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Psychedelic Restricted Drugs: Legal Access Pathways

Health Canada

CAPRA Webinar
August 18, 2022

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Speaker Introductions

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Health Canada Branches and Mandates

Health Products and Food Branch (HPFB)

- HPFB's mandate is to manage the health-related risks and benefits of health products and food
- Administers the *Food and Drugs Act* (FDA)

Controlled Substances and Cannabis Branch (CSCB)

- CSCB's mandate is to reduce or prevent the harms associated with many different controlled drugs and substances in Canada
- Administers various legislation: *Controlled Drugs and Substances Act* (CDSA), *Tobacco and Vaping Products Act*, *Cannabis Act*

What are psychedelics and how are they regulated?

- A group of psychoactive substances that produce changes in perception, mood, and cognition.
- There are different types of psychedelics; some occur naturally, whereas others are made in laboratories.
- Consistent with the international treatment of these substances, most psychedelics are controlled under the *Controlled Drugs and Substances Act* (CDSA) as "controlled substances".
  - Such substances are controlled internationally under the United Nations Drug Control Conventions.
- Because of their biological effects, psychedelics meet the definition of "drug" and are also subject to the *Food and Drugs Act*.

Regulatory Status of Various Psychedelics

Drug Name	Also known as or found in:	CDSA	FDA
Ketamine	Esketamine, Special K	Narcotic (*Narcotic Control Regulations*)	All psychedelics are "drugs" and therefore subject to the *Food and Drugs Act* * Ibogaine is on the Prescription Drug List
Psilocybin	Magic Mushrooms	Restricted drugs (Part J of the *Food and Drug Regulations*)	
MDMA	Ecstasy		
LSD	Acid		
DMT	Ayahuasca & Daime Tea		
Ibogaine	Iboga	Not controlled	

Requirements to Conduct Activities with Psychedelic Controlled Substances

- Activities with controlled substances, such as sale, possession, and production, are illegal unless authorized under the regulations or through an exemption granted under section 56 of the CDSA.
  - Regulations under the CDSA provide a framework within which legitimate activities with controlled substances are permitted

- To legally conduct activities with controlled substances, an authorization from Health Canada's Office of Controlled Substances is needed.
  - To apply for a dealer's licence: hc.cds-sdc.sc@canada.ca
  - To apply for an authorization to conduct research with controlled substances: exemption@hc-sc.gc.ca

Legal Access Pathways for Psilocybin

- Health Canada recognizes there are times when access to unauthorized drugs may be appropriate.
- In some circumstances, with the support of a regulated health care practitioner, it may be possible for individuals to legally access psilocybin through one of three pathways:

1. Clinical trials
2. Special Access Program
3. Individual subsection 56(1) exemptions from the CDSA

CLINICAL TRIALS

Food and Drug Regulations, Part C, Division 5
Drugs for Clinical Trials Involving Human Subjects

Why clinical trials?

- Clinical trials provide access to drugs that have not yet undergone the rigorous review process required to be authorized for sale in Canada.
- They aim to determine the safety and efficacy of a drug to treat a particular indication.
- Health Canada strongly encourages potential sponsors seeking access to psychedelic restricted drugs to pursue a clinical trial and help build the evidence base.

Protect the health and safety of patients

Generate evidence re: safety and efficacy

What is a clinical trial?

Clinical trial means an “investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify:

- the clinical, pharmacological or pharmacodynamic effects of the drug;
- identify any adverse events in respect of the drug;
- study the absorption, distribution, metabolism and excretion of the drug; or
- ascertain the safety or efficacy of the drug”.

Source: FDR C.05.001

Division 5 of the *Food and Drug Regulations*

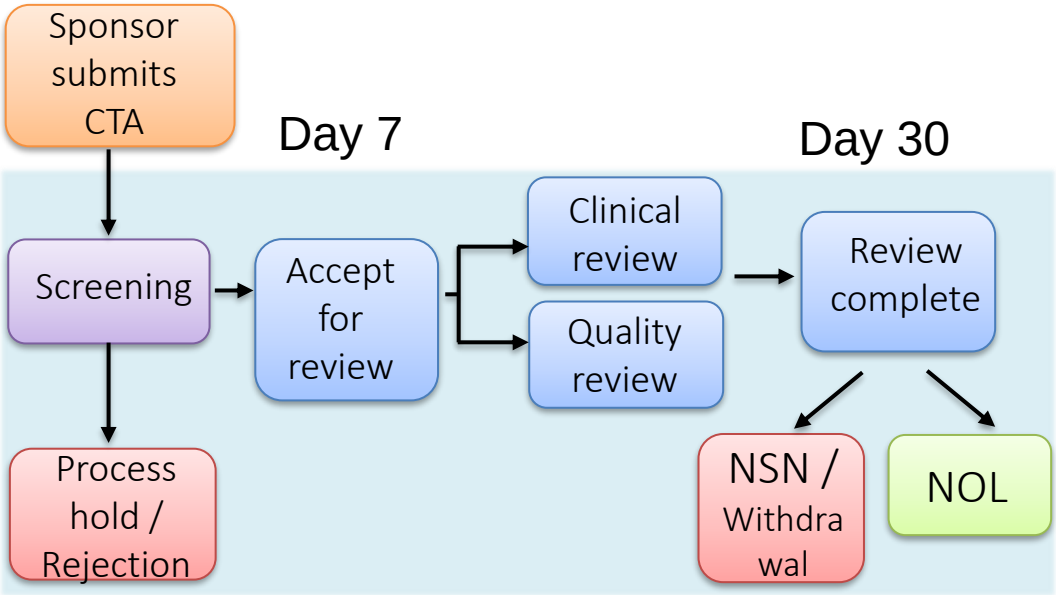
- Allows the sale and importation of an unauthorized use of a drug in a clinical trial
- Default system: the Minister has 30 calendar days from the date of receipt of a complete application to raise objection to the trial (if no objection, issues a “No Objection Letter” (NOL))
- Incorporates essential components of Good Clinical Practices, including the need to use a product produced in accordance with good manufacturing practices (GMP)

Health Canada's Role

Actions to minimize the risks to which participants may be exposed in a clinical trial setting:

- Assess the protocol, Informed Consent Form, Investigator's Brochure and quality-related information
- Monitor Adverse Drug Reactions – Safety Database in place to collect such information while trial is ongoing
- Good Clinical Practice (GCP) inspection program
- Suspend or cancel the authorization of a clinical trial

Clinical Trial Application (CTA) Regulatory Process & Timeline



NSN: Non-Satisfactory Notice
NOL: No Objection Letter
Clock starts on the day a COMPLETE application is received by the Office of Clinical Trials

Reasons the Office of Clinical Trials Might Object to a Clinical Trial

Regulations state that a sponsor may not sell or import the drug for a clinical trial if:

- there is insufficient information to assess the risks of the drug or the trial
- the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person
- the clinical trial is contrary to the best interests of a clinical trial subject
- the objectives of the clinical trial will not be achieved

Source: FDR C.05.006

Content of an application

As defined under C.05.005 of the *Food and Drug Regulations,* a CTA should contain*:*

- Protocol
- Statement on risks and anticipated benefits as set out in the Informed Consent form
- Form 3011
- Details on any refusal from a Research Ethics Board, if known at the time of the application
- Investigator's Brochure
- The chemistry and manufacturing information
- Proposed date of commencement at each clinical trial site, if known at the time of the application

Must be provided in "Non-eCTD electronic only" format

Common deficiencies noted at screening

- A protocol number has not been assigned
  - Must appear on Appendix 3 of Form 3011, Protocol title page and Informed Consent Form
- Appendix 3 of Form 3011 is missing
- Access letter to Drug Master File not included
  - for drugs not approved in Canada, when the sponsor of the trial is not the manufacturer
- Investigator's Brochure is not up to date
  - must be < 1 year old or include attestation that the information has not changed in the past year
- The following elements are missing from the protocol:
  - Attestation that the clinical trial will be conducted according to Good Clinical Practices
  - Confirmation that records will be kept for 15 years

Common deficiencies noted during review

- The hypothesis tested is not specified
- The unmet medical need is not specified
- The parameters for assessment are not appropriate to answer the question
- The choice of the dose is not supported
- Inadequate type or duration of contraception
- The sample size is insufficient
- Risk mitigation measures are insufficient

Also required before initiating the clinical trial

- Research Ethics Board (REB) approval
  - Investigators affiliated with a Canadian university or hospital will typically have access to an REB through that institution
  - There are also private REBs that can be accessed by investigators who don't otherwise have access to an REB
- Submission of clinical trial site information
  - Information on investigator and research ethics board for each site
- Authorization under the CDSA to use a controlled substance for scientific purposes
  - Contact exemption@hc-sc.gc.ca for more information

Post-authorization requirements: Safety

- Serious Unexpected Adverse Drug Reactions Reporting
  - If fatal or life-threatening, within 7 days of becoming aware of the information
  - Otherwise, within 15 days of becoming aware of the information
- Annual update of the Investigator's Brochure
- Notification of any serious safety issue that requires an immediate change to the protocol

Post-authorization requirements: Amendments

A clinical trial amendment application is required before implementing:

- Amendments to the protocol that:
  - Affect the selection, monitoring or dismissal of a clinical trial participant
  - Affect the evaluation of the efficacy of the drug
  - Alter the risk to the health of a clinical trial participant
  - Affect the safety evaluation of the trial
  - Extend the duration of the trial
- Amendments to the chemistry and manufacturing information that may affect the safety or quality of the drug

Post-authorization requirements: Amendments

- However, if the clinical trial or the use of the drug endangers the health of participants, the sponsor may implement changes immediately but must:
  - Immediately notify Health Canada
  - Submit a clinical trial amendment application within 15 days

Suspension and cancellation of trials

The regulations allow for the suspension or cancellation of a clinical trial if:

> (a) the sponsor has contravened the Regulations or any provisions of the Act relating to the drug;
>
> (b) any information submitted in respect of the drug or clinical trial is false or misleading;
>
> (c) the sponsor has failed to comply with good clinical practices;
>
> (d) the sponsor has failed to provide information requested under the regulations; or
>
> (e) there is reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a clinical trial subject or other person

Source: FDR C.05.016 and C.05.017

SPECIAL ACCESS PROGRAM

Food and Drug Regulations C.08.010 and C.08.011

Sale of New Drug for Emergency Treatment

Special Access Program (SAP) for Drugs

- Health Canada may authorize the sale of a non-marketed drug for emergency treatment of an individual patient
- Requirements:
  - The patient suffers from a serious or life-threatening condition
  - Conventional therapies have been tried and failed, considered but deemed unsuitable, or are unavailable in Canada
  - There is sufficient data to support the requested use

SAP request

- Request can only be submitted by licensed practitioners who are allowed to treat patients with a prescription drug
- Request is patient-specific and must include details that demonstrate the requirements have been met
  - Condition of the patient
  - Therapies tried or considered
  - Supporting evidence for use of the drug for the specific indication
- Request must indicate the quantity requested
  - Drug cannot be transferred to another patient without seeking authorization from the SAP

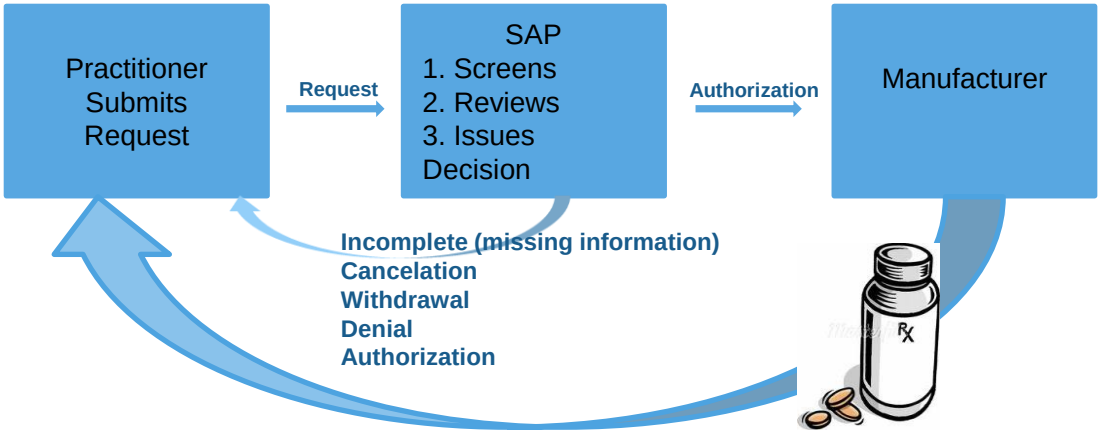
SAP request

- The practitioner agrees to
  - provide a report to the manufacturer of the new drug **and** to Health Canada describing the results obtained following the use of the new drug, including information respecting any adverse drug reactions observed by the practitioner; and
  - account to Health Canada, on request, for all quantities of the new drug received

SAP Requests Decision Making and Processing

Consideration of requests involves:

1. Determining whether the patient suffers from a serious or life-threatening condition;
2. Confirming that other therapies have been tried or at least considered, or unavailable;
3. Reviewing data respecting the use, safety and efficacy of the drug for the condition being treated.



The SAP confirms with the manufacturer that the drug is manufactured according to GMP

SAP timelines

- Generally processed within 1-2 working days of receipt (longer if new drug or new indication)
  - Delays in issuing decisions are usually related to missing information from the practitioner (incomplete request) or missing information from the manufacturer
- Before authorizing a drug for the first time, Health Canada must contact the manufacturer and
  - Explain the Special Access Program
  - Confirm willingness to provide the drug
  - Seek information about the drug (i.e. confirm evidence of safety, efficacy and quality)
  - Obtain commitment to provide information to practitioner and inform us of new safety concerns

Reasons for denials

- Denials
  - Condition is not serious or life-threatening
  - Other drugs are available and have not been considered
  - Insufficient data to support the use of the drug for the treatment of the patient's condition
- Reconsideration process
  - Provides the practitioner with an opportunity to be heard when the SAP is considering issuing a Denial
  - Provides an opportunity to request an independent review following the issuance of a denial recommendation

Additional information

- Advertising of unauthorized drugs accessed through the SAP is prohibited.

- Health care professionals wishing to access psychedelic drugs for professional training purposes are not eligible for the SAP. However, clinical trials remain an option.

CDSA Subsection 56(1) class exemption for psilocybin and MDMA accessed through the SAP

- On January 5, 2022, a subsection 56(1) class exemption was issued for practitioners, agents, pharmacists, persons in charge of a hospital, hospital employees, and licensed dealers which allows them to conduct activities with psilocybin and MDMA when the sale of these substances has been authorized through the SAP.
  - https://www.canada.ca/en/health-canada/services/health-concerns/controlled-substances-precursor-chemicals/policy-regulations/policy-documents/subsection-56-1-class-exemption-conducting-activities-psilocybin-mdma-special-access-program-authorization.html
- This class exemption does not allow the following:
  - Shipping to a community pharmacy;
  - Possession or transport of the drug by the patient.

INDIVIDUAL CDSA SUBSECTION 56(1) EXEMPTIONS

Subsection 56(1) of the CDSA

"The Minister may, on any terms and conditions that the Minister considers necessary, exempt from the application of all or any of the provisions of this Act or the regulations any person or class of persons or any controlled substance or precursor or any class of either of them if, in the opinion of the Minister, the exemption is necessary for a medical or scientific purpose or is otherwise in the public interest."

Individual subsection 56(1) exemptions

- The Special Access Program and individual exemptions from the CDSA are not mechanisms to encourage the early use of unauthorized drugs, nor are they meant to be used as a means of circumventing clinical development or the established drug review and approval process.

- Clinical trials and the Special Access Program are existing regulatory options through which a legal source of psilocybin may be accessed. These pathways should generally be pursued instead of an individual exemption under the CDSA, unless it can be demonstrated that access to psilocybin is not possible or suitable through these existing legal routes.

Questions?

Clinical trials: oct.enquiries-requetes.bec@hc-sc.gc.ca

SAP: sapd-pasm@hc-sc.gc.ca

Exemptions from the CDSA: exemption@hc-sc.gc.ca

Dealer's licences: hc.cds-sdc.sc@canada.ca