Health Canada Santé Canada

August 13, 2008

# NOTICE

Our file number: 08-108225-127

**Revision to Guidance Document: *Submission of Pharmacogenomic Information***

Health Canada has adopted the International Conference on Harmonization (ICH) guideline *Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories*, ICH Topic E15. The ICH guideline is available on the Health Canada website.
http:/www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/ich/efficac/e15-eng.php

The Health Canada guidance document *Submission of Pharmacogenomic Information* has been revised to incorporate the ICH definition of pharmacogenomics and to further clarify where and when to submit applications for investigational testing for pharmacogenomic tests.

Comments or questions related to this guidance document may be directed to:

*For pharmaceuticals:*
Regulatory Project Management Division
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Therapeutic Products Directorate
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Canada

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# GUIDANCE DOCUMENT

## Submission of Pharmacogenomic Information

Published by authority of the
Minister of Health

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**Health Products and Food Branch**

Canada

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| Our mission is to help the people of Canada maintain and improve their health.<br>*Health Canada* | HPFB's Mandate is to take an integrated approach to managing the health-related risks and benefits of health products and food by:<br>• minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for health products and food; and,<br>• promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health.<br>*Health Products and Food Branch* |



***Également disponible en français sous le titre:*** *Présentation de l'information pharmacogénomique*

# FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document ***may be*** acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

| Document Change Log | | | |
|---|---|---|---|
| **File Number** | 08-108225-127 | **Replaces** | 07-103797-737 |
| **File name** | pharmaco_2008.pdf | **Replaces** | pharmaco_guid_ld_2007-02.pdf |
| **Date** | May 23, 2008 | **Date** | February 14, 2007 |

| Section | Change |
|---|---|
| Abbreviations and definitions | Pharmacogenomics definition replaced with the ICH definition |
| Clinical trial applications involving pharmacogenomic testing | Text added to clarify where and when investigational testing applications should be submitted. |

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# 1.0 INTRODUCTION

## 1.1 Objectives

Health Canada, the federal regulatory authority that evaluates the safety, efficacy, and quality of health products available in Canada, recognizes that the application of pharmacogenomics (PGx) is increasingly becoming an integral part of the drug discovery and development processes. This document is intended to provide guidance to sponsors on how and when to submit PGx information to Health Canada.

## 1.2 Scope and Application

This guidance document applies to sponsors intending to submit PGx information to Health Canada, either in support of an application or submission for a drug, biologic drug, or medical device intended for human use, or as part of ongoing post-market activities.

In this guidance document, “shall” is used to express a requirement, i.e., a provision that the user is obliged to satisfy in order to comply with the regulatory requirements; “should” is used to express a recommendation or that which is advised but not required; and “may” is used to express an option or that which is permissible within the limits of the guidance document.

## 1.3 Policy Statements

Health Canada encourages the application of PGx to the drug development process and recognizes that some testing and data collection will be for exploratory research purposes.

When clinical trial sponsors intend to collect samples for exploratory PGx testing outside the scope of a main clinical trial, informed consent should be obtained separately from that of the main trial. This will enable subjects to decline consent to the collection of samples for research use without prejudicing their participation in the main trial.

PGx tests that are licenced for sale in Canada or authorized by Health Canada for investigational testing are required if the test results are to be used for diagnostic purposes, patient management, or are to be submitted to Health Canada in support of a clinical trial application or drug submission.

Health Canada does not request sponsors to submit 'voluntary genomic data submissions' as done by other jurisdictions, such as the United States Food and Drug Administration and the European Medicines Agency. Sponsors are encouraged to request pre-submission consultation meetings prior to filing PGx applications or submissions.

## 1.4 Abbreviations and Definitions

### *1.4.1 Abbreviations*

| | |
|---|---|
| ADR | Adverse Drug Reaction |
| ANDS | Abbreviated New Drug Submission |
| BGTD | Biologics and Genetic Therapies Directorate |
| CTA | Clinical Trial Application |
| CTA-A | Clinical Trial Application Amendment |
| CTD | Common Technical Document |
| DNA | Deoxyribonucleic acid |
| ICH | International Conference on Harmonization |
| IVDD | *In Vitro* Diagnostic Device |
| MAH | Market Authorization Holder |
| MDB | Medical Devices Bureau |
| MHPD | Marketed Health Products Directorate |
| NDS | New Drug Submission |
| PGx | Pharmacogenomics |
| RNA | Ribonucleic acid |
| SNDS | Supplemental New Drug Submission |
| SNP | Single Nucleotide Polymorphism |
| TPD | Therapeutic Products Directorate |

### *1.4.2 Definitions*

*Adverse Drug Reaction:*
A noxious and unintended response to a drug, which occurs at doses normally used or tested for the diagnosis, treatment or prevention of a disease or the modification of an organic function. [C.01.001]

*Biologic Drug:*
A drug listed in Schedule D to the *Food and Drugs Act* that is in dosage form, or a drug that is a bulk process intermediate that can be used in the preparation of a drug listed in Schedule D to the Act. [C.04.001]

Schedule D includes names of individual products (such as “insulin”), product classes (such as “immunizing agents”), references to particular sources (such as “drugs, other than antibiotics, prepared from microorganisms”) and methodology (such as “drugs obtained by recombinant DNA procedures”). Drugs or biological preparations similar to those listed in Schedule D for which there are special safety, efficacy and quality concerns, are treated as biologics for regulatory purposes.

*Device:*
Any article, instrument, apparatus or contrivance, including any component, part or accessory thereof, manufactured, sold or represented for use in
a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings or animals,
b) restoring, correcting or modifying a body function or the body structure of human beings or animals,
c) the diagnosis of pregnancy in human beings or animals, or
d) the care of human beings or animals during pregnancy and at and after birth of the offspring, including care of the offspring, and includes a contraceptive device but does not include a drug. [Section 2 of the *Food and Drugs Act*]

*Drug:*
Any substance or mixture of substances manufactured, sold or represented for use in:
a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, or abnormal physical state, or its symptoms, in human beings or animals;
b) restoring, correcting or modifying organic functions in human beings or animals; or
c) disinfection in premises in which food is manufactured, prepared or kept. [Section 2 of the *Food and Drugs Act*]

*In Vitro Diagnostic Device*:
A medical device that is intended to be used *in vitro* for the examination of specimens taken from the body. [Section 1 of the *Medical Devices Regulations*]

*Medical Device:*
A device within the meaning of the Act, but does not include any device that is intended for use in relation to animals [Section 1 of the Medical Devices Regulations]

*Pharmacogenomics*[1]*:*
Pharmacogenomics (PGx) is defined as the study of variations of DNA and RNA characteristics as related to drug response.

[1] International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Tripartite Guideline: Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories E15, 2007.

*Pharmacogenomic Test:*
A test intended to identify inter-individual variations in whole-genomes or candidate genes, single-nucleotide polymorphisms, haplotype markers, or alterations in gene expression that may be correlated with pharmacological function and therapeutic response.

*Single Nucleotide Polymorphism*[2]*:*
A chromosomal locus at which a single base variation exists stably within populations (typically defined as each variant form being present in at least 1-2% of individuals).

## 1.5 Background

There is a growing understanding of how genes and genetic variation contribute to drug responses, including non-response and toxicity. This understanding, coupled with the sequencing of the human genome and corresponding potential for understanding gene function/interaction, offer new opportunities for drug development and health care.

Many sponsors are considering integrating PGx into the drug discovery and development processes, and there are increasing efforts by regulators to determine the most appropriate means of using PGx information within the context of pre-market and post-market drug evaluation and regulatory decision-making.

PGx is a rapidly evolving field of research, and as such, it will take a concerted effort between sponsors and regulators to harness the benefits that it has to offer.

PGx may have utility in areas such as:

- the determination of drug disposition (such as metabolism, transport, receptor site) and response where genetic variation may affect the expression or activity of one or more critical components;
- the surveillance or monitoring of disease-based expression to determine disease stage and whether therapeutic intervention has an affect on disease progression;
- the identification of target patient population that may either have greater or reduced response to a drug (altered efficacy) or risk of developing a drug-related adverse reaction (altered safety); and
- the investigation of the genetic basis of unexpected adverse drug reactions (ADR) in the context of a risk management programme.

[2] Council for International Organizations of Medical Sciences (CIOMS). Pharmacogenetics; Towards improving treatment with medicines. World Health Organization, 2005.

### General Considerations for Pharmacogenomic Studies

Testing in clinical trials, including PGx testing should be done without compromising the well-being of patients. When a drug is studied in one geographical area and/or specific subgroup(s), the intrinsic (e.g. PGx) and extrinsic (e.g. diet) factors that could impact on the extrapolation of data to other geographical area(s) and/or specific subgroup(s) should be considered. Hence a study that stratifies or excludes patients on the basis of PGx should be examined in the context of the study and not extrapolated further. Special attention may be required when applying PGx due to one or more of the following: the nature of the subgroup involved, the probabilistic rather than definitive nature of PGx information, the interpretation and validation of the tests used, the variable phenotypic expression of genotype, the variation in haplotypes among different populations, the complexity of multiple genetic expressions, environmental factors which may affect expression of genomic characteristics, re-evaluation of existing therapies in the PGx context, re-labelling of currently marketed drugs, and education.

## 2.0 SUBMISSION OF PHARMACOGENOMIC INFORMATION

In Canada, pharmaceutical drugs are regulated by the Therapeutic Products Directorate (TPD) and biologic drugs are regulated by the Biologics and Genetic Therapies Directorate (BGTD) in accordance with the *Food and Drugs Act* and the *Food and Drug Regulations*. *In vitro* diagnostic devices (IVDD) are regulated by TPD's Medical Devices Bureau (MDB) in accordance with the *Food and Drugs Act* and the *Medical Devices Regulations*. This section provides guidance to sponsors on how the *Food and Drugs Act* and its associated regulations apply to the submission of PGx information to Health Canada.

### 2.1 Information Requirements for Clinical Trial Applications

Clinical trials involving PGx testing are subject to Part C, Division 5 of the *Food and Drug Regulations* which outlines the requirements applicable to the sale and importation of drugs for use in human clinical trials in Canada. CTAs should be submitted in accordance with Health Canada's *Guidance for Clinical Trial Sponsors: Clinical Trial Applications* and the *Clinical Trials Manual.*

In accordance with C.05.005 (e), sponsors are required to submit PGx data that pertain to the pharmacological or pharmacodynamic aspects, pharmacokinetics, and toxicological effects of the drug if the PGx data is relevant to, or supports the use of the investigational product in the proposed clinical trial.

Any PGx results from clinical pharmacokinetic studies of the drug as well as any information regarding drug safety, pharmacodynamics, efficacy and dose responses of the drug that were obtained from previous clinical trials in humans shall be submitted as part of the CTA in

accordance with C.05.005 (e) if the results support the safety and/or efficacy of the drug for which the application is being filed.

If PGx data are being used by the sponsor to support the design of the proposed clinical trial or animal study, to justify testing in humans, or to support the proposed indication(s)/labelling of the drug, it shall be submitted as part of the CTA.

As per C.05.009, Health Canada reserves the right to request any additional information that is required to assess the safety and risks of the drug intended for use in the proposed clinical trial, and which could include PGx information. Additional information would be requested in accordance with Health Canada's *Management of Drug Submissions Guidance Document*.

### *2.1.1 Clinical Trial Applications Involving Pharmacogenomic Testing*

At the clinical trial stage, PGx testing used for diagnostic purposes or patient management can be achieved in two ways:

(i) Use of a PGx test that is licenced for sale in Canada;

(ii) Use of a PGx test that is authorized for investigational testing

(i) PGx test that is licenced for sale in Canada
If a sponsor of a clinical trial intends to collect data using a PGx test that is already licenced for sale in Canada, the sponsor should include in their CTA the name, description, and licence number of the IVDD and whether the device will be used for its intended purpose. If the device is to be used for a purpose that is different from the purpose for which it was licenced, the manufacturer/device sponsor shall obtain an authorization for investigational testing from MDB. Refer to item (ii) below.

(ii) PGx test that requires authorization for investigational testing
If a sponsor of a clinical trial intends to collect PGx data using an IVDD that is not licenced or is not already authorized for investigational testing by Health Canada, the manufacturer/device sponsor shall obtain an authorization for investigational testing from MDB.[3]

[3] Part 3, Section 80 (2) of the *Medical Devices Regulations* states that no person shall import or sell a Class II, III or IV medical device to a qualified investigator for the purpose of conducting investigational testing unless the manufacturer or importer holds an authorization issued under subsection 83(1) and possesses records that contain all the information and documents required by section 81.

To obtain authorization, sponsors should refer to Part 3 of the *Medical Devices Regulations* and use the guidance document, *Preparation of an Application for Investigational Testing - In Vitro Diagnostic Devices (IVDD)* to guide the preparation of documents to be submitted to MDB. Manufacturers/device sponsors are encouraged to apply for the investigational testing authorization prior to submitting a CTA. The investigational testing authorization shall be obtained and the CTA shall be authorized prior to using the medical device or initiating the proposed clinical trial.

It is especially important that the analytical validity of a PGx test be established if the test is used to determine subject eligibility, select the dose, assess safety or efficacy of a drug, or otherwise used to manage the health and safety of subjects enrolled in a clinical trial. Once a sponsor has established the analytical validity of the test, its clinical validity and utility can be investigated in a clinical trial only after obtaining an authorization for investigational testing. Every study based on PGx data should provide evidence that the performance characteristics of the test used were validated.

CTAs that involve the use of an investigational IVDD with a pharmaceutical or biologic drug should be submitted, respectively, to the Office of Clinical Trials within TPD or the Regulatory Affairs Division within BGTD. When filing a CTA, the sponsor should indicate in the covering letter that the proposed study involves the use of an investigational medical device, and include the name and/or description of the investigational IVDD being used and the date that an application for investigational testing was filed or granted by MDB (if available at time of filing). If authorization of the investigational IVDD is not yet available at the time the CTA is filed, the sponsor should indicate on the covering letter for the CTA that authorization will be obtained for the IVDD prior to initiating the clinical trial in accordance with the *Medical Devices Regulations*.

### *2.1.2 Pharmacogenomic Testing for Exploratory Research Purposes*

Health Canada recognizes that PGx testing is often conducted for exploratory research purposes[4]. Authorization is not required for such PGx testing :

(i) if the test is **not** manufactured, sold or represented for *in vitro* diagnostic use[5]; or

[4] For the purpose of this document, exploratory research refers to research studies that fall outside of the scope of the clinical trial and/or where there is no intention of submitting the results to Health Canada.

[5] The term diagnostic refers to the examination of specimens for the purpose of providing information concerning a physiological state, state of health or disease or congenital abnormality.

(ii) if the test is labeled "For Research Use Only" and is not otherwise labeled or otherwise represented for a specific diagnostic application.

Sponsors should refer to the Health Canada document, *Guidance for the Risk Based Classification System of In Vitro Diagnostic Devices* to determine when the PGx test is subject to the Medical Devices Regulations. Sponsors are encouraged to consult with the MDB if further clarification is required.

### *2.1.3 Informed Consent*

As set out in Division 5 of the *Food and Drug Regulations* and in the Good Clinical Practice Guidelines, written informed consent, given in accordance with the applicable laws governing consent, shall be obtained from every person prior to their participation in a clinical trial. Sponsors should refer to the document titled: *Good Clinical Practice: Consolidated Guideline, ICH Topic E6* for further guidance on informed consent of trial subjects.

As PGx is an emerging field, Health Canada recognizes that there are several scenarios under which samples for PGx testing may be collected. These may include, but are not limited to:

(i) PGx testing carried out within the context of the main clinical trial
In this case, consent to PGx testing would be inherent to the conduct of the trial and, therefore, a condition for participation in the clinical trial.

(ii) PGx testing as a sub-study that is not linked, but may be indirectly related to the main clinical trial.
In this case, consent should be sought separately from consent to the main trial, either by using separate informed consent forms or by using the same form. The participant should have the ability to decline consent to the collection of samples for research use without prejudicing their participation in the main trial.

(iii) For future use (banking) as in exploratory studies[6].

The informed consent documentation for clinical trials involving the use of PGx testing should specify that PGx testing will be conducted and the research aim, the sample and data coding strategy, and the storage, destruction, and security measures used around

[6] Sponsors intending to collect samples and bank samples for future use in exploratory research studies should seek guidance for such research from the *Tri-Council Policy Statement for the Ethical Conduct of Research Involving Humans*, provincial legislation, professional and institutional policies, and other relevant documents

sample and data preservation. Constraints and conditions and any other general guidelines set by each local Research Ethics Boards shall be respected, in addition to any applicable Federal and/or Provincial legislation.

## 2.2 Information Requirements for New Drug Submissions, Supplemental New Drug Submissions, Abbreviated New Drug Submissions

Part C, Division 8 of the *Food and Drug Regulations* defines the requirements for the sale of new drugs in Canada and prohibits the sale of new drugs unless the manufacturer has filed a submission that is satisfactory to the Minister. Sections C.08.002., C.08.002.1, and C.08.003 outline the requirements for submission of a New Drug Submission (NDS), Abbreviated NDS (ANDS), and Supplemental New Drug Submission (SNDS) respectively. Submissions should be filed in accordance with the Health Canada guidance document, *Preparation of New Drug Submissions in the CTD Format*.

In order to comply with the above-mentioned sections, sponsors shall submit PGx data if it provides evidence of the safety and/or clinical effectiveness of the new drug in the context of its proposed indications. Similarly, if PGx data is being used to support the proposed dosage of the drug, the claims to be made for the drug, or the contra-indications and adverse reactions of the drug, the data shall be submitted by the sponsor.

Part C, Division 8 of the regulations enables Health Canada to request any additional information or material respecting the safety and effectiveness of the new drug, which could include relevant PGx information.

### *2.2.1 NDS, SNDS, or ANDS involving Pharmacogenomic Tests*

Health Canada encourages sponsors intending to use a PGx test to support a therapeutic decision (eg. the choice or dosing of a drug) to apply for a medical device licence as they progress through their drug development program if a licenced test is not already available for use in Canada.

If the sponsor used a PGx test that is already licenced in Canada, the sponsor should indicate in their submission, the name, description, and licence number of the IVDD that was used.

In Canada, all devices intended to be used for PGx testing are classified as Class III medical devices and require a pre-market scientific assessment of the safety and effectiveness by the MDB[7]. The requirements for an application for a new Class III medical device are described in the guidance document: *Preparation of a Premarket Review Document for Class III and Class IV Device Licence Applications,* and in Section 32 of the *Medical Devices Regulations.*

Since these devices may have profound impact on the safety and effectiveness of the drug for which the assay/test is performed, data for pre-market review will be required. When in doubt as to the classification of a test, manufacturers are encouraged to contact MDB prior to submitting a licence application.

### *2.2.2 Labelling Considerations*

Sponsors shall comply with all of the applicable labelling requirements in the *Food and Drugs Act* and *Regulations*. Sponsors should refer to the *Guidance for Industry: Product Monograph* for guidance on the development of a product monograph. When developing the product monograph and labelling, sponsors should consider whether there is evidence to support the inclusion of PGx information. For example,

- when PGx data demonstrate that subgroups of patients experience higher or lower clinical efficacy, specific labelling may be warranted to identify and define the population subgroup(s) that may derive the greatest benefit;
- when PGx data demonstrate that subgroups of patients may be at increased or decreased risk for ADR(s), specific labelling may be warranted to identify and define the specific subgroup(s);
- when there is sufficient evidence to support special dosage considerations for specific population subgroup(s), these should be defined (for example, when there is evidence to support dosage reductions for particular patient subgroups to avoid ADRs);
- when testing is recommended or required in order to optimize the use of the drug (e.g. if testing is recommended prior to selecting or prescribing treatment).
- When the medical and technical aspects of the submission have been evaluated, staff from the relevant review division will be available to discuss the development of an appropriate product monograph with the sponsor.

[7] Sponsors may refer to the Health Canada document: *Guidance for the Risk Based Classification System of In Vitro Diagnostic Devices*.

## 3.0 PRE-SUBMISSION CONSULTATION MEETINGS

Sponsors are encouraged to request consultation meetings with the relevant Directorates prior to submitting CTA or NDS that contain PGx information or that use a PGx test. These consultations will enable sponsors and Health Canada to share information and knowledge pertaining to the integration of PGx in the drug development and approval process and will help familiarize Health Canada staff with industry activities related to PGx.

For drugs and biologics, pre-CTA and pre-submission meetings should be requested as per the process outlined in the *Guidance for Clinical Trial Sponsors: Clinical Trial Applications,* and the *Management of Drug Submission,* respectively. In the meeting request and Information Package, sponsors should indicate whether an associated application for an investigational PGx test has been submitted to the MDB. Where applicable, representatives from the MDB will attend the meeting.

## 4.0 POST-MARKET PHARMACOGENOMIC CONSIDERATIONS

PGx may enhance the ability to identify safety and efficacy issues associated with therapeutic products in the post-market setting, particularly in products with variable pharmacokinetic/ pharmacodynamic properties and narrow therapeutic indices. Sources of post-market PGx data may include, but are not limited to, post-market studies, results from independent research, and information from spontaneous ADR reports.

Sponsors/MAHs are reminded of mandatory post-market reporting requirements for drugs under the relevant regulations, as well as mandatory problem reports for problems with licenced PGx tests[8,9].

Sponsors/MAHs are also encouraged to consult with MHPD regarding the integration of PGx into post-market activities. Should safety and/or efficacy issues involving therapeutic products arise from PGx data in the post-market setting, both MHPD and the relevant pre-market directorate may discuss appropriate strategies to address the issue. A post-market PGx issue may include the following situations:

- PGx data suggests reduced or no efficacy of a therapeutic product in specific subpopulations;

[8] C.01.016 of the *Food and Drug Regulations* details post-market reporting requirements for drugs.

[9] Part 1, Sections 59-61 of the *Medical Devices Regulations* detail the requirements for mandatory problem reporting for medical devices, which include pharmacogenomic tests (Class III devices).

- PGx data identifies sub-populations vulnerable to certain ADRs or classes of ADRs have been identified from PGx-derived data.

PGx information obtained post-market that may warrant a change(s) to a section of the Canadian Product Monograph are to be submitted to the relevant pre-market review directorate under the appropriate submission (e.g. changes to the indication(s) or dosing recommendations would require the submission of an SNDS).

For the analysis of post-market safety/efficacy issues arising from PGx data, information required by Health Canada to assess the risk should at minimum include the ADR(s) in question (including lack of efficacy), the suspected single nucleotide polymorphism (SNP)/haplotype involved, and validation information on the PGx test used.[10] Additional contextual information may also be required in order to interpret the significance of the link between the safety/efficacy issues and the SNP/haplotype. Such information may include, but is not restricted to, the following:

- information on related metabolic enzymes or transport proteins associated with the SNP/haplotype, particularly where more than one known or suspected biological pathway may be involved;
- non-genetic intrinsic and extrinsic factors that may be confounding variables, including age, gender, race/ethnicity, co-medications (including natural health products, supplements, and foods), smoking and alcohol use, co-morbidities, possible failure of compliance, weight/nutritional status, etc;
- summary information on other common characteristics of the patient population that may also explain the occurrence of the ADR(s) in question (e.g. pediatric population).

In addition, the sponsor/MAH should provide a summary analysis of the significance of this information on the overall safety/efficacy of the product for its given indication(s). A comprehensive risk management strategy should be proposed to ensure that risks associated with the health product are appropriately addressed.

It should be noted that Health Canada has initiated the process of implementing the ICH E2E guidance document on Pharmacovigilance Planning.[11] This document is intended to aid in planning pharmacovigilance activities, particularly during the early post-marketing period after a therapeutic product is licenced. Where feasible and relevant, sponsors/MAHs are encouraged to integrate PGx testing as part of ICH E2E, Pharmacovigilance Planning.

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[10] If the test is licenced in Canada, the validation documentation would not have to be resubmitted.

[11] ICH E2E: Pharmacovigilance Planning. Document can be found at: http://www.ich.org/cache/compo/276-254-1.html

## 5.0 ADDITIONAL INFORMATION

PGx is an emerging field. On an ongoing basis, Health Canada may update its guidance in response to new scientific knowledge, best practices, and/or based on experience gained by the department.

Questions concerning the submission of PGx information to Health Canada should be directed to:

*For pharmaceuticals:*
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E-mail: RPM_Division-GPR_Division@hc-sc.gc.ca

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Email: MHPD_DPSC@hc-sc.gc.ca

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1. Council for International Organizations of Medical Sciences (CIOMS). *Pharmacogenetics;Towards improving treatment with medicines.* World Health Organization, 2005.

2. Food and Drug Administration. *Guidance for Industry: Pharmacogenomic Data Submissions*. U.S. Department of Health and Human Services, 2005.

3. Health Canada. *Clinical Trials Manual*. Published August 2006. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/clini/cta_intro-eng.php

4. Health Canada. *Guidance for Clinical Trial Sponsors: Clinical Trial Applications.* Public Works and Government Services Canada, 2003.

5. Health Canada. *Guidance for Industry: Product Monograph*. Public Works and Government Services Canada, 2004.

6. Health Canada. *Guidance for the Risk Based Classification System of In Vitro Diagnostic Devices (Draft).* Public Works and Government Services Canada, 1998.

7. Health Canada. *Guidance for Industry: Management of Drug Submissions*. Public Works and Government Services Canada, 2005.

8. Health Canada. *Draft Guidance for Industry: Preparation of Drug Submissions in the CTD Format*. Public Works and Government Services Canada, 2003.

9. Health Canada. *Preparation of an Application for Investigational Testing - In Vitro Diagnostic Devices (IVDD).* Public Works and Government Services Canada, 1999.

10. Health Canada. *Preparation of a Premarket Review Document for Class III and Class IV Device Licence Applications.* Public Works and Government Services Canada, 1998.

11. Interagency Secretariat on Research Ethics. *Tri-Council Policy Statement for the Ethical Conduct of Research Involving Humans.* Public Works and Government Services Canada, 2005.

12. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Tripartite Guideline: Good Clinical Practice E6, 1996.

13. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Tripartite Guideline: Pharmacovigilance Planning E2E, 2004.

14. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Tripartite Guideline: Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories E15, 2007.