

CANNABIS ADVERSE REACTION REPORTING GUIDE

**Adverse Reaction Reporting Guidance for
Licence Holders under the *Cannabis
Regulations***



Government
of Canada

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Canada

Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. Health Canada is committed to improving the lives of all of Canada's people and to making this country's population among the healthiest in the world as measured by longevity, lifestyle and effective use of the public health care system.

Disclaimer: Guidance documents provide information on how to comply with the requirements of the governing statutes and regulations. Alternate approaches to the principles and practices in this document may be acceptable if they meet the requirements of the *Cannabis Regulations*. This document should be read in conjunction with relevant sections of the *Cannabis Act* and its regulations. In cases of discrepancies between this document and the *Cannabis Act* and its regulations, the latter shall prevail.

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.

Publication Date: June 30, 2020

Également disponible en français sous le titre :
Guide sur la déclaration des effets indésirables du cannabis

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Cat.: H134-16/2020E-PDF
ISBN: 978-0-660-35058-5
Pub.: 200049

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1.0 Purpose

The document provides guidance for federal licence holders with respect to meeting mandatory reporting requirements for adverse reactions with cannabis products as outlined under section 248 of the *Cannabis Regulations*, as well as good case management practices that should be followed in meeting these requirements.

Adverse reaction reporting plays an important role in the post-market surveillance of cannabis products in the marketplace as it can help Health Canada and licence holders to identify and respond to emerging health and safety issues with cannabis products. Licence holders regulated under the *Cannabis Act* and its regulations should have procedures in place to enable them to react appropriately to reports of adverse reactions, including the activities of monitoring, reporting, assessing, and understanding their nature in order to minimize preventable harms.

This guidance may also be useful for others who may report adverse reactions to Health Canada on a voluntary basis, including patients, consumers, health care practitioners, health care institutions, and provincial/territorial-authorized retailers.

2.0 Background

The *Cannabis Act* and its regulations sets out the framework for legal access to cannabis while controlling and regulating its production, distribution and sale.

This guide describes Health Canada's expectations pertaining to adverse reaction reporting including the form and manner for submitting adverse reaction reports and the information that should be included in these reports.

Health Canada has published other guidance documents and information on its website that may be used in conjunction with this document to assist licence holders in complying with the *Cannabis Act* and regulations. In order to maintain consistency and transparency, this guide, as well as other guidance documents and information, will be updated, as required, to reflect changes to policies or operations. For more information, please visit Health Canada's website.

Health Canada has harmonized to the greatest extent possible with the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceutical for Human Use (ICH) guidance documents.

3.0 Scope

The scope of this guide pertains to adverse reaction reporting by federal licence holders who are subject to the requirements under the *Cannabis Act* and its regulations. Mandatory adverse reaction reporting requirements are outlined in section 248 of the *Cannabis Regulations*, and apply to licence holders that are authorized to sell or distribute a cannabis product for medical or non-medical purposes.

For the purposes of this guide, this applies to licence holders selling or distributing cannabis products intended for human consumption:

- Holders of a licence for processing (including standard and micro)
- Holders of a licence for sale for medical purposes

Note: This guidance also applies to licence holders who are conducting observational studies with cannabis products, and licence holders who are conducting research involving human subjects that does not meet the definition of a clinical trial in the *Food and Drugs Regulations* (for example, taste-testing).

This guide does not apply to:

- Holders of a licence under the *Industrial Hemp Regulations*, unless they are also a holder of a licence under the *Cannabis Regulations*.
- Holders of a drug identification number (DIN) for a drug containing cannabis (such as Sativex®) or cannabinoids (such as Cesamet®) that are regulated under the *Food and Drugs Act* and its regulations.
- A company who manufactures or sells cannabis as an active pharmaceutical ingredient (drug) for use in a clinical trial as defined in C.05.001 of the *Food and Drug Regulations*.
- Holders of a research licence conducting clinical trials (as defined in C.05.001).

4.0 Definitions and Abbreviations

4.1 Definitions

The *Cannabis Act* and its regulations contain definitions of terms, some of which are included here for ease of use. Other relevant definitions are also included.

Adverse reaction:

As defined in subsection 248(3) of the *Cannabis Regulations*, means a noxious and unintended response to a cannabis product. For purposes of reporting, it means that a causal relationship between a cannabis product and the occurrence of the adverse reaction is suspected.

Brand name:

Means a product name including modifiers or extensions (trademark, style, or logo) that is reasonably associated with a cannabis product.

Canada Vigilance:

The Canada Vigilance Adverse Reaction database collects case reports of adverse reactions, including for cannabis products.

Cannabis:

As defined in subsection 2(1) of the *Cannabis Act*, means a cannabis plant and anything referred to in Schedule 1 to the Act but does not include anything in Schedule 2 of the Act. For the purpose of this guide, the term cannabis includes any class of cannabis listed in Schedule 4 to the Act, as well as any cannabis accessory that contains cannabis, a discrete unit of cannabis or a cannabis product. This excludes a drug containing cannabis (cannabis drug) under the *Food and Drugs Act*.

Cannabis accessory:

As defined in subsection 2(1) of the Act means:

- a. A thing, including rolling papers or wraps, holders, pipes, water pipes, bongs and vaporizers, that is represented to be used in the consumption of cannabis; or
- b. A thing that is deemed under subsection (3) to be represented to be used in the consumption of cannabis.

Cannabis drug:

Refer to **Drug**.

Cannabis-naive consumer:

A person who has not previously used cannabis or a cannabis product.

Cannabis product:

Cannabis of only one of the classes that are set out in Schedule 4 to the Act- or a cannabis accessory if that accessory contains such cannabis - after it has been packaged and labelled for sale to a consumer at the retail level. It does not include a cannabis product that is intended for an animal, a cannabis accessory that contains cannabis that is intended for an animal, or a drug containing cannabis.

Causality:

For adverse reactions with cannabis products, causality refers to a determination of the likelihood that the cannabis products caused the adverse reaction (that is, the relationship between cause and effect).

Clinical trial:

As defined in Division 5 of the *Food and Drug Regulations*, means an investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug, or ascertain the safety or efficacy of the drug. For purposes of this guidance document, this means any clinical trial using a cannabis product, whether it is commercially available or not under the *Cannabis Act* and its regulations. Certain types of research involving human subjects may not meet the above definition, for example, taste-testing cannabis for assessing consumer preference of edible cannabis products.

Concomitant product:

A product used by a patient or consumer that is not suspected in the causal relationship to the adverse reaction by the reporter, but was being taken at the time of the adverse reaction.

Consumer:

An individual who uses a cannabis product for medical or non-medical purposes. In the adverse reaction reporting forms, this may be referred to as the 'patient'.

Distribute:

Includes administering, giving, transferring, transporting, sending, delivering, providing or otherwise making available in any manner, whether directly or indirectly, and offering to distribute. For purposes of adverse reaction reporting requirements, the definition does not apply to distribution for analytical testing.

Domestic adverse reaction:

An adverse reaction occurring in Canada with a cannabis product sold or distributed in the Canadian marketplace.

Drug:

Cannabis that is an active pharmaceutical ingredient as defined in Division C.01A.001(1) of the *Food and Drugs Regulations* or that is manufactured or sold for use in a clinical trial as defined in Division C.05.001 of those regulations.

Expedited reporting:

For purposes of this guidance document, expedited reporting is reflective of the following: any serious adverse reaction must be reported no later than 15 calendar days of initial receipt of the information by the licence holder; irrespective of whether the report is domestic or foreign.

Foreign adverse reaction:

An adverse reaction occurring outside Canada with a cannabis product exported by a licence holder for medical purposes that is identical or equivalent to a cannabis product (in composition) sold or distributed in Canada, regardless of the brand name used for purposes of export. For purposes of this guidance, this does not apply to cannabis exported for scientific research involving humans (that is, clinical trials) which falls under other applicable adverse reaction reporting obligations.

Health care practitioner:

For the purpose of this guidance document, means a health care professional in a clinical field, including medicine, surgery, dentistry, pharmacy, nursing, midwifery, naturopathic medicine or other allied health professions.

Licence holder:

The holder of a licence issued under the *Cannabis Act*, other than a holder of a licence that is subject to the *Industrial Hemp Regulations*.

MedDRA:

Is the Medical Dictionary for Regulatory Activities, developed and maintained by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), as a standardized set of clinically validated terms for symptoms, signs, diseases, syndromes and diagnoses. The terminology is organized into five distinct levels of hierarchy ranging from System Organ Class (SOC), High Level Group Term (LGT), High Level Term (HLT), Preferred Term (PT) and Low Level Term (LLT). These groupings aid in the retrieval, evaluation and presentation of adverse reaction data coded with MedDRA.

Medically important:

An adverse reaction that may not be immediately life threatening or result in death or hospitalization but may jeopardize the patient or consumer or may require medical intervention to prevent one of the other outcomes listed in the serious definition from the *Cannabis Regulations*.

Noxious:

Harmful, injurious or detrimental to health. This response may be temporary (transient) or lead to persistent or permanent incapacity or disability, or death.

Observational study:

A study in which the investigator strictly observes and evaluates the outcomes or the use of cannabis products in a population (that is, real world use), without controlling the administration or prescription of the cannabis product (that is, no interventions assigned). This may also be referred to as an epidemiological study or non-interventional study, or post-market study.



Patient:

With respect to adverse reaction reporting, is the person who experienced the adverse reaction following the use of a product. For purposes of this guidance, this may include an individual (patient or consumer) who experienced an adverse reaction to a cannabis product for either medical or non-medical purposes. For solicited adverse reaction reports, this would also refer to a person who experienced an adverse reaction to cannabis under conditions of a research study involving humans (for example, for taste testing) that is not a clinical trial.

Post-market adverse reaction:

Any adverse reaction associated with a cannabis product from a licence holder under the *Cannabis Act* and its regulations once it has entered the marketplace inside or outside of Canada.

Post-market surveillance:

The practice of monitoring the safety of a cannabis product after it has been released into the marketplace inside or outside of Canada. Post-market surveillance is an important component of the science of vigilance of cannabis products.

Qualified person:

For the purposes of this guidance, is an individual in charge of adverse reaction reporting obligations, practices and procedures including monitoring and screening of adverse reactions. A qualified person should have knowledge of the applicable sections of the *Cannabis Act* and its regulations and be qualified through training and experience relevant to their assigned responsibilities to conduct screening and follow-up of adverse reactions; assessment of adverse reactions including causality assessment; interpretation of clinical data; and, interpretation of seriousness for purposes of expedited reporting to Health Canada. This may include a qualified health practitioner (for example, medical, nursing or pharmacist) or other qualified professional with relevant scientific, health or clinical training and experience. More than one qualified person may be part of a team responsible for adverse reaction reporting.

Risk management:

Activities undertaken to identify, characterize, prevent or minimize risks with the use of cannabis products.

Reporter:

A person who reports an adverse reaction either for himself or herself or on behalf of another person. This may include a consumer, patient, family member, friend, caregiver, health care practitioner, hospital or other health care institution, provincial or territorial-authorized retailer or other.

Sale:

Includes offer for sale, expose for sale and have in possession for sale.

Serious adverse reaction:

A noxious and unintended response to a cannabis product that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life threatening or results in death.

Suspect product:

A product that is suspected to have caused the adverse reaction. This may include cannabis products alone or in combination with other suspect health products. More than one suspect product may exist in an adverse reaction report. For example, an interaction between a suspect cannabis product and a suspect health product that results in an adverse reaction.

Unintended response:

A response or effect that is not planned or intended. For purposes of the definition of serious adverse reaction reporting under subsection 248(3), this would include all serious adverse reactions. This does not pertain to 'unexpected' in reference to an effect of a drug (including a cannabis drug) being inconsistent with the applicable product information under the *Food and Drugs Act* and its regulations (for example, Investigator's Brochure or Product Monograph).

Unsolicited report:

An adverse reaction report received from an unsolicited communication or spontaneous source (for example, community members, including consumers, patients, family members, health care practitioners and retailers) that is not derived from a study or organized data collection system.

Vigilance:

Defined as the collection, evaluation and monitoring of adverse reactions (serious and non-serious) associated with the use of a cannabis product. This includes a set of methods and tools allowing the surveillance and evaluation of the safety of cannabis products, and contributing to real world data and evidence-based decision-making process and knowledge translation. This may also be referred to as post-market surveillance, cannabis vigilance or pharmacovigilance.

4.2 Abbreviations

AER

Adverse reaction report number

CTA

Clinical trial application

FDA

Food and Drugs Act

ICH

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

CIOMS

Council for International Organizations of Medical Sciences

MedDRA

Medical Dictionary for Regulatory Activities

SOP

Standard Operating Procedure

WHO

World Health Organization

4.3 Icons



Important: Key or cautionary information.



Tip: Information that could be helpful.

5.0 Adverse Reactions Associated with Cannabis Products

Adverse reactions, also known as side effects, are defined as noxious and unintended responses to a cannabis product, and may be serious or non-serious. Adverse reactions are usually spontaneously reported based on the suspicions of a reporter (unsolicited reports), but they may also be collected under conditions of a study or other organized data collection system (solicited reports). All instances of adverse reactions known to licence holders, whether solicited or unsolicited, or involving a complaint (such as, side effect associated with a complaint about product quality issues) regardless of the source of the report, should be considered a reportable adverse reaction if they meet the minimum criteria, as described below.

Adverse reactions may be associated with one or more cannabis products alone, or in combination with drugs (prescription or non-prescription drugs, biologic drugs), natural health products, cosmetics, foods, alcohol, tobacco or other substances.

5.1 Regulations Pertaining to Adverse Reaction Reporting

As outlined in section 248 of the *Cannabis Regulations*:

A holder of a licence that sells or distributes a cannabis product **must**:

- a. within 15 days after becoming aware of a serious adverse reaction to the cannabis product, provide the Minister with a detailed report containing all information in their possession that is associated with the use of the cannabis product by the individual who experienced the reaction; and
- b. prepare an annual summary report that contains a concise and critical analysis of all adverse reactions to the cannabis product that the holder became aware of during the previous 12 months.

These reporting obligations apply to all licence holders who sell or distribute a cannabis product, whether inside or outside of Canada. Sale includes directly to patients for medical purposes, as well as sale to consumers through provincial or territorial-authorized retailers for non-medical purposes. This also applies to distribution or sale of a finished cannabis product from one licence holder to another (such as, for sale for medical purposes, for export for medical sale, or for resale).

5.2 Serious Adverse Reactions

A serious adverse reaction is defined in section 248 of the *Cannabis Regulations* as a “noxious and unintended response to a cannabis product that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death.”

An adverse reaction should not be downgraded from serious to non-serious by a licence holder, even if the licence holder disagrees with the seriousness assigned by the reporter. The opinions of both the reporter and the licence holder should be recorded in the adverse reaction report and identified as such.

Medical and scientific judgement by a qualified health professional should be exercised in deciding whether an adverse reaction is medically important and should be reported to Health Canada on an expedited basis as well. According to ICH guidance, this should also be considered serious as a medically important event ([ICH E2B](#)). For example, an allergic reaction that caused breathing difficulties and that required treatment in an emergency room or a seizure (convulsion) that did not result in hospitalization but involved a medical intervention or consultation with their health care practitioner.



Medically important events are those that may not be immediately life threatening or result in death or in-patient hospitalization but may jeopardize the patient or may require medical or surgical intervention to prevent one of the other outcomes listed in the serious adverse reaction definition from the *Cannabis Regulations*. Health Canada asks that these cases be reported on an expedited basis as well.

5.3 Non-serious Adverse Reactions

A non-serious adverse reaction is one that does not meet any of the criteria for a serious adverse reaction under the *Cannabis Regulations*, or is not judged to be medically important. A licence holder may voluntarily submit these adverse reactions, particularly if a new or unexpected issue is observed (for example, change in severity or frequency of adverse reactions; trend or cluster of related cases). Additionally, all adverse reactions, including non-serious adverse reactions, must be collected and critically analyzed as part of the annual summary report.



Tip: A list of important medical events (**MedDRA** terms) has been developed by the European Medicines Agency^a; however, this is only provided as guidance tool and medical and scientific judgement should be used by a qualified individual.

5.4 Domestic and Foreign Adverse Reactions

As outlined in section 248 of the *Cannabis Regulations*, licence holders must submit all serious adverse reactions to Health Canada within 15 days of becoming aware of them. This includes both domestic adverse reactions (that is, those occurring inside Canada) and foreign adverse reactions (that is, those occurring outside of Canada) associated with a cannabis product that is sold by a licence holder in Canada or other country.

Licence holders should indicate in the report if the case occurred in Canada or outside of Canada and indicate in which country the reaction occurred.

5.5 Other Adverse Reaction Report Types

Adverse reactions with recalled products, discontinued products or previously available products that are submitted to licence holders are still required to be reported to Health Canada. Section 248 does not solely apply to currently marketed products, as discontinued or recalled products may still be in possession by individuals.

Cases of overdose (accidental or intentional), dosing errors and other instances of direct exposure to a cannabis product and resulting in a serious adverse reaction must also be reported to Health Canada.

In instances of pregnancy and breastfeeding exposure, licence holders are expected to follow-up on reports received from health care practitioners, consumers or patients where *in utero* or neonatal exposure could have occurred, to determine whether any adverse outcomes occurred in the foetus or newborn.

^a European Medicines Agency. Inclusion / Exclusion criteria for the “Important Medical Events” list. https://www.ema.europa.eu/en/documents/other/eudravigilance-inclusion/exclusion-criteria-important-medical-events-list_en.pdf [07 March 2019]



Tip: Adverse reactions occurring in a parent and a foetus are considered two separate adverse reaction reports.

6.0 Good Vigilance Practices

6.1 Procedures

Every licence holder who sells or distributes a cannabis product should have written procedures in place for example, standard operating procedures (SOPs) outlining the collection, follow-up, evaluation, reporting and record keeping for all adverse reactions with cannabis products. Licence holders should verify their complaint records to ensure that all serious adverse reactions are identified, followed-up and reported to Health Canada.

Appropriate follow-up procedures should exist in order to obtain pertinent details for including in adverse reaction reports (refer to section 7.5 Follow-Up Information). Reports should be accurate, legible and as complete as possible.

In general, adverse reaction reporting procedures (good vigilance practices) should define:

- key responsibilities
- responsible personnel
- investigating adverse reactions
- reporting adverse reactions
- record keeping activities

Relevant steps in the processes may include but are not limited to:

- monitoring and handling of adverse reactions from reporters received spontaneously (unsolicited reports) through email, telephone, letter or social media; or collected in studies or other organized data collection sources (solicited reports)
- determining if a complaint includes an adverse reaction
- assigning a unique identifier to each case for tracking and follow-up purposes
- following-up with reporters to obtain as much information, including products, patient medical history and outcomes
- investigating to provide opinion on causality and possible causes (for example, root cause)
- submitting adverse reaction reports to Health Canada

- record keeping, including all adverse reaction reports and documentation of investigations (for example, causality, root cause analysis, certificates of analysis)

6.2 Contractual Agreements

The distribution and sale of cannabis products may take place through contractual or supply agreements between a licence holder and other parties (for example, subsidiary, corporation, consultant or other third party). The sections below discuss responsibilities in regards to adverse reaction reporting.

6.2.1 Adverse Reaction Reporting by a Licence Holder

Licence holders are responsible for mandatory adverse reaction reporting under section 248 of the *Cannabis Regulations*. This applies to a holder of a processing licence that sells or distributes a cannabis product for non-medical purposes to a provincial/territorial authorized retailer or to another licence holder. This also applies to a holder of a licence for medical sale who may also hold a processing licence, or holder of a medical sale licence only that sells products from other licence holders.

If a licence holder sells a cannabis product produced by another licence holder, it is expected that proper procedures are in place (for example, SOPs) for meeting mandatory adverse reaction reporting obligations to Health Canada. These procedures should include submitting adverse reaction reports to the licence holder who produced the cannabis product so they may also meet their adverse reaction reporting obligations. In such instances, the report should indicate if it was also submitted to the licence holder who produced the cannabis product for record keeping purposes.

6.2.2 Adverse Reaction Reporting Conducted on Behalf of a Licence Holder

It is important that if adverse reaction reporting to Health Canada occurs on behalf of a licence holder by a corporation or third party company, a written agreement between the licence holder and third party be established, to:

1. authorize the collection of information by the other party on behalf of the licence holder; and,
2. ensure that the reports submitted would meet the legal requirements of the *Cannabis Regulations*, such as the timelines and required content.

Examples of such arrangements could include a corporation who reports adverse reactions on behalf of a subsidiary who is a licence holder, or a third party who conducts adverse reaction reporting activities on behalf of a licence holder.

Whatever the nature of the arrangement, it is ultimately the responsibility of licence holders who sell or distribute a cannabis product to meet the adverse reaction reporting requirements under section 248 of the *Cannabis Regulations*.

Written agreements should exist with every party that conducts adverse reaction reporting activities, including but not limited to:

- mandatory reporting of serious adverse reactions to Health Canada
- preparing and maintaining annual summary reports of all adverse reactions

If such written arrangements are made it is encouraged to notify Health Canada proactively for transparency (refer to section 10 Contact Information).

6.3 Record Keeping Requirements

Good documentation is an important part of a quality assurance system for adverse reaction reporting. Under subsection 248(2) of the *Cannabis Regulations*, licence holders must maintain the adverse reaction reports for at least 25 years after the day on which they are prepared, including both individual adverse reaction reports and annual summary reports.

As such, licence holders should ensure that adverse reaction reports are stored appropriately in order to protect personal information.

If adverse reaction reports are transmitted between stakeholders with contractual agreements or between licence holders, this should be done while ensuring privacy and data security of personal information.

A qualified person should verify adverse reaction data for appropriateness, completeness, follow-up and determination of seriousness, especially if customer care representatives are initially receiving adverse reactions among other types of incidents or complaints (for example, collected within a broader complaints system or process).

If case reports are coded, verbatim from the reporter should always be maintained in the narrative, and reflect as much detail as possible about the reaction.

For purposes of verifying record keeping requirements, information should be readily available to Health Canada. This includes written procedures for handling reports, conducting follow-up and analysis of adverse reaction reports, record keeping of individual case reports as well as annual summary reports. These records should be easily accessible to permit submission upon request to Health Canada as per section 248 of the *Cannabis Regulations* and for auditing purposes during an inspection.

6.4 Personnel and Training

Licence holders should have qualified personnel who are responsible for screening and assessing adverse reactions submitted to the licence holder. The qualified personnel should have necessary qualifications, experience and training relevant to the responsibilities of adverse reaction reporting (for example, background in medical or health-related fields, experience in interpretation of medical information in adverse reaction reports, and knowledge of the *Cannabis Regulations*). For the purpose of reporting serious adverse reactions, clinical judgement by a qualified health professional should be exercised in deciding whether an adverse

reaction report is serious and must be submitted to Health Canada. Clinical judgement is also important in determining if an adverse reaction is medically important and should be submitted, as well as determining if the case is related to the product itself or due to other factors (causality assessment). Qualified personnel should also be involved in determining the completeness of the case report and whether follow-up is required, and determining if there is significant new information from follow-up that requires expedited reporting based on clinical judgement.



Tip: A responsible person should be designated for adverse reaction reporting that is identifiable in reports submitted to Health Canada in case of questions or follow-up. An alternate person may also be designated in case the primary contact is not available.

The qualified personnel are responsible for establishing and maintaining a system whereby adverse reaction data is collected, monitored, followed-up, and properly assessed. All personnel involved in collecting reports of complaints or adverse reactions (for example, customer care service) should have their responsibilities outlined in writing.

Adequate and ongoing training should be provided to personnel as necessary. Third party companies that have a contractual agreement for adverse reaction reporting on behalf of a licence holder should also have the necessary qualifications, training and experience to conduct adverse reaction reporting activities.

7.0 Good Case Management Practices



An individual report must be submitted to Health Canada for each consumer or patient who experienced a serious adverse reaction associated with a cannabis product. In instances of a cannabis product being shared among two or more individuals, a report should be filled out for each person.

7.1 How to Report Individual Reports

Licence holders should report adverse reactions to Health Canada through one of the following forms for mandatory reporting:

- [Mandatory Adverse Reaction Reporting Form for Industry \(Health Canada Form\)](#)
- [Council for International Organizations of Medical Sciences \(CIOMS Form\)](#)

7.1.1 Method for Submitting Reports to Health Canada:

Complete the applicable form and send to the Canada Vigilance Program:

Send by fax at: 613-957-0335

Mail to:

Canada Vigilance Program
Health Canada
Address Locator 1908C
Ottawa, Ontario
K1A 0K9

Certain companies may already be enrolled with Canada Vigilance as trading partners to submit adverse reaction reports electronically in accordance with the technical requirements and business (validation) rules set out for users of the E2B portal. If this method of transmission is used for submitting adverse reactions for cannabis products, it is important to follow best practices for electronic transmission of adverse reaction reports ([ICH E2B guidance](#)). It is also important that sufficient details about suspect cannabis products are captured in the report so they may be coded appropriately by Health Canada. For further information, see Appendix 4 of Health Canada's guidance document "[Reporting Adverse Reactions to Marketed Health Products](#)".



Tip: For solicited adverse reactions that are derived from a study or organized data collection system, section 8.2.3 provides further details on submitting reports to Health Canada.

7.2 Minimum Criteria for an Adverse Reaction Report

The minimum criteria for reporting an adverse reaction to Health Canada are:

- an identifiable reporter (source)
- an identifiable patient or consumer
- a suspect cannabis product
- a description of the adverse reaction

If these four minimum criteria are met, a case is considered reportable to Health Canada, and for serious adverse reactions, must be submitted to Health Canada within 15 days of the licence holder becoming aware of the serious adverse reaction.

In the above context, an identifiable patient/consumer and reporter refers to the ability to verify the existence of a patient/consumer and a reporter. One or more of the following should qualify

a patient as being identifiable: age or age category, sex, unique identifier or reference to a patient.

In the context of a suspect cannabis product, this refers to a cannabis product that an individual consumed (intentional or unintentional) and that is suspected of having caused the adverse reaction (causal relationship is suspected).

It is expected that licence holders collect as much information as possible so that reports submitted to Health Canada capture clinically relevant and complete information for evaluation. Key data elements are outlined below in order to assist licence holders in submitting detailed adverse reaction reports.

The following key data elements may also be useful for reports submitted to Health Canada from other sources, including health care practitioners, consumers/patients, retailers or others.

7.3 Key Data Elements



The following key data elements apply to both unsolicited adverse reaction reports and solicited adverse reaction reports. Refer to [section 8.0 Adverse reaction reports by source](#) for further information.

7.3.1 Reporter Information

- Report source (origin of information): Spontaneous / Study / Unknown / Other
- Reporter type (initial reporter): Consumer / Patient / Health care practitioner / Lawyer / Retailer / Other
- The reporter also sent a report to the Canada Vigilance Program: Yes / No / Unknown
- Contact office: Name of responsible person and address of licence holder (or company submitting report on behalf of licence holder, with name of licence holder for which the report is being submitted)
- Report number: Identification number assigned by the licence holder to a report for record-keeping purposes. For a follow-up report on the same case, the report number should be the same as the number assigned to the initial report
- Type of report: Initial / Follow-up
- Date of when the licence holder received the information for this report
- Date the report is being sent to Health Canada

7.3.2 Patient/Consumer Information

- Unique identifier: patient identifier in order to readily locate the case for follow-up purposes. For privacy purposes, do not use the patient's name or initials

- Age at the time of the reaction (according to date of birth and date of reaction/event; or, age at the time of the reaction/event; or, patient age group according to available information)
- Sex
- Height and weight
- Relevant medical history, including family history of disease, pre-existing health conditions (e.g., allergies, acute or chronic disease), history of use of other substances (e.g., tobacco, nicotine, alcohol, controlled drugs, illicit substances) including the duration and frequency of use, if known
- Medication history, including the use of pharmaceutical drugs (prescription and non-prescription), biologic drugs and natural health products, including the duration and frequency of use, if known
- Whether the patient is a regular cannabis consumer (past or present) or a new cannabis consumer (cannabis naïve). If past history is known, provide relevant information such as dates, product names, dosage forms, route of administrations, and frequency of use

7.3.3 Adverse Reaction Information

- Country in which the adverse reaction occurred
- Date that the adverse reaction occurred
- Full description of the adverse reaction, including body site and severity, and any relevant clinical information (reported signs and symptoms, clinical course, specific diagnosis, etc.)
- Whether the report is serious and criterion for seriousness
- Onset date (and time), stop date (and time), and duration of adverse reaction
- Outcome (recovered or not; sequelae or not)
- Setting (hospital in-patient, out-patient, home, nursing home, other)
- Relevant diagnostic tests and laboratory data
- For a fatal outcome, stated cause of death
- Relevant autopsy or post-mortem findings

7.3.4 Suspected Cannabis Product(s)

More than one cannabis product may be involved in a case. Include all details of the cannabis products suspected in the adverse reaction, including:

- product name
 - brand name assigned by the licence holder under which it is sold, including any name extensions or modifiers
- product class

- dried or fresh cannabis
 - cannabis extract
 - cannabis topical
 - edible cannabis
 - cannabis accessory that contains any of these
- product form
 - dried flower: pre-rolled, milled, whole flower
 - extracts: oil, capsule, oral spray, vaping liquid, vaping cartridge, hash, “shatter”, “budder”, wax
 - edible cannabis: beverage, confectionary, baked good
 - topicals: cream, lotion, gel, transdermal
- Quantity or concentration of THC, THCA, CBD and CBDA
- List of other constituents (terpenes) or other ingredients (for example, carrier oil, food ingredients)
- Batch or lot number as well as UPC/SKU/GTIN (as applicable)
- Route of administration (for example, oral [ingested, buccal, sublingual]; inhaled [vaped or smoked]; intranasal; topical)
- Device or accessory used (include details such as brand name and model number, place of purchase)
- Daily dose and frequency of use (for example, once a day, or if used multiple times a day, specify dose and regimen)
- Duration of use (include start and stop dates)
- Indication: specify if the cannabis product was being used for medical or non-medical purposes. If the product was being used for medical purposes, describe the reason for use. Specify whether the patient has a medical authorization document
- Dechallenge information: Reaction abated after stopping the product, reducing dose, or changing route of administration
- Rechallenge information: Reaction re-appeared after the product was re-started

7.3.5 Other Suspected Health Products or Substances

Describe if any drugs or health products are also suspected in the reported adverse reactions (such as, co-suspected in the adverse reaction with the cannabis product).

7.3.6 Concomitant Health Products or Other Substances

Describe if any concomitant products or substances were used concurrently but not considered suspected in the adverse reaction. These may include prescription or non-prescription drugs, natural health products, drugs, alcohol, tobacco.

7.3.7 Treatment of the Adverse Reaction

Describe the treatment of the adverse reaction, including any health products or therapies that were used.

7.4 Narrative Information

Narrative information in case reports is important for describing the clinical course of the adverse reaction. Include as much narrative information as possible, including:

- Additional details of past medical history
- History of use of suspect products (including cannabis products)
- Clinical course of the adverse reaction (including time to onset)
- Diagnosis (including investigations)
- Outcome (including sequelae or no sequelae)
- Any other information that may support or rule out a causal association, such as positive de-challenge and re-challenge information

Licence holders should also include their assessment of causality and root cause analysis of the adverse reaction, including whether product quality or other factors are suspected of being involved.

7.5 Follow-up Information

Adverse reaction reports should be followed-up to obtain as much detail as possible. This additional information should be submitted to Health Canada in a follow-up report citing the original adverse reaction number regardless of how much time has elapsed since the initial report was submitted to Health Canada. Follow-up information may include additional information submitted by the original reporter (for example, notes, medical history, discharge records, product details) or additional information from the licence holder themselves (for example, certificate of analysis of the lot involved in the adverse reaction report, information pertaining to root cause analysis).

It is expected that licence holders exercise due diligence in obtaining as much detail about an adverse reaction from a reporter for assessment. Follow-up should be attempted for each case report, especially for serious adverse reactions that must be submitted to Health Canada. This may help to minimize requests for information from Health Canada when evaluating the cases.

7.6 Assessment of Adverse Reactions Associated with Cannabis Products

All adverse reaction reports received by licence holders should be reviewed by a qualified person, including:

- screening of complaint records to ensure that all adverse reactions are documented and reported in accordance with section 248 of the *Cannabis Regulations*
- reviewing the adverse reaction report to ensure quality and completeness of the information
- conducting follow-up, particularly on serious or medically important cases
- determining seriousness for expedited reporting purposes
- conducting an investigation of the adverse reaction, including evaluating the likelihood that the suspect product caused the adverse reaction (causality analysis) and possible underlying cause (root cause). If causality has already been attributed by the original reporter, this should not be changed, but the licence holder can identify in the report their own opinion of causality in addition to that reported by the original reporter
- determining whether product quality is involved or not
- if corrective or preventive actions have been taken for a particular issue involving an adverse reaction according to an investigation of quality (subsections 19(2) and 88(1) of the *Cannabis Regulations*), these details should be included as follow-up to the adverse reaction report

For further information on the World Health Organization's criteria for causality, please refer to Appendix 6 of the Health Canada guidance [Reporting Adverse Reactions to Marketed Health Products](#). Further information on root cause analysis may be found in the [Good Production Practices Guide for Cannabis](#).

7.7 Duplicate or Linked Reports

Adverse reaction reports may be submitted to licence holders from more than one source, such as a consumer or patient in addition to a health care practitioner, retailer or other source. If a duplicate or follow-up report is received after the initial report has been submitted, a licence holder should report these to Health Canada and cite the original adverse reaction number. It is important to indicate whether the report is a follow-up (same reporter) or duplicate (different reporter) to the initial report. The proper identification of duplicate reports will also help licence holders to reflect the accurate number of unique cases, particularly for serious adverse reactions, for signal detection purposes and to avoid issues related to multiple counting of a single case when developing the annual summary report. Licence holders should have in place a system or method for identification and management of duplicate and linked reports.

7.8 Handling and Coding of Reports

Licence holders should have a system, database or program to collect and analyze adverse reaction data. This may include an electronic system (for example, Argus Safety Case Management system) to collect information in a standardized manner. The use of international standardized medical terminology (such as, MedDRA) is recommended as a tool to code adverse reaction data for cannabis adverse reactions in order to classify, search and retrieve adverse reaction reports. Further, it is also helpful for reporting purposes (for example, for individual case reports and for the preparation of annual summary reports). If standardized medical terminology is used, the report should still include the initial reporter verbatim details in the narrative to ensure that all details are captured.

8.0 Adverse Reaction Reports by Source

8.1 Surveillance of Adverse Reaction Reports

It is expected that licence holders monitor and analyze adverse reactions, which may originate from various sources, including:

- Submitted to licence holders spontaneously by consumers/patients, health care practitioners, retailers, as unsolicited reports
- Submitted directly to Health Canada and identified through routine monitoring of the Canada Vigilance Adverse Reaction Online database by licence holders
- Published in the scientific literature
- Reported on social media platforms that licence holders are responsible for
- Collected from an epidemiological study, research study involving humans (outside of the scope of a clinical trial), or other organized data collection systems as solicited reports

8.2 Spontaneous Reports

8.2.1 Spontaneous Reports Submitted Directly to Licence Holders

Spontaneous reports are those received on an unsolicited basis from consumers, patients, health care practitioners or other reporters (for example, retailers) that describe an adverse reaction in a consumer or patient with one or more cannabis products and that does not originate from a study or any organized data collection system (for example, patient registries or monitoring programs).

If a spontaneous report is submitted to a licence holder, even if the relationship is unknown or unstated, it is considered a reportable adverse reaction based on the suspicion of the initial reporter that there is a suspected relatedness between a cannabis product and the adverse reaction.

Certain spontaneous reports may be stimulated by certain factors, for example, advisories, recalls or other information that communicates about reporting of adverse reactions. These reports should be considered unsolicited and must be reported to Health Canada.

8.2.2 Spontaneous Reports Submitted Directly to Health Canada

In order to ensure that adverse reaction report records held by licence holders are complete, licence holders should be monitoring the [Canada Vigilance Adverse Reaction Online Database](#), in order to identify any adverse reaction reports with their cannabis products submitted directly by the public to Health Canada.

Licence holders should verify the online database to identify adverse reaction reports with their cannabis products, by licence holder name or brand name of cannabis product. Only reports involving a cannabis product from the applicable licence holder are expected to be retrieved and included in the annual summary report.

Reports originating from the Canada Vigilance Adverse Reaction Online Database do not need to be resubmitted to Health Canada except if the licence holder has additional information about the case. If additional information exists, the licence holder should submit a follow-up report (citing original adverse reaction number). However, for purposes of preparing an annual summary report, Health Canada expects all adverse reactions known to the licence holder to be included, including those originating from the Canada Vigilance Adverse Reaction Database as well as from other regulatory authorities, if applicable (for example, cannabis product exported for medical purposes by a licence holder).

8.2.3 Scientific Literature Reports

Licence holders are expected to screen the medical and scientific literature for case reports with their cannabis products. If a licence holder becomes aware of a published case report or a study reporting a serious adverse reaction with their cannabis product (such as, explicitly reported in the publication, or implicitly known by the licence holder), it is the responsibility of the licence holder to submit this adverse reaction to Health Canada. This only applies in instances where the publication's authors have identified at least a possible causal association with the cannabis products, irrespective if the published case report occurred inside or outside of Canada.

A single report should be created for each individual patient identified in a publication, and all relevant case details (including citation of the publication) should be included. The publication authors would be considered the primary reporters and the full literature citation should be provided.

8.2.4 Social Media or Media Reports

If a licence holder becomes aware of a serious adverse reaction report in the media or social media with one of their cannabis products, it is considered a reportable case if it meets the four

minimum criteria. Given the limited nature of these sources, effort should be made to obtain as much detail as possible. Although these are considered spontaneous reports, they should be identified as originating from the media or social media in the adverse reaction reporting form.

8.3 Study Reports



Adverse reactions that occur under conditions of a clinical trial are outside of the scope of this guidance document. Under the *Cannabis Exemption (Food and Drugs Act) Regulations*, cannabis used for the purpose of a clinical trial is subject to the requirements of Part C, Division 5: Drugs for Clinical Trials Involving Human Subjects of the *Food and Drug Regulations*.



Additional information about clinical trials can be found at:

- [Guidance Document for Clinical Trial Sponsors: Clinical Trial Applications](#)
- [Health Products Containing Cannabis or for Use with Cannabis: Guidance for the Cannabis Act, the Food and Drugs Act, and Related Regulations](#)

For the purposes of this guidance, study reports are defined as adverse reactions that are derived from epidemiological studies or other types of organized data collection systems where data is actively collected or solicited, such as registries, or patient utilization or monitoring programs. Study reports are also referred to as “solicited reports.”

Epidemiological studies are non-interventional studies in which investigators do not assign cannabis products as an intervention, but rather, study or observe the use of cannabis products in a defined group or populations using epidemiological methods.

Study reports also in scope of this guidance include adverse reactions originating from research studies in humans involving cannabis that do not meet the definition of a clinical trial as defined under Division 5 of the *Food and Drug Regulations* (for example, sensory testing).

Serious adverse reactions derived from a study or organized data collection system (that is, solicited reports) in scope of this guidance must be submitted to Health Canada if there is a suspicion that the cannabis product caused the adverse reaction, as determined by a qualified person using clinical judgement. In other words, a serious adverse reaction from a study must be submitted if there is a reasonable possibility that cannabis product caused the adverse reaction (that is, the relationship cannot be ruled out).

8.3.1 Study Reports from Licence Holders

Licence holders who are conducting studies with cannabis products should be monitoring adverse reactions (that is, included in the protocol) in order to meet serious adverse reaction obligations under section 248 of the *Cannabis Regulations*, including both domestic and foreign adverse reactions.

When reporting serious adverse reactions from studies, the following information should be included:

- Study ID and title
- Study type (for example, cohort study, case-control, survey, other)
- Location of study
- Status of study (ongoing or completed, with dates)

Licence holders should use the forms outlined in section 7.1 to submit the adverse reactions to Health Canada. All principles outlined in this guidance document should be applied including key information, determination of seriousness, and determination of causality.

If an adverse reaction is reported outside of the parameters of an epidemiological study or organized data collection scheme (such as, after the study has been completed), it should be considered to be a spontaneous report.

8.3.2 Study Reports from Other Stakeholders

It is possible that a licence holder receives reports of serious adverse reactions with one or more of their cannabis products derived from studies conducted by other stakeholders (for example, private investigator, academic center or other licence holder or market authorization holder). In such instances, licence holders should attempt to obtain follow-up information from the other stakeholder, and the report treated according to the principles outlined above for mandatory reporting of serious adverse reactions to Health Canada. A licence holder should not alter the causality provided by the initial reporter (for example, investigator) and should identify their own causality in the report.

8.3.3 Research in Humans Involving Cannabis

A clinical trial is defined in the *Food and Drug Regulations* as an “investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug or ascertain the safety or efficacy of the drug.”

Health Canada considers certain specific and limited types of research in humans involving cannabis to fall outside of this definition. An example would include a taste test study

investigating the palatability of an edible cannabis product, or other type of sensory testing study.

These studies in humans involving cannabis that do not fit the definition of a clinical trial must be authorized under the terms of a Cannabis Research Licence from the Controlled Substances and Cannabis Branch. Licences allowing for this specific and limited type of human research include a number of conditions, including the requirements to submit all serious adverse reactions and prepare an annual summary report, similarly to what is outlined section 248 of the *Cannabis Regulations*, for all cannabis (in its final form) that is administered or distributed to human research subjects.

Any holder of a research licence that conducts human research involving cannabis outside of a clinical trial must submit a detailed report of any serious adverse reaction to the cannabis to Health Canada within 15 days after they become aware of a serious adverse reaction. This report must contain all information in their possession that is associated with the use of the cannabis by the individual who experienced the reaction.

When submitting adverse reaction reports to Health Canada, the report must include:

- The research licence number and title of the study; and
- A description of the cannabis material (in its final form), including the list of ingredients, description of the cannabis product form and composition (for example, amount or concentration of each ingredient and function)

Licence holders should use the forms outlined in section 7.1 to submit the adverse reactions to Health Canada. All principles outlined in this guidance document should be applied including key information, determination of seriousness, and determination of causality.

Additionally, any adverse reactions to the cannabis that licence holders become aware of during the last 12 months must be included in an annual summary report that contains a concise and critical analysis of all adverse reactions to the cannabis. This report must also include the research licence number for the study and a description of the cannabis, including the list of ingredients, description of the cannabis form and class and its composition (for example, relative abundance of each ingredient).

All records (all individual adverse reaction reports and annual summary reports) must be retained for at least 25 years after the day on which they are prepared.

9.0 Contact Us

Licence holders who have questions about the information or requirements in this guide are invited to contact the Controlled Substances and Cannabis Branch at cannabis@canada.ca.



10.0 Feedback: Help Us Improve

Health Canada is committed to providing all stakeholders with timely, accurate and reliable information. This includes providing applicants and licence holders with the information they need to comply with the *Cannabis Act* and its regulations.

We would appreciate receiving your feedback on whether this guide was useful, and we welcome your suggestions for improvement. Email your feedback to us at cannabis@canada.ca and indicate in the subject line Feedback on the Cannabis Adverse Reaction Reporting Guide.

Your comments will help us improve this guide.