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REVIEW ARTICLE

REGULATORY PERSPECTIVE OF GENERIC ANTI CANCER DRUG DEVELOPMENT PROCESS IN EUROPE AND USA

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ABSTRACT

The role of regulatory affairs is to develop and execute a regulatory strategy to ensure that the collective efforts of the drug development team results in a product that is approvable by global regulators but is also differentiated from the competition in some way and also is to ensure that the company's activities, from non-clinical research through to advertising and promotion, are conducted in accordance with the regulations and guidelines established by regulatory authoritiesEvery country's ultimate goal is to protect their people's health and safety. Particularly Canada is showing much more attention on their people because of the diseases relevant to the different climatic conditions. Time and tide waits for none and Hence, It is the objective to know regulatory requirements for compilation of Generic drugs (ANDA's) in Canada by following guidelines and regulations of Health Canada and proceeding of ANDA's by considering CTD along with ICH regulations.The chances of empowering the market with the generic drugs increase, when the patent protection of the innovator (NOTICE OF COMPLIANCE) molecule expires. Compilation of Dossiers for generic drugs in Canada has become more stringent than so many other countries. Because of these high stringent regulations, health Canada has explored better exclusivities than other countries. CTD is Common Technical Document that gives the common format for the preparation of a well-structured technical document for applications that will be submitted to regulatory authorities. Regulatory reviews and communication with the applicants will be facilitated by a standard document of common elements. To compile ANDS, it is very necessary to submit the requirementsModule-2(QOS),Module-3(QUALITY) and comparative bioavailability studies to prove the quality of our generic product.

Keywords: ANDA, ICH Guidelines, Canada

INTRODUCTION

In Canada, a 'new drug' has been defined in section C.08.001 of the Food & Drug Regulations as a drug which contains a substance which has not been sold in Canada for a sufficient time and in sufficient quantity to establish its safety and efficacy. Thus, 'new drug' includes both novel products as well as drugs 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 properties). 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.

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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 [5].

The Food and Drug Regulations contain data exclusivity provisions that add to the protection offered to brand companies under the Patent Act. Data exclusivity periods prevent disclosure of information submitted by brand companies for a minimum of eight years. As a result, data exclusivity prevents generic manufacturers from obtaining data upon which it can rely to file its ANDS.

The third regulatory scheme, entitled the Patented Medicines (Notice of Compliance) Regulations (NOC regulations), attempts to balance the protection afforded by the Patent Act and the Food and Drug Act by setting forth a simplified approval process for generic manufacturers that is linked to patents that cover the brand product. The NOC regulations are administered by the Office of Patented Medicines Liaison within the Therapeutic Products Directorate (TPD) of Health Canada.

The aim of the present study was explains about Compilation of dossiers for generic drugs (ANDS) in Canada and 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 regulations.

METHODOLOGY

ANDS Eligibility[6]

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 bioequivalent 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 product.”
6) Generally, subsequent market entry products which satisfy the above criteria would be eligible for filing as an ANDS.

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Pharmaceutical Equivalence

As stated in the section C.08.001.1 of the “Food and Drug 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 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.

Outline of CTD modules

Module 1: Administrative Information and Prescribing Information

1.1 Table of Contents (Modules 1-5)

1.2 Application 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)

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Module 5: Clinical Study Reports

5.1 Table of Contents for Module 5

5.2 Tabular Listing of all Clinical Studies

5.3 Clinical Study Reports

5.3.1 Biopharmaceutical Studies

5.3.1.2 Comparative Bioavailability and Bioequivalence Study Reports

5.3.1.3 In vitro-In vivo Correlation Study Reports

5.3.1.4 Reports of Bio analytical and Analytical Method for Human Studies

5.3.7 Case Report Forms and Individual Patient Listings

5.4 Literature References

In this, the review is mainly focused on the QOS and QUALITY module of dossiers. To assess the quality of product, sponsor has to submit the required information with CTD format to get market approval.

Module 1: Administrative information and prescribing information

Module 1 is to include regional administrative documents and proposed labelling for use in the region. The information to be included in Module 1 and its outline is identified in section 4.1 of the Guidance for Industry - Preparation of New Drug Submissions in the CTD Format.

1.1 Table of Contents (Modules 1-5)

1.2 Application Information

1.2.1 Drug Submission Application Form (HC/SC 3011)

1.2.2 Submission Fee Application Form

1.2.3 Submission Certification Form

1.2.4 Patent Information

1.2.5 Good Manufacturing Practices (GMP) and Establishment Licensing (EL) Information

1.2.6 Letters of Access

1.2.7 International Registration Status

1.2.8 Other Application Information

This section serves as a placeholder for other administration information that may be filed by the applicant in relation to the submission.

a. Canadian Reference Product Confirmation

Confirmation that the Canadian reference product was used in the comparative bioavailability study may be provided in the form of a purchase receipt(s), signed confirmation in writing that the reference was purchased in Canada, or a photocopy of the product label(s) which clearly shows the trade name, product strength, lot #, expiry date, and Drug Identification Number (DIN) of the product administered in the bio-study. Pursuant to paragraph (c) of section

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C.08.001.1 of the "Food and Drug Regulations", the use of a Canadian reference product purchased outside of Canada, must be supported by a justification statement that should be provided in this section. The justification should address all of the criteria outlined in the TPD Canadian Reference Productpolicy and will include supporting data (e.g., comparative dissolution) which should be provided in the relevant modules of the CTD submission (i.e., Modules 2-5).

b. Waiver Requests

Generally, results from comparative bioavailability studies should be provided in support of the safety and efficacy of each proposed product and each proposed strength included in an ANDS. In the absence of such studies, a justification supporting a waiver of this requirement should be provided in this section for each product and for each strength.

For example, if there are several strengths of the proposed product, and comparative bioavailability data has not been submitted for all strengths, the sponsor should provide a scientific justification for not conducting studies on every strength of dosage form. This justification may address issues such as the nature of the kinetics of the drug (e.g., linear versus non-linear), and the proportionality of the strengths for which a waiver is sought to the strength on which a comparative bioavailability study was conducted.

The statement of justification for waiver will include supporting data (e.g., comparative dissolution data) which should be provided in the relevant module(s) of the CTD submission (i.e., Modules 2-5). For example, comparative dissolution profiles should be provided in Module 3, section 3.2.P.2 (Pharmaceutical Development).

c. Certificates of Analyses

Certificates of Analyses should be provided in this section in order to verify the potency (as a percent of the label claim) for both the Test and Reference products.

1.3 Product Labelling

1.3.1 Product Monograph

The Product Monograph for second and subsequent market entry products must provide information directly relevant to the safe and effective use of the new drug. Please note that the conditions of use for the new drug must fall within the conditions of the use of the Canadian reference product. A copy of the current labelling and Product Monograph for the reference product must be included in the submission (in this section). Any differences between the Product Monographs must be annotated to supporting data. Copies of data or references to support such differences must be included in the submission. Please note that the labelling must be current at the time the NOC is issued.

The Product Monograph must include the Summary Table(s) of the Comparative Bioavailability Data. The location of the summary table(s) within the Product Monograph is outlined in the most current TPD guidance document(s).

1.3.2 All Inner and Outer Labels

1.3.3 Non-Canadian Package Inserts

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1.4 Health Canada Summaries

1.4.1 Certified Product Information Document

1.4.2 Comprehensive Summary: Bioequivalence

A completed paper copy of the Comprehensive Summary: Bioequivalence (CS-BE) for Pivotal bioequivalence studies are to be included in this module. The electronic copy is to

Be provided in Module 1.6.

Note: If the Comprehensive Summary: Bioequivalence (CS-BE) is completed for submissions that rely solely on pivotal comparative bioavailability studies to establish safety and efficacy, Modules 2.4-2.7 of the CTD do not need to be completed.

If the dossier includes a pivotal comparative bioavailability study (ies) as well as other types of safety and efficacy studies, Modules 2.4-2.7 must be completed, as applicable, irregardless of whether or not the CS-BE was completed for the pivotal comparative bioavailability study(ies).

If the submission involves only a solution for parenteral use, and the Product Monograph has been provided as described above, and data concerning the pharmaceutical equivalency and characteristics of the formulation have been provided in the Chemistry and Manufacturing portion of the submission, then no additional information under Module 5 of this guidance is required.

The CS-BE is pivotal in the review process. It should provide a comprehensive, integrated summary of the overall content of information in the submission as it pertains to the comparability of the product with the Canadian reference product of proven safety and effectiveness under the proposed conditions of use. This should include a scientific rationale and justification for the study design used, the parameters assessed and the standards applied. It must also be cross-referenced to the supporting documents provided in Module 5 (Clinical Study Reports).

The CS-BE template provides placeholders for the following information (which may not necessarily be a component of the clinical study report(s) submitted in Module 5).

Physicochemical Characteristics

This section should provide information characterizing the physicochemical properties of the drug, e.g., pKa, molecular weight, solubility in water (g/mL), chirality and polymorphism.

Pharmacology

This section should include a concise synopsis of the salient features of the drug's pharmacologic actions, e.g., site and mechanism of action.

Pharmacokinetics

Information on the absorption, distribution, metabolism and elimination of the drug should be presented here. The nature and extent of any first pass effect, whether plasma concentrations are directly related to dose (i.e., are the pharmacokinetics linear), and values of half-life (T½), clearance, volume of distribution and fraction excreted should be established on the basis of the information summarized in this section. This information, together with that provided under

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Drug Product Classification, is important in establishing the type and number of studies to be conducted in support of each ANDS.

• **Absorption**- Information characterizing the following properties of the drug is required; area under the curve (AUC), time of maximum observed concentration (Tmax), maximum observed concentration (Cmax), time of onset of action and food effect on absorption. Other characteristics of absorption kinetics (e.g., stereospecificity and dose or concentration dependence of absorption) must also be reported.

• **Distribution**- Degree of protein binding, information identifying sites of distribution is required, including reference to whether the drug crosses the blood-brain barrier.

• **Metabolism**- Identify the site(s) and pathway(s) of metabolism. Metabolites should be characterized as to biological/pharmacological activity and whether or not drug metabolizing enzymes are induced. Specify the degree of first-pass metabolism and whether metabolism is capacity limited.

Elimination- Identify the route(s), percent of elimination and terminal half-life (T½).

Drug Product Classification

On the basis of the scientific and medical information summarized above, the drug product is to be characterized as one of the following:

i. conventional (immediate) release formulation with uncomplicated or non-variable pharmacokinetics

ii. modified release formulation with uncomplicated or non-variable pharmacokinetics

iii. conventional release formulation with complicated or variable pharmacokinetics

iv. modified release formulation with complicated or variable pharmacokinetics

The study design, pharmacokinetic parameters and standards of bioequivalence to be used for a declaration of equivalence must be appropriate for the drug product characteristics. In this regard, characteristics of the medicinal ingredient (active drug substance) and the drug product (dosage form) must be taken into consideration. For a description of the characteristics to be used to classify the drug product refer to the TPD guidance

"Conduct and Analysis of Bioavailability and Bioequivalence Studies" -- Part A, and Part B, and the Expert Advisory Committee on Bioavailability -- Report C.

Summary of the Bioavailability/Bioequivalence Studies

This portion of the CS-BE should include summaries of each study performed to establish the bioavailability and bioequivalence of each formulation and be cross referenced to the supporting documents provided in Module 5 (Clinical Study Reports).

All requests for waivers and justification statements should be included in Module 1.2.8 (Other Application Information).

For example, when a product is to be marketed in more than one strength, if the formulation of each strength contains the same medicinal and non-medicinal ingredients in the same proportion, the results of a single comparative bioavailability study may be extrapolated to all strengths in the series. In this regard, refer to the TPD policy on "Bioequivalence of Proportional

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Formulations - Solid Oral Dosage Forms". In all cases, however, if comparative bioavailability data is not provided for each formulation, the sponsor must provide a scientific justification for waiver of this requirement.

Similarly, if the submission involves a solution (e.g., oral solution, syrup, topical) which the sponsor believes should not require a comparative bioavailability study, a scientific justification must be presented for the waiver of this requirement (e.g., TPD policy: Waiver of Comparative Bioavailability Requirements for Oral Solutions, Submissions for Generic Topical Drugs, Submissions for Generic Parenteral Drugs).

REVIEW OF DRUGS IN CANADA[10]

Guidance document for the Management of Drug Submissions is applicable for all types documents (NDS, SNDS, SNDS-C, PSUR-C, ANDS, SANDS, NC, DINA, DINB, DIND, CTA-A).All submitted information and material will be screened to ensure that it is complete and of suitable quality to be reviewed. The same management principles will be applied consistently to all submission types. Time frames referred to in this guidance are the current Health Canada Target Performance Standards. Submissions shall contain all the information and material required for purposes of Part C of the Food and Drug Regulations.

Drugs are authorized for sale in Canada once they have successfully gone through the drug review process. This process is the means by which a drug application is reviewed by scientists in the Therapeutic Products Directorate (TPD) of Health Canada, and on occasion, outside experts, to assess the safety, efficacy and quality of a drug.

Health Canada has published numerous guidelines and policies to assist sponsors in the preparation and filing of drug submissions. Sponsors of pharmaceutical or biological drug Submissions should refer regularly to the Health Canada web site for those guidelines and policies relating to a particular submission type of interest. Note: The web site is subject to continual update and improvement.

The updated screening criteria for Abbreviated New Drug Submissions (ANDS) and their supplements (SANDS) will help assess the completeness of the drug submission and identify significant deficiencies prior to the review process. A key component to the screening of the ANDS will include an attestation checklist to assist sponsors in ensuring that the submission filed is complete and that key required information in support of the submission is provided in the filing. Generic manufacturers will be expected to include a completed attestation form in their submission to indicate that this required information has been provided. This attestation will be assessed as part of the screening process. Sponsors are asked to include the completed attestation form in **both PDF and Word format** in their ANDS or supplement in section 1.2.3. Failure to provide a completed attestation form will result in the issuance of a Screening Deficiency Notice.

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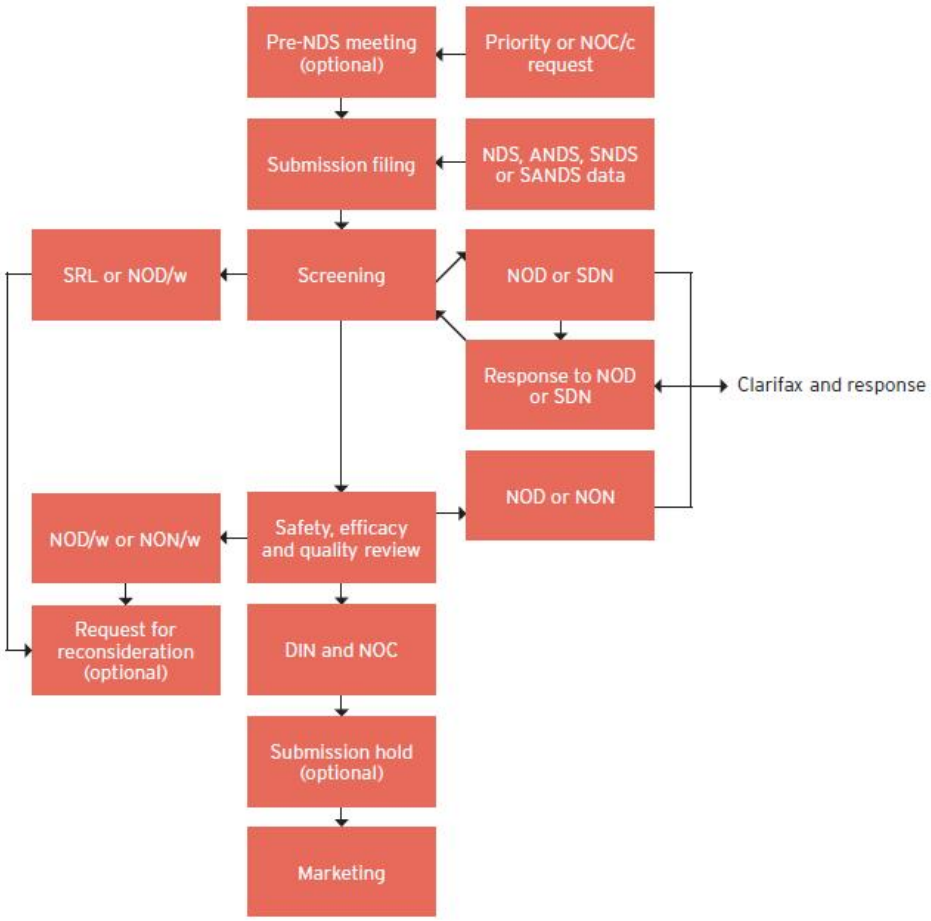

Fig.no.1: Review process of a new drug in Canada

It includes the following steps:

NOC: Notice of Compliance

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

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

NOD/w: Notice of Deficiency/withdrawal letter

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

SDN: Screening Deficiency Notice—sponsor has 45 days 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 15 days to respond

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Submission filing

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 calendar days. A response for a review under the NOC/c guidelines should be received 10 working days 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 60 days.

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 calendar 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 calendar days to respond and resolve any identified deficiencies. The TPD notes that submissions containing interim analyses of pivotal data or safety studies will be considered deficient. If a sponsor's response to a screening deficiency notice contains unsolicited information, 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 calendar 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 30 days to decide and then notify the TPD if it will submit additional information. The sponsor then has a further 60 days 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 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 calendar 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)

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If there are significant deficiencies or omissions in a submission 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 90 days 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 90 days 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/c)

The NOC/c policy at Health Canada was formulated with the goal of providing physicians and patients early access to a drug as well as a means to 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 appear on the product's label.

Reviewer reports

The reviewer reports will be provided to the sponsor within seven calendar 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 calendar days.

Brief Introduction regarding Exclusivities in Canada:[7]

1. Brand companies must list their patents for an approved drug on the Patent register.

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2. When filing an abbreviated new drug submission (ANDS) the generic companies must address the patents 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 year 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 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.

Brief Discussion regarding Marketing of generic drugs in Canada[2]

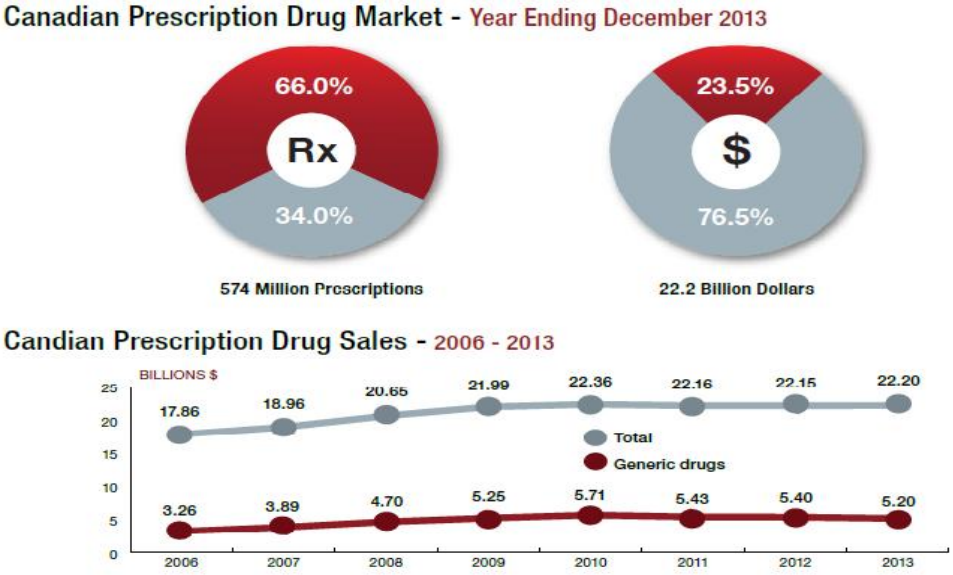

Fig.No:2: **Marketing of generic drugs in Canada**

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1. Pharmaceutical sector is one of the most innovative and profitable industries especially in Canada.
2. Canada has total 3% share of the global market in pharmaceuticals.
3. Canadian Pharmaceutical market is the 9th largest market in the world.
4. Because of generic drugs and innovative drugs having the same Quality, safety and efficacy considerations Shared by brand-name and generic drug companies, Canadians are showing more interest on using generics unless they are suffering from severe health diseases.
5. Canada only contains More than 390 pharmaceuticals and More than 400 biotechs.
6. But Mechanisms of protection much less extensive than the U.S. and more stringent regulatory requirements to market generics of different countries in Canada.

In 2013, the generic share of the number of retail prescriptions was 66.0% equating to 379 million generic prescriptions. Growth of generic prescriptions was 6.9% compared to the previous year. Yet, generic pharmaceutical sales accounted for only 23.5% of the total cost of the Canadian prescription drug market, totalling 5.2-billion dollars in drugstore and hospital sales. Canada's total prescription drug expenditures now exceed 22.2-billion dollars.

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 work 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.

Acknowledgment

The author was very thankful to the guide, principal and management for supporting in entire research work.

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