



# Greetings

Health Canada is pleased to provide you with our new pre-inspection package to assist your organization in complying with Health Canada regulations and preparing for an inspection by the Health Products and Food Inspectorate.

Inspections are conducted to assess compliance with Division 5 of the ***Food and Drug Regulations – Drugs for Clinical Trials Involving Human Subjects*** — with the legislative authority for the regulations stemming from the ***Food and Drugs Act***. You can find all applicable laws and regulations regarding Clinical Trials at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

The Inspectorate is committed to providing the health products industry with information and guidance toward achieving world class excellence in safety and quality standards. In fact, the Inspectorate's regulatory practices with respect to clinical trials are recognized globally and are harmonized with those of other major industrialized countries through the principles of Good Clinical Practices (GCP), as described by the ***International Conference on Harmonization*** at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

Our commitment to providing you with guidance reflects the shared responsibility of health product safety. As the regulator, we recognize that safety can only be achieved through the involvement of government, industry, research ethics boards, healthcare providers and patients.

The following information is contained in this package:

- Fact sheets outlining the mandate and the activities of the Health Products and Food Inspectorate and, specifically, as they pertain to clinical trials;
- Frequently Asked Questions;
- A checklist to help your organization prepare for an inspection;
- A checklist of documents that should be available for an inspection;
- A Summary Report outlining the findings of inspections conducted in support of Division 5 of the *Food and Drug Regulations*; and
- An opportunity to tell us what you think about the new pre-inspection package.

In addition, we recommend that you review the guidance documents entitled ***Classification of Observations Made in the Conduct of Inspections of Clinical Trials (GUI-0043)*** and ***Guidance for Records Related to Clinical Trials (GUI-0068)*** which can be found at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

If you have any questions related to this letter or the referenced documentation, please do not hesitate to contact us by e-mail at [GCP-BPC@hc-sc.gc.ca](mailto:GCP-BPC@hc-sc.gc.ca), telephone at 613-952-8173 or fax at 613-952-9805.



# Good Clinical Practices

Protecting Canadians. Sharing the responsibility.

## Canada's Health Products Regulatory Enforcement Authority

The Health Products and Food Inspectorate is responsible for the activities concerning the compliance and enforcement of the *Food and Drugs Act* (with the exception of products regulated as foods which are the responsibility of the Canadian Food Inspection Agency).

The Inspectorate's activities include the enforcement of the regulations on clinical trials (Division 5 of the *Food and Drugs Regulations - Drugs for Clinical Trials Involving Human Subjects*).

## Safety

Inspections, investigations and compliance verifications of clinical trials are carried out so that participants are not subjected to undue health risks.

## Informed Consent

All clinical trial participants must be informed in writing of the anticipated risks and benefits associated with the study.

## Global Standard

The Inspectorate's regulatory practices for clinical trials are recognized globally, and are harmonized with those of other major industrialized countries.

Health Canada has adopted the *International Conference on Harmonization (ICH) Guideline on Good Clinical Practices (ICH E6)*.

## Shared Responsibility

The safety of participants in clinical trials is a shared responsibility, among healthcare providers, industry, Research Ethics Boards, government and all Canadians.

The Health Products and Food Inspectorate

1-800-267-9675

[www.hc-sc.gc/gcp](http://www.hc-sc.gc/gcp)



# Good Clinical Practices Frequently Asked Questions

## GENERAL INFORMATION

### >>1. Why is my site being inspected?

Health Canada's goal is to inspect approximately 2% of all clinical trial sites in Canada annually. The number of inspections conducted in Canada is consistent with that done by other Regulatory Agencies in the world.

The objectives of the inspection are to ensure that participants in clinical trials are not subjected to undue risks, to validate the data generated, to investigate complaints and to assess compliance with Division 5 of the *Food and Drug Regulations* - Drugs for Clinical Trials.

The results of these inspections may be used in the evaluation of subsequent submissions to the Therapeutic Products Directorate (TPD) and/or the Biologics and Genetic Therapies Directorate (BGTD).

### >>2. How was my site selected?

A list of clinical trial sites is obtained from TPD and BGTD, by the Inspectorate every fiscal year. The Inspectorate then selects up to 2% of the sites for inspection, in consultation with TPD and BGTD. It should be noted that the Inspectorate may contact other parties (e.g., Research Ethics Boards (REBs), Research Departments, clinical trials sites, etc.), during the selection process, in order to obtain clarification and/or additional information regarding a clinical trial and/or a site.

When deciding if a site should be selected for an inspection, the following may be taken into consideration:

- >>The number of trials being conducted at the site;
- >>The status of the trial(s) being conducted at the site (i.e., if the trial(s) is still ongoing);
- >>The number of subjects enrolled in the trial(s);
- >>The drug(s) involved in the trial(s);
- >>The number of sites where the trial(s) is being conducted (i.e., if it is a single-centre or a multi-centre trial);
- >>In the case of a multi-centre trial, if the other site(s) is going to be or has been inspected;
- >>If the sponsor/contract research organization/qualified investigator has been inspected before;
- >>The compliance history of the site, if an inspection was previously conducted.

### >>3. *What does an Inspector plan to look at during an inspection?*

The following is an example\* of a high-level inspection plan used by the Inspectorate:

- >>Identify the key study personnel and their delegated responsibilities, and review their education, training and experience;
- >>Review of the correspondence with Health Canada and the Research Ethics Board (REB) to ensure that the REB has provided written approval of the protocol, the Informed Consent Form (ICF) and other information provided to the subjects before the trial begins; to verify that the REB has approved any amendments to the protocol and informed consent form;
- >>Review the procedure for obtaining informed consent and ensure that the statements of risks and benefits in the Informed Consent Form are consistent with those requested by Health Canada and the REB;
- >>Verify that the Informed Consent Form used to administer informed consent is the correct version (i.e., the most recently approved and in the appropriate language of the subject population) and is signed and dated by the subject or the subject's legally acceptable representative and by the person who obtained consent, before the subject is enrolled in the trial for all subjects enrolled in the trial.
- >>Ensure that the investigator has adhered to the protocol/amended protocol that has been approved by Health Canada and the REB. Verify, for instance that the subjects were selected in accordance with the inclusion/exclusion criteria, drug dosages are administered in accordance with the protocol, use of concomitant medications is documented, data with respect to safety and efficacy are documented and criteria for removal of subjects from the study are followed;
- >>Verify that the data has been accurately transcribed from source documents (e.g., original medical records) to case report forms;
- >>Ensure that all adverse events are documented and that adverse drug reactions are reported in accordance with the protocol and regulatory requirements. To do so, verify records to assess the timeliness, accuracy and completion of all required reporting;
- >>Ensure that all quantities of all lots are reconciled by checking records for drug receipt at the site, dispensing records, returns to sponsor etc.;
- >>Verify that adequate supervision of medical care by the qualified investigator is provided;
- >>Verify that the drug is manufactured, handled and stored in accordance with the applicable good manufacturing practices, protocol and labelling requirements;
- >>Review sponsor monitoring reports or correspondence with the sponsor/monitor to ensure that all monitor findings are documented and corrected;
- >>Verify that the test samples for clinical testing (if applicable) are handled in accordance with the protocol; and
- >>Confirm if there are provisions for records to be retained for 25 years.
- >>Ensure that the investigational drug(s) is labeled in accordance with Section C.05.011 of Division 5 of the Food and Drug Regulations.

*\* The above represents an example of areas an inspector may focus on during an inspection. It should be noted that the above inspection plan is not all inclusive, and is not provided in any order of priority; it could vary depending on the type of site and/or clinical trial inspected. For additional guidance, please refer to International Conference on Harmonization (ICH) guideline E6: Good Clinical Practices which can be found on our website at the following address: [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp)*

## >>4. What are the documents to collect in preparation for a GCP inspection?

>>Copy of the Study Protocol, including any amendments;  
>>Copy of the Informed Consent Form, including any amendments;  
>>Copy of the Principal (Qualified) Investigator's declaration;  
>>Copy of REB Attestation (applicable to REBs only);  
>>Delegation of Responsibilities Chart or list;  
>>Research Centre Organisational Chart;  
>>Research staff résumés;  
>>Standard Operating Procedures (e.g., informed consent process, adverse drug reaction reporting, training, etc.);  
>>Training records;  
>>Correspondence files between:

- Sponsor and Health Canada;
- Sponsor and the site (e.g., Qualified Investigator, Contract Research Organization); this would include Sponsor monitor reports, etc.;
- Site and Research Ethics Boards (e.g., approval of protocol, amendments, Informed Consent Form, advertising, etc.);

>>Adverse Event and Serious Adverse Event documentation (e.g., list, reports, etc.);  
>>Investigational Drug Accountability Records;  
>>Service providers' contracts (e.g., laboratories, drug supplier, storage, equipment, etc.);  
>>Records of calibration, maintenance and temperature monitoring for the applicable research equipment;  
>>Investigator Brochure or Product Monograph, as applicable;  
>>Source data (e.g., Informed Consent Forms, pharmacy records, subject medical records, etc.);  
>>Case Report Forms;  
>>Subject enrollment log.

*\* It should be noted that this list is not all inclusive and it is not provided in any order of priority; additional documents may be requested prior to, during and/or after the inspection. In addition, some of the above documents may not be applicable in all cases. For additional guidance, please refer to the International Conference on Harmonization (ICH) Guideline E6: Good Clinical Practices which can be found on our website at: [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).*

## INFORMED CONSENT

### >>5. Why does Health Canada review the Informed Consent Form during a Good Clinical Practice inspection when it has received Research Ethics Board approval and was submitted to Health Canada with the application for authorization of a clinical trial?

Statements of anticipated risks and benefits that will be set out in the Informed Consent Form are reviewed by Health Canada when the application for authorization of the trial is reviewed.

During a clinical trial inspection, the Informed Consent Form is reviewed to ensure that the correct version has been signed and dated by the subjects, that the statements of risk and benefits submitted to Health Canada are included, and that additional and specific requests from Health Canada and/or the Research Ethics Board and Institution/Hospital have been included in the Informed Consent Form to protect subjects, and that all the elements under Section 4.8.10 of the *International Conference on Harmonization Guideline E6: Good Clinical Practices* (ICH E6) are included.

The review of the Informed Consent Form also ensures that new information concerning the safety of the patients/subjects has been included in the Informed Consent Form and that the subjects have been informed.

*>>6. Should every page of the Informed Consent document(s) be initialled and dated?*

Health Canada's preference is that every page of the Informed Consent document be initialled and dated to ensure that the patient has read and understood every page.

However, we do understand the strain this can put on subjects that are unwell and/or debilitated.

A statement could be included at the end of the Informed Consent document(s) stating that the subject has read and understood the number of pages of the informed consent document(s). The informed consent document(s) should be paginated to ensure that the complete document is presented to the subject.

## SPONSOR

*>>7. When a clinical trial is conducted by a group of physicians at different sites, one of whom is identified on the clinical trial application as the sponsor, is this person required to monitor the trial at all investigative sites?*

The physician identified on the clinical trial application as the sponsor must assume the responsibilities of both the sponsor and the qualified investigator. This would include ensuring that all of the Sponsor's Obligations under section C.05.010 (Good Clinical Practices) of Division 5 the *Food and Drug Regulations* (FDR) are met at all of the different sites, as well as all other applicable sections of Division 5.

Section 5.18 of ICH E6 provides guidance with respect to monitoring. This document can be found on our website at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

*>>8. What are the Sponsor's responsibilities when drugs used in clinical trials conducted in Canada are shipped directly to the clinical trial site from a foreign manufacturer?*

The sponsor is ultimately responsible for all regulatory requirements regarding the importation of clinical trial material. The sponsor must have a representative in Canada who is responsible for the sale of the drug as per C.05.003 (c) (VIII) of Division 5 of the *Food and Drug Regulations* (FDR). It should be noted that Division 5 of the FDR does not differentiate between a commercial and non-commercial sponsor.

The sponsor's representative in Canada must be able to demonstrate adherence to all applicable regulatory requirements.

In addition, drugs may be shipped directly to a clinical trial site provided the following conditions are met and the following documents are available:

*>>For drugs used in clinical trials conducted in Canada, a No Objection Letter (NOL), issued by Health Canada, is required to allow the importation of the clinical trial material; in accordance with section C.05.006 or C.05.008 of the FDR;*

*>>A list of all Qualified Investigators and the location of Canadian sites is provided to Health Canada;*

*>>Certificates of manufacture and certificates of analysis (or Batch Certificates) for the lots of clinical trial material imported into Canada;*

*>>Evidence of approved lot release;*

*>>Systems in place for the monitoring of storage and transportation conditions from the foreign source to the various clinical trial sites across Canada;*

*>>Accountability of the imported drugs used in clinical trials and distributed to various clinical trial sites located in Canada;*

*>>The disposition of drugs returned from the clinical trial sites;*

*>>Written agreements with third parties who have been delegated some of the sponsor's responsibilities;*

*>>Evidence that the drugs used in clinical trials conducted in Canada meet the Good Manufacturing Practices (GMP) requirements. Please refer to Annex 2 of the GMP Guide (Guide-0036).*

## QUALIFIED INVESTIGATOR

*>>9. What are the Qualified Investigator's responsibilities when drugs used in clinical trials conducted in Canada are shipped directly to the clinical trial site from a foreign manufacturer?*

Drugs may be shipped directly to a clinical trial site provided the following conditions are met:

- >>A written agreement is in place between the sponsor and the QI describing their specific responsibilities;*
- >>The agreement is available at the clinical trial site;*
- >>At the time of filing the Clinical trial Application, the site is listed as an importer in Appendix I of the HC-SC 30011 form;*
- >>The QI has the means in place to check the transportation and storage conditions of the drugs used in the clinical trial(s).*

These conditions may be verified during an inspection conducted at a qualified investigator's site where drugs are received directly from the foreign source. Please refer to the response provided under Question 8 for additional requirements regarding the importation of drugs used in a clinical trial.

*>>10. Does the Qualified Investigator (QI) for a clinical trial conducted in Canada need to be a physician or a dentist?*

Yes, as per Section C.05.001 of Division 5 of the *Food and Drug Regulations*, the Qualified Investigator (QI) must be "entitled to provide health care under the laws of the province where that clinical trial site is located and ..., in the case of a clinical trial respecting a drug to be used for dental purposes only, a physician or dentist and a member in good standing of a professional medical or dental association; and, in any other case, a physician and a member in good standing of a professional medical association."

Another individual may be the lead investigator in charge of the trial, but the QI is responsible for medical care and medical decisions in respect of the clinical trial.

The lead investigator may sign as the Senior Medical or Scientific Officer in Canada in Box 87 of the HC-SC 3011 form (Drug Application for Human, Veterinary, or Disinfectant Drugs and Clinical Trial Applications/Attestation), but only a licensed physician or dentist entitled to provide health care under the laws of the province where that clinical trial site is located can be listed as the Qualified Investigator on the Qualified Investigator Undertaking Form.

It should be noted that Section C.05.010(e) of Division 5 of the *Food and Drug Regulations* also states that there be no more than one QI at each clinical trial site.

## RECORDS

### >>11. *What are the requirements for record retention and who has to keep the records?*

Records have to be maintained as per Section C.05.012 of Division 5 of the *Food and Drug Regulations*. The Sponsor is responsible for maintaining and retaining these records.

However, the Sponsor may delegate these responsibilities to a third party. Therefore, if the Sponsor delegates its responsibility to a third party, they will be responsible for retaining those records.

As of September 1st, 2001, the retention of records is required for a period of 25 years. The guidance document entitled *Guidance for Records Related to Clinical Trials (Guide-0068)*, as well as Sections 4.9 and 8 of ICH E6 provides additional information.

These guidance documents are available on the Health Canada website at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

### >>12. *In what medium should source documents be kept?*

As per *Guidance for Records Related to Clinical Trials (Guide-0068)*, source documents should preferably be kept for the entire retention period and in their original medium. Transfer of source documents from their original medium to a secondary medium can be acceptable, preferably at the completion of a trial, and only if:

- >>*the corrections to the original data can be clearly captured in the secondary medium;*
- >>*the person that performs the task of transferring source documents from the original to the secondary medium attests (i.e., signs and dates an attestation), that the secondary documents are true copies of their respective primary documents, and;*
- >>*the transfer process has been fully validated. Evidence of validation should be available for inspection.*

In addition, Annex 11 to the PIC/S Good Manufacturing Practices Guide: Computerized Systems can also be consulted.

The Qualified Investigator should always consult the sponsor prior to the destruction of records created during the conduct of clinical trials. Please see the response provided under Question #11 for additional guidance. Guidance documents pertaining to record keeping are available on the Health Canada website at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

>>13. *Does the 25 year record retention requirement apply to clinical trials conducted before Division 5 of the Food and Drug Regulations came into force on September 1st, 2001?*

Since Division 5 of the *Food and Drug Regulations* came into effect on September 1, 2001, clinical trial applications submitted to Health Canada on or after that date are subject to these requirements.

Although clinical trial applications submitted to Health Canada prior to September 1, 2001 are not required to comply with this requirement (i.e., 25 year record retention), other requirements pertaining to record retention were in effect prior to 2001. In May of 1997, Health Canada adopted ICH Topic E6: Good Clinical Practice. Record retention requirements are outlined in sections 3.4, 4.9 and 8 of this guidance document.

Finally, there may be additional record retention requirements under provincial jurisdiction, contractual agreements with Sponsors, Research Ethics Boards or others, which should be considered.

Link to the ICH Topic E6: Good Clinical Practice at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp).

## LABELLING

>>14. *What are the lot number labelling requirements for clinical trial drugs?*

The purpose of having a lot number on the drug label is to ensure traceability to the manufacturing lot and ensure a recall would be possible.

However, for blinded clinical trials the sponsor must ensure that the label information does not compromise the blinding. Labelling of a clinical trial drug with a drug manufacturing lot number could potentially compromise a blinded clinical trial.

Identifiers other than a “lot” or “(L)” number, for example a batch number, a kit number or a bar code, may be considered in compliance with Section C.05.011(e) of Division 5 of the *Food and Drug Regulations*, provided the drug label allows for traceability to the manufacturing lot. In the case where a bar code is included as the identifier on the label, the code on the drug label should allow ready access to information, such as the lot number and expiration date, through a validated computerized system.

During an inspection, Health Canada may verify that there is a system of traceability in place to ensure patient safety and that the computerized system, if applicable, is fully validated.

## >>15. What are the expiration date labelling requirements for clinical trial drugs?

The sponsor is responsible for ensuring that the clinical trial drug, in its original packaging, meets the requirements of Section C.05.011 of Division 5 of the *Food and Drug Regulations*, which includes an expiration date.

As per Section C.01.0111 of Division 5 of the *Food and Drugs Act*, an expiration date is defined as:

“(a) the date, expressed at minimum as a year and a month, up to and including which a drug maintains its labelled potency, purity and physical characteristics; or

(b) the date, expressed at minimum as a year and a month, after which the manufacturer recommends that the drug not be used.”

During an inspection, Health Canada may verify that the clinical trial drug(s) has an expiration date to ensure that the drug(s) meets the standards for potency, purity and physical characteristics to protect subject safety.

If stability studies to support expiry dating for a clinical trial drug are still ongoing at the time of labelling, the following approaches may be considered acceptable:

*>>A re-test date on the label would be acceptable in lieu of the expiration date, if the sponsor has data to support the extended shelf-life of the drug.*

*>>If only the manufacturing date is listed on the label, the clinical trial site where the drug is dispensed must have a document from the sponsor stating the shelf-life of the drug. The sponsor must have data to support the shelf-life of the drug. As an example, this principle would apply to radiopharmaceuticals.*

*>>In the case where a drug product requires reconstitution or further preparation prior to being administered to a subject/patient, the sponsor is responsible for demonstrating that the drug used at the clinical trial site meets all of the requirements of Division 5 of the Food and Drug Regulations. The reconstitution or preparation of a clinical trial drug must be done in accordance with the clinical trial protocol and must be documented.*

*>>When reconstitution or further preparation is required prior to the use of the drug, the drug label should provide the expiration date of the drug in the original packaging. Information on reconstitution or preparation and the required storage conditions should be included in accompanying documentation. The sponsor must be able to demonstrate that the reconstituted drug keeps its characteristics of potency, quality and safety during this period of use.*

Regardless of the approach taken, data should in place at all times to support the ongoing suitability of the clinical trial drug at the time of use.

In the case where a bar code is included as the identifier on the label, the code on the drug label should allow ready access to information, such as the lot number and expiration date, through a validated computerized system.

Please refer to *Annex 2 to the Current Edition of the Good Manufacturing Practices Guidelines: Manufacture of Drugs Used in Clinical Trials (GUI-0036)* for additional guidance.

>>16. *Must all of the required information appear on a label attached to the drug?*

As defined in the *Food and Drugs Act*, a label includes any legend, word or mark attached to, included in, belonging to or accompanying any food, drug, cosmetic, device or package.

The required information, outlined in Section C.05.011 of Division 5 the *Food and Drug Regulations*, must be attached to, included with, or accompany each container of the drug product.

In the case where a bar code is included as the identifier on the label, the code on the drug label should allow ready access to information, such as the lot number and expiration date, through a validated computerized system.

>>17. *When a marketed drug is used as a comparator in a clinical trial, can it be labelled in accordance with the marketing authorization, rather than in accordance with Section C.05.011 of Division 5 of the Food and Drug Regulations?*

Yes, it would be acceptable for the marketed drug to be labelled in accordance with its marketing authorization, including all relevant sections of the *Food and Drugs Act* and its associated Regulations, provided that the labelling on the marketed drug is appropriate for the trial. The response provided under Question 14 should also be taken under consideration, specifically for blinded clinical trials.

## OTHER

>>18. *Do Phase IV clinical trials have to comply with the requirements of Division 5, Section C.05.010 of the Food and Drug Regulations?*

Phase IV clinical trials, which are clinical trials that are conducted for conditions of use previously authorized, do not require the filing of an application for authorization with Health Canada, as per Section C.05.006(2) of the *Food and Drug Regulations* (FDR).

However, sponsors of Phase IV trials are required to conduct the trial according to Good Clinical Practices (Section C.05.010 of Division 5 the FDR), obtain REB approval and keep the required records. Please refer to Section C.05.002 (2) of Division 5 of the FDR for references to the other sections of Division 5 of the *FDR* that pertain to phase IV trials.

Where a clinical trial is conducted on a marketed drug to test the safety or efficacy of the product under new conditions of use (i.e., outside the parameters of the Drug Identification Number or Notice of Compliance) the sponsor will be required to file an application for authorization to conduct the clinical trial with Health Canada.

### >>19. *How is traceability of the investigational product assessed during an inspection?*

The sponsor of a clinical trial is responsible for ensuring that the drug is manufactured, stored and handled in accordance with good manufacturing practices. The sponsor should establish and maintain a system to ensure that clinical trial material can be traced through the sourcing, manufacturing, packaging, storage, transport and delivery to the qualified investigator/clinical trial site where the product is used, administration of the product to the study subject, reconciliation and disposal or destruction of the product. The system should contain sufficient detail to allow linking of each individual product to the individual subject who received the product. Where multiple parties are involved, the sponsor should ensure that the role of each is clearly outlined in writing.

Records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product(s) should be available in order to demonstrate traceability. These records should include dates, quantities, batch/serial numbers, expiration dates and the unique code numbers assigned to the investigational product(s) and trial subjects.

### >>20. *Why are storage and transportation conditions verified during an inspection?*

Traceability of the investigational product is ensured in many ways, such as with proper labelling (e.g., lot number, expiry date, etc.) and adequate storage and transportation conditions. For additional information regarding labelling requirements, please refer to Section C.05.011 of the *Food and Drug Regulations*, as well as the responses provided under questions 14 to 17. For additional information regarding the requirements pertaining to transportation conditions, please refer to *Annex 2 to the Current Edition of the Good Manufacturing Practices Guidelines: Manufacture of Drugs Used in Clinical Trials (GUI-0036)*, as well as the *Guidelines for Temperature Control of Drug Products during Storage and Transportation (GUI-0069)*. It should be noted that these requirements do apply to products stored at ambient room temperature.

These guidelines are available on Health Canada's Compliance and Enforcement website at [www.hc-sc.gc.ca/gmp](http://www.hc-sc.gc.ca/gmp).



# Good Clinical Practices

## Inspection Plan Checklist\*

- Identify the key study personnel and their delegated responsibilities, and review their education, training and experience.
- Review the correspondence with Health Canada and the Research Ethics Board (REB) to ensure that the REB has provided written approval of the protocol, the Informed Consent Form (ICF) and other information provided to the subjects before the trial begins, to verify the REB has approved every amendment to the protocol and Informed Consent Form.
- Review the procedure for obtaining informed consent and ensure that the statements of risks and benefits in the Informed Consent Form are consistent with those requested by Health Canada and the REB.
- Verify that the Informed Consent Form used to administer informed consent is the correct version (e.g., the most recently approved and in the appropriate language of the subject population) and is signed and dated by the subject or the subject's legally acceptable representative and by the person who obtained consent, before the subject is enrolled in the trial and this for all subjects enrolled in the trial.
- Ensure that the investigator has adhered to the protocol/amended protocol that has been approved by Health Canada and the REB. Verify, for instance, that the subjects were selected in accordance with the inclusion/exclusion criteria, drug dosages are administered in accordance with the protocol, use of concomitant medications is documented, data with respect to safety and efficacy are documented and criteria for removal of subjects from the study are followed, etc.
- Verify that the data has been accurately transcribed from source documents (e.g., original medical records) to case report forms.
- Ensure that all adverse events are documented and that adverse drug reactions are reported in accordance with the protocol and regulatory requirements. To do so, verify records to assess the timeliness, accuracy and completion of all required reporting.
- Ensure that all quantities of all lots are reconciled by checking records for drug receipt at the site, dispensing records, returns to sponsor, etc.
- Verify that adequate supervision of medical care by the qualified investigator is provided.
- Verify that the drug is manufactured, handled and stored in accordance with the applicable good manufacturing practices, protocol and labelling requirements.
- Review sponsor monitoring reports or correspondence with the sponsor/monitor to ensure that all monitor findings are documented and corrected.
- Review sponsor monitoring reports or correspondence with the sponsor/monitor. All monitor findings should be documented, as well as the action(s) taken to correct them.
- Verify that the test samples for clinical testing (if applicable) are handled in accordance with the protocol.
- Confirm if there are provisions for records to be retained for 25 years.
- Ensure that the investigational drug(s) is labeled in accordance with Section C.05.011 of Division 5 of the *Food and Drug Regulations*.

\* The above represents an example of areas an inspector may focus on during an inspection. It should be noted that the above inspection plan is not all inclusive, and is not provided in any order of priority; it could vary depending on the type of site and/or clinical trial inspected, etc. For additional guidance, please refer to International Conference on Harmonization (ICH) guideline E6: Good Clinical Practices which can be found on our website at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp)



# Good Clinical Practices Inspection Document Checklist\*

- Copy of the Study Protocol, including any amendments.
- Copy of Informed Consent Form, including any amendments.
- Copy of the Principal (Qualified) Investigator's declaration.
- Copy of REB Attestation (applicable to REBs only).
- Delegation of Responsibilities chart or list.
- Research Centre Organizational Chart.
- Research staff résumés.
- Standard Operating Procedures (e.g., informed consent process, adverse drug reaction reporting, training, etc.).
- Training records.
- Correspondence files between :
  - Sponsor and Health Canada.
  - Sponsor and the site (e.g., Qualified Investigator, Contract Research Organization—this would include Sponsor monitor reports, etc.).
  - Site and Research Ethics Boards (e.g., approval of protocol, amendments, Informed Consent Form, advertising, etc.).
- Adverse Event and Serious Adverse Event documentation (e.g., list, reports, etc.).
- Investigational Drug Accountability Records.
- Service providers' contracts (e.g., laboratories, drug supplier, storage, equipment, etc.).
- Records of calibration, maintenance and temperature monitoring for the applicable research equipment.
- Investigator Brochure or Product Monograph, as applicable.
- Source data (e.g., Informed Consent Forms, pharmacy records, subject medical records, etc.).
- Case Report Forms.
- Subject enrollment log.

\* It should be noted that this list is not all inclusive, and is not provided in any order of priority; additional documents may be requested prior to and/or after the inspection. In addition, some of the above documents may not be applicable in all cases. For additional guidance, please refer to the International Conference on Harmonization (ICH) guideline E6: Good Clinical Practices which can be found on our website at [www.hc-sc.gc.ca/gcp](http://www.hc-sc.gc.ca/gcp)



# Tell us what you think.

The Health Products and Food Inspectorate is committed to providing the health products industry with information and guidance toward achieving world class excellence in safety and quality standards.

Our new pre-inspection information package is just one way we are working to support our commitment. We are continually looking at new ways of helping you achieve international standards. To help us develop better and more effective tools in support of our shared goals, please don't hesitate to tell us what you think.

1. Did you find the new pre-inspection package helpful?

- Strongly Agree       Agree       Disagree       Strongly Disagree

2. Did the new pre-inspection package answer most of your questions related to the inspection process?

- Strongly Agree       Agree       Disagree       Strongly Disagree

3. Please comment on other information or tools that you believe could help you better prepare for an inspection?

Please e-mail your feedback to: [gcp\\_bpc@hc-sc.gc.ca](mailto:gcp_bpc@hc-sc.gc.ca) or fax to: 613-952-9805

# The Health Products and Food Branch Inspectorate



## Canada's health products regulatory enforcement authority

We are responsible for activities concerning compliance and enforcement of the *Food and Drugs Act* (with the exception of products regulated as foods which are the responsibility of the Canadian Food Inspection Agency (CFIA)).

## Health Products

- Pharmaceuticals
- Non-Prescription Medicines
- Natural Health Products
- Veterinary Drugs
- Vaccines
- Blood and Blood Components
- Human Tissues
- Medical Devices

*"Protecting health and safety is in everyone's interest. That includes Canadians, governments, Canada's trading partners, and industries"*

-Canada's Food and Consumer Safety Action Plan, 2008.

## HPFB Inspectorate

Toll-Free Complaint Line  
1-800-267-9675  
or Visit

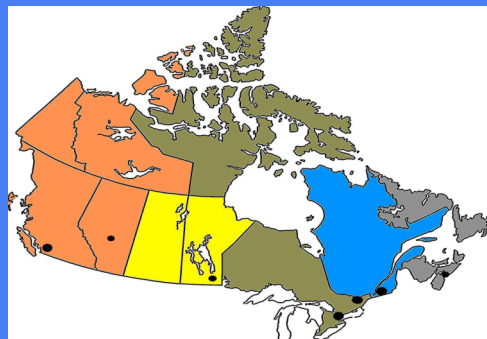
[www.hc-sc.gc.ca/dhp-mps/compli-conform/index\\_e.html](http://www.hc-sc.gc.ca/dhp-mps/compli-conform/index_e.html)

## World Class Standards

Our regulatory practices and standards are recognized globally, and are harmonized with those of other major industrialized countries.

By following **Good Manufacturing Practices (GMP)** and **Good Clinical Practices (GCP)**, Canada's industry is able to meet the standards necessary for entry into key markets throughout the world.

## National Commitment



Our enforcement activities are carried out by five Regional Operational Centres and a coordination centre in Ottawa:

- Halifax (Atlantic)
- Longueuil (Quebec)
- Toronto (Ontario and North)
- Winnipeg (Manitoba and Saskatchewan)
- Vancouver (Western)

The HPFB Inspectorate also operates two labs: one in Longueuil, the other in Toronto; as well as offices in Edmonton, AB and St. John's, NF.

## Main Activities (2007-2008)

### Inspections

**900** inspections of human drug, veterinary drug, medical device, semen, and blood establishments - this includes inspections of clinical trial sites.

### Compliance Verifications and Investigations

**7,260** compliance verifications and investigations of incidents in which a health risk was suspected.

### Laboratory Testing

**500** samples analyzed in support of HPFB enforcement activities, as well as those activities of our regulatory partners both within and outside Canada.

### Recall Monitoring

**720** recalls of health products.

### Establishment Licensing

**750** licensed drug establishments.  
**1,630** licensed medical device establishments.