



Health
Canada

Santé
Canada

Guidance Document

Special Access Program for Drugs: Guidance Document for Industry and Practitioners

| | |
|-----------------|------------|
| Date adopted: | 2020/09/30 |
| Effective date: | 2020/09/30 |
| Revised date: | 2022/04/11 |



Health Canada is responsible for helping Canadians maintain and improve their health. It ensures that high-quality health services are accessible, and works to reduce health risks.

Également disponible en français sous le titre :

Programme d'accès spécial aux médicaments : Ligne directrice à l'intention de l'industrie et des praticiens

To obtain additional information, please contact:

Health Canada

Address Locator 0900C2

Ottawa, ON K1A 0K9

Tel.: 613-957-2991

Toll free: 1-866-225-0709

Fax: 613-941-5366

TTY: 1-800-465-7735

E-mail: publications-publications@hc-sc.gc.ca

© Her Majesty the Queen in Right of Canada, as represented by the Minister of Health, 2022

Publication date: April 2022

This publication may be reproduced for personal or internal use only without permission provided the source is fully acknowledged.

Cat.: H164-303/2022E-1-PDF

ISBN: 978-0-660-42826-0

Pub.: 220002

Document change log

| Date | Change | Location (section, paragraph) | Nature of and/or reason for change |
|-----------------|--|-------------------------------|---|
| January 5, 2022 | The section on controlled substances has been updated. | Section 3.1.3 | This section was updated to reflect the regulatory amendments that restore the possibility of restricted drugs being requested through the SAP. |
| April 11, 2022 | The section on personalized service has been updated. | Section 3.2.4 | This section was updated to better reflect the scope of the personalized service. |

Foreword

Guidance documents are meant to provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent, and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document may be acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy, or quality of a therapeutic product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

Table of Contents

| | |
|---|----|
| 1. Introduction | 7 |
| 1.1 Purpose/overview | 7 |
| 1.2 Scope and application | 7 |
| 1.3 Policy objectives | 7 |
| 1.4 Policy statements | 8 |
| 1.5 Background..... | 9 |
| 2. Overview of the regulatory framework | 9 |
| 2.1 Section C.08.010: Practitioner requesting a drug | 10 |
| 2.1.1 Information to be submitted with new drug requests..... | 10 |
| 2.1.1(a) Information about the medical emergency: Patient(s) may be known or unknown at the time of request..... | 10 |
| 2.1.1(b) Information about the use, safety and efficacy of the drug | 11 |
| 2.1.1(c) Shipping address..... | 11 |
| 2.1.1(d) Other information the Minister may request | 11 |
| 2.2 Manufacturer to share new information | 11 |
| 2.3 Practitioner reporting requirements..... | 12 |
| 2.4 Manufacturer’s request to pre-position a drug in Canada | 12 |
| 2.4.1 Request for information | 13 |
| 2.4.2 Importer requirements for pre-positioning drugs on behalf of manufacturers | 13 |
| 2.4.3 Distribution of the pre-positioned drug to a practitioner by a Canadian importer | 14 |
| 2.5 Effect of a letter of authorization..... | 14 |
| 3. Guidance for implementation..... | 15 |
| 3.1 Drugs eligible for request through the Special Access Program | 15 |
| 3.1.1 Drugs that have received a negative decision to a drug submission filed with a regulatory agency | 15 |
| 3.1.2 Marketed drugs with compliance actions in Canada | 16 |
| 3.1.3 Drugs that contain a controlled substance..... | 16 |
| 3.1.4 Drug shortages and discontinued drugs | 17 |
| 3.2 Practitioners filing a drug request..... | 17 |
| 3.2.1 Special Access Request (SAR) form..... | 18 |

| | |
|---|----|
| 3.2.2 Filing a drug request | 18 |
| 3.2.2.1 Information that must be provided to support a request..... | 18 |
| 3.2.3 Submitting the request | 20 |
| 3.2.4 Personalized service for urgent life-threatening or end-of-life situations..... | 21 |
| 3.3 Practitioner obligations to report | 21 |
| 3.3.1 Adverse Drug Reaction Reporting..... | 21 |
| 3.3.2 Follow-up reporting | 22 |
| 3.4 Special Access Program | 22 |
| 3.4.1 Review of Special Access Request (SAR) and supporting information | 22 |
| 3.5 Issuance of an authorization | 23 |
| 3.5.1 Manufacturers’ responsibilities when receiving a Letter of Authorization..... | 24 |
| 4. Manufacturers filing a pre-positioning request..... | 24 |
| 4.1 Manufacturer filing a request for pre-positioning (Form D: Pre-positioning request)..... | 25 |
| 4.2 Review of the pre-positioning request and supporting information | 25 |
| 5. Sending request forms and reporting forms to Health Canada’s SAP | 26 |
| 6. Refusal to issue an authorization to a practitioner request | 26 |
| 6.1 Reconsideration review process | 27 |
| 6.1(i) Review of denial recommendation | 27 |
| 7. Amendments to a Letter of Authorization to sell a drug to a practitioner or to pre-position a drug in Canada | 27 |
| 8. Drugs authorized through the Special Access Program that receive market authorization in Canada | 28 |
| 9. Hours of operation..... | 29 |
| 10. Return of unused stock..... | 29 |
| 11. Advertising | 29 |
| Appendix A: Glossary | 30 |

1. Introduction

1.1 Purpose/overview

Health Canada's Special Access Program for drugs (SAP) enables drugs that are not marketed in Canada to be requested by practitioners for the treatment, diagnosis, or prevention of serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable. Non-marketed drugs may be unauthorized if they have not been approved by Health Canada. This means they have not been assessed for safety, effectiveness and quality. It may also mean that the sale of the drug has not commenced in Canada, or the product has been discontinued or removed from the market due to regulatory actions under the *Food and Drug Regulations* (https://laws-lois.justice.gc.ca/eng/regulations/c.r.c.,_c._870/index.html) (FDR).

The SAP administers the sale¹ of these drugs for “emergency treatment” under Part C Division 8 of the FDR. An authorization for the sale of drugs that are not available on the Canadian market is based on sufficient evidence supporting the requested use and the drug information available to the SAP at the time of the request.

This guidance document explains the regulatory information requirements and conditions to be met when requesting a drug. It is intended to assist practitioners and manufacturers who use the SAP.

1.2 Scope and application

This guidance document explains the mandate, intent and scope of the SAP including:

- the process to request a drug for a medical emergency that cannot otherwise be sold or distributed in Canada
- the responsibilities of practitioners and manufacturers
- the reconsideration process
- the personalized service for urgent life-threatening or end-of-life situations
- the process and conditions to be met by manufacturers who request to pre-position a drug

For the purpose of this guidance document, "drug" includes pharmaceuticals, biologics, radiopharmaceuticals, and natural health products². It excludes medical devices³, veterinary drugs⁴ and active pharmaceutical ingredients⁵ (APIs). While the term “treatment” refers throughout the document to how the drug is used, it is defined to also include the use of a drug to diagnose, or prevent a serious or life-threatening condition in a patient.

1.3 Policy objectives

To ensure requests for special access to unauthorized drugs are managed in accordance with Part C, Division 8, sections C.08.010 and C.08.011 of the FDR.

1.4 Policy statements

Health Canada is authorized under the *Food and Drugs Act* (FDA) (<https://laws-lois.justice.gc.ca/eng/acts/f-27/>) to regulate the safety, efficacy and quality of therapeutic products, including drugs (pharmaceuticals, biologics and radiopharmaceuticals), natural health products and medical devices. Prior to market authorization of a drug, access is usually limited to clinical trials sponsored by a manufacturer or research organization, and authorized by Health Canada through a clinical trial application. Health Canada also authorizes clinical trial applications for as few as one patient enrollment. Clinical trials ensure that the best interests of patients are protected and that a product is administered in accordance with national and international ethical, medical, and scientific standards. In certain situations when a drug is not available through enrollment in a clinical trial, Health Canada may allow an exemption from the FDA and the FDR to permit the sale of an unauthorized drug for a medical emergency.

Special access by Canadian health practitioners to unauthorized drugs is for serious or life-threatening conditions where conventional therapies have failed, are unsuitable, or are unavailable either as marketed products, or through enrollment in clinical trials. In situations where there is a public health emergency, other regulatory mechanisms allow access to unauthorized drugs such as the *List of Drugs for an Urgent Public Health Need*, or the issuance of Interim Orders by the Minister of Health. Emergency access should be exceptional and where possible, open label or compassionate access trials should be incorporated into drug development plans to meet the needs of patients not eligible for enrollment in other pivotal trials.

The regulatory authority supporting the SAP is discretionary. A decision to authorize or deny a request is made on a case-by-case basis by taking into consideration the nature of the medical emergency, the availability of marketed alternatives and the information provided in support of the request regarding the use, safety and efficacy of the drug. If an authorization is granted, the practitioner agrees to report on the use of the drug including any observed adverse drug reactions and, when requested, must account for all quantities received.

The SAP is not a mechanism to encourage the early use of drugs nor is it a means of circumventing drug clinical development or the regulatory review of a submission for marketing. Access to any drug through the SAP should be limited in duration and quantity to meet emergency needs only. In the event that a drug submission is under regulatory review, access will be limited until that review is complete and the drug is marketed.

Drugs accessed through the SAP do not undergo the scrutiny of a benefit-risk assessment that is part of the regulatory framework for a new drug submission or a clinical trial application. These drugs are exempt from the *Food and Drugs Act* and its regulations. The decisions to authorize a drug through the SAP are based on a practitioner's rationale about the use of the drug for the medical emergency and how it would benefit their patient based on the patient's clinical history. Accordingly, an authorization through the SAP does not constitute an opinion that a drug is safe, efficacious or of high quality. A manufacturer is under no obligation to sell an unauthorized drug through the SAP and Health Canada cannot compel a manufacturer to do so.

1.5 Background

Prior to selling a drug on the Canadian market, a manufacturer is required to submit information on a drug's safety, efficacy and quality and to comply with the provisions of the FDA and the FDR, including obtaining market authorization from Health Canada. The FDR require drug manufacturers to submit substantial evidence of a new drug's clinical efficacy and safety for the purpose and recommended conditions of use. This type of evidence can only be obtained through the conduct of clinical trials in humans. As the development of a drug and its market authorization can take a number of years, it may be many years before a drug is available to patients. Therefore, a regulatory mechanism that allows drugs to be available for medical emergencies when the drug is not available in Canada and other therapeutic options have been exhausted is needed.

2. Overview of the regulatory framework

Under the FDR, provisions regarding the sale of a new drug for a medical emergency (Sections C.08.010 and C.08.011), provide the Minister with discretionary authority to issue a letter of authorization that:

- (i) allows the sale of a quantity of a new drug, that is otherwise unauthorized for sale in Canada, to the practitioner named in the letter of authorization for use in the emergency treatment of a patient (or patients) under his/her care, or unknown at the time of the request
- (ii) allows the sale of a quantity of drug that on at least one occasion has been previously authorized by the SAP and is approved for the same requested use by the United States Food and Drug Administration or the European Medicines Agency
- (iii) allows a manufacturer to pre-position a drug in Canada that can only be sold if Health Canada receives and authorizes a request from a practitioner for that drug

As per the regulations, drugs requested under these provisions must be non-marketed drugs in Canada. An overview of the types of drugs that are eligible for requests through the Program and the criteria the SAP uses when considering such requests is provided in section 3.1 "Drugs eligible for request through the SAP" of this guidance.

The Regulations do not expressly define the term "medical emergency". However, Health Canada has interpreted this term as "serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable in Canada".

"Conventional therapies" are widely accepted treatments that are used by most health care professionals or, well supported by substantial medical evidence and are considered standard-of-care in the medical profession.

"Unavailable" is defined as a conventional therapy that is not marketed in Canada or not accessible due to a shortage or the discontinuation of the therapy from the Canadian market. Cost is not a consideration in the SAP's decision-making matrix and does not fall within the Program's interpretation of "unavailable". Drug funding and reimbursement decisions are exclusively within the jurisdiction of the federal, provincial and territorial public drug plan and private insurance providers.

In determining what is a serious or life-threatening condition in a patient, several factors are considered. Such factors include but are not limited to:

- the need for hospitalization or in-patient admission/care
- the risk of adverse pregnancy outcome
- the risk of persistent or significant disability in the absence of treatment
- the prognosis of the condition

2.1 Section C.08.010: Practitioner requesting a drug

Under sections C.08.010(1) of the regulations, the Minister may issue a letter of authorization allowing a manufacturer to sell a drug to a requesting practitioner to treat one, or several patients in a medical emergency.

The Minister's authority to issue a letter of authorization is discretionary. This means the Minister may authorize or deny access to a drug based on the information supplied by the practitioner and other information that the Program may have in its possession. This discretion is carefully exercised by considering all information provided, the nature of the medical emergency, and the extent to which the information submitted in support of the request is credible and relevant to the specified medical emergency.

Practitioners filing a request must be entitled under the laws of a province to treat patients with a prescription drug, and must be practicing their profession in that province as per the definition of practitioner in Part C of the FDR, Division 1, section C.01.001. That is, "a practitioner is a person who (a) is entitled under the laws of a province to treat patients with a prescription drug, and (b) is practising their profession in that province".

2.1.1 Information to be submitted with new drug requests

Subsection C.08.010(1)(a) requires a practitioner to submit information and details about the medical emergency. This includes information the practitioner has, with respect to the use, safety and efficacy of the drug, which supports the decision to prescribe the drug and the civic address to which the drug is to be shipped. It can also include any additional information the Minister may request in respect of the medical emergency, or the safety and efficacy of the new drug in relation to the medical emergency.

2.1.1(a) Information about the medical emergency: Patient(s) may be known or unknown at the time of request

The practitioner must provide sufficient information on the condition of the patient to justify that the condition is serious or life-threatening. The practitioner must also identify what treatments have been considered or tried and describe how they have either failed, are unsuitable for the patient or unavailable on the market.

In cases where the patient is unknown at the time of the request, the practitioner must provide a rationale as to why the drug is needed in anticipation of a medical emergency for the treatment of a specified condition or disease.

2.1.1(b) Information about the use, safety and efficacy of the drug

To support a request, the practitioner must provide information on the use, safety and efficacy of the drug being requested. This may include but is not limited to data/references and/or resources in the practitioner's possession that support the decision to prescribe the drug e.g., articles from medical literature, treatment guidelines, investigator brochures, foreign prescribing information, etc.

If the drug has been previously authorized by the Program, a practitioner is not required to submit information about the use, safety and efficacy of the drug for the specified emergency if the following conditions are met:

- the European Medicines Agency or the United States Food and Drug Administration has authorized the drug to be sold without terms or conditions in its jurisdiction for the same use for which the drug is requested, and
- the Minister has not cancelled the drug identification number of a Canadian drug as a result of a manufacturer failing to provide Health Canada with sufficient evidence regarding the safety and efficacy of the drug for its recommended use, or a manufacturer failing to comply with an order issued by the Minister (as per paragraphs C.01.014.6(2)(b) or (c) or subsection C.01.014.6(3))

2.1.1(c) Shipping address

Practitioners must specify where the drug is to be shipped, for example: a practitioner's office, a hospital pharmacy, a nuclear medicine department, a blood bank or a community pharmacy. Practitioners must include the name and the civic address of the facility to which the drug will be shipped and the person responsible for receiving the shipment. The person who receives the drug for distribution or administration to a patient, must be a practitioner or a pharmacist (subsection C.08.010(1)(c)).

The requirement for a Drug Establishment Licence (DEL) does not apply to practitioners receiving the drug directly. A DEL is only required for facilities that are importing and subsequently storing drugs for a foreign manufacturer who requests to pre-position a drug in Canada. It is not required for practitioner offices, hospital or community pharmacies, nuclear medicine departments or blood banks that are receiving a shipment of drug for use.

2.1.1(d) Other information the Minister may request

Access to a drug under the medical emergency provisions of the FDR takes into account not only information about the drug, but also the individual health status of the patient. When the information submitted to support the request for a drug is not sufficient to allow the Minister to make a final decision regarding the issuance of an authorization, the Minister may request additional information.

2.2 Manufacturer to share new information

Manufacturers are expected to ensure that significant new information respecting the safety, efficacy and quality of drugs released under the SAP is made available to practitioners and the Program as soon as it is known. This information should be vetted through the SAP prior to communication with practitioners.

2.3 Practitioner reporting requirements

As per subsection C.08.010(1)(b), the practitioner must:

- (i) provide a report to the manufacturer of the new drug and to the Minister containing the results obtained following the use of the drug including information respecting any adverse drug reactions observed by the practitioner, and
- (ii) account to the Minister, on request, for all quantities of the new drug received

The practitioner who requested the drug is responsible to account for the quantity of drug received. For drugs shipped to a community pharmacy, or a location other than the practitioner's office, the requesting practitioner remains responsible to account for the quantity received.

2.4 Manufacturer's request to pre-position a drug in Canada

Subsection C.08.011.1(1) provides the Minister with the authority to allow a drug from a foreign manufacturer to be imported into Canada for pre-positioning purposes, in advance of a SAP authorization allowing a manufacturer to sell to a requesting practitioner.

To request permission to pre-position a drug, a manufacturer must provide information concerning the labelled indications of the drug and a rationale as to why the product needs to be pre-positioned in Canada, for instance, an explanation describing the importance of timely access and administration, which might be otherwise delayed if the drug were to be shipped from a foreign jurisdiction.

The manufacturer must identify the Canadian importer who will pre-position the drug in a Canadian facility. The Canadian importer must hold a Drug Establishment Licence (DEL) in Canada. As per subsection C.08.011.1(1)(b), the DEL enables the holder of the licence to import the drug for the purpose of pre-positioning as long as it falls within the same category identified on the licence.

The civic address of the facility where the drug is to be stored in Canada must be provided, and any other information the Minister may request to determine whether to issue an authorization.

The Minister may refuse to issue an authorization if the manufacturer has not met all requirements. Examples of this include when:

- the quantity of drug requested to be pre-positioned exceeds the amount that is likely required to address potential medical emergencies
- the drug to be pre-positioned does not fall within the same category as that on the importer's DEL
- the manufacturer has not supplied information the Minister requested under subsection C.08.011.1(a)(v), or
- the information provided in response to a request by the Minister regarding the medical emergency, or the safety and efficacy of the drug in relation to the medical emergency does not support the issuance of an authorization to pre-position the drug

2.4.1 Request for information

As per subsection C.08.011.1(1)(a)(v), the Minister may require a manufacturer who is requesting to pre-position a drug in Canada, to provide Health Canada with any other information that would help the Minister to determine whether to issue the letter of authorization. This information request may include information that was submitted to a foreign regulatory authority for monitoring the safety, efficacy or quality of the drug.

2.4.2 Importer requirements for pre-positioning drugs on behalf of manufacturers

Manufacturers wishing to pre-position drugs intended for medical emergencies must identify a Canadian importer who is the holder of a DEL to import the SAP drug. To do so, the SAP drug to be imported must fall within a category of drug that is identified on the importer's DEL for the activity to import. DEL holders who import SAP drugs for medical emergencies on behalf of foreign manufacturers that have received authorization to pre-position, are conducting such activities as part of their regular business.

A DEL should not be requested solely for the purposes of importing a SAP drug.

For the purposes of pre-positioning a drug under the SAP, the DEL holder does not require the following:

- the importer is not required to have the relevant foreign buildings listed on either its DEL's foreign building annex or active pharmaceutical ingredient annex
- the importer is not required to hold a DEL authorizing the specific dosage form class of the drug

Subsection C.08.011.2(2) lists the relevant sections of Divisions 2 to 4 that apply to the importation of a SAP drug as it relates to storage and distribution under the pre-positioning provisions of the regulations:

- (a) sections C.02.003.1 and C.02.004 which require that the drug be stored and kept in sanitary conditions by the licensee to preserve the integrity of the product and avoid contamination of the drug
- (b) section C.02.006 which requires the drug be stored under the supervision of personnel who, having regard to the duties and responsibilities involved, have had technical, academic and other training as the Minister considers satisfactory in the interests of the health of the consumer or purchaser
- (c) subsection C.02.012(1) which requires the importer to maintain a system of control that permits complete and rapid recall of any lot or batch of the drug that is distributed; and a program of self-inspection
- (d) sections C.02.013 and C.02.014 which require quality control and specific measures regarding quality control
 - quality control for pre-positioned drugs ensures the appropriate handling and distribution of the drug to practitioners
- (e) section C.02.015 which requires proper storage and transportation procedures and investigation of complaints

- (f) subsection C.02.021(1) as it applies to the storage of the new drug by the holder of a DEL, for instance, maintaining all records and evidence of the storage of the drug in dosage form that are required to be maintained for a period of one year after the expiration date of the drug unless the person's DEL specifies some other period
- (g) subsection C.02.022(1) which requires record retention of sales of each lot or batch of the drug, for one year after the expiration date of that lot or batch unless their DEL specifies some other period to enable recall measures
 - for pre-positioned drugs, the number of drugs received and distributed must be accounted for
 - this number must be the same quantity as stated in the Letter of Authorization
 - this includes record keeping of where and to whom the drug was distributed
- (h) section C.02.023 states what is required when dealing with a complaint including retaining records of results of any investigations, contact information, and record retention for a period of one year after the expiration date of the lot or batch of the drug
- (i) subsections C.02.024(1) which requires record retention of the results of the self-inspection programs for a period of three years
 - self-inspection programs are to include drugs pre-positioned under the SAP to ensure they are stored and distributed according to letters of authorization issued to manufacturers authorizing the sale of the drug to practitioners
- (j) section C.03.013 prohibits importation of a drug that is derived from animal tissue unless the tissue is obtained from a healthy animal free from infectious disease, and
- (k) section C.04.001.1 as it applies to the storage of the new drug by the holder of a DEL, for instance, prohibits the distribution of a drug unless it has been stored according to the Division

2.4.3 Distribution of the pre-positioned drug to a practitioner by a Canadian importer

As per subsection C.08.011.3(1), new drugs that have been pre-positioned can only be distributed to a practitioner by the importer once the foreign manufacturer of the drug has received a letter of authorization from the Minister that permits the sale of a quantity of the drug to a named practitioner under section C.08.010(1). The Letter of Authorization specifies the name and civic address of the person to whom the drug may be shipped. The quantity of drug distributed cannot exceed the quantity specified in the Letter of Authorization.

2.5 Effect of a letter of authorization

Under the regulations, there are two separate letters of authorization:

- (i) a letter of authorization to a manufacturer to allow the sale of a specified quantity of drug to a practitioner for use in a medical emergency
- (ii) a letter of authorization to a manufacturer to allow the import of a specified quantity of drug for pre-positioning purposes, by a Canadian DEL holder

The sale of the quantity of drug identified in either authorization is exempt from the *Food and Drugs Act* (FDA) and the *Food and Drug Regulations* (FDR). Drugs can only be distributed and/or sold for the use stated in the authorization. Advertisement of drugs authorized under these provisions is prohibited as per section C.08.002 of the FDRs and section 3 of the FDA.

Under the Letter of Authorization to a manufacturer that allows the sale of a specified quantity of drug to a practitioner for use in a medical emergency, practitioners, who are in possession of stock that has expired, cannot use the expired product. To replenish expired stock, practitioners must submit a new request to the SAP.

For the Letter of Authorization that allows the importation of a specified quantity of drug for pre-positioning purposes, by a Canadian DEL holder, the pre-positioned drug may expire before an authorization for a manufacturer to sell to a practitioner is issued. Should this happen, the authorization to pre-position is no longer valid and the drug cannot be distributed. Manufacturers wishing to replenish expired pre-positioned products must submit a new request.

3. Guidance for implementation

3.1 Drugs eligible for request through the Special Access Program

Drugs for sale through the SAP are not authorized for sale to the general Canadian public. The majority have not undergone regulatory review in Canada as marketed drugs.

Practitioners who wish to use drugs approved for sale on the Canadian market for an indication that is different from the approved indication(s) do not need to file a SAP request to do so.

The SAP will consider requests for drugs that had a market authorization in Canada at one time and were discontinued from the market and drugs that were reviewed by Health Canada but never received a market authorization. The Program will also consider requests for drugs that are under regulatory review such as in a clinical trials, or under review for a market authorization in Canada. Once a drug accessed through the SAP receives marketing authorization, it may continue to be accessed through the program for a short period of time in order to allow the manufacturer to launch the drug on the Canadian market.

3.1.1 Drugs that have received a negative decision to a drug submission filed with a regulatory agency

The SAP will consider requests for drugs that received a negative decision in another regulatory jurisdiction or following the review of a drug submission filed with Health Canada (i.e., Notice of Deficiency-Withdrawal (NOD/W), or Notice of Non-Compliance-Withdrawal (NON/W)). In addition to determining that the patient will not be at undue risk, the SAP will:

- verify that the manufacturer agrees to disclose the concerns raised by the relevant regulator to the requesting practitioner(s)
- have the manufacturer draft a letter to requesting practitioners that includes the concerns that prompted the negative decision
- have the relevant review bureau at Health Canada verify that the concerns regarding the negative decision issued for a Canadian drug submission are well described

These steps ensure that requesting practitioners and their patients are aware of all relevant information respecting the drug and its use.

3.1.2 Marketed drugs with compliance actions in Canada

The SAP will consider authorizing access to drugs that were subject to compliance actions such as the cancellation or suspension of a license or market authorization, provided that:

- the drug is considered to be medically necessary for the treatment, diagnosis or prevention of a serious or life-threatening condition
- the manufacturer is willing to disclose to the SAP and the practitioner the reasons for regulatory action
- there are no other dosage forms of the drug on the market that would be considered a reasonable alternative
- there are no other drugs or therapies that would be considered reasonable alternatives
- a clinical trial is inappropriate for gathering new or confirmatory evidence of the safety and efficacy of the drug

3.1.3 Drugs that contain a controlled substance

The *Controlled Drugs and Substances Act* (CDSA) (<https://laws-lois.justice.gc.ca/eng/acts/c-38.8/>) is the federal statute that provides a framework for the control of substances that can alter mental processes and may produce harm to health or society when diverted to an illegal market or misused. All controlled substances are listed in Schedules I – V of the CDSA. Health care practitioners may request access to controlled substances (including restricted drugs), through the Special Access Program, for the purposes of the emergency treatment of patients with a serious or life-threatening condition when other therapies have failed, are unsuitable or are not available in Canada, and where there is sufficient evidence of safety and efficacy for the treatment of the patient's condition. Such requests will be assessed on a case-by-case basis, as with any other request to the SAP. Note that controlled substances are drugs that are subject to both the CDSA and the FDA.

Restricted drugs are a category of controlled substances listed in Schedule J of the FDR and are controlled under the CDSA, meaning activities such as the sale, possession, production, etc. of these substances are illegal unless authorized. If a restricted drug is authorized for sale through the SAP, an exemption under subsection 56(1) of the CDSA is needed to allow parties to legally conduct activities (e.g. possession, transport, etc.) with the restricted drug. A class exemption (<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>) has been issued to cover some types of potential SAP authorizations for restricted drugs, thereby avoiding the need for individual exemptions; however, it is important to note that the class exemption does not guarantee that a request will be authorized through the SAP as all requests are assessed on a case-by-case basis. If a SAP authorization for a restricted drug is granted and it is covered by the class exemption, anyone conducting activities in relation to the authorization must adhere to the terms and conditions set out in the class exemption (e.g., record keeping and security). Please note that the class exemption does not allow patients to possess or transport restricted drugs, which means that it has to be used in the presence of the practitioner or the health care professional to whom the practitioner has delegated this

activity. If a SAP authorization for a restricted drug is not covered by the class exemption, an individual exemption (<https://www.canada.ca/en/health-canada/services/health-concerns/controlled-substances-precursor-chemicals/exemptions.html>) will be required. If the manufacturer of the restricted drug is located in Canada, they must be a licensed dealer under the CDSA and the restricted drug must be listed on their licence. If the drug is coming from outside of Canada, the restricted drug must be imported by a licensed dealer who has the restricted drug listed on their licence and has obtained an import permit from Health Canada.

Anyone implicated in a SAP authorization for a controlled substance that is not a restricted drug, (a narcotic, targeted substance, or controlled drug) is not subject to the class exemption but is subject to the requirements of the relevant regulations under the CDSA, namely the *Narcotic Control Regulations*, the *Benzodiazepines and Other Targeted Substances Regulations*, or Part G of the FDR.

3.1.4 Drug shortages and discontinued drugs

In circumstances where a drug is in short supply or discontinued from the market, the SAP will consider requests on a case-by-case basis for an alternative to an otherwise marketed drug to address a medical emergency. The decision to use the SAP to manage a drug shortage is a coordinated process between Health Canada and the provincial and territorial stakeholders, led by Health Canada's Regulatory Operations and Enforcement Branch (ROEB) where a foreign manufacturer may be available for drug provision.

When considering requests for an alternative to a marketed drug the Program takes into account the following:

- the drug is necessary to treat, mitigate, or diagnose a serious or life-threatening condition in a patient(s), or to prevent such conditions
- the manufacturer is willing to disclose the reasons for the drug shortage or discontinuance if this information is not available on the Drug Shortages Canada website
- there are no other dosage forms of the drug on the market that would be considered a reasonable alternative
- there are no other drugs or therapies that would be considered reasonable alternatives

In addition, the SAP considers the following factors:

- the manufacturer demonstrates that extraordinary efforts have been made to avoid and manage the shortage such as inventory control, rationing, etc.,
- other options to manage the shortage have been ruled out
- the scope of the shortage is operationally manageable by the SAP

3.2 Practitioners filing a drug request

A practitioner (or their delegate) may file a request for an individual patient, for multiple patients with the same serious or life-threatening condition, or for future patient(s) in anticipation of a medical emergency (for example, a drug needed in the emergency room for a patient that is unknown at the time of the request). Practitioners are not required to have a Drug Establishment License (DEL) to request a drug for a medical emergency.

To request a drug through the SAP, practitioners must gather the required information described in section 3.2.2.1 “Information that must be provided to support a request” and must complete the appropriate forms.

3.2.1 Special Access Request (SAR) form

The Special Access Request (SAR): Form A, is used to request access to a drug for immediate use for one or multiple patient(s).

The SAR for Future Use: Form B is used to request access to a drug that is required on-site within a facility, in anticipation of patients presenting with a medical emergency.

Form A or B can also be used to request drugs that have been previously authorized by the Program for a specific patient, or an unknown patient(s). Repeat requests for the same use do not require the submission of safety, efficacy and use data.

3.2.2 Filing a drug request

Prior to filing a request, practitioners are encouraged to contact individual manufacturers to confirm the availability of the drug and to obtain the most recent drug information such as prescribing information and other data that supports the use of the drug.

In deciding to request a drug through the SAP, the practitioner assumes the liability and responsibility for the use of that drug.

3.2.2.1 Information that must be provided to support a request

Drug details

The requester must provide the following:

- name of the drug and information concerning the medical emergency for which the drug is required
- the most recent information available (e.g. data, references, resources) in the practitioner’s possession that support the decision to prescribe the drug
- information from sources such as medical literature, clinical protocols, investigator brochures, foreign prescribing information, etc.
- a complete citation including journal and article titles, author(s), volume, issue, date, and page information, or a copy of the reference

Should information on the use, safety and efficacy of the drug change, the Minister may ask the practitioner to provide additional information. Failure to provide that information could lead to issuance of a denial.

For repeat requests for the same use, the practitioner does not need to provide drug information and references regarding its use, safety and effectiveness.

Information on the drug details is not needed to support requests if the drug has previously been determined by the SAP as being suitable for authorization for the same clinical circumstances **and** the drug has been authorized by the European Medicines Agency (EMA) or the United States Food and Drug Administration (US FDA) to be sold in those jurisdictions

without terms or conditions for the same indication as the one being requested for the medical emergency in Canada. However, information on the use, safety and efficacy of the drug may change due to the drug's safety profile changing, regulatory actions taken by the EMA or the US FDA, or the addition of certain conditions or restrictions regarding the use of the drug. In such cases, the practitioner making the request would be required to provide the necessary information regarding the safety, efficacy, and quality of the drug for the medical emergency.

Patient details

New patient to the Special Access Program

If the request is for a new patient, the requester must provide the following information:

- specific information about the patient(s)'s medical history;
- therapies that have been considered, ruled out and/or have failed or that are unsuitable and/or unavailable to achieve an adequate response for the specific patient(s)
- why the requested drug is the best choice for the patient(s) (e.g. mechanism of action, drug class, dosage form).

Each rationale should be patient specific based on their medical condition and history.

Repeat request for same patient

When the request relates to the same patient for the same medical emergency, only a patient update is required. The practitioner must:

- provide information on the patient(s)'s condition since treatment was initiated;
- describe the patient(s)'s response to the drug relative to the initial treatment goal(s),
- provide a rationale for requesting continued access
- attest that there have been no changes to the information about the drug or the patient(s)'s medical history provided in the previous request
 - if there is a change in the patient(s)' medical condition, the practitioner must update the patient(s)' current medical state by providing a full description

Future use requests for anticipated medical emergencies

There are circumstances where certain non-marketed drugs need to be available on-site at a Canadian institution or organization in anticipation of an emergency when the shipping time from a manufacturer would compromise timely medical care for patients. This includes drugs that might need to be readily available at hospital emergency departments, zoos, workplaces where hazardous materials are handled and with first responders (for example, fire and police departments and paramedic services).

The SAP considers future use requests where practitioners:

- include a clinical rationale as to why the drug is required on-site in advance of a medical emergency
- explain the conditions and clinical circumstances under which the drug will be used

Quantity of drug requested

The quantity of drug requested must always be specified. The following information must also be provided:

- the precise number of tablets, vials, etc. for each patient
- the total quantity, for instance, the sum of the quantities for all patients; and
- for future use requests, the anticipated need for X # patients or # months

If the amount of drug required is not clearly stated, the request will be returned seeking clarification. The quantity of drug authorized will depend on the nature of the medical emergency and the patient(s)'s medical condition(s). The quantity of the drug in the Letter of Authorization must be the same as the quantity being shipped. If the quantity in the bottle being shipped is different than the quantity needed, this must be specified in the request form so that it can be included in the Letter of Authorization.

Shipping information

The civic address where the drug will be shipped is to be provided (for example, hospital pharmacy, practitioner's office, nuclear medicine department, blood bank or community pharmacy).

If the SAP authorized the drug to be shipped to a location that is not the practitioner's office, the practitioner must ensure that he/she will be informed of the quantity that was received in the shipment.

Transfer a drug to another patient

Practitioners wishing to transfer the supply of drug to another patient must receive authorization from the SAP prior to treatment. The practitioner must complete Section E of Form A.

The practitioner must reference the request number of the initial request (original patient) and indicate to whom and where the supply is being transferred. The amount being transferred will need to be specified in the quantity section and information provided to support the transfer of the drug for use in another patient(s). Consideration/authorization by the SAP and the manufacturer is required prior to transferring the drug to start treatment.

3.2.3 Submitting the request

Practitioners submitting forms should refer to section 5 "Sending request forms and reporting forms to Health Canada's SAP" of this guidance for contact information. Requests must be legible, signed and dated by the practitioner.

Upon receipt of a request by the SAP, the information is screened to ensure that it is complete.

The SAP assesses the information that has been submitted to support the need for a drug to be used in a medical emergency for a patient or multiple patients. When the data submitted is not sufficient to allow the SAP to make a final decision regarding the issuance of an authorization, the Program may request additional information. A decision will be made to deny or authorize the request once all information has been provided.

Most requests are processed within one working day of receipt. However, given the mandate of the Program and the potential volume of requests received, requests are triaged to ensure that more urgent matters are given priority, e.g., requests for blood products and certain antibiotics.

3.2.4 Personalized service for urgent life-threatening or end-of-life situations

The Special Access Program provides personalized assistance and support for practitioners treating patients who are in an urgent life-threatening or end of life situations due to an emergency, critical or terminal illness. The service is available during and after business hours.

It is important to note that manufacturers still have the final decision on whether the drug will be supplied to the physician and whether any restrictions or conditions will be imposed on the release of the drug. A manufacturer is under no obligation to sell an unauthorized drug through the SAP and Health Canada cannot compel a manufacturer to do so.

3.3 Practitioner obligations to report

Practitioners initiating requests on behalf of their patients are responsible to ensure the patients are informed of the possible risks and benefits of the drug being requested and its development status. Manufacturers of drugs authorized by the SAP are not regulated under the Food and Drugs Act and its Regulations as is the case for Canadian marketed products. Because of this, practitioners requesting drugs through the SAP are responsible to monitor their patients and the outcomes of the use of the drug. Practitioners must report, to the manufacturer and to Health Canada, the outcome experienced by the patient using the drug and any observed adverse drug reactions (ADRs).

3.3.1 Adverse Drug Reaction Reporting

Practitioners are required to report any adverse drug reactions experienced with a SAP drug. For the purposes of a SAP drug, the definition of adverse drug reaction is the same as the one for clinical trials. That is, adverse drug reaction is defined in section C.05.001 of the *Food and Drug Regulations* as any noxious and unintended response to a drug that is caused by the administration of any dose of the drug. The adverse drug reaction is to be reported when its nature, severity or frequency is not consistent with the terms or description used in the product labelling, the Investigator's Brochure and/or in the foreign prescribing information. The SAP has adopted the International Conference of Harmonization (ICH) guidelines⁶ for ADR reporting in regards to what is to be reported and the associated timeframes.

The practitioner shall inform the SAP of any serious and unexpected adverse drug reactions within 15 days after becoming aware of the information. If the reaction is fatal or life threatening, the practitioner should report such adverse reactions within seven days after becoming aware of the information. ADRs are to be reported using the Council for International Organizations of Medical Sciences (CIOMS) forms (<https://cioms.ch/cioms-i-form/>) and should be sent through Canada Vigilance.

The regulations require practitioners to provide a report to the manufacturer of the drug and to Health Canada. Since manufacturers are not marketing their drug in Canada, providing adverse drug reaction reports to the manufacturer allows the manufacturer to track and add this information to their surveillance databases and systems.

3.3.2 Follow-up reporting

Reporting on the use of the drug should be on a patient-by-patient basis. Information to be provided includes how the patient responded to treatment with the drug, and whether or not the patient experienced any serious and/or unexpected adverse reactions.

Practitioners, who want to continue to treat their patient with the drug, must provide a follow-up report on the outcome of the use of the drug prior to requesting more using Form A. Section E of Form A is to be completed by the practitioner for repeat patients. The practitioner is to provide a follow-up on the patient(s)'s clinical status and outcome with the use of the drug. The practitioner must provide the patient's response to the drug relative to the initial treatment goals when submitting subsequent requests.

Form C is to be used for follow up reporting when a drug was requested for a patient only once, that is when no subsequent requests will be submitted for the same patient, on the same drug.

3.4 Special Access Program

3.4.1 Review of Special Access Request (SAR) and supporting information

In deciding whether to issue an authorization, the SAP considers if the data supporting the request is credible and supportive of the need for the drug for the identified emergency.

The SAP assesses requests from practitioners on a case-by-case basis. When assessing the information provided, the Program may request additional information from the practitioner to allow appropriate consideration of the request. For example, additional information on the patient's condition may be needed to confirm whether the condition is serious.

The SAP may further consult with expert reviewers within Health Canada to seek additional information. The Program also confirms there are no marketed alternatives in Canada, there are no clinical trials in Canada for which a patient might be eligible to enroll and, as needed, the Canadian and international development and regulatory status of the drug.

The Program undertakes the following risk management activities when considering requests:

- emphasizing that marketed alternatives should always be considered and/or tried before considering the use of unauthorized drugs
- recommending alternative mechanisms, such as clinical trials, to provide emergency access to unauthorized drugs
- encouraging the exchange of information about drugs released through the SAP between manufacturers, practitioners and the SAP
- reviewing documentation supporting emergency use of an unauthorized drug prior to its first release through the SAP
- working with the manufacturer to gather and document information about a drug, its development and regulatory status as part of their commitment to supply the drug, and in turn ensuring practitioners have access to current and relevant information respecting a drug available through the Program

Each request represents a unique set of circumstances and is supported to varying degrees by information provided by the practitioner. In addition to the SAP's overarching risk management activities, the Program takes into account and balances the following factors to ensure that a medical emergency exists and there is credible data to support the request:

- seriousness of the condition: description of the condition for which the drug is requested and why it represents a medical emergency
- clinical status of patient: description of current clinical status of the patient, including prognosis
- other therapies tried and/or ruled out: summary of marketed therapies that have failed, have been considered and ruled out, or are unavailable
- prior patient experience with the drug: summary of a patient's past experience with the drug, including evidence of efficacy and adverse drug reactions
 - references must be provided with the most recent information (no later than 10 years) that is relevant to the medical emergency ranging from:
 - prescribing information/package insert from the jurisdiction where the drug may be marketed
 - references to data from the literature outlining the results of clinical trials
 - references to treatment recommendations or guidelines published by expert or responsible health authorities
- case series and individual case reports from the literature
 - other data the SAP may require includes any additional information in respect of the medical emergency or the safety and efficacy of the drug in relation to that medical emergency
- data available to the SAP
 - medical literature, treatment guidelines, investigator's brochures, information obtained from the manufacturer, clinical trial reports, etc.
 - consultations with expert reviewers within Health Canada
 - consultation with Canadian and or international experts
 - confirmation of the Canadian and international development /regulatory status of the drug
- availability of clinical trials to determine if enrollment in clinical trials is an option for an individual patient

3.5 Issuance of an authorization

Following consideration of the Special Access Request Form (SAR), the SAP will either authorize or deny the request. If the Program is satisfied with the information submitted by the practitioner a letter of authorization will be issued to the manufacturer of the drug. The authorization allows the sale of a quantity of the requested drug to the named practitioner. For requests submitted by a manufacturer for pre-positioning, the authorization allows the importation of the drug for pre-positioning purposes only. Manufacturers may impose conditions on the use of the drug with the SAP prior to the issuance of the authorization to sell to a practitioner and/or pre-positioning.

The letter of authorization allowing the sale of a quantity of drug to a practitioner is sent electronically to the manufacturer with a copy to the practitioner, or via fax for requests received in paper format.

3.5.1 Manufacturers' responsibilities when receiving a Letter of Authorization

Manufacturers receiving a Letter of Authorization are allowed to sell the identified quantity of drug for the specified use indicated in the authorization. Shipping arrangements are made directly with the practitioner or institution named in the Letter of Authorization.

A decision to charge for a requested drug authorized by the SAP rests with the manufacturer. Manufacturers are responsible for determining price, if any, and may consult the Patented Medicines and Pricing Review Board (PMPRB) in this regard if necessary.

Foreign manufacturers are responsible for ensuring that they meet the regulatory requirements of their own country with respect to the export of drugs to Canada, especially in the case of a controlled substance. In addition, Health Canada's Office of Controlled Substances must issue an Import Permit to the importer. This permit allows the controlled drug supplies to be shipped to Canada without contravening the *Controlled Drugs and Substances Act* (CDSA). If a drug is a controlled substance, the DEL holder must comply with the rules under the CDSA including those relating to dealer's licences.

Manufacturers should clearly display the Letter of Authorization with other related documents, such as export permits, to facilitate clearance by the Canada Border Services Agency (CBSA).

Manufacturers may impose conditions on the sale of a drug to ensure the drug is used in accordance with the latest information available. For instance, the manufacturer may restrict the amount of the drug sold, request further patient information, or offer a protocol for the use of the drug. Manufacturers are also responsible for providing all relevant information, such as an Investigator's Brochure, to requesting practitioners.

Manufacturers are expected to ensure that significant new information respecting the safety, efficacy and quality of drugs released under the SAP is made available to practitioners and the SAP expeditiously. Should new information about a drug become available in other jurisdictions, this information should be vetted through the SAP prior to communication with practitioners.

Manufacturers should also maintain complete and accurate records of all transactions in a manner that permits rapid response to specific requests.

4. Manufacturers filing a pre-positioning request

To allow for a shorter shipping time to the practitioner, the Program may allow foreign manufacturers to pre-position drugs in Canada that could be requested through the SAP in advance of a request for the drug by a practitioner and authorization by the Program. This is particularly important for medical emergencies that require the timely administration of the drug.

4.1 Manufacturer filing a request for pre-positioning (Form D: Pre-positioning request)

To pre-position a drug in Canada, foreign manufacturers must identify a Canadian importer who has a DEL that meets the requirements as described in section 2.5.2 “Importer requirements for pre-positioning drugs on behalf of manufacturers” of this guidance. Obligations placed on the importer are for activities that are part of the regular business of a DEL holder.

Manufacturers may wish to store their product in a Canadian facility that is not the identified importer’s facility. The storage facility is hereafter referred to as “warehouse”. While the warehouse does not require to be listed on the importer’s DEL to store SAP drugs, the importer, or the foreign manufacturer must provide the address of the warehouse where the new drug is to be stored in Canada to the SAP. It is to be noted that the importer is required to keep records on the drug’s storage and distribution (sales).

Using Form D, the foreign manufacturer must provide the contact information of the importer, the DEL number, shipping and storage facility address, and the quantity of drug to be pre-positioned.

Form D requires the manufacturer to attest to the following:

- The product will only be distributed once an individual SAP authorization is issued allowing the sale of the drug from the manufacturer to the practitioner who made the request; and
- Records will be kept (including quantities and dates) with respect to the amount of product imported, released or destroyed. These records are to be made available to the SAP upon request.

While not required by the regulations, manufacturers should keep records for a period of three years from the distribution date of the drug from the facility to a named practitioner. The quantity of drugs received by the importer, and distributed, should be accounted for. This number should be the same as the quantity stated in the authorization letters. Record keeping should not only include the quantity of drug, but also where and to whom the drug was distributed.

Manufacturers must also provide a rationale as to why the product should be pre-positioned in Canada.

4.2 Review of the pre-positioning request and supporting information

The SAP will consider the authorization of pre-positioning requests based on the indications for use of the drug and if they are for medical emergencies, and the urgency for the delivery of the drug for patient use. The SAP considers the following factors for pre-positioning:

- if the Program authorized sales of this drug in the recent past
- if the use of the drug is for a serious or life-threatening condition
- if alternative drugs exist on the Canadian market
- if the requested product is currently under review in Canada and what is its submission status

In addition, the SAP performs an assessment to support why the product should be pre-positioned which includes:

- whether or not timely administration of the drug is required
- whether or not the product's stability is vulnerable due to a short half-life
- the quantity of the drug being pre-positioned

The SAP may refuse to issue an authorization if:

- the quantity of drug requested to be pre-positioned exceeds the amount that is determined by Health Canada to be required to address potential emergencies and the requestor does not agree to a reduced amount to be authorized
- the importer does not have a valid establishment license to import the drug, or
- the information requested by the Minister regarding the medical emergency or the safety and efficacy of the drug in relation to the medical emergency does not support the request to pre-position the drug

A pre-positioned drug cannot be sold or distributed to a practitioner until a Letter of Authorization has been issued to a manufacturer authorizing the sale of the drug to a named practitioner.

5. Sending request forms and reporting forms to Health Canada's SAP

Completed forms must be submitted via fax or by mail:

Special Access Program
Health Canada, Tunney's Pasture
Address Locator 3105A
K1A 0K9

Telephone: 613-941-2108

Fax: 613-941-3194

E-mail: sapd-pasm@hc-sc.gc.ca

Forms sent by facsimile do not require a cover sheet. Telephone requests should be reserved for life-threatening situations requiring immediate attention. By telephone, practitioners should be prepared to provide all of the required information using the form as a guide.

6. Refusal to issue an authorization to a practitioner request

SARs that are denied will be returned promptly to the practitioner with an explanation. If the SAR is denied, the SAP will send (or fax) a letter to the practitioner only, with an explanation.

The SAP may refuse to issue an authorization to a practitioner if:

- an alternative treatment is available in Canada
- the clinical rationale and other required information does not support the use of the drug in the medical emergency, or
- the application does not otherwise meet the regulatory requirements

6.1 Reconsideration review process

The main objective of the Reconsideration Review Process (RRP) is to provide the practitioner with an opportunity to be heard when the SAP is considering issuing a denial. It allows for an independent review of the recommendation and involves direct communication between the reconsideration reviewer and the requesting practitioner.

6.1(i) Review of denial recommendation

All reconsiderations are reviewed by a health professional. The health professional, who may be a pharmacist or practitioner within Health Canada, conducts a full independent review of the request and the supporting information. If the health professional determines that the information provided supports an authorization, a Letter of Authorization is issued. If the health professional cannot make a decision based on the information provided, the practitioner is contacted and specific information is solicited to facilitate decision-making. Following review of the solicited information, if the health professional deems the information supportive of the request, a Letter of Authorization is issued and the request is considered closed.

If the information does not support the authorization, the health professional will contact the practitioner to discuss the recommendation to deny the request. If the practitioner does not have any further supporting information to provide, the SAP will issue a Letter of Denial. The practitioner may choose to withdraw the request rather than receiving a denial.

7. Amendments to a Letter of Authorization to sell a drug to a practitioner or to pre-position a drug in Canada

Amendments to a Letter of Authorization may be issued if there are factual errors noted by the practitioner, the manufacturer or SAP. Amendments can be handled informally and are dealt with expeditiously by the Program so as not to hold up shipping and delivery. Most requests for amendments can be handled by telephone or by emailing the Program at the contact information provided in section 5 “Sending request forms and reporting forms to Health Canada’s SAP” of this document.

Substantial changes to a request such as changing the indication for the use of the drug, a new or different route of administration, or an increased quantity of drug to be sold/imported from what was initially requested, requires the submission of a new request form.

8. Drugs authorized through the Special Access Program that receive market authorization in Canada

Drugs authorized through the SAP may be under development in Canada at the time of a practitioner's request; for instance, they may be undergoing clinical trials or submission review. In the event that a drug submission is under regulatory review, SAP will continue to consider requests until the review is complete. Following regulatory review and the issuance of a Notice of Compliance (NOC), some manufacturers will launch a drug onto the Canadian market quickly while others might wait.

The SAP may become aware that a submission is under regulatory review either by manufacturers currently supplying their drug through the Program providing information on the status of their drug in Canada, or by obtaining this information from the drug review bureaus of Health Canada. SAP drugs that are under regulatory review are added to a "Watch List" that is monitored regularly in anticipation of a final decision. Close to the target date for review of the drug submission, the SAP will contact the manufacturer to request information on the company's transition plan for the drug to the Canadian market and an anticipated launch date.

When necessary, the SAP considers, on a case-by-case basis, a transition period that allows continued access to a drug until the marketed drug is available. In such situations, the SAP may adjust the quantities considered for authorization to reflect the launch date provided by the manufacturer. Regular updates from manufacturers on review status and marketing developments help to facilitate an effective transition of a drug from the SAP to the Canadian market. In general, the SAP allows a transition time of no more than 90 days.

Once a manufacturer receives an NOC and marketed supply of the drug is available, access via the SAP ends.

In determining if access via the SAP is to continue until the marketed authorized drug is available, the following guiding principles are considered:

- patient safety is a priority
 - therefore, once a marketed alternative is available, patients should access the marketed drug since it will be compliant with Canadian regulations and subject to post-market regulatory requirements
- once a drug receives market authorization, access through the SAP should be limited to meet an unmet medical need with a supply up to 90 days
 - the SAP will consider authorizing a continued supply of the drug to meet an unmet medical need should the marketed alternative not be medically suitable for the patient

Practitioners should contact the manufacturer if they require more information on the plans for marketing the drug in Canada. Practitioners may consult Health Canada's website to view the list of drug submissions under review, entitled "Drug and health product submissions under review (SUR)"⁷.

9. Hours of operation

The SAP operates 24 hours a day, 365 days a year. Regular business hours are weekdays from 8:30 am to 4:30 pm Eastern Standard Time. Outside of regular business hours and during statutory holidays⁸, an On Call service is available.

10. Return of unused stock

As a general rule, unused supplies of a drug should be returned to the manufacturer. It is anticipated that the practitioner will discuss with the manufacturer how to proceed should the return of stock be necessary. Some manufacturers require and enforce this policy.

11. Advertising

In accordance with section C.08.002 of the *Food and Drug Regulations*, advertising of unauthorized drugs accessed through the SAP is prohibited. Furthermore, it is Health Canada's position that advertising of an unauthorized drug is inconsistent with Section 9(1) of the *Food and Drugs Act* (FDA), which prohibits advertising a drug in a manner that is false, misleading or deceptive, or is likely to create an erroneous impression regarding its character, value, quantity, composition, merit or safety.

Health Canada encourages the maker of a drug that is on SAP to not engage in activities deemed to promote a drug to health care professionals or the public. Health Canada uses its policy document entitled "The Distinction Between Advertising and Other Activities" to distinguish between activities intended to promote the sale of a health product and non-promotional ones. If a message regarding a health product is deemed promotional, it is subject to the advertising provisions of the FDA, the *Controlled Drugs and Substances Act*, and associated Regulations.

Appendix A: Glossary

Adverse drug reaction (ADR): As defined in section C.05.001 of the FDR, means any noxious and unintended response to a drug that is caused by the administration of any dose of the drug.

ADR reports: A summary of the patient's unexpected adverse drug reactions to the drug. For the most part, ADRs are only suspected associations however, a temporal or possible association is sufficient for a report to be made. Reporting an ADR does not imply a causal link, rather it is a precautionary measure.

Conventional therapy: A treatment that is widely accepted and used by most health care professionals or, are well supported by substantial medical evidence and are considered standard-of-care in the medical profession.

Unavailable drug: A conventional therapy that is not marketed in Canada or not accessible due to a shortage or the therapy has been discontinued from the Canadian market. The affordability of a drug is not considered when considering a drug as being “unavailable”.

Medical emergency: Serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable.

Notice of Compliance (NOC): A notification, issued pursuant to paragraph C.08.004(1)(a) or C.08.004(3)(a), indicating that a manufacturer has complied with sections C.08.002 or C.08.003 and C.08.005.1 of the *Food and Drug Regulations*. Notices of Compliance are issued to a manufacturer following the satisfactory review of a drug submission.

Notice of Deficiency (NOD): If deficiencies and/or significant omissions that preclude continuing the review of a drug submission are identified, a NOD will be issued.

Notice of Deficiency - Withdrawal (NOD/W): When the response to a NOD is received, a new Screening 1 period (with an associated performance target) begins. If during the screening process, the response to a NOD is found to contain unsolicited information, is incomplete or deficient, the response to the NOD will be rejected and the submission will be considered withdrawn without prejudice to a refiling. A NOD-Withdrawal Letter will be issued by Health Canada.

Notice of Non-compliance (NON): After the comprehensive review of a submission is complete, a NON will be issued if the submission is deficient or incomplete in complying with the requirements outlined in the *Food and Drugs Act and Regulations*.

Notice of Non-compliance - Withdrawal (NON/W): When the response to a NON is received, a Screening 2 period begins (with an associated performance target). If during the screening process, the response to a NON is found to contain unsolicited information, is incomplete or deficient, the response to the NON will be rejected and the submission will be considered withdrawn without prejudice to a refiling. A NON-Withdrawal Letter will be issued by the responsible Health Canada Directorate.

Practitioner: As per section C.01.001 of the FDR, a person who is entitled under the laws of a province to treat patients with a prescription drug and is practicing their profession in that province.

Pre-positioning a drug: A drug that is placed in a Canadian facility in advance of a request for the drug by a practitioner and authorization by the SAP.

Serious adverse drug reaction: As defined in section C.05.001 of the FDR, means an adverse drug reaction that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death.

Special Access Request (SAR): A standard form used by the SAP to facilitate the request procedure. Practitioners fill out the SAR with the necessary information and submit it to the SAP.

¹According to the *Food and Drugs Act*, "sell" includes offer for sale, expose for sale, have in possession for sale and distribute, whether or not the distribution is made for consideration.

² The Natural Health Products (NHPs) finds its authority under the *Natural Health Products Regulations* (NHPR), however section 103.1, "Sale of Natural Health Product for Emergency Treatment" refers to section C.08.010 and C.08.011 of the *Food and Drug Regulations*, which provide the authority that, allows practitioners to request products that are unauthorized in Canada for use in a medical emergency.

³ The Medical Device Bureau administers its own Special Access Program and has its own Special Access Regulations contained in the *Medical Devices Regulations*. Information on how to access a medical device through the Program is available on the Health Canada website.

⁴ The Veterinary Drugs Directorate also finds its authority under Part C, Division 8, sections C.08.010 and C.08.011 of the *Food and Drug Regulations* and administers a similar program called Emergency Drug Release (EDR). Information on the Veterinary EDR is available on the Veterinary Drugs Directorate website.

⁵Active Pharmaceutical Ingredients (APIs) for pharmaceutical compounding are subject to the requirements of the *Food and Drug Regulations*, Division 1A: Establishment Licensing and Division 2: Good Manufacturing Practices (GMP).

⁶ E2A: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting

⁷ Drug and health product submissions under review (SUR) (<https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review.html>)

⁸ New Year's Day: January 1; Good Friday: Friday before Easter Sunday; Easter Monday; Victoria Day: Monday on or before May 24; Canada Day: July 1; Civic Holiday: first Monday in August; Labour Day: first Monday in September; Thanksgiving Day: second Monday in October; Remembrance Day: November 11; Christmas Day: December 25; Boxing Day: December 26.