicited information or is found to be deficient during screening, the response will be rejected and the submission withdrawn from further review.

If a sponsor failed to respond for an NON on time, or if the response is unacceptable, then the TPD will issue a Notice of Non-compliance --Withdrawal (NON/w). The submission will be considered withdrawn but the sponsor can re-file at a later date without prejudice.

Notice of Compliance with Conditions (NOC/s)

The NOC/s policy at Health Canada was formulated with the goal of providing physicians and patients early access to a drug as well as a means effectively monitor and report on the safety of the drug through enhanced post-marketing surveillance. The NOC/c policy is restricted to products for serious, life-threatening or severely debilitating diseases or conditions.

Notice of Compliance (NOC)

Once a submission is found acceptable, a sponsor receives a Notice of Compliance. This identifies the Drug Identification Number (DIN) that is assigned to the product and is required to appears on the product's label.

Reviewer reports

The reviewer reports will be provided to the sponsor within seven calender days following the issuance of an NOD, an NOD/w, an NON or an NON/w. Sponsors may request a

reviewer's report following the issuance of an NOC, and it is supposed to be provided within 30 calender days.

4.4 Brief Introduction regarding Exclusivities in Canada

1. Brand companies must list their patents for an approved drugs on the patent register
2. When filing an abbreviated new drug submission (ANDS) the generic companies must address the patent listed on the Patent register.
3. If the generic challenges the validity or infringement of the patent, the innovator may apply to the court for an order prohibiting the minister (Health Canada).
4. Minister cannot issue a NOC to the generic for a period of up to 24 months.
5. Products first authorized prior to June 17, 2006; 5 years exclusivity.
6. products first authorized after June 17, 2006;

6 years -- Applications for generics cannot be submitted

8 years (6+2) -- No-marketing period during which a notice of compliance will not be granted to manufacturer.

7. Further 6 months of data exclusivity can be added for active ingredients that have been the subject of paediatric studies designed and conducted with the purpose of increasing.
8. Knowledge about the use of the drug 20 years of patent protection under the Canadian Patent Act.
9. Unlike most industrial countries, NO patent term restoration or patent term extension in Canada.

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30. This application contains the following items *(Continued; select all that apply)*

☐ 9. Safety update report *(e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)*	☐ 10. Statistical section *(e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)*
☐ 11. Case report tabulations *(e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)*	☐ 12. Case report forms *(e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)*
☐ 13. Patent information on any patent that claims the drug/ biologic *(21 U.S.C. 355(b) or (c))*	☐ 14. A patent certification with respect to any patent that claims the drug/biologic *(21 U.S.C. 355 (b)(2) or (j)(2)(A))*
☐ 15. Establishment description *(21 CFR Part 600, if applicable)*	☐ 16. Debarment certification *(FD&C Act 306 (k)(1))*
☐ 17. Field copy certification *(21 CFR 314.50 (l)(3))*	☐ 18. User Fee Cover Sheet *(PDUFA Form FDA 3397, GDUFA Form FDA 3794, BsUFA Form FDA 3792, or MDUFA Form FDA 3601)*
☐ 19. Financial Disclosure Information *(21 CFR Part 54)*	
☐ 20. Other *(Specify)*: _____	

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to, the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state, and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge, are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

31. Typed Name and Title of Applicant's Responsible Official		32. Date *(mm/dd/yyyy)*
33. Telephone Number *(Include country code if applicable and area code)*	34. FAX Number *(Include country code if applicable and area code)*	35. Email Address

36. Address of Applicant's Responsible Official

Address 1 *(Street address, P.O. box, company name c/o)*	
Address 2 *(Apartment, suite, unit, building, floor, etc.)*	
City	State/Province/Region
Country	ZIP or Postal Code

37. Signature of Applicant's Responsible Official or Other Authorized Official — Sign	38. Countersignature of Authorized U.S. Agent — Sign

The information below applies only to requirements of the Paperwork Reduction Act of 1995.

The burden time for this collection of information is estimated to average 24 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the address to the right:

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FORM FDA 356h (08/18 - PREVIOUS EDITIONS OBSOLETE) Page 3 of

RESULTS AND DISCUSSION

1. Compilation of dossier for generic drugs (ANDS) in Canada includes all modules as per ICH guidelines in CTD format electronically.
2. Majority of bulk drugs companies (sponsors) file their dossiers by collecting the all revelant data from R&D, their documents from QC dept and which are finally authorized by QA dept regarding particular product.

3. Comparative BA/BE studies information of that generic drugs are gathered from contract Research Organization (CRO's) which will conduct clinical trails, bioavailability of different drugs especially.
4. All of these data included in the dossier should be submitted to the agent for our company who is very familiar with pre-submission meetings and updating guidelines of that regulatory authority.
5. The agent verify the Dossier and inform to the company if any requirements, documents, letters are needed and collect them and finally submit to the federal regulatory authority i.e., Health Canada (TPD).
6. Experts and scientists will review of these submissions as per regulatory norms regarding Quality, Safety & Efficacy of that product compared to Canadian reference product.
7. Once the dossier is found to be acceptable, then sponsor will get the NOC/DIN for that particular generic drug.
8. Then the generic product is acceptable to market that product in Canada.

CONCLUSION

I worked on "Compilation of dossiers for generic drugs (ANDS) in Canada" as a part of my project specification. The regulatory requirements for this ANDS submission, guidelines and regulations of Health Canada and proceeding ANDS by considering CTD format with ICH guidelines which were discussed in the Methodology of this submission.

In this dissertation mainly focused on the QOS and MODULE 3 (Quality) and brief introduction regarding the BA/BE studies also. Exclusivities for marketing pharmaceuticals in Canada are also briefly mentioned in the methodology. Here by included that the abbreviated new drug dossier preparation, development and also review of submission in Canada. Here by concluded that the brief information regarding marketing of generic drugs in Canada also explored in this thesis.

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