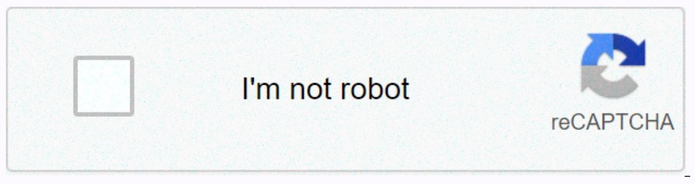

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Adverse reaction reporting guidance document

Guidance on reporting adverse reactions to license holders under the Cannabis Regulations On this page, disclaimers contain: Guidance documents provide information on how to comply with the requirements of applicable statutes and regulations. Alternative approaches to the principles and practices of this document may be acceptable if they meet the requirements of the cannabis regulations. This document must be read in conjunction with relevant sections of the Cannabis Act and its provisions. In the event of inconsistencies between this document and the Cannabis Act and its provisions, the latter shall take precedence. Guidance documents also provide assistance to staff on how Health Canada's mandates and objectives should be implemented in a fair, consistent and effective manner. 1.0 Purpose The document provides guidance to holders of federal licensees to meet mandatory reporting requirements for adverse effects with cannabis products as described in section 248 of the Cannabis Regulations, as well as good case management practices that should be followed to meet these requirements. Reporting of adverse reactions plays an important role in post-marketing monitoring of cannabis products on the market, as it can help Health Canada and licenseholders identify and respond to new health and safety problems with cannabis products. Licence holders regulated under the Cannabis Act and its provisions should have procedures in place to enable them to respond appropriately to adverse reaction reports, including activities such as monitoring, reporting, assessing and understanding their nature to minimise preventable harm. This guide may also be useful for others who can report adverse reactions to Health Canada on a voluntary basis, including patients, consumers, health care professionals, health care institutions, and provincial/territorial-authorized retailers. 2.0 Background The Cannabis Act and its regulations establish the framework for legal access to cannabis, while at the same time controlled and regulating production, distribution and sales. This guide describes Health Canada's expectations for adverse reaction reporting, including the form and manner of 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 can be used in connection with this document to help license holders comply with the Cannabis Act and regulations. In order to maintain consistency and transparency, this guidance, as well as other guidance documents and information, will be updated as necessary to reflect changes in policies or operations. For more information, please visit Health Canada's website. As far as possible, Health Canada has harmonised with the International Council for the Harmonisation of Technical Requirements for the Registration of Medicinal Products for Human Use (ICH) indicative 3.0 Scope Scope The scope of this guide relates to the reporting of adverse reactions by federal license holders subject to the requirements of the Cannabis Act and its provisions. Mandatory adverse event reporting requirements are set out in section 248 of the Cannabis Re-Regulations and apply to licence holders authorised to sell or distribute a cannabis product for medical or non-medicinal purposes. For the purposes of this guide, this is true for license holders who sell or distribute cannabis products intended for human consumption: Holders of a license for processing (including standard and micro) Holders of a license for sale for medicinal purposes Note: This guide also applies to certificate holders conducting observational studies with cannabis products, and license holders conducting research involving subjects who do not meet the definition of a clinical trial in food and drug regulations (e.g. taste tests). This guide does not apply to: Holders of a licence under the industrial hemp provisions, unless they also hold 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 rules. A company that 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 authorisation conducting clinical trials (as defined in C.05.001). 4.0 Definitions and abbreviations 4.1 Definitions The Cannabis Act and its provisions contain definitions of terms, some of which are included here for ease of use. Other relevant definitions are also included. Side effect: As defined in subsection 248(3) of the cannabis regulations, a harmful and unintended reaction to a cannabis product. For reporting purposes, this means that a causal link between a cannabis product and the occurrence of the adverse reaction is suspected. Trademark name: A product name, including modifiers or extensions (trademark, style or logo) that is reasonably associated with a cannabis product. Canada Vigilance: Canada Vigilance Adverse Reaction database collects case reports of side effects, including for cannabis products. Cannabis: As defined in subsection 2(1) of the Cannabis Act, a cannabis plant means everything mentioned in Schedule 1 of the Act, but nothing in Schedule 2 of the Act. For the purposes of this guide, the concept of cannabis includes any class of cannabis listed in Table 4 of the Act, as well as cannabis accessories containing cannabis, a discreet unit of cannabis or a cannabis product. This excludes a drug containing cannabis (cannabis drug) under the Food and Drugs Act. Cannabis accessories: As defined in 2 (1) in law means: One thing, including rolling papers or wraps, wraps, pipes, water pipes, bongs and vaporizers represented to be used in the consumption of cannabis; or A thing considered under subsection (3) to be represented to be used in the consumption of cannabis. Cannabis Drug: See 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 specified in Schedule 4 of the law or cannabis accessories if the accessory contains such cannabis - after it has been packaged and labelled for sale to a retail consumer. It does not include a cannabis product intended for an animal, a cannabis accessory containing cannabis intended for an animal, or a medicinal product containing cannabis. Causality: For side effects with cannabis products, causality refers to a determination of the likelihood that cannabis products caused the side effect (i.e. the cause-to-effect relationship). Clinical trial: As defined in section 5 of the Food and Drug Regulations, a study on a human-related medicinal product intended to detect or verify the clinical, pharmacological or pharmacodynamic effects of the medicinal product, identify any adverse reactions associated with the medicinal product, examine absorption, distribution, metabolism and excretion of the medicinal product, or determine the safety or efficacy of the medicinal product. For the purposes of this guidance document, this means any clinical trial of a cannabis product, whether commercially available or not, under the Cannabis Act and its provisions. Certain types of research involving humans may not meet the above definition, for example, in the case of human beings. Concurrent product: A product used by a patient or consumer who is not suspected in causation with the adverse reaction of the reporter but was taken at the time of the adverse reaction. Consumer: A person using a cannabis product for medical or non-medical purposes. In the adverse reaction reporting forms, this can be called the patient. Distribute: Includes administration, transfer, transfer, transportation, shipment, delivery, delivery or otherwise available in any way, either directly or indirectly, and offers to distribute. For the purposes of reporting adverse reactions, the definition does not apply to distribution for analytical testing. Domestic side effect: A side effect that occurs in Canada with a cannabis product sold or distributed on the Canadian market. Medicinal product: Cannabis that is an active pharmaceutical ingredient as defined in section C.01A.001(1) of the Food and Drugs Regulations or which is manufactured or sold for use in a clinical trial as defined in section C.05.001 of these Regulations. Expedited reporting: For the purposes of this guidance document, accelerated reporting reflects the following: any serious adverse reaction must be reported within 15 calendar days of receipt of the information by the licence holder. whether the report is domestic or foreign. Foreign side effects: A side effect that occurs outside Of Canada with a cannabis product exported by a licensee for medicinal purposes that is identical to or similar to a cannabis product (in composition) sold or distributed in Canada, regardless of the trademark used for export. For this guide, this does not apply to cannabis exported for scientific research involving humans (i.e. clinical trials) that fall under other applicable risk-taking obligations. Physician: For the purposes of this guidance document, this guidance document shall mean a healthcare professional in a clinical field, including medicine, surgery, dentistry, pharmacy, nursing, midwife, naturopathic medicine or other related health professions. Licence holder: Holder of a licence issued under the Cannabis Act, with the exception of a licence holder subject to the provisions on industrial hemp. MedDRA: Is the Medical Dictionary for Regulatory Activities, developed and maintained by the International Council for the Harmonisation of Technical Requirements for Medicinal Products for Human Use (ICH), as a standardized set of clinically validated conditions for symptoms, signs, diseases, syndromes and diagnoses. The terminology is organized into five different 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 groups support the retrieval, evaluation and presentation of adverse reaction data encoded with MedDRA. Medically important: A side effect that may not be immediately life-threatening or result in death or hospitalization, but may endanger the patient or consumer or may require medical intervention to prevent one of the other results listed in the serious definition from cannabis regulations. Harmful: Harmful, harmful or harmful to health. This reaction may be temporary (transient) or lead to permanent or permanent incapacity or disability or death. Observational study: A study in which the investigator closely observes and evaluates the results or use of cannabis products in a population (i.e. real-world use) without controlling the administration or prescribing of the cannabis product (i.e. no assigned interventions). This may also be referred to as an epidemiological or non-intervention study or post-market study. Patient: Regarding adverse reaction reporting, the person who experienced the adverse reaction after using a product. For the purposes of this guide, this may include a person (patient or consumer) who has experienced a side effect of a cannabis product for either medical or non-medical purposes. For bivirkningsindberetninger bivirkningsindberetninger also refers to a person who has experienced a side effect of cannabis under conditions in a research study involving people (e.g. for taste testing), which is not a clinical trial. Post-marketing adverse reactions: Any adverse reaction to a cannabis product by a licensee under the Cannabis Act and its provisions once it has entered the market inside or outside Of Canada. Post-marketing monitoring: The practice of monitoring the safety of a cannabis product after it has been released to the market inside or outside Canada. Post-marketing surveillance is an important part of the science of vigilance of cannabis products. Qualified person: In this guide, a person responsible for obligations, practices and procedures for reporting adverse reactions, including monitoring and screening of adverse reactions. A qualified person should be aware of the applicable parts of the Cannabis Act and its provisions and be qualified through training and experience relevant to their responsibility to carry out screening and follow-up of adverse reactions; assessment of adverse reactions, including assessment of causation interpretation of clinical data and interpretation of severity for the purpose of accelerated reporting to Health Canada. This may include a qualified healthcare professional (e.g. doctor, nurse 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, characterise, prevent or minimise risks associated with the use of cannabis products. Reporter: A person reporting a side effect either for himself 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 dealer or others. Sale: Includes offers for sale, defer to sale and holds for sale. Serious adverse reaction: A harmful and unintended reaction to a cannabis product requiring hospitalisation or prolongation of existing hospitalisation, causing congenital malformation, resulting in persistent or significant disability or incapacity, is life-threatening or results in death. Suspicious product: A product suspected of having caused the side effect. This may include cannabis products alone or in combination with other suspicious health products. More than one suspicious product may appear in an adverse reaction report. For example, an interaction between a suspected cannabis product and a suspected health product that results in a side effect. Unintended response: A response or effect that is not planned or intended. For the purposes of the definition of serious in accordance with Subsection 248(3), (3), all serious side effects. This is not unexpected ly related on the grounds that an effect of a medicinal product (including a cannabis substance) does not comply with the applicable product information under the Food and Drugs Act and its provisions (e.g. Unsolicited Report: An adverse reaction report received from an unsolicited source of communication or spontaneous (e.g. members of the local community, including consumers, patients, family members, practitioners and retailers) that is not derived from a survey or an organised 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 number of methods and tools that enable the safety of cannabis products to be monitored and evaluated and contribute to data and evidence-based decision-making and real-world knowledge translation. This can also be referred to as post-marketing surveillance, surveillance of cannabis or pharmacovigilance. 4.2 Abbreviates AER Adverse Reaction Report number CTA Clinical trial application FDA Food and Drugs Act ICH International Council for Harmonisation of Technical Requirements for Medicinal Products for Human Use CIOMS Council of International Organizations for Medical Sciences MedDRA Medical Dictionary for Activities Regulatory SOP Standard Operating Procedure WHO World Health Organization 5.0 Side Effects associated with Cannabis Products Side effects, also known as side effects, are defined as harmful and unintended reactions to a cannabis product and may be serious or non-serious. Adverse reactions are usually reported spontaneously on the basis of the suspicion of a reporter (unsolicited reports), but they can also be collected under conditions in a survey or other organised data collection system (requested reports). All cases of adverse reactions known to licence holders, whether requested or unsolicited or involving a complaint (e.g. adverse reaction in relation to a complaint about product quality issues), regardless of the source of the report, should be considered as a reported adverse reaction if they meet the minimum criteria as described below. Side effects 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 on the reporting of adverse reactions As described in Section 248 of the Cannabis Regulations: A holder of a licence selling or distributing a cannabis product must: within 15 days of becoming aware of a serious adverse reaction of the cannabis product, the Minister shall have a detailed report containing all the information in their possession and related to that person's use of the cannabis product; who have experienced the reaction. and prepare annual synthesis report containing a concise and critical analysis of all adverse effects of the cannabis product that the holder became aware of during the previous 12 months. These reporting obligations apply to all licenseholders who sell or distribute a cannabis product, whether inside or outside Of Canada. Sales include direct to patients for medical purposes as well as sales to consumers through provincial or territorial dealers for non-medical purposes. This also applies to the distribution or sale of a finished cannabis product from one licence holder to another (e.g. 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 Re-Regulations as a harmful and unintended reaction to a cannabis product requiring hospitalisation or prolongation of existing hospitalisation, causing congenital malformation, resulting in persistent or significant disability or incapacity, being life-threatening or resulting in death. A licence holder should not downgrade a side effect from serious to non-serious, even if the certificate holder disagrees with the seriousness of the task of the reporter. The opinions of both the reporter and the holder of the certificate should be recorded in the adverse reaction report and identified as such. Medical and scientific assessment of a qualified healthcare professional should be exercised in deciding whether a side effect is medically important and should be reported to Health Canada on an expedited basis. According to ich's guidance, this should also be considered a medically important event (ICH E2B). For example, an allergic reaction that caused respiratory problems and which required treatment in an emergency room or a seizure (convulsions) that did not result in hospitalization, but involved a medical intervention or consultation with their doctor. Important: Medically important events are those that may not be immediately life-threatening or result in death or hospitalized hospitalization, but may endanger the patient or may require medical or surgical intervention to prevent any of the other results listed in the serious side effect definition from cannabis regulations. Health Canada requests that these cases be reported on an expedited basis as well. 5.3 Non-serious side effects A non-serious side effect is a side effect that does not meet any of the criteria for a serious adverse reaction under the cannabis regulations or that is not considered to be medically important. A licensee may voluntarily submit these side effects, especially if a new or unexpected problem is observed (e.g. change in severity or frequency of side effects, tendency or cluster of related cases). In addition, all adverse reactions, including non-serious adverse reactions, should be critically collected and analysed as a of the annual synthesis report. Report. Domestic and foreign side effects As described in section 248 of the Cannabis Regulations, licensees must submit all serious adverse reactions to Health Canada within 15 days of becoming aware of them. This includes both domestic side effects (i.e. adverse reactions occurring in Canada) and foreign side effects (i.e. adverse reactions occurring outside Of Canada) associated with a cannabis product sold by a licensee in Canada or another country. Licence holders shall indicate in the report whether the case occurred in Canada or outside Canada and indicate the country in which the reaction occurred. 5.5 Other adverse reaction types Adverse reactions with recalled products, discontinued products or previously available products submitted to licensees must still be reported to Health Canada. Section 248 does not apply only to products currently placed on the market, as discontinued or recalled products may still be in the possession of individuals. Cases of overdose (accidental or intentional), dosing errors and other cases of direct exposure to a cannabis product and resulting in a serious adverse reaction should also be reported to Health Canada. In the case of pregnancy and lactation exposure, certificate holders are expected to follow up on reports from doctors, consumers or patients where exposure in the uterus or neonatal may have been found to determine whether there were adverse reactions in the foetus or newborn. 6.0 Good Vigilance Practices 6.1 Procedures Any licensee who sells or distributes a cannabis product should have written procedures outlining the collection, follow-up, evaluation, reporting and recording of all adverse reactions with cannabis products. Licence holders should check their complaint records to ensure that all serious adverse reactions are identified, followed up and reported to Health Canada. Appropriate follow-up procedures should be carried out to obtain relevant information, including in adverse reaction reports (see section 7.5 Follow-up information). The reports shall be accurate, legible and as complete as possible. In general, adverse reporting procedures (good vigilance practices) should define: key responsible personnel investigating adverse reactions reporting adverse reactions, which clay etching activities Relevant steps in the processes may include, but are not limited to: monitoring and management of adverse reactions from journalists who have received spontaneously (unsolicited reports) via email, telephone, letter or social media; or collected in surveys or other organised data collection sources (requested reports) that determine whether a complaint includes an adverse reaction that assigns a unique identifier to each case for the purpose of tracking and follow-up with journalists in order to obtain as much information, including products, patient records and investigation into causal link and possible causes (e.g. root cause) submission of adverse reaction reports to Health Canada registration, including all adverse reaction reports and evidence of studies (e.g. causation, root year analysis), certificates of analysis) 6.2 Contractual agreements Distribution and sale of cannabis products may take place through contractual or supply agreements between a licence holder and other parties (e.g. subsidiary, company, consultant or other third party). The sections below discuss responsibilities with regard to the reporting of adverse reactions. 6.2.1 Reporting of adverse reactions from licence holders is responsible for mandatory reporting of adverse reactions under section 248 of the Cannabis Regulations. This applies to a holder of a processing licence who sells or distributes a cannabis product for non-medical purposes to a provincial/territorial authorised dealer or to another licence holder. This also applies to a holder of a licence for the sale of medicinal products which may also hold a processing licence, or only the holder of a medical sales licence selling products from other licence holders. If a licence holder sells a cannabis product produced by another licence holder, it is expected that (e.g. these procedures should include the submission of adverse reaction reports to the licence holder who manufactured the cannabis product so that they can also fulfil their adverse reaction reporting obligations). In such cases, the report should indicate whether it has also been submitted to the licence holder who manufactured the cannabis product for registration purposes. 6.2.2 Reporting of adverse reactions made on behalf of a licensee is important that if a company or a third-party company, on behalf of a licenseholder, makes a written agreement between the licensee and the third party that: allow the other party, on behalf of the licensee, to collect information on behalf of the license holder; and ensure that the reports submitted meet the legal requirements of the cannabis regulations, such as deadlines and required content. Examples of such schemes may include a company reporting adverse reactions on behalf of a subsidiary that is the licensee or a third party carrying out adverse reaction reporting activities on behalf of a licensee. Regardless of the nature of the scheme, it is ultimately the responsibility of licence holders when they sell or distribute a cannabis product in order to meet the requirements for reporting adverse reactions under Section 248 of the Cannabis Regulations. Written agreements should be made with all parties carrying out adverse reaction reporting activities, including but not limited to: mandatory reporting of serious adverse reactions to Health Canada; maintaining annual summary reports on all adverse reactions If such written measures are taken, it is encouraged to proactively notify Health Canada of transparency (see section 10 Contact Details). 6.3 Registration requirements Good documentation is an important part of a quality assurance system for reporting adverse reactions. Under sub-section 248(2) of the Cannabis Regulations, licence holders are required to keep adverse reaction reports for at least 25 years after the day on which they are produced, including both individual adverse reaction reports and annual summary reports. Licence holders should therefore ensure that adverse reaction reports are properly kept to protect personal data. Where adverse reaction reports are sent between stakeholders with contractual agreements or between licence holders, this should be done while protecting and protecting personal data. A qualified person should check adverse reaction data for appropriateness, completeness, follow-up and severity determination, especially if customer care representatives initially receive side effects among other types of incidents or complaints (e.g. collected within a broader complaint system or process). If case reports are coded, verbatim from the journalist should always be maintained in the narrative, and reflect as much detail as possible about the reaction. In order to verify registration requirements, health information should be readily available to Health Canada. This includes written procedures for handling reports, carrying out follow-up and analysis of adverse reaction reports, recording individual case reports and annual summary reports. These registries should be readily available so that they can be submitted to Health Canada upon request in accordance with Section 248 of the Cannabis Regulations and for review during an inspection. 6.4 Holders of staff and training certificates should have qualified staff responsible for screening and assessing adverse reactions submitted to the licence holder. Qualified personnel should have the necessary qualifications, experience and training relevant to the reporting of adverse reactions (e.g. background in medical or health-related areas, experience in interpreting medical information in adverse reaction reports and knowledge of cannabis regulations). For the purpose of reporting serious adverse reactions, a clinical assessment by a qualified healthcare professional should be carried out to determine whether an adverse reaction report is serious and should be submitted to Health Canada. Clinical assessment is also important to determine whether a side effect is medically important and should be submitted, as well as determine whether the case is related to the product itself or due to other factors (causality assessment). Qualified staff should also be involved in determining whether the case is and whether follow-up is needed and determine whether significant new information is available from follow-up requiring rapid reporting based on clinical assessment. Qualified personnel are responsible for establishing and maintaining a system whereby adverse reaction data is collected, monitored, followed up and properly assessed. All staff involved in the collection of reports of complaints or adverse reactions (e.g. customer service) should have their responsibilities outlined in writing. Staff should, if necessary, receive adequate and continuous training. Third-party companies that have a contractual agreement to report adverse reactions on behalf of a licensee should also have the necessary qualifications, training and experience to carry out adverse reactions reporting activities. 7.0 Good Practice for Good Case Management Important: An individual report must be submitted to Health Canada for each consumer or patient who has experienced a serious adverse reaction to a cannabis product. In the event that a cannabis product is shared between two or more persons, a report should be completed for each person. 7.1 How to report individual alerts Licenseholders must report adverse reactions to Health Canada via one of the following mandatory reporting forms: 7.1.1 Method of submitting reports to Health Canada: Fill out the relevant form and send to canada Vigilance Program: Send by fax at: 613-957-0335 Mail to: Canada Vigilance Health Canada Address Locator 1908C OttawaC, 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 for users of the E2B portal. If this transfer method is used to transmit adverse reactions for cannabis products, it is important to follow best practices for electronic reporting of adverse reaction reports (ICH E2B guidance). It is also important that sufficient information about suspicious cannabis products is captured in the report so that they can be coded correctly by Health Canada. For more information, see Appendix 4 to Health Canada's Guidance Reporting Adverse Reactions to Marketed Health Products. 7.2 Minimum criteria for an adverse reaction report The minimum criteria for reporting a side effect to Health Canada are: An identifiable reporter (source) an identifiable patient or consumer of a suspected cannabis product a description of the adverse reaction If these four minimum criteria are met, a case is considered to be reportable to Health Canada and for serious adverse reactions must be submitted to Health Canada within 15 days of the certificate 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 and a reporter. One or more more of the following should qualify a patient as identifiable: age or age category, gender, unique identifier or reference to a patient. In the case of a suspicious cannabis product, this refers to a cannabis product taken by a person who is ingested (intentionally or unintentionally) and is suspected of having caused the adverse reaction (causal link is suspected). Licence holders are expected to collect as much information as possible so that reports submitted to Health Canada record clinically relevant and complete information for evaluation. The main data elements are outlined below to help certificate holders submit detailed adverse reaction reports. The following key data elements may also be useful for reports submitted to Health Canada from other sources, including healthcare professionals, consumers/patients, retailers, or others. 7.3 Key data elements 7.3.1 Reporter information Report source (origin of information): Spontaneous/ Investigation/Unknown/Unknown Reporter type (introductory reporter): Consumer/Patient/Health care practitioner/Lawyer/Dealer/Other Reporter also sent a report to the Canada Vigilance Program: Yes/No/Unknown Contact Office: Name of Responsible Person and Address License Holder (or Company Submit Report on Behalf of License Holder, report number: Identification number assigned to a report by the licence holder for registration. For a follow-up report on the same case, the report number must be the same as the number assigned to the original reportReport type: Initial/Follow-up date when the certificate holder received the information for this report Date, where the report is sent to Health Canada 7.3.2 Patient/Consumer Information Unique identifier: patient ID to easily locate the case for follow-up purposes. For privacy reasons, the patient's name or initials Age on the reaction time day (according to date of birth and date of birth/event or age at the time of the reaction/event or patient age group according to available information) Gender height and weight Relevant medical history, including medical history, pre-existing health conditions (e.g. allergies, acute or chronic illness), past use of other substances (e.g. tobacco, nicotine, alcohol, controlled substances, illicit substances), including the duration and frequency of use, the known history of medicines, including the use of medicinal products (prescription and non-prescription), biologic drugs and natural health products, including the duration and frequency of use, if it is known whether the patient is a regular cannabis consumer (past or present) or a new cannabis consumer (cannabis nause). If past history is known, provide relevant information such as dates, product names, dosage forms, route of and frequency of use 7.3.3 Side effect information Country Country adverse reaction occurred Date of the adverse reaction occurring Complete description of the adverse reaction, including the body site and severity, and all relevant clinical information (reported signs and symptoms, clinical course, specific diagnosis) Whether the report is serious, and severity criterion Date (and time), stop date (and time) and duration of adverse reaction (recovered or not, sequelae or not) Setting (hospitalization, 600, home, nursing home, other) Relevant diagnostic tests and laboratory data For a fatal result, stated cause of death Relevant autopsy or post-findings 7.3.4 cannabis products More than one cannabis product may be involved in a case. Contain all information about the cannabis products suspected to be covered by the adverse reaction, including: product name assigned by the licensee 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 containing one of these product form dried flower: pre-rolled, milled, whole flower extract: oil, oral capsule spray, vaping liquid, vaping cartridge, hash, budder, wax edible cannabis: beverage, confectionery, baked good tops: cream, lotion, gel, transdermal quantity or concentration of THC, THCA, CBD and CBDA List of other ingredients (terpenes) or other ingredients (for example, carrier oil, food ingredient batch lot number as well as UPC / SKU / GTIN (as applicable) Administration pathway (e.g., oral [ingested, buccal, sublingual]; inhaled [vaped or smoked] intranasal current) Used equipment or accessories (including information such as brand name and model number ((e.g. once a day, or if used several times a day, indicate dose and regimen) Duration of use (includes start and stop dates) Indication: Indicate whether the cannabis product was used for medical or non-medical purposes. If the product was used for medical purposes, it describes the cause of use. Indicate whether the patient has a medical approval document Dechallenge: Reaction slowed after stopping the product, reduction of dose or modification of administration path Rechallenge information: The reaction resurfaced after the product was re-administered 7.3.5 Other suspected health products or substances Describe whether medicines or health products are also suspected in the reported side effects (e.g. with suspicion of the adverse reaction to the cannabis product). 7.3.6 Concomitant sanctive products or other substances Describe whether concurrent products or substances were used at the same time, but not as a suspicion of the adverse reaction. These may include prescription or non-prescription drugs, natural health products, drugs, alcohol, tobacco. 7.3.7 Treatment of adverse reactionsThe treatment of the adverse reaction, including or treatments that were used. 7.4 Narrative information Narrative information in case reports is important for describing the clinical course of adverse reaction. Include as much narrative information as possible, including: Additional information about past medical history Past medical history All other information that may support or exclude a causal relationship, such as positive de-challenge and re-challenge information Licensees should also include their assessment of causation and causation of the adverse reaction, including whether product quality or other factors are suspected. 7.5 Follow-up reports should be followed up in order to get as much detail as possible. This additional information should be submitted to Health Canada in a follow-up report, referring to the original adverse reaction number, regardless of how long it has taken since the first report was submitted to Health Canada. Follow-up information may include additional information from the original reporter (e.g. notes, medical history, discharge, product information) or additional information from the certificate holder himself (e.g. evidence of analysis of the batch involved in the adverse reaction report, information relating to the analysis of the root cause). It is expected that licence holders exercise due diligence in obtaining so much detail about a side effect from a reporter for assessment. Follow-up should be required for each case report, in particular for serious adverse reactions to be submitted to Health Canada. This can help minimize requests for information from Health Canada when evaluating cases. 7.6 Assessment of adverse reactions to cannabis products All adverse reaction reports received by certificate 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, which reviews the adverse reaction report to ensure the quality and completeness of the information making the follow-up, in particular in serious or important medical cases; , which determines the seriousness of accelerated reporting and conducts an investigation into the adverse reaction, including the assessment of the likelihood that the suspicious product caused the adverse reaction (cause analysis) and possible underlying cause (cause). If the original reporter has already attributed causality, this should not be changed, but the licence holder may identify in the report his or her own perception of causality beyond that reported by the original reporter and determine whether or not product quality is involved if corrective or preventive measures have been taken; a particular problem involving an adverse reaction following a quality study (subsection 19(2) and Article 88(1) of the Cannabis Regulations), this information should be included as a follow-up to the adverse reaction report For further information on the World Health Organisation's causal criteria, please refer to Appendix 6 to the Health Canada Guide, which reports adverse reactions to marketed health products. Further information on root cause analysis can be found in the guide on good production practices for cannabis. 7.7 Double reports or linked reports may be submitted to licence holders from more than one source, such as a consumer or patient, in addition to a healthcare professional, dealer or other source. If a double or follow-up report is received after the first report has been submitted, the license holder shall report them to Health Canada and mention the original adverse reaction number. It is important to indicate whether the report is a follow-up (same reporter) or duplicate (other reporter) to the original report. Proper identification of double alerts will also help licence holders to reflect the exact number of unique cases, in particular for serious adverse reactions, for signal detection purposes and to avoid multiple case counting problems when preparing the annual synthesis report. Licence holders should have a system or methodology for identifying and managing double reports and linked reports in place. 7.8 The handling and coding of reports Licensees should have a system, database or program for collecting and analysing adverse reaction data. This may include an electronic system (e.g. The use of international standardized medical terminology (such as MedDRA) is recommended as a tool to encode adverse reaction data for cannabis side effects in order to classify, seek and obtain adverse reaction reports. In addition, it is also useful for reporting (e.g. individual case reports and preparation of annual summary reports). If standardized medical terminology is used, the report should still include the first reporter verbatim details of the narrative to ensure that all the details are captured. 8.0 Adverse reaction reports from source 8.1 Monitoring of adverse reaction reports that licenseholders monitor and analyze side effects that may originate from various sources, including: Sent to license holders spontaneously by consumers/patients, healthcare professionals, retailers, who unsolicited reports Submitted directly to Health Canada and identified through routine monitoring of the Canada Vigilance Adverse Reaction Online database by licensees Published in the scientific literature Reported on social media platforms that licensees are responsible for collected from epidemiological study, research study research study people (outside the framework of a clinical trial) or other organised data collection systems which requested reports 8.2 Spontaneous reports 8.2.1 Spontaneous alerts, submitted directly to licence holders Spontaneous alerts are those received on an unsolicited basis from consumers, patients, healthcare professionals or other journalists (e.g. retailers) who describe a side effect of a consumer or patient with one or more cannabis products and who do not originate from a survey or an organised data collection system (e.g. patient registries or monitoring programmes). Where a spontaneous alert is submitted to a certificate holder, it shall be considered to be a reportable adverse reaction justified by the suspicion that the first reporter suspects that there is a suspicion of a suspected link between a cannabis product and the adverse reaction. Some spontaneous alerts may be stimulated by certain factors, such as These reports should be considered unsolicited and should be reported to Health Canada. 8.2.2 Spontaneous alerts submitted directly to Health Canada To ensure that the adverse reaction reports held by licensees are complete, licensees should monitor the Online Database for Adverse Surveillance reported by their cannabis products and submitted directly by the public to Health Canada. Licence holders should check the online database to identify adverse reaction reports with their cannabis products according to the licence holder's name or trade mark on the cannabis product. Only reports involving a cannabis product from the licence holder concerned are expected to be retrieved and included in the annual synthesis report. Alerts from Canada's online audit response database do not need to be resealed to Health Canada unless the license holder has additional information on the matter. If further information is available, the certificate holder must submit a follow-up report (with reference to the original adverse reaction number). However, for the preparation of an annual synthesis report, Health Canada expects all adverse reactions known to the licence holder, including those from the Canada Monitoring Information Database, as well as other regulatory authorities, if applicable (e.g. cannabis product exported for medicinal 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 study reporting a serious adverse reaction to their cannabis product (e.g. explicitly reported in the publication or implicitly known by the licence holder), it is the licensee who is responsible for submitting the adverse reaction to Health Canada. This applies only in cases where the authors of the publication have at least identified a possible causal link with the cannabis products, regardless of whether the published case report took place inside or outside Canada. A single report should be created for each patient identified in a publication and all relevant case information (including reference to the publication) should be included. The publication authors will be considered as the primary journalists and the full literature reference should be given. 8.2.4 Reports on social media or media If a licence holder becomes aware of a serious adverse reaction report on the media or on 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, efforts 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 Important: Adverse reactions occurring under conditions in a clinical trial are outside the scope of this guidance document. Under the Food and Drugs Act, cannabis used in a clinical trial is subject to the requirements of Part C, Section 5: Medicinal products for clinical trials involving persons in food and drug regulations. In this guide, study reports are defined as adverse reactions derived from epidemiological studies or other types of organised data collection systems where data is actively collected or requested, such as registries or patient exploitation or monitoring programmes. Survey reports are also called requested reports. Epidemiological studies are non-interventional studies in which investigators do not assign cannabis products as an intervention, but rather examine or observe the use of cannabis products in a defined group or populations using epidemiological methods. Study reports also covered by this guide include adverse reactions stemming from research studies in people involving cannabis that do not meet the definition of a clinical trial as defined in section 5 of the Food and Drug Regulations (e.g. sensory testing). Serious adverse reactions derived from a study or an organised data collection system (i.e. requested reports) in connection with this guide shall 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 assessment. In other words, a serious adverse reaction from an investigation must be submitted if there is a reasonable possibility that the cannabis product caused the adverse reaction (i.e. the relationship cannot be excluded). Investigation reports from licence holders carrying out tests on cannabis products should be adverse reactions (i.e. included in the Protocol) 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 (e.g. cohort study, case-control, study, other) Study status of the study (ongoing or completed, with dates) Licensee holders should use the forms described in section 7.1 to submit the adverse reactions to Health Canada. All the principles outlined in this guidance document should be applied, including important information, determination of seriousness and determination of causation. If an adverse reaction is reported outside the parameters of an epidemiological study or an organised data collection scheme (e.g. after the investigation has been completed), it should be considered as a spontaneous report. 8.3.2 Survey 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 by other stakeholders (e.g. private investigator, academic centre or other licence holder or marketing authorisation holder). In such cases, licence holders should seek follow-up information from the other stakeholder and the report processed in accordance with the above principles for mandatory reporting of serious adverse reactions by Health Canada. A certificate holder should not alter the causal link provided by the original reporter (e.g. investigator) and should identify their own causal link in the report. 8.3.3 Research in humans involving cannabis A clinical trial is defined in the Food and Drug Regulations as a study of a human-related medicinal product which aims to detect or verify the clinical, pharmacological or pharmacodynamic effects of the medicinal product, to identify any adverse reactions associated with the medicinal product, to investigate the absorption, distribution, metabolism and excretion of the medicinal product, or to determine the safety or efficacy of the medicinal product. Health Canada considers certain specific and limited forms of research in people involving cannabis to fall outside this definition. One example could include a taste test study that examines the taste of an edible cannabis product or some other form of sensory test study. These studies in people involving cannabis that do not fit the definition of a clinical trial must be approved under a cannabis research license from the Controlled Substances and Cannabis Division. Licences allowing for this specific and limited form of human research include a number of conditions, including the requirement to serious adverse reactions and prepare an annual summary report in the same way as that outlined in section 248 of the Cannabis Regulations for all cannabis (in its final form) which administered or distributed to human research topics. Any holder of a research permit carrying out human research involving cannabis outside a clinical trial shall submit a detailed report on any serious adverse reaction of cannabis to Health Canada within 15 days of their knowledge of a serious adverse reaction. This report shall contain all information in their possession associated with the use of cannabis by the person who experienced the reaction. When submitting adverse reaction reports to Health Canada, the report shall include: Study certificate number and title A description of the cannabis material (in its final form), including the list of ingredients, description of the cannabis product form and composition (e.g. quantity or concentration of each ingredient and function) Licence holders should use the forms described in section 7.1 to submit the adverse reactions to Health Canada. All the principles outlined in this guidance document should be applied, including important information, determination of seriousness and determination of causation. In addition, any adverse effects of cannabis that licence holders have become aware of over the past 12 months shall be included in an annual synthesis report containing a concise and critical analysis of all adverse effects of cannabis. This report shall also include the research certificate number of the study and a description of cannabis, including the list of ingredients, description of the form and class of cannabis and its composition (e.g. relative presence of each ingredient). All records (all individual adverse reaction reports and annual summary reports) shall be kept for at least 25 years after the day on which they are drawn up. 9.0 Contact us Licence holders who have questions about the information or requirements of this guide are encouraged to contact the Controlled Substances and Cannabis 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 rules. We would appreciate receiving your feedback on whether this guide was useful, and we welcome your suggestions for improvements. Send your feedback to us at cannabis@canada.ca and provide feedback in the Feedback subject line on the Cannabis Adverse Reaction Reporting Guide for license holders. Your comments will help us improve this guide. Footnote 1 European Medicines Agency. Inclusion/exclusion criteria for the Important Medical Events list. [07 March 2019] Back to Footnote 1 referrers referrers