DATA ON CANNABIS ADVERSE REACTIONS: 2022 ANNUAL REPORT

Adverse reactions associated with cannabis reported to Health Canada between January 1, 2022 to December 31, 2022

Government of Canada Gouvernement du Canada

Canada

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KEY HIGHLIGHTS

In 2022, Health Canada received 159 reports of adverse reactions (including duplicates, such as multiple reporters of the same adverse reaction) associated with cannabis as a suspected substance (including cases of polysubstance use).

Out of the 159 reports, 92 were unique cases associated with legal cannabis products.

Of the cases involving legal cannabis products:

- 40% involved males and 28% involved females
- 51% involved cannabis used for medical purposes (self-reported)
- 53% involved ingestible cannabis liquid extracts (that is, ingestible cannabis oils and softgels)
- 38% were missing age-related information and 22% of cases involved adults aged 18 to 44 years
- 75% were reported as serious, with other (medically important condition) as the most frequently reported reason for seriousness

The most frequently reported adverse events across all cases involving legal cannabis products where causality was assessed as certain, probable or possible included:

- headache (n=8)
- seizure (n=6)
- hallucination (n=6)
- dyspnoea (n=6)
- drug ineffective (n=6)

In 2022, there was 1 suspected case of vaping-associated lung injury (VALI) that was reported as involving a legal cannabis product.

Most findings have remained consistent from 2021 to 2022, however, some changes were observed, namely:

- a decrease in the total number of cases (serious and non-serious)
- route of administration reported (inhalation versus oral administration)
- a shift in some of the reasons for seriousness being selected by reporters
- the types of adverse events reported, and, in some instances, the type of individuals involved in adverse reaction cases (for example, the distribution of age and sex)

However, further years of data are required to conduct proper trend analysis and to assess any long-term changes in findings.

Health Canada continues to monitor, assess and report on adverse reactions associated with cannabis, and findings continue to be used to inform evidence-based educational materials on health and safety risks with cannabis, including risk communications and educational resources.

INTRODUCTION

This report describes the findings of the domestic case reports of adverse reactions associated with cannabis submitted to Health Canada's Canada Vigilance database and analyzed by the Office of Cannabis Science and Surveillance of the Controlled Substances and Cannabis Branch in Health Canada. This work forms part of the Vigilance Framework for Cannabis that has been in place since the coming into force of the *Cannabis Act* and *Cannabis Regulations* (October 17, 2018).

This fourth annual data report presents a summary of all domestic case reports of adverse reactions submitted to Health Canada between January 1, 2022, and December 31, 2022, suspected of being associated with a cannabis product as defined under the *Cannabis Act* or its Regulations, intended for human consumption.

For the purposes of this report:

- A **legal cannabis product** means cannabis of 1 of the classes set out in Schedule 4 to the Act, or a cannabis accessory that contains such cannabis, after it has been packaged and labelled for sale to a consumer at the retail level. It does not include:
    - cannabis that is intended for an animal
    - health products containing cannabis or for use with cannabis
    - a cannabis accessory that contains cannabis that is intended for an animal
- An **adverse reaction** is a noxious and unintended response to cannabis or a cannabis accessory that contains cannabis
- A **serious adverse reaction** is an adverse reaction that requires inpatient hospitalization or a prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death

Licence holders who sell or distribute a cannabis product provide Health Canada with a detailed report must within 15 days of becoming aware of a serious adverse reaction to the cannabis product . This report must contain all information in their possession associated with the use of the cannabis product by the individual who experienced the reaction.

The following groups may also submit adverse reaction reports on a voluntary basis to Health Canada:

- patients
- consumers
- health care practitioners
- medical cannabis clinics
- other reporters such as provincial and territorial authorized retailers

Reports may also be received from market authorization holders of licensed health products that submit adverse reaction reports for other suspect health products (such as prescription or non-prescription drugs, or natural health products) in which cannabis is also identified as a co-suspect product.

Adverse reaction reports with cannabis may involve cannabis that is:

- from an illegal source
- a legal cannabis product

- cultivated[1] or produced[2] in the home for personal use
- undefined (cannabis as a substance not otherwise specified)

For the purposes of this report, case reports involving a legal cannabis product (that is, identifiable by product brand name or licence holder) are classified according to the intended use of the cannabis products as follows:

- **Cannabis use for non-medical purposes:** If there is no reported medical or therapeutic indication or reason for use provided in the adverse reaction report, minimal details or the intended use is for non-medical purposes, the case is classified as "non-medical use of cannabis".
- **Cannabis use for medical purposes:** This includes cases described as involving the cannabis being used pursuant to a medical authorization document provided by a health care practitioner or cases that report the use of the cannabis for a medical or therapeutic purpose, without mention of a medical authorization document. This definition aligns with the definition of medical use within the Canadian Cannabis Survey. This is broader in scope than the definition of cannabis uses for medical purposes under the *Cannabis Regulations*; which only includes cannabis being used pursuant to a medical authorization document from a health care practitioner.

Adverse reaction reports are collected and housed in the Canada Vigilance database. Most adverse reaction case reports submitted to Health Canada with cannabis are reported spontaneously by consumers, patients, health care practitioners or by licence holders (referred to as market authorization holder [MAH] in the Canada Vigilance database). However, reports may also originate from research studies, including:

- published case studies
- observational studies (non-interventional, real-world)
- interventional human studies involving cannabis that fall outside of the definition of a clinical trial (for example, non-therapeutic research on cannabis studies)
- other organized data collection systems (for example, patient registries)

While reports originating from clinical trials may be included in the broader Canada Vigilance dataset, these reports are excluded from this data report as they fall under the purview of the Clinical Trials Framework.

Health Canada conducts near-time monitoring, detection, assessment and associated activities for cases of adverse reactions involving cannabis products as part of the Vigilance Framework for Cannabis. Health Canada also monitors cases involving cannabis as a substance for broader issues of public health importance such as:

- vaping-associated lung illness
- cases involving pediatric populations
- other potential emerging safety issues

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[1] Under the *Cannabis Act* and Regulations adults are allowed to legally grow up to a maximum of 4 cannabis plants for personal use. This is in addition to any plants that may be authorized for personal and designated production for medical purposes, which can vary across the provinces and territories. However, rules surrounding home growing for non-medical purposes may vary based on the rules and regulations of individual provinces or territories.

[2] Under the *Cannabis Act* and Regulations adults are allowed to make products at home for personal consumption using cannabis that they have grown legally or using cannabis that they obtained from other legal sources.

The purpose of this report is to provide a brief summary of adverse reaction reports involving cannabis, as well as a descriptive analysis of adverse reaction data associated with legal cannabis products, submitted to Health Canada between January 1, 2022, and December 31, 2022.

In addition to the descriptive analysis of cases from 2022, comparisons to the previous reporting period (January 1, 2021, to December 31, 2021) have been made, where appropriate. These comparisons are largely descriptive, and differences have not been tested for statistical significance in most cases due to the limited nature of the data. Therefore, caution should be taken with the interpretation of these changes in results over the 2 reporting periods.

Data for other reporting periods, including trends across periods, are also publicly available:

- Cannabis-related side effects: Key findings
- Data on cannabis adverse reactions: 2021 annual report
- Data on cannabis adverse reactions: 2020 annual report
- Data on cannabis adverse reactions: 2018-2019

This report does not cover adverse reaction data associated with health products, including drugs containing cannabis, which are regulated under the *Food and Drugs Act* and its Regulations. A summary of adverse reactions associated with other health products received by Canada Vigilance in 2022 are described in Health Canada's InfoWatch Newsletter: Adverse reactions to health products - annual report 2022.

Considerations

Certain caveats should be considered when interpreting the adverse reaction data in this report.

Adverse reactions are generally spontaneously submitted to Health Canada and cannot be used to determine the incidence or prevalence of adverse reactions to cannabis in the general population.

Serious adverse reactions have a greater representation in this dataset as licence holders have a regulatory obligation to report these to Health Canada under section 248.1 of the *Cannabis Regulations*. The submission of non-serious adverse reactions by licence holders to Health Canada as individual case reports is voluntary,[3] therefore, the non-serious cases are likely underreported and likely underrepresented in this dataset.

Reporting of adverse reactions for cannabis products is voluntary for:

- hospitals
- consumers
- medical cannabis clinics
- health care practitioners
- provincial and territorial retailers

Therefore, both serious and non-serious cases from these sources are likely underreported.

[3] As per paragraph 248.1(1)(b) of the *Cannabis Regulations*, all adverse reactions, including non-serious adverse reactions, must be maintained in an annual summary report by the licence holder, which can be requested by Health Canada.

Individuals experiencing serious outcomes or using cannabis products for medical purposes may be more motivated to report or seek out medical attention.

Several factors may influence the number and quality of case reports submitted to Health Canada such as:

- media coverage
- reason for cannabis use
- consumer or patient medical history
- length of time a product is on the market
- awareness, motivation and ability to report
- nature of reports (spontaneous reports versus studies or other organized data-collection systems)

This report includes information on cannabis for medical and non-medical purposes; however, the number of cases elsewhere may not directly align with what is presented in this current data report due to different dates of extraction from the Canada Vigilance database (for example, in the adverse reactions to health products - annual report 2022).

The inclusion of a particular report in the database does not necessarily mean that there is a causal relationship between the reported cannabis products and adverse events. Additional scientific investigations are required to establish a cause-and-effect relationship.

ADVERSE REACTIONS WITH CANNABIS

Adverse reactions associated with cannabis as a substance

Figure 1: Reports associated with cannabis as a substance

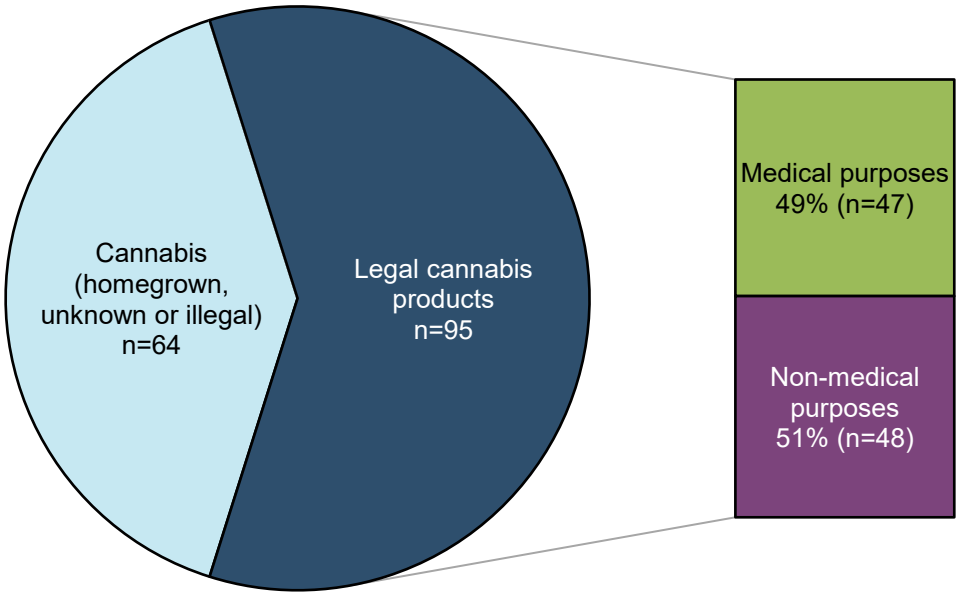

Figure 1 – Text description

	Number of reports	Proportion (%)
Cannabis (homegrown, undefined or illegal)	64	40
Legal cannabis products- Medical purposes	47	29
Legal cannabis products – Non-medical purposes	48	30
Total	**160**	**100**

Caveats:

- This figure represents all reports involving cannabis as a suspected substance that were submitted to Canada Vigilance database in 2022, including duplicate reports where the case details are the same, but reporters differ (n=25)
- Reports are classified for internal reporting purposes within Canada Vigilance depending on whether they report using legal cannabis products used for either for medical or non-medical purposes (1 classification per case). Cases that do not involve cannabis products from legal sources are not assigned a classification and remain classified as cannabis as a substance only (undefined or illegal cannabis)
- Under the *Cannabis Act* and Regulations adults are allowed to legally grow up to a maximum of 4 cannabis plants for personal use. However, this cannabis cannot legally be packaged and labeled for sale at the retail level. Therefore, adverse reaction reports involving homegrown cannabis are kept separate from reporting involving legal cannabis products

A total of 159 reports (includes duplicates[4]) associated with cannabis as a suspect substance were submitted to Health Canada between January 1, 2022, and December 31, 2022. Most of these reports involved legal cannabis products (60%, n=95). There was an almost even distribution between reports involving cannabis use for self-reported medical purposes (49%, n=47) and non-medical purposes (51%, n=48). Of the reports involving unknown or illegal cannabis (40%, n=64) (for example, reports involving 'cannabis' or 'marijuana' without specific details, the product listed is unverifiable), 19% (n=12) involved additional co-suspect substances or health products (for example, polysubstance or polypharmacy reports) in addition to cannabis, a decrease from 28% in 2021. 1 report included the transformation of cannabis, from an unknown source, into an edible format.

Report of vaping-associated lung illness (VALI)

There was 1 suspected report of VALI involving cannabis reported to the Canada Vigilance database in 2022. However, this case was initially received by Health Canada in 2021 and is also included in the 2021 Annual report of cannabis adverse reactions. This case is referenced here despite it having been initially reported in late 2021, as the 2 responsible licence holders submitted complete reports to Health Canada, per their mandatory reporting obligations, in early 2022.

Of note, the Chief Public Health Officer of Canada and the President of the Public Health Agency of Canada (PHAC) declared the VALI outbreak over in Canada as of August 2021, with the publication of a Public Health Notice and an update of the Government of Canada's VALI webpage:

- Public Health Notice: Outbreak of Vaping-Associated Lung Illness (VALI) from September 2019 to August 2021 in Canada
- Vaping-associated lung illness

[4] Duplicate cases may exist if an adverse reaction report about the same adverse reaction event was received from different reporters (for example, from a health professional, consumer, hospital, and/or manufacturer).

Reports involving the pediatric population (under 18 years)

In 2022, there were 39 reports of adverse reactions to cannabis involving the pediatric population (aged under 18 years), a decrease from 47 in 2021:

- 72% (n=28) of the reports involved cannabis from an unknown source
- 23% (n=9) involved cannabis from an identifiable or suspected illegal source
- 2 reports involved legal cannabis products, authorized for medical purposes

In terms of route of administration:

- 69% (n=27) of these reports involved cannabis consumed orally, mostly in an edible format (n=19)
- 19% (n=7) involved inhalation as a route of administration, mostly smoking (n=4)
- route of administration was unknown in 4 reports

Health Canada also monitors reports of accidental ingestion of cannabis in the pediatric population (under 18 years of age). 67% (n=26) of the reports involving the pediatric population involved accidental or unintentional exposure to cannabis, and all of these reports involved cannabis from an unknown or illegal source. Reports originate from several Canadian surveillance programs including the Canadian Surveillance System for Poison Information and the Canadian Pediatric Surveillance Program's study on non-medical cannabis use in children and youth: Serious and life-threatening events associated with non-medical (recreational) cannabis use in Canadian children and youth.

Health Canada continues to monitor pediatric exposures suspected to be associated with cannabis and will continue to take appropriate risk mitigation strategies as necessary. In March 2023, Health Canada launched a public education campaign on preventing and identifying cannabis poisonings in children. In May 2023, Health Canada issued an updated public advisory on the accidental ingestion of edible cannabis by children. These can be found at:

- Cannabis in Canada: Get the facts
- Public advisory: Accidental ingestion of illegal "copycat" edible cannabis products causing serious harm to children

Case reports involving cannabis products for self-reported medical and non-medical purposes from the legal marketplace and regulated under the *Cannabis Act* and its Regulations form the basis for the remaining portions of this Annual Report.

Adverse reactions associated with legal cannabis products

Figure 2: Reports by reporting month and seriousness

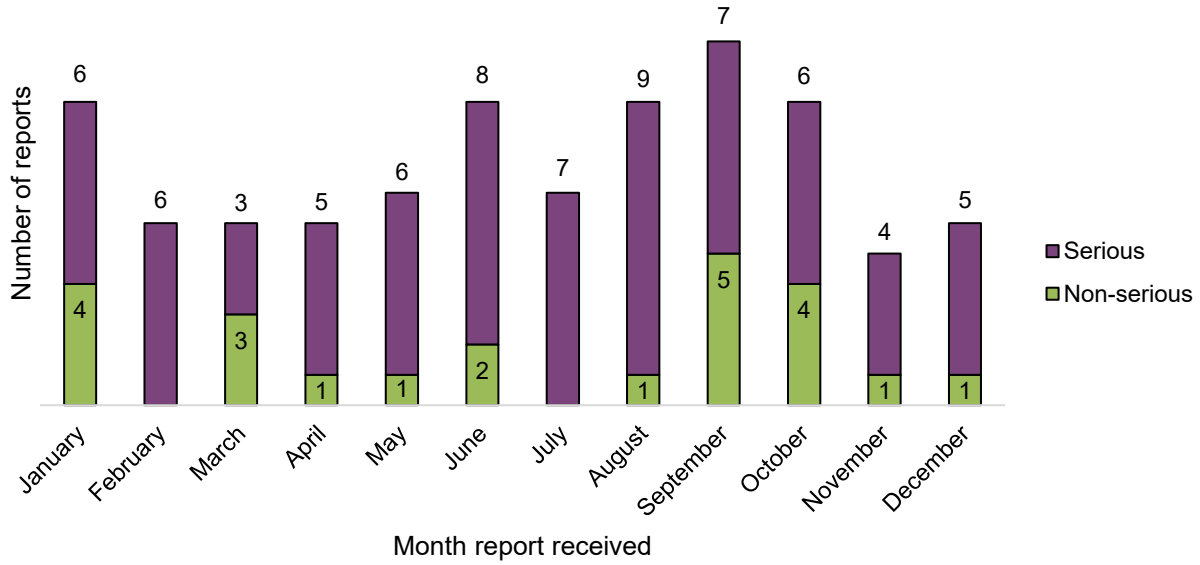

Figure 2 – Text description

Month report received	Number of reports by seriousness		
	Serious	Non-serious	Total
January	6	4	10
February	6	0	6
March	3	3	6
April	5	1	6
May	6	1	7
June	8	2	10
July	7	0	7
August	9	1	10
September	7	5	12
October	6	4	10
November	4	1	5
December	5	1	6
Total	**72**	**23**	**95**

Caveats:

- This figure includes duplicate reports where the case details are the same, but reporters differ (n=5)
- Seriousness is based on the initial report and may be subject to change if additional information is submitted to Health Canada
- Reports are presented according to the initial date of receipt by the Canada Vigilance database. The actual date of the adverse reaction may not align with the month that the report was received (lag time between event and reporting)

There were no clear temporal trends observed in the total number of adverse reaction case reports involving legal cannabis products submitted to Health Canada in 2022. The average number of reports received by Health Canada per month during the reporting period was 7.9, ranging from 5 to 12 cases per month.

Some descriptive trends were observed in 2022 compared to 2021. The total number of reports overall (serious and non-serious) and the average number of serious and non-serious reports per month, decreased in 2022 (total reports: from 179 to 95, average reports per month: from 14.5 to 7.9. In contrast, the total number of serious and non-serious reports submitted to Health Canada decreased (serious: from 108 reports in 2021 to 72 reports in 2022, non-serious: from 71 in 2021 to 23 in 2022).

Figure 3: Cases by reason for seriousness in serious cases

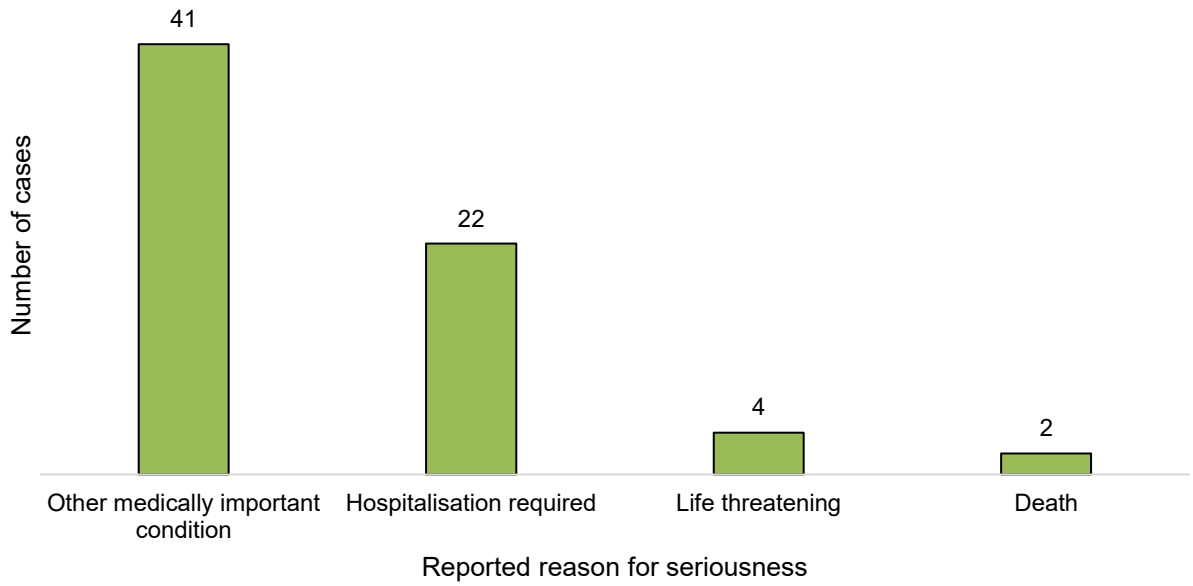

Figure 3 – Text description

Reason for seriousness	Number of cases
Other medically important condition	41
Hospitalisation required	22
Life threatening	4
Death	2
Total	**69**

Caveats:

- This figure includes unique cases where the reporter indicated that the adverse reaction was serious (n=69)
- Each serious case may have more than 1 reason for seriousness as the reporter may select multiple reasons

In 2022, all serious cases submitted to Health Canada involved 1 reason for seriousness, for a total of 69 responses for seriousness, spanning 4 categories, selected by reporters (Figure 3). The most frequently selected category was “other medically important condition” (59%, n=41), followed by “hospitalization

required" (32%, n=22). The category of "other medically important condition" includes events that are not immediately life threatening or result in death or hospitalization but may jeopardize the patient or may require a medical intervention (for example, ambulatory services, emergency department visits, outpatient visits with a health care practitioner or at-home medical interventions) to prevent a serious outcome. In 2021, the most common reported reason for seriousness was also "other medically important condition" (62%, n=65).

2 cases associated with legal cannabis products involved fatal outcomes. More details regarding these 2 cases can be found in Fatal cases during the reporting period. Comparatively, 2 fatal outcomes were reported in 2021. 4 cases were reported as life threatening (a decrease from 6 cases in 2021) and no cases reported disability (a decrease from 4 cases in 2021).

Figure 4: Reports by initial reporter type and report source

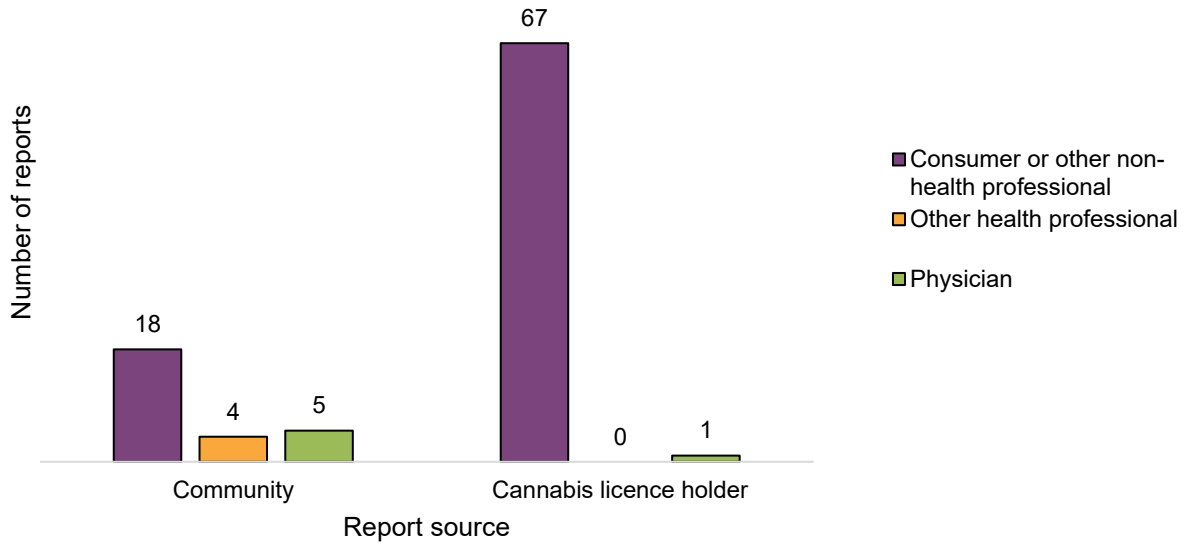

Figure 4 – Text description

Report source	Reporter type			
	Consumer or other non-health professional	Other health professional	Physician	Total
Community	18	4	5	27
Cannabis licence holder	67	0	1	68
Total	**85**	**4**	**6**	**95**

Caveats:

- This figure includes duplicate reports where the case details are the same, but reporters differ (n=5)

- Reports from health care practitioners are considered medically confirmed as per international guidelines,[5] therefore are distinct from consumer reports
- For purposes of this figure, each report source is further subdivided according to initial reporter type (consumer or health care practitioners, meaning physician, pharmacist or other health professional)
- Report source is reflective from whom Health Canada received the report (community, hospital or market authorization holder [for legal cannabis products, this would reflect and is labelled as a licence holder])

Most adverse reaction reports involving legal cannabis products were from cannabis licence holders (72%, n=68). Among cannabis licence holder reports, the main initial reporter type was primarily a consumer (99%, n=67). Consumers were also the main initial reporter type from the community (that is, reports submitted directly to Health Canada). Reports from these descriptive reporting trends are consistent with observations from 2021 in that consumers are more inclined to report adverse reactions directly to the licence holder who then submits a report to Health Canada as per their reporting obligations. Health care practitioners tend to report on behalf of their patients directly to Health Canada. However, compared to previous years, there has been a steady decrease in the number of serious and non-serious adverse reaction reports originating from health care practitioners with a slight increase in 2022 (2018 to 2019: n=36; 2020: n=18; 2021: n=8; 2022: n=10). There were no reports of adverse reactions received from hospitals that identified legal cannabis products in 2022, consistent with 2021.

Under the *Protecting Canadians from Unsafe Drugs Act* (that is, Vanessa's Law), as of December 16, 2019, hospitals are required to submit all serious adverse reactions to Health Canada involving suspect drugs (including drugs containing cannabis) with or without other suspect products. Reports involving a co-suspect drug and co-suspect cannabis are also required to be submitted to Health Canada. However, under the *Cannabis Act* and its Regulations, hospitals may consider submitting, on a voluntary basis, any adverse reactions involving cannabis as the sole suspect product.

[5] World Health Organization (2012). Safety monitoring of medicinal products. Reporting system for the general public. Available from: https://www.who.int/publications/i/item/9789241503198.

Demographics

Figure 5: Cases by age group

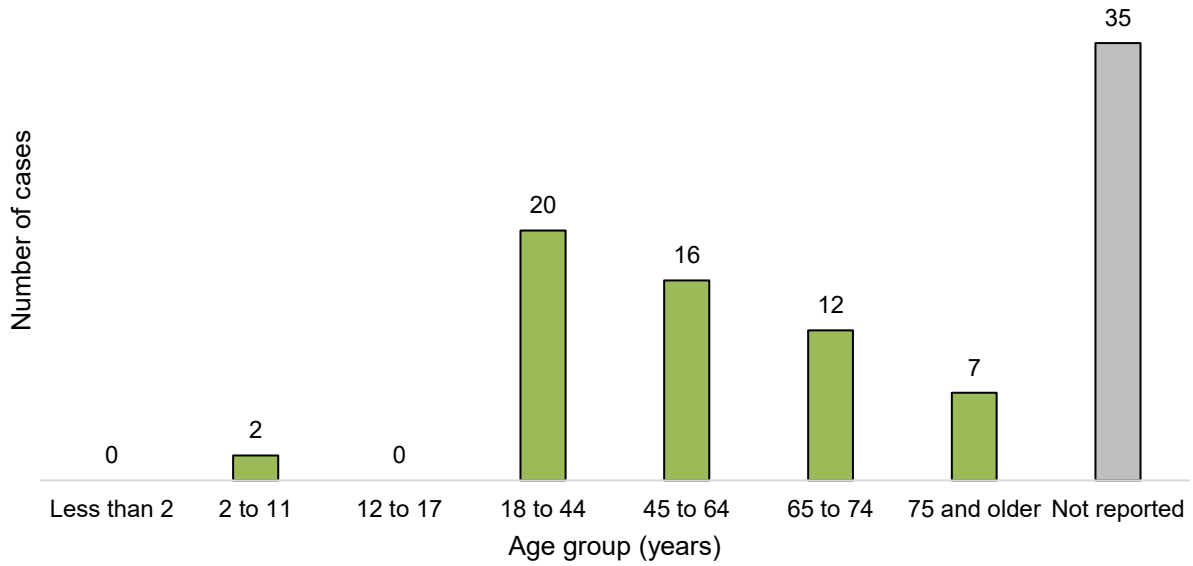

Figure 5 – Text description

Age group (years)	Number of cases
Less than 2	0
2 to 11	2
12 to 17	0
18 to 44	20
45 to 64	16
65 to 74	12
75 and older	7
Not reported	35
Total	**92**

Caveats:

- In cases where the year of birth and the date of reaction are listed in the report, then the age is calculated
- In cases where the year of birth is listed without a date of reaction, the date the report was submitted is used to calculate the age

The average age of individuals in cases involving adverse reactions to legal cannabis products in 2022 was approximately 52 years (95% CI: 46-57) with a range of 3 years to 97 years. This did not differ significantly from 2021 where the average age was 59 years (95% CI: 55-63) with a range of 18 years to 99 years.

When classified using the World Health Organization's Vigilyze database (Vigibase) age groupings, most cases involved persons aged 18 to 44 years (22%, n=20). This differs from 2021 where 45 to 64 years was the most common age group (17%, n=30). Adults aged 65 years and older represented 21% of cases (n=19), as a composite category, a decrease from 26% in 2021. 2 pediatric cases (under 18 years

of age) were submitted to Health Canada involving legal cannabis products (both authorised for medical purposes) in 2022 compared to no cases in 2021.

Many cases in 2022 lacked age-related information (38%, n=35), a similar proportion as 2021 (43%, n=74).

Figure 6: Cases by sex

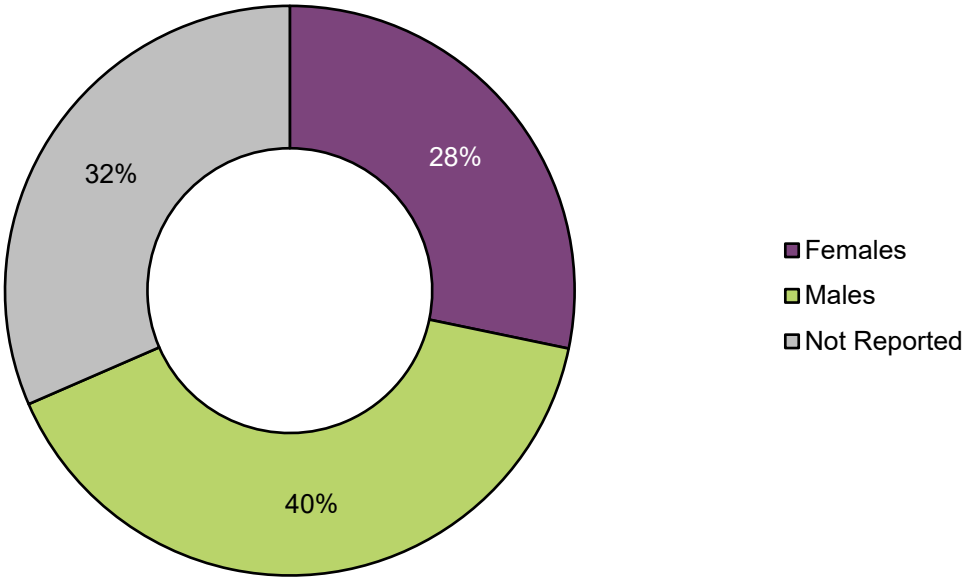

Figure 6 – Text description

Sex	Number of cases	Proportion (%)
Females	26	28
Males	37	40
Not reported	29	32
Total	**92**	**100**

Most adverse reaction cases submitted to Health Canada in 2022 involved males (40%, n=37), while 28% involved females (n=26) and 32% (n=29) did not indicate the sex of the individual. The distribution of cases by sex was different than what was observed in 2021 as females made up a greater proportion of the cases compared to males (males: 30%; females: 42%). The proportion of cases not reporting sex continued to increase from 28% in 2021 and 8% in 2020.

Sex and age may not be reported for several reasons, including consumers not wanting to disclose this information to licence holders or Health Canada or cases originating from other reporting forms such as the Cannabis Reporting Form, which do not capture this type of demographic information.

Suspected cannabis products

Most adverse reaction cases reported in 2022 were associated with legal cannabis products as the sole suspect product (93%, n=86), meaning that no other health products were reported as co-suspects. Health products may include:

- natural health products
- prescription or non-prescription drugs

- other types of health products regulated under the *Food and Drugs Act*

However, 38% of cases (n=35) included at least 1 concomitant product. A concomitant product is a product that is used at the time of the adverse reaction but not considered suspect by the reporter as having been responsible for the adverse reaction. These may be:

- health products
- illegal substances
- other regulated substances (for example, alcohol, tobacco or other vaping products such as nicotine or flavors)

A small proportion of cases (7%, n=6) reported in 2022 had 2 or more suspect cannabis products reported, with a range of 2 to 3 cannabis products, a decrease from 2021 (13%, n=23). Of note, suspect products are based on the suspicion of the reporter and the involvement of other products, substances or factors cannot always be ruled out. These considerations form part of the clinical evaluation in the clinical summary portion of this report.

Figure 7: Cases by route of administration

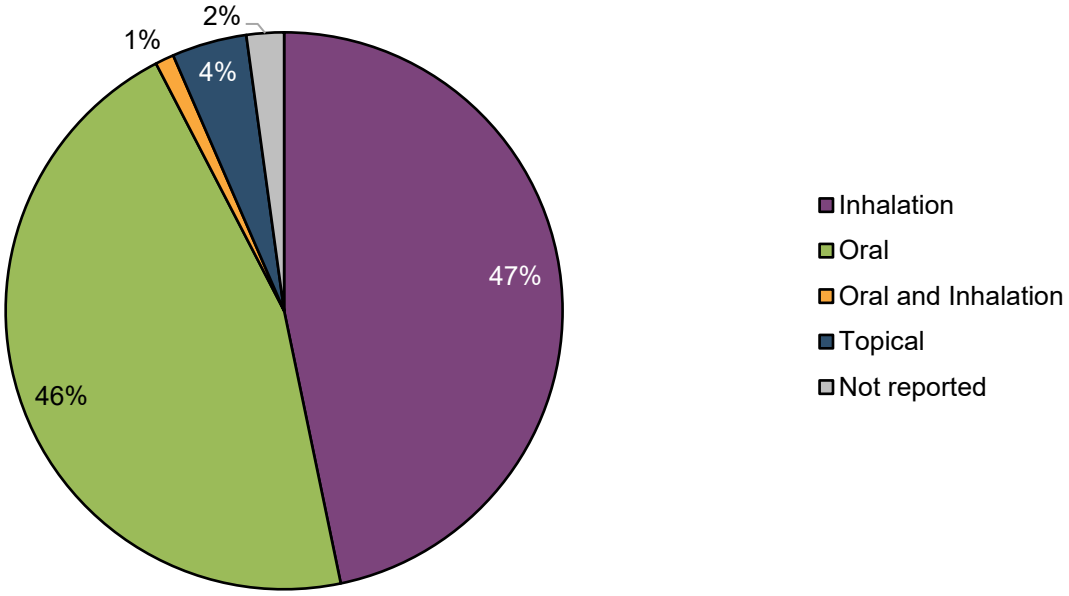

Figure 7 – Text description

Route of administration	Number of cases	Proportion (%)
Inhalation	43	47
Oral	42	46
Oral and inhalation	1	1
Topical	4	4
Not reported	2	2
Total	**92**	**100**

Caveats:

- This figure describes route of administration of suspect cannabis products in cases, which is coded separately from dosage form (that is, a cannabis oil product may be ingested, applied topically)

- Cases may involve more than 1 suspect cannabis product; therefore, multiple routes of administration may appear for a single case
- Inhalation refers to consuming cannabis through the respiratory tract and may involve smoking or vaporization, among others
- Oral administration refers to consuming cannabis by mouth and may involve ingestion, buccal administration, sublingual administration, etc. meaning that absorption may occur at the level of the gastrointestinal tract as well directly into the bloodstream through oral mucosal tissue

Suspect cannabis products associated with adverse reaction cases almost equally involved cannabis being consumed via general inhalation (47%, n=43) and orally (46%, n=42), which is largely cannabis extracts for ingestion. Topical application was involved in 4% of cases and 1 case involved multiple routes of administration. There were no instances of sublingual administration.

These results differ from 2021 where consumption via oral administration was much more frequent than inhalation (63% versus 31% respectively).

Figure 8: Cases by product class and reason for use

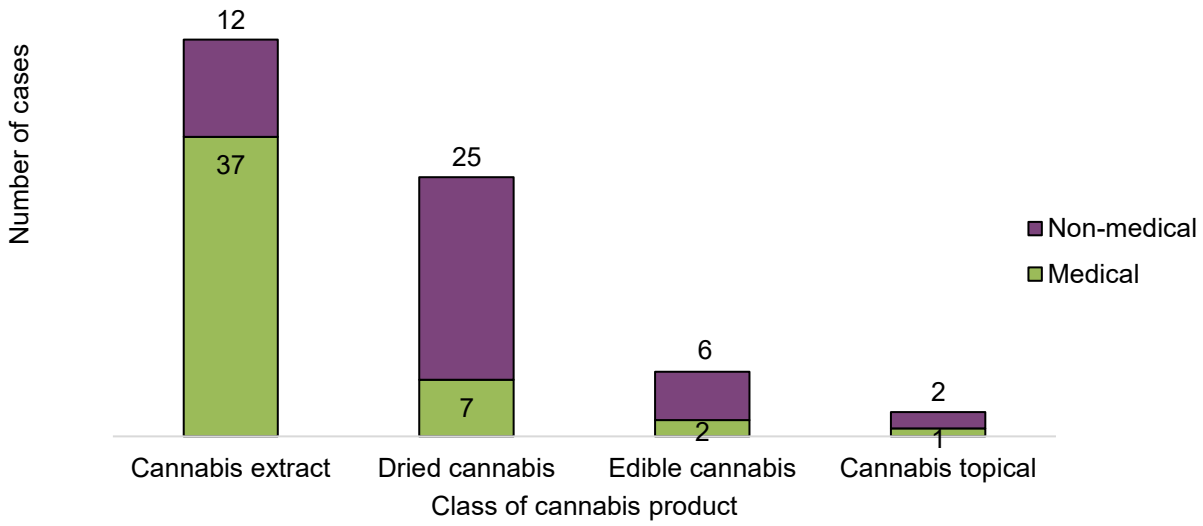

Figure 8 – Text description

Class of cannabis product	**Reason for use**		
	Medical	Non-medical	Total
Cannabis extract	37	12	49
Dried cannabis	7	25	32
Edible cannabis	2	6	8
Cannabis topical	1	2	3
Total	**47**	**45**	**92**

An almost equal number of adverse reaction cases submitted in 2022 were associated with cannabis products used for self-reported medical purposes (51%, n=47) versus non-medical purposes (49%,

n=45). All of the cases involving cannabis products for medical purposes were serious (100%, n=47). In contrast, an almost equal number of cases involving cannabis products for non-medical purposes were serious (49%, n=22) versus non-serious (51%, n=23).

Cases were associated with 4 main classes of legal cannabis products (Figure 8):

- cannabis extracts (n=49)
- dried cannabis (n=32)
- edible cannabis (n=8)
- cannabis topicals (n=3)

No cases in 2022 were associated with fresh cannabis. Most cases involving cannabis extract products were used for medical purposes (76%, n=37), unlike cases involving dried cannabis (22%, n=7). These descriptive observations are consistent with observations from 2021.

No cases involving transformation of legal cannabis products into homemade edible cannabis were reported 2022.

Figure 9: Cases by suspect cannabis product sub-class and seriousness

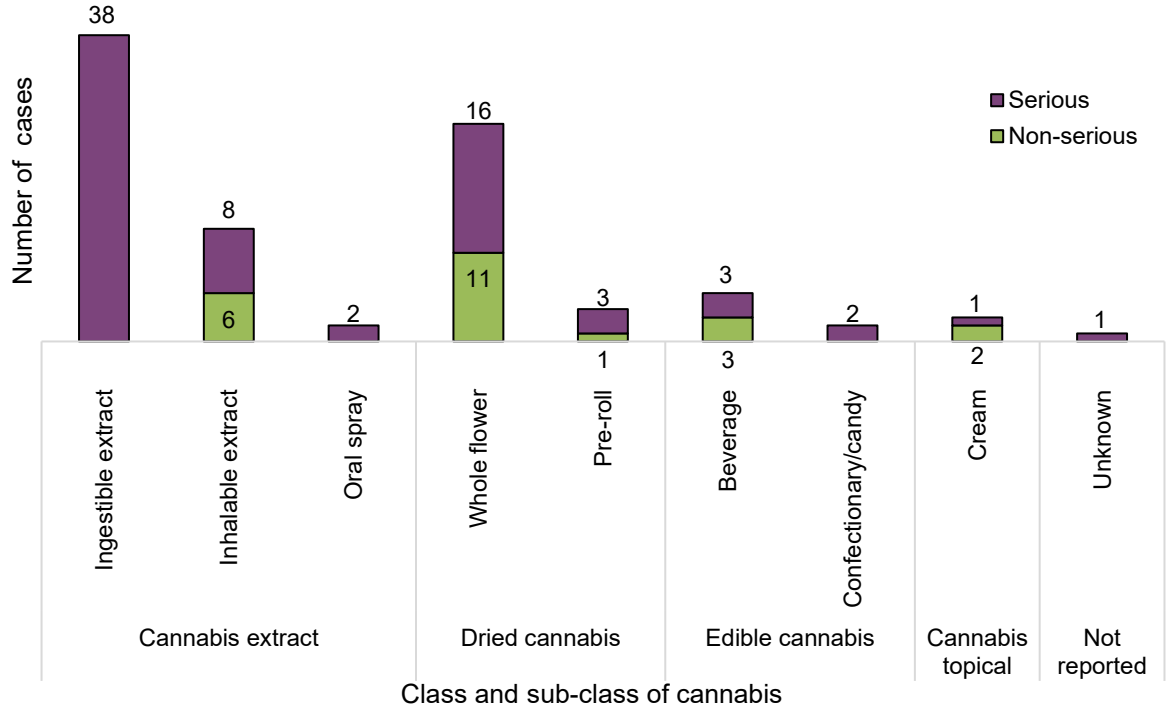

Figure 9 – Text description

Class of cannabis product	Sub-class of cannabis product	Total number of products by seriousness		
		Serious	Non-serious	Total
Cannabis extract	Ingestible extract	38	0	38
	Inhalable extract	8	6	14
	Oral spray	2	0	2
Dried cannabis	Whole flower	16	11	27

	Pre-roll	3	1	4
Edible cannabis	Beverage	3	3	6
	Confectionary/candy	2	0	2
Cannabis topical	Cream	1	2	3
Not reported	Unknown	1	0	1
Total		**74**	**23**	**97**

Caveats:

- This figure was developed by Health Canada through manual categorization of cases according to their sub-class of suspect cannabis products
- Cases may have multiple suspected cannabis product reported across different sub-classes of cannabis. For this reason, the total number reflected in the table according to count of suspect products by sub-classes and seriousness may exceed the number of unique cases
- Cannabis extracts as a class involves a diverse group of product forms including oral liquids or drops, softgels, capsules or tablets, sublingual sprays, dissolvable strips or highly concentrated extracts like shatter, wax, rosin, resin or vaping liquids. Dried cannabis includes whole dried flower, milled flower, and pre-rolls. Edibles includes food-like formats (chocolate, confectionary, mints) and beverages
- Oral sprays (ingestible) are noted separately from ingestible liquid extracts based to their intended sublingual or oro-mucosal use (that is, inside the mouth) that may absorb directly into the bloodstream

As noted above, cannabis extracts were among the most frequently reported class of cannabis products involved in adverse reaction cases, along with dried cannabis. Within the category of cannabis extracts, ingestible oils in liquid form (bottled oils with dropper) and inhalable liquid extracts (vaping liquids) were most frequently involved subclasses, representing 48% (n=26) and 26% (n=14) of adverse reaction cases involving cannabis extracts respectively. Ingestible oils in softgel/capsule form represented 22% (n=12). This is generally consistent with observations from 2021, where ingestible oils in liquid form were the most frequently involved product subclass (56%), followed by ingestible oils in capsule form (20%) and inhalable liquid extracts (18%).

Inconsistent with 2021, cannabis extracts were the most frequently reported class across all age groups (under 18 years, 18 to 64 years and 65 years or older) in 2022. When disaggregated by sub-class, young to middle aged adult groups (18 to 64 years) were more frequently involved in adverse reaction cases with vaping liquids, oral sprays and cannabis topicals, while older adults (65 years or older) were more frequently involved in adverse reaction cases with ingestible oils in liquid form and softgel capsules. This is generally consistent with data from 2021 where young to middle aged adult groups (18 to 64 years) were more frequently involved in adverse reaction cases with vaping liquids and oral sprays, while older adults (65 years or older) were more frequently involved in adverse reaction cases with ingestible oils in liquid form and softgel capsules.

Some consumers or patients may preferentially select ingestible cannabis oil products for 1 or more reasons such as:

- for duration of effect
- to avoid inhaling cannabis
- for cannabinoid concentration
- for the ability to draw or titrate a specific measured dose
- other reasons

In addition, adults over 55 years of age may be more sensitive to cannabis and have a higher risk of experiencing adverse reactions. This is especially true when they have certain medical conditions or use other health products, which may increase the risk of possible interactions, thereby contributing to an increased risk of experiencing adverse reactions.

Types of individual events reported

Figure 10: Breakdown of individual events by system organ class (SOC)

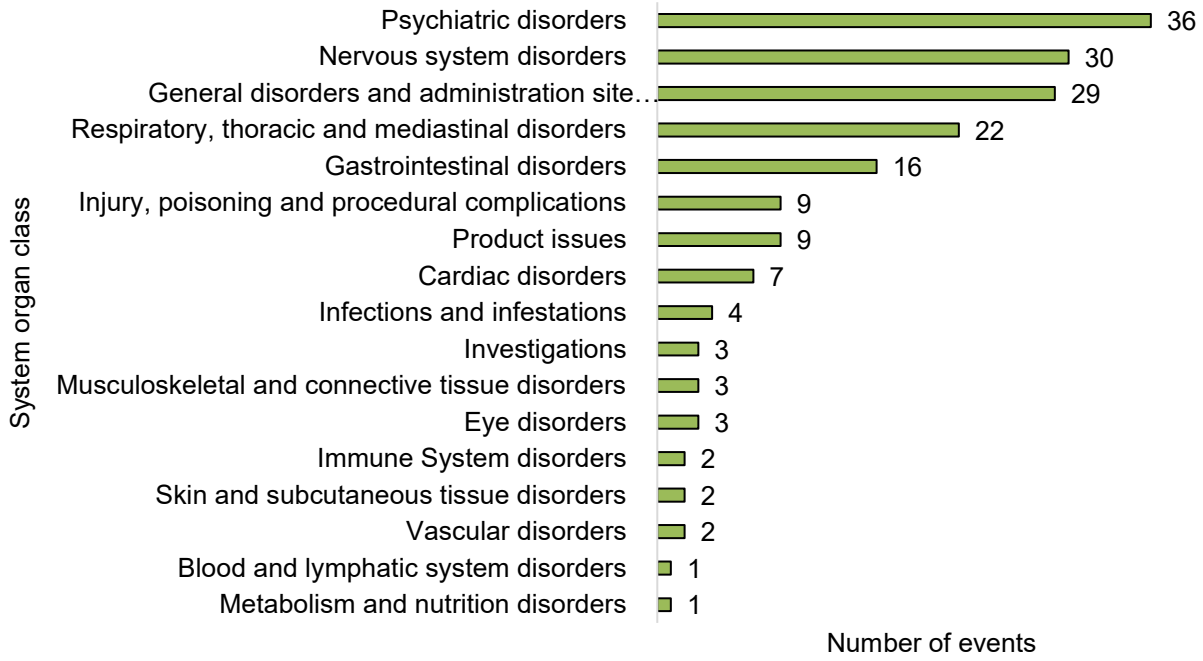

Figure 10 – Text description

System organ class	Number of events
Psychiatric disorders	36
Nervous system disorders	30
General disorders and administration site conditions	29
Respiratory, thoracic and mediastinal disorders	22
Gastrointestinal disorders	16
Injury, poisoning and procedural complications	9
Product issues	9
Cardiac disorders	7
Infections and infestations	4
Investigations	3
Musculoskeletal and connective tissue disorders	3
Eye disorders	3
Immune System disorders	2
Skin and subcutaneous tissue disorders	2
Vascular disorders	2
Blood and lymphatic system disorders	1

Metabolism and nutrition disorders	1

Caveats:

- This figure shows SOCs across all adverse reaction cases where the suspect product was assessed by Health Canada as being certainly, probably or possibly related to the reported event (that is, causality assessment)
- Each case may describe 1 or more individual medical events reflective of signs, symptoms, diseases, diagnoses, investigations, and procedures
- Events are coded according to MedDRA, which provides standardized medical terminology in hierarchical groupings. The highest-level grouping is the SOC
- 1 adverse reaction case may be represented across multiple SOCs, and is influenced by how individual events (signs, symptoms, observations or diagnostics) are reported

Health Canada assessed a total of 310 adverse events for causality. Of these, 179 individual adverse events (representing 117 unique event categories) were assessed as being certainly, probably or possibly related to the suspected cannabis product for cases received in 2022.

When grouped at the broadest grouping level (that is, SOC) the 5 most frequent categories were:

- psychiatric disorders (20%)
- nervous system disorders (17%)
- general disorders and administration site conditions (16%)
- respiratory, thoracic and mediastinal disorders (12%)
- gastrointestinal disorders (9%)

These top 5 SOCs for 2022 are consistent with the top 5 SOCs reported in 2021, but in varying order.

Figure 11: Frequency of individual events

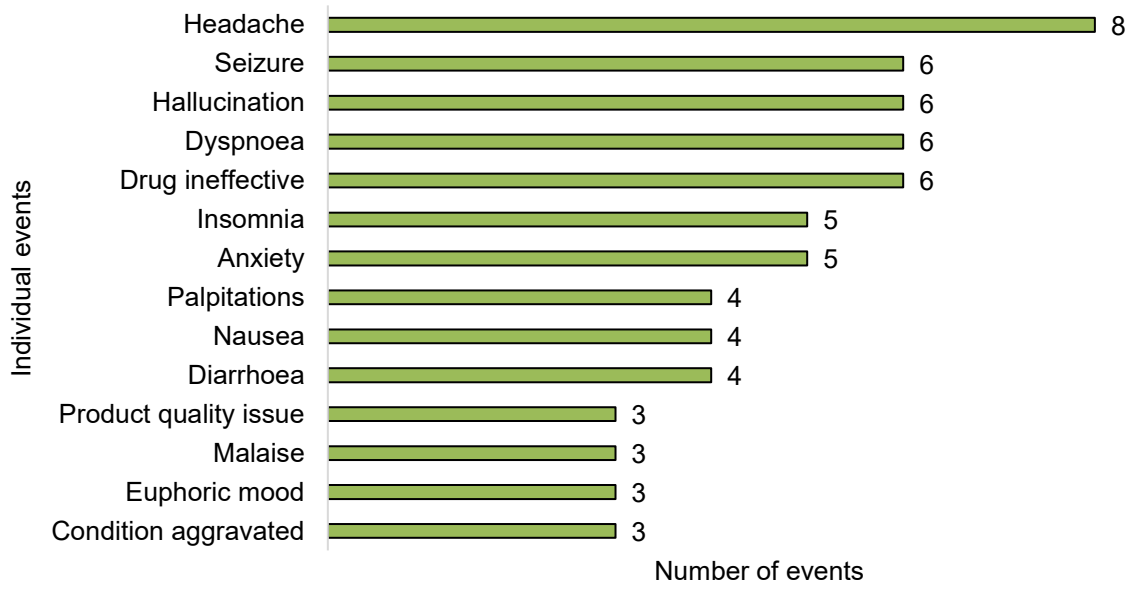

Figure 11 – Text description

Individual events	Number of events
Headache	8
Seizure	6
Hallucination	6
Drug ineffective	6
Dyspnoea	6
Insomnia	5
Anxiety	5
Palpitations	4
Nausea	4
Diarrhoea	4
Product quality issue	3
Malaise	3
Euphoric mood	3
Condition aggravated	3

Caveats:

- This figure focuses on the most frequently reported individual events across adverse reaction cases where the suspect product was assessed by Health Canada as being certainly, probably or possibly related to the reported event (that is, causality assessment). Other individual events reported less frequently do not appear in this figure
- Individual events are coded using MedDRA terminology based on the verbatim described in the case report
- Each case can have multiple individual events reported therefore the number of individual events exceeds the total number of unique cases
- Several types of hallucination were combined to create an all-inclusive hallucination category. These included auditory hallucination, visual hallucination, mixed hallucination, hypnagogic hallucination and pseudohallucination

As noted in Figure 11, the top 5 most frequently reported individual events assessed by Health Canada as being certainly, probably or possibly related to the suspected cannabis product for cases received in 2022 were:

- headache (4%)
- seizure (3%)
- hallucination (3%)
- dyspnoea (3%)
- drug ineffective (3%)

Figure 12: Frequency of individual events by cannabinoid ratio

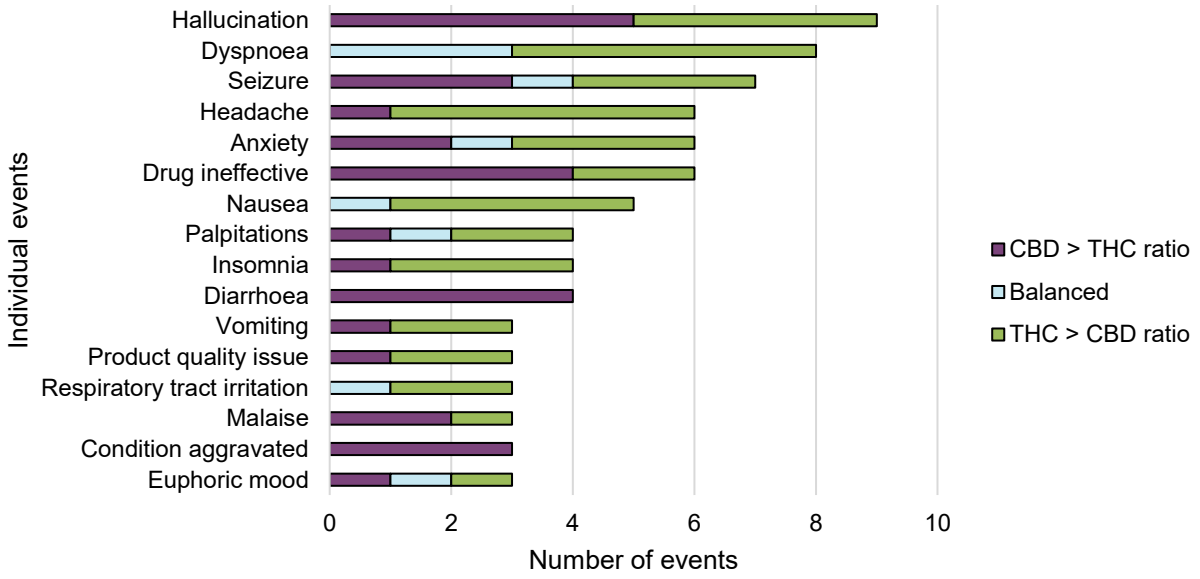

Figure 12 – Text description

Individual events	**Cannabinoid dominance**			
	CBD > THC ratio	Balanced	THC > CBD ratio	Total
Hallucination	5	0	4	9
Dyspnoea	0	3	5	8
Seizure	3	1	3	7
Headache	1	0	5	6
Anxiety	2	1	3	6
Drug ineffective	4	0	2	6
Nausea	0	1	4	5
Palpitations	1	1	2	4
Insomnia	1	0	3	4
Diarrhoea	4	0	0	4
Vomiting	1	0	2	3
Product quality issue	1	0	2	3
Respiratory tract irritation	0	1	2	3
Malaise	2	0	1	3
Condition aggravated	3	0	0	3
Euphoric mood	1	1	1	3

Caveats:

- This figure focuses on the most frequently reported individual events across adverse reaction cases after stratification by cannabinoid ratio, where the suspect product was assessed by Health Canada as being certainly, probably or possibly related to the reported event (that is, causality assessment). This figure excludes cases without sufficient information for assignment of cannabinoid ratio (that is, unclassified), therefore, the events in this figure may differ from those

observed in Figure 11. Other events were reported during the reporting period but do not appear in this figure

- This figure was manually created by Health Canada by classifying each suspect cannabis product to a cannabinoid ratio based on available product details and assigning all individual events within a case to all reported suspect cannabis products and their cannabinoid ratio (weighted equally for all events). Therefore, this may over-estimate the correlation between cannabinoid ratio and individual events
- The category “balance” is considered a THC:CBD ratio between 1.2:1 and 1:1.2.

Overall, adverse reaction cases from 2022 more frequently involved products with a greater THC to CBD ratio (that is, a THC:CBD ratio greater than 1.2:1) compared to products containing a greater CBD to THC ratio (that is, a CBD:THC ratio greater than 1.2:1). As highlighted in Figure 12, certain individual medical events were more frequently reported with products containing a greater ratio of THC to CBD, whereas others were more frequently reported with products containing a greater ratio of CBD to THC.

For example, the following were more frequently reported with products containing a greater ratio of THC to CBD:

- anxiety
- nausea
- insomnia
- vomiting
- dyspnoea
- headache
- product quality issue
- respiratory tract infection

Whereas the following were more frequently reported with products containing a greater ratio of CBD relative to THC:

- malaise
- diarrhoea
- hallucination
- drug ineffective
- condition aggravated

These are reported events only and other factors may be contributing to these events including:

- dosage
- route of administration
- knowledge or awareness of effects of cannabis and cannabinoids
- prior exposure to cannabis (for example, cannabis naïve consumers)
- reporting factors such as motivation to report, risk tolerance or awareness of reporting
- the age and health status of patients (including pre-existing health conditions and use of concomitant medications)

However, the ability to draw strong conclusions is limited due to the complex nature of the available data.

SEX AND GENDER BASED ANALYSIS PLUS OF 2022 ADVERSE REACTION DATA

Figure 13 – SGBA plus: Cases by sex

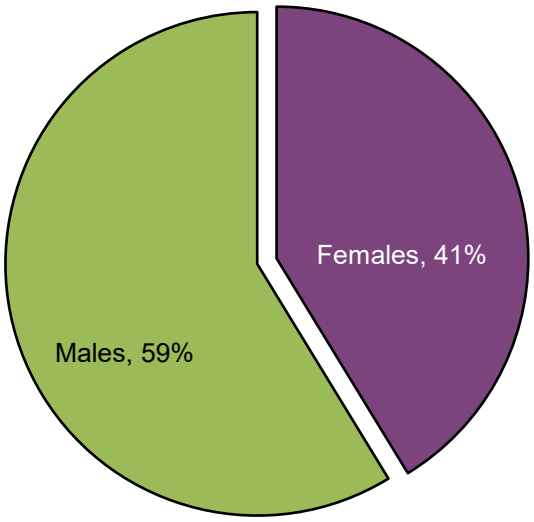

Figure 13 – Text description

Sex	Number of cases	Proportion (%) of total
Females	26	41
Males	37	59
Total	**63**	**100**

A total of 63 adverse reaction cases included a designation for sex in 2022. Of these cases 59% (n=37) involved males. Males were involved in 54% of all serious cases with a reported sex, and females and males equally reported use of cannabis for medical purposes (n=21 each). Non-serious cases and use for non-medical purposes more frequently involved males than females.

Females involved in adverse reaction cases associated with cannabis products were generally older than males. Where age was reported (n=51), the average age of females was 61.9 years (95% CI: 54.1-69.6) and 48.0 years for males (95% CI: 39.7-56.3).

Under 65 years:
Females, n=10; males, n=22

65 years or older:
Females, n=11; males, n=8

Figure 14 – SGBA plus: Cases by age group (years)

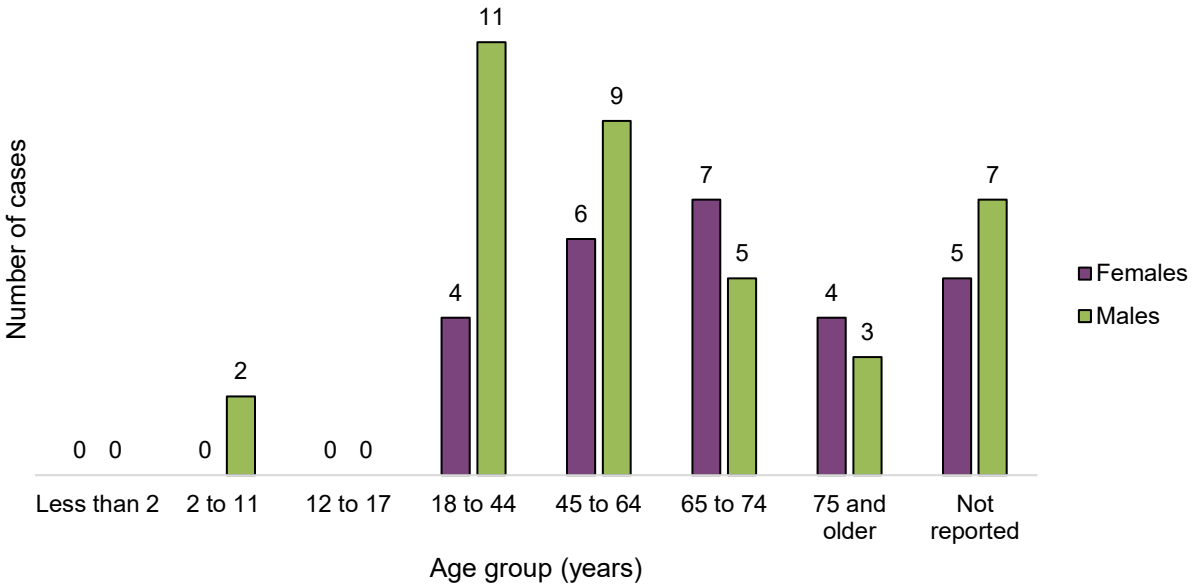

Figure 14 – Text description

Age group (years)	**Number of cases**	
	Females	Males
Less than 2	0	0
2 to 11	0	2
12 to 17	0	0
18 to 44	4	11
45 to 64	6	9
65 to 74	7	5
75 and older	4	3
Not reported	5	7
Total	**26**	**37**

Adverse reactions cases involving ingestible cannabis extracts in liquid format (bottled oils), inhalable liquid extracts (vapes), oral sprays and dried cannabis more frequently involved males than females. Conversely, edibles (beverages and confectionaries) more frequently involved females than males.

Males were more frequently involved in adverse reaction cases where multiple suspect cannabis products were reported compared to females (4 versus 1 case with multiple products, respectively).

Table 1: Top individual events reported by sex	
Females	*Males*
Hallucination* (n=4)	Dyspnoea (n=5)
Diarrhoea (n=3)	Drug ineffective (n=4)
Seizure (n=3)	Hallucination* (n=4)

* including visual, auditory, mixed, hypnagogic and pseudohallucination.

CLINICAL EVALUATION OF SERIOUS AND MEDICALLY IMPORTANT CASES

Summary of serious and medically important adverse reactions

All individual events within an adverse reaction case that is reported as serious to Health Canada are assessed for causality. The causality of individual events is based on the information reported in the cases and through follow-up where possible. Cases may lack sufficient information to assess the causal association between events and exposure to the cannabis products. Causality assessment is a clinical investigation of cases and is a routine practice in pharmacovigilance to determine the likelihood of association between the products and the adverse reactions. This practice supports the identification of potential safety concerns that may require further investigation or actions by the regulatory authority (such as Health Canada) or the licence holder.

Table 2: Causality assessment of serious cases	
Causality Assigned	*Number of events*
Certain	3
Probable	8
Possible	167
Unlikely	41
Unassessable	49
Total	268

Overall, most events were assigned a causality of “Possible” (62%, n=167), meaning there was a reasonable possibility that the cannabis product may have contributed to the adverse reaction, but the contribution of other factors could not be ruled out (for example, concomitant medications or co-morbidities).

3 events were assigned a causality of “Certain” (1%), for which a stringent level of evidence is required, including both laboratory and medical confirmation. As well, the case must lack any other alternative explanations.

The 3 events assigned a causality of “Certain” (n=3 cases) all involved procurement or administration issues, namely:

1. incorrect dose being administered
2. wrong product administered
3. wrong product procured

Each case involved a legal cannabis extract product for ingestion (softgel capsules, n=2; oils, n=1), no co-suspect products were reported. All individuals had pre-existing medical conditions, reported use of concomitant health products and were using cannabis products for self-reported medical purposes (indications of use included epilepsy, sleep disorder, cancer-related pain or neuralgia).

There were 8 events assigned a causality of “Probable” (3%), meaning there was sufficient information to judge that the cannabis product probably contributed to the adverse reaction and the contribution of other factors was considered to be unlikely.

The 8 events assigned a causality of “Probable” represented 4 cases:

- 2 were associated with legal cannabis extract products for ingestion (softgel capsules, n=1; oral spray, n=1)
- 1 was associated with edible cannabis
- 1 involved multiple co-suspect products (oil and vape)

Among these cases, 3 out of 4 reported cannabis as a sole suspect product, meaning that no other health products were reported as co-suspects. In addition, all 4 cases had pre-existing medical conditions and were using cannabis products for self-reported medical purposes (indications of use included anxiety, pain or epilepsy). All but 1 case reported use of concomitant health products (75%, n=3).

There were 49 events determined to be “Unassessable” (18%), meaning there was insufficient information to establish a causal association between the cannabis product and the reported adverse reaction.

There were 41 events assigned a causality of “Unlikely” (15%), meaning that the cannabis product was judged to not play a causative role in the reported adverse reaction (other probable factors identified).

Important identified risks during the reporting period

During this reporting period, no serious or medically important cases were classified as having new important identified risks by Health Canada. An identified risk means that the association between a drug (for example, cannabis) and event has been proven, and that this risk could have implications for public health.[6]

[6] European Medicines Agency. (2017). Guideline on good pharmacovigilance practices (GVP): Annex I - Definitions (Rev 4). https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-annex-i-definitions-rev-4_en.pdf

Most serious or medically important cases with 'Probable' causality were considered to involve known identified risks (that is, the risk is has already been identified and characterised in Health Canada's Information for Health Care Professionals document; last updated: Spring 2018). These include:

- Neurological reactions (for example, headache, light-headedness)
- Psychiatric reactions (for example, panic, anxiety, hallucinations)
- Respiratory non-infectious reactions (for example, throat irritation)
- Cardiovascular reactions (for example, atrial fibrillation, palpitations, tachycardia)
- Hypersensitivity /allergic reactions (for example, systemic hypersensitivity reactions)

Important potential risks during the reporting period

2 important potential risks were observed in adverse reaction data with cannabis products during this reporting period.

A potential risk means that there is suspicion of association between a drug (for example, cannabis) and the event, which is yet to be proven, and that this risk could have implications for public health.[6]

Risk of new onset of seizure in individuals without pre-existing seizure disorder with the use of cannabis products (THC, CBD, balanced)

While there is some research to suggest that cannabis, specifically CBD, may be helpful in the treatment of seizure-related symptoms and disorders, little is known about the potential for cannabis to cause seizure in individuals without pre-existing seizure conditions. After receiving several reports of convulsion and seizure associated with cannabis products, Health Canada initiated in 2022 a preliminary signal assessment to assess the potential risk of new onset seizure in healthy individuals consuming licensed cannabis products (THC, CBD, balanced). A total of 16 domestic case reports were identified in which convulsion or seizure was reported and assessed as being "probably" (n=3) or "possibly" (n=13) associated with the cannabis products; 8 cases were submitted in 2022, the rest were submitted in other years. Most cases involved females and young to middle-aged adults (18-64 years). Most individuals were using cannabis for medical purposes and, therefore, had pre-existing conditions (other than seizure disorder or convulsion). Likewise, most individuals were consuming other concomitant health products. As such, there may be several contributing factors influencing these outcomes. An in-depth assessment (signal assessment) will be conducted, which will include a review of domestic and foreign data, as well as evidence from the published literature to determine whether this important potential risk warrants any risk mitigation.

Risk of arrythmia with the use of cannabis products (THC, CBD, balanced)

This important potential risk was identified at the end of 2022 and is currently being assessed by Health Canada.

Ongoing monitoring of safety signals

Health Canada will continue to monitor for any new literature and adverse reaction reports for the following risks:

- hypoglycemia events amongst cannabis users
- hallucinations amongst consumers using cannabidiol-containing products
- cannabis-drug interactions (for example, warfarin, topiramate, clobazam, metronidazole, lorazepam)
- blood clotting in individuals that concurrently use cannabis products and estrogen containing combined oral contraceptives

Fatal cases during the reporting period

During this reporting period, Health Canada conducted a comprehensive assessment on 2 fatal cases involving cannabis products for medical purposes.

Case 1

The first fatal case was initially received by Health Canada 2021 and is also included in the 2021 Annual report of cannabis adverse reactions. This case is referenced here despite it having been initially reported in late 2021, as the 2 responsible licence holders submitted complete reports to Health Canada, per their mandatory reporting obligations, in early 2022. This case involved 2 cannabis vaping products with other concomitant medications in a patient with complex medical history and several risk factors who experienced seizures which led to hospital admission then death. The outcome of death was determined to be from multi-organ failure and sepsis. The sepsis was most likely due to a staphylococcal infection, of which the source was the temporary hemodialysis line placed in the patient to address deteriorating kidney function. The use of a cannabis vape product may have been a cause of the initial seizure but is less likely to be the cause of the patient's death. However, Health Canada cannot rule out the contribution of the THC vaping products to some of the underlying lung and kidney injury prior admission.

Case 2

The second fatal case received in 2022 involved a single ingestible cannabis oil product used for medical purposes (authorization present) to treat symptoms related to arthralgia. The individual had a complex medical history and was using multiple concomitant health medications, in addition to the cannabis product. Reported events included seizure and death. Total daily dose at the time of the seizure was 12 mg of THC and 14.4-18 mg of CBD. Based on the available case information, Health Canada assessed the event of seizure as possibly related to the cannabis product while the outcome of death was assessed as unlikely.

NOTE TO READERS

Adverse reaction case reports with cannabis submitted to Health Canada are received and entered into the Canada Vigilance database. The Marketed Health Product Directorate (MHPD) of the Health Products and Food Branch (HPFB) collects, monitors and analyses adverse reactions submitted to the Canada Vigilance database, amongst other activities, and codes and houses adverse reaction reports for cannabis. The Controlled Substances and Cannabis Branch (CSCB) is responsible for the monitoring, detection, prioritization, evaluation and aggregate reporting of adverse reactions associated with cannabis (pharmacovigilance).

Voluntary reports from the public may be received via the online reporting form, through the toll-free number or through the printable form via electronic fax or mailing to Health Canada. Mandatory reports are submitted by licence holders to meet their regulatory reporting obligations for serious adverse reactions under the *Cannabis Regulations* and are submitted through fax or mail, unless the company is registered to submit electronic reports directly to the Canada Vigilance database (specific format must be met). Cannabis complaints and product quality issues may also be referred via the Cannabis Reporting Form from Health Canada. Incidents involving cannabis accessories (for example, mechanical, physical or electrical issue or failure of a cannabis accessory and associated injuries) can be reported via the Consumer Product Incident Reporting Form from the Healthy Environment and Consumer Safety Branch. All cannabis adverse reaction cases are coded in the following manner:

1. Case reports are translated into electronic data into the Canada Vigilance database. All individual events are coded using the MedDRA, which is developed, maintained and updated by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human

Use as an international set of standardized medical terms for symptoms, signs, diseases, syndromes and diagnoses.

2. Case reports involving cannabis as a substance in a suspected role are coded as 'cannabis sativa' at the active ingredient level, irrespective of the identity of the cannabis product (legal, illegal, unspecified, undetermined).
3. Case reports involving a legal cannabis product in a suspected role (identified either by product name or licence holder) are classified according to the intended use: cannabis product used for medical purposes (medical cannabis) or used for non-medical purposes (non-medical cannabis), based on the information in the report. Cannabis use for medical purposes includes reports described having a medical authorization document; or, a reported medical or therapeutic purpose or indication, without mention of a medical authorization document. If there is no reported reason for use provided in the report, minimal details or intended use for non-medical purposes, the report is classified as non-medical cannabis.
4. Case reports are coded as serious as reported if at least 1 criterion for seriousness is selected:
    - death
    - life-threatening
    - admitted to the hospital
    - lengthened hospital stay
    - disability
    - birth defect
    - other medically important condition may also be selected by the reporter
5. According to international pharmacovigilance guidelines (ICH guidelines[7]), medically important conditions may also be considered serious under certain circumstances and therefore are an option to select when reporting an adverse reaction to Health Canada, and any adverse reaction case identified as such are further reviewed. However, these cases technically fall outside of the regulatory definition of a serious adverse reaction under the *Cannabis Regulations*.

Health Canada conducts routine monitoring, detection, assessment and associated activities for all cannabis adverse reaction reports, which involves:

- Screening of all new cannabis case reports to ensure they are:
    - coded appropriately according to MedDRA
    - classified as either cannabis for medical or non-medical purposes (legal classes)
    - product names are accurate
- Case reports involving a suspected non-compliance (for example, the presence of visual mould, metallic taste, unusual odour) are referred to the Compliance Directorate for verification.
- Non-serious reports are screened by Health Canada and those deemed to be medically important events are included for further assessment (causality assessment).
- All serious and medically important case reports undergo further investigation and assessment, including:
    - conducting follow-up for additional information on product details or clinical details of cases to aid in assessment
    - conducting a cursory causality assessment for each event reported in the case report. Causality assessment is based primarily on the WHO-UMC system for standardised case causality assessment

[7] European Medicines Agency (2004). ICH Topic E2D: Post Approval Safety Data Management Step 5. https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-12.pdf

    - undergoing a comprehensive individual causality assessment for all fatal and life-threatening cases, which, are considered priority reports
- Any cases involving new or unexpected adverse reactions of interest undergo preliminary assessment (signal prioritization) to determine if they should be further evaluated
- A case series evaluation (signal assessment) is conducted in the event of a cluster or related cases involving new adverse reactions of interest. These comprehensive assessments involve the determination of biological plausibility based on published literature, domestic as well as international adverse reaction data (WHO Vigibase)

REPORTING AN ADVERSE REACTION INVOLVING A CANNABIS PRODUCT

Licence holders must submit serious adverse reaction reports, as defined by the *Cannabis Regulations*, involving a cannabis product. They are encouraged to voluntarily submit non-serious adverse reaction reports involving a cannabis product. More information can be found in the *Cannabis adverse reaction reporting guide for licence holders*.

Consumers and health care practitioners are encouraged to report any adverse reaction to a cannabis product directly to Health Canada. Consumers and health care practitioners may also send a report to the licence holder of the cannabis product.

Report an adverse reaction to Health Canada

CONTACT US

Any questions or comments on this report, including any requests for the data used to support this report, should be directed to cannabis_oss-cannabis_bss@hc-sc.gc.ca.