Health Canada Santé Canada

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Draft Guidance Document

Public or Canadian Armed Forces Health Emergencies - Drugs for Immediate Use or Stockpiling

This guidance document is being distributed for comment purposes only.

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Canada

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 :
Ébauche de la ligne directrice : Urgences en matière de Santé Publique ou touchant les Forces Armées Canadiennes – utilisation immédiate ou mise en réserve de drogue

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.

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1. Introduction

1.1 Purpose/overview

Prior to selling a drug in Canada, a manufacturer is required to submit information on a drug's safety, efficacy and quality and to comply with the provisions of the Food and Drugs Act (FDA) and the Food and Drug Regulations (FDR), including obtaining market authorization from Health Canada. However, not all drugs that are considered the best treatment for an emergency, event, or incident are available on the Canadian market, as it is a manufacturer's decision whether or not to seek market authorization in Canada. If a drug has not received market authorization in Canada, regulatory amendments are proposed that may permit access to drugs to support emergency preparedness and response activities by Medical Officers of Health (MOHs) responsible for public health and to the Surgeon General (SG) of the Canadian Armed Forces (CAF) responsible for military health.

Federal, Provincial, Territorial Chief Medical Officers of Health (CMOH) (F/P/T), Municipal[1] (M) MOHs and the SG of the CAF, referred to herein as "public health officials (PHOs)", perform population-based emergency preparedness and response activities on a routine basis. Each province and territory, and the CAF, has legislative and regulatory tools governing their activities for public or military population health. As a part of their regular, routine business PHOs prepare, manage and respond to emergencies. This includes making decisions regarding which drugs are the best treatments to use in an event, incident or emergency situation. These drugs are then purchased for either immediate use or potential use in an event, incident or emergency.

The proposed regulatory framework entitled Public or Canadian Armed Forces Health Emergencies - Drugs for Immediate Use or Stockpiling provides a regulatory mechanism that enables a PHO to request that a manufacturer sell them a quantity of drug that is not authorized for sale in Canada in order to respond to, or prepare for a public or military health event, incident or emergency.

1.2 Scope and application

This guidance document explains the intent and scope of the proposed regulatory provisions under Division 11 of the FDR for the sale of an unauthorized drug to facilitate emergency preparedness and response activities for mass populations. It further provides:

- the information required to comply with Part C, Division 11 of the Food and Drug Regulations
- the process to be followed to request authorization for sale of a drug that cannot otherwise be sold or distributed in Canada for use in a public or military health event, incident or emergency and
- the responsibilities of the PHOs and manufacturers in that process.

For the purposes of this guidance document:

i. "drugs" include pharmaceuticals, radiopharmaceuticals, biologics and natural health products[2] for human use and

ii. emergency includes emergency, incident and event. An incident is an action, whether intended or unintended, that is likely to lead to grave consequences; an event is an immediate and significant risk to public health; an emergency is an occurrence or imminent threat of a health hazard or disease that poses a significant risk to the public health.

Also, the proposed regulations will be referred to as "proposed block release regulations".

1.3 Policy objectives

To provide a regulatory mechanism and process that enables requests for access to unauthorized[3] drugs to prepare for and/or respond to a public or military health event, incident or emergency for a mass population. Requests will be received, processed and decided upon in accordance with the proposed Division 11 of the FDR.

1.4 Policy statements

- Emergency access to drugs should be exceptional and where possible, drugs available on the Canadian market (including extraordinary use new drugs[4]) should be the first choice of treatment for public or military health emergencies.
- The regulatory authority supporting considerations of access to unauthorized drugs is discretionary. A decision to authorize or deny a request is made on a case-by-case basis taking into consideration the nature of the public or military health emergency, the availability of marketed alternatives and the supporting information provided with the request regarding the use, safety and efficacy of the drug to be used in a population.
- PHOs are responsible for monitoring and reporting on the drug's distribution and are accountable for all quantities received, distributed and used, including the reporting of serious adverse drug reactions.
- Monitoring patient response to use of the drug as well as reporting on adverse drug reactions provides useful information to the PHO when assessing whether or not the drug continues to be the best choice for a public or military health emergency.
- An authorization through this proposed regulatory framework does not imply that Health Canada has reviewed the drug's data for safety, efficacy and quality.
- The dissemination of drug information by the PHO is needed for the safe prescribing, dispensing and use of a drug.
- Health Canada recognizes that, due to ethical considerations, some drugs have never been tested in humans, under the proposed conditions of use. For these types of drugs additional safety measures should be taken to monitor their administration as well as follow up on the results of using the drug, when feasible.

2. The regulatory framework

2.1 Overview of the requirements

The Federal Minister of Health (herein referred to as "Minister") may grant authorization to allow drugs, which are otherwise unauthorized for sale in Canada, to be sold for the purposes of emergency preparedness and response activities carried out by PHOs. Under the proposed

provisions in Part C, Division 11 of the FDR, entitled Public or Canadian Armed Forces Health Emergencies - Drugs for Immediate Use or Stockpiling (referred hereto as block release), PHOs can request an authorization from Health Canada that will permit the sale of a specific quantity of an unauthorized drug for an identified use, to address a potential, imminent or actual public or military health emergency[5]. Health Canada's Special Access Program for drugs (SAP) is responsible for administering these proposed regulations.

Provincial legislation governing emergency preparedness and response activities vary in how emergencies are defined, however they are all similar in that the emergencies present a significant health risk to the public which may result in a mass population of individuals being faced with a serious or life-threatening disease or condition. Rather than defining emergencies that would trigger use of this proposed regulatory framework, the proposed regulations set out conditions to be met for an authorization of a drug. The sale of a requested drug is permitted only when the conditions have been met and the information provided by PHOs support the requested use of the drug in an emergency.

For a drug to be considered under this proposed regulatory framework, the existing drugs marketed in Canada are either, ineffective, unsuitable or unavailable to diagnose, treat, mitigate or prevent a disease or condition, in the population affected or at risk, resulting from an imminent, actual or potential public or military health emergency. Also, the drug must not have been assigned a Drug Identification Number (DIN) in Canada or issued a Notice of Compliance (NOC).

PHOs wishing to procure a drug under the proposed block release regulations for emergency preparedness (i.e., stockpiling), or to respond to an imminent or actual emergency, are expected to demonstrate that the requested drug is appropriate for use based on available information on the drug and based on a risk/threat assessment of the emergency or event.

If the drug requested is for an actual public health or military emergency and it has been authorized for sale in the United States, the European Union, or Switzerland for the specified use, the regulatory framework Urgent Public Health Need - Foreign Approved Drugs (Part C, Division 10, of the FDR) may also be a viable access mechanism.

2.1.1 Application requirements - conditions to be met when requesting a drug

When considering use of this proposed regulatory framework the PHO is expected to have identified a drug to be used in a particular emergency based on available information on the drug and based on a risk/threat assessment of the public or military health emergency.

Several conditions must be met in order for the PHO to seek authorization for the sale of a drug that is not marketed in Canada. As required by the proposed subsection C.11.003(2)(i), the PHO must make a statement attesting that the following conditions are met:

(i) there is an actual, imminent or potential emergency, event or incident affecting public health or the health of the members of the Canadian Armed Forces, that is likely to result, in humans, in a disease, disorder or abnormal physical state that is serious or life-threatening

(ii) immediate action is or would likely be required to diagnose, treat, mitigate or prevent the disease, disorder or abnormal physical state, or its symptoms

(iii) conventional therapies, if any, have failed, are unsuitable or are unavailable in Canada at the time the application is made and

(iv) the known and potential benefits associated with the use of the drug outweigh the known and potential risks associated with that use

"Conventional therapies" are treatments that are widely accepted and used by most health care professionals using authorized drugs that have been approved for an indication in Canada either through a new drug submission or an extraordinary use new drug submission. Treatment with medical devices are also considered conventional therapies when widely accepted and used by most health care professionals as well as procedures that are not subject to Health Canada approval (for example: surgery, radiotherapy, etc.).

PHOs are required to provide any information or documents available to them concerning the use, safety, efficacy and quality of the drug for its intended use including, but not limited to, information published in a medical or scientific journal, as well as a list of countries that have authorized the drug for that use, or any other use, i.e., the drug's foreign-approved indications.

Other information required at the time of the request include:

- foreign regulatory authorities[6] that have authorized the requested drug and its approved indication (if any) in the foreign country
- foreign regulatory authorities that have refused to issue the requested drug a market authorization and the reasons for refusal. PHOs should discuss this requirement with the manufacturer who will be selling them the drug

2.1.2 Authorization of a drug under the proposed Block Release Regulations

According to section C.11.004 (1), the Minister may issue a Letter of Authorization which permits the sale of a requested quantity of drug for use in an identified emergency or event, whether it is for immediate use (i.e., emergency response), or for stockpiling purposes to support preparedness planning in anticipation of the drug's actual use in an emergency.

Information submitted to Health Canada to support a request to authorize a drug under the proposed regulations will not undergo regulatory and scientific review by Health Canada as is the case when a drug is reviewed to receive market authorization in Canada for the general public. Health Canada reviews the information provided by the PHO to support the use of the requested drug for the identified event, incident or emergency. The Department also takes into account information that may be available to the Program, on the drug and its use or purpose in the specified event, incident or emergency, at the time of the request.

While drugs authorized under this proposed regulatory framework are exempt from certain provisions of the FDR[7] (as per the proposed section C.11.005), several obligations and requirements have been retained to mitigate the risks associated with the use of an unauthorized drug intended for a mass population. Part A of the FDRs applies. The FDA will also apply thereby enabling inspections of facilities where the drugs are stockpiled.

Drugs authorized under this proposed regulatory framework may have undergone regulatory review and received marketing authorization from a foreign regulatory agency. Drugs in

development may be considered for emergency use if evidence supports such use, and the benefits are anticipated to outweigh the risks for using the drug in this emergency context. Drugs authorized under these proposed regulations may only be used for the public or military health emergency identified in an authorization.

2.1.3 Refusal of an authorization

The Minister may refuse to issue an authorization if the conditions have not been met. In the case of a request for stockpiling, when there is an alternative mechanism that would permit the sale of the drug or already a stockpile of the drug in Canada in a quantity that could address the emergency, the Minister may refuse to issue an authorization as per the proposed section C.11.004(2).

Examples of alternative mechanisms that would permit the sale of the drug include:

- A request is made for a drug to be stockpiled. The requested drug is under review in Canada and may be made available for purchase at a future date. If the emergency is not imminent, the PHO could wait to stockpile the drug and purchase it once it is available in Canada.
- For drugs that are under development where human clinical trial data may not be available to support a full regulatory drug submission due to the ethical aspect of having to test the drug in a human trial, Health Canada may request a sponsor to file an extraordinary use new drug submission[8]. Should a sponsor agree to do so, the PHO may wait to stockpile a quantity of drug.

In an actual emergency, should the SAP receive requests for a drug which is already stockpiled in Canada, the Department may suggest to the PHO requesting the drug that he/she contact the PHO from either the federal, provincial, territorial or municipal jurisdiction, who has possession of a stockpile for the requested drug. This may reduce the amount of unused stock that, with time, would expire and then require destruction or need to be returned to the manufacturer) if no emergency occurred in a jurisdiction. The PHO who received authorization for the original stockpile remains responsible for the quantity of drug distributed and used.

Refusals are based on the information provided with the request and any other information that may be available to the Department at the time of the request.

2.1.4 Effect of the authorization

An authorization allows a manufacturer to sell the quantity of drug identified in the authorization for the specified use. The authorization is valid until the quantity of drug identified in the authorization is depleted, or expired. If the drug expires before stock is depleted, the authorization is no longer valid. PHOs should have a plan as to how they will dispose of stock, or ensure their contractual agreements include arrangements with the manufacturer regarding how the stock would be handled should an authorization no longer be valid.

The sale of the quantity of drug identified in an authorization is subject to the FDA and Part A of the FDRs. Drugs can only be distributed and/or sold for the use stated in the authorization. If a drug is already authorized but is required for a new use or emergency, the PHO must file a separate request for that new use or emergency.

The sale of these drugs and the quantity of the drug are exempt from the FDR except for Part A which sets out inspection powers as well as requirements on importing and exporting. It is to be noted however that if an authorization has been cancelled as per the proposed subsection C.11.013(1), the FDR would apply to any unused quantity of the drug as of the day that the cancellation comes in effect (as proposed in subsection C.11.013(2)). An authorization may be cancelled due to serious safety concerns with the drug. Refer to section 2.1.11 of this guidance document.

A drug that is no longer authorized for use should either be destroyed or returned to the manufacturer.

2.1.5 Public Health Officials must provide information about the drug and its use

Section C.11.006 of the proposed regulation requires the PHO who distributes the quantity, or a portion of the quantity, of the drug obtained under an authorization for the purpose of immediate use in an emergency to make the following information available in English and French to the patient to whom the drug is administered and to the persons who are administering the drug:

- Information about the known and potential benefits and risks associated with the uses of the drug for which the sale of the drug is authorized. This should include all warnings and precautions in respect of the use of the drug.
- The recommended duration of use, if any, of the drug.

In addition, the PHO must provide the following information to the persons administering the drug:

- the name and contact information of the public health official
- the name and contact information of the manufacturer
- the use of the drug that is authorized to address the emergency, event or incident, as the case may be and
- specific information about the drug:
    i. its brand name, if any, and either its proper name, common name and chemical name or its identifying name, code, number or mark
    ii. its medicinal ingredients
    iii. its strength
    iv. its dosage form and
    v. its recommended route of administration

As proposed in subsection C.11.006 (2), after becoming aware of any changes to information that was provided, the PHO is responsible to notify the relevant persons of such changes.

2.1.6 Labelling of stockpiled drugs - information requirements

Since drugs authorized under these proposed regulations are unauthorized products for use by the general public in Canada, the following requirements are intended to mitigate risks posed by these products and ensure the safety of the patient and anyone who is handling the drug through the labelling of the drug. This is to ensure the drug and its intended use, any precautions, and storage requirements are clearly identified.

In the case of a drug to be stockpiled, subsection C.11.007(1) proposes requirements that the public health official or any other person who obtains the quantity, or a portion of the quantity, of the drug for which an authorization was issued for the purpose of stockpiling must ensure that, before stockpiling, the drug bears a label or is accompanied by a package insert that clearly sets out the following information in English and French:

(a) the name and address of the manufacturer of the drug
(b) a statement that the Minister has authorized the sale of the drug to address the emergency, event or incident specified in the authorization
(c) a statement that the drug is to be used only for the use specified in the authorization
(d) the brand name of the drug, if any, and either its proper name, common name and chemical name or its identifying name, code, number or mark
(e) the medicinal ingredients
(f) the strength of the drug
(g) the dosage form
(h) the recommended dosage and route of administration
(i) the lot number of the drug, if known
(j) all warnings and precautions in respect of the use of the drug, if any
(k) the expiration date of the drug, if any, or its stability testing or retesting date, as specified by the manufacturer
(l) the recommended storage conditions for the drug and
(m) a statement of the net contents of the container of the drug in terms of weight, measure or number

2.1.6.1 New Information in respect of the safety of the drug or other

As per the proposed subsection C.11.007(2), the PHO is responsible to ensure, without delay, that he/she notify in writing to any persons who has possession of the drug in stockpile of any new information in respect of the safety of the drug, or of changes to the name and address of the manufacturer; warnings and precautions in respect of the use of the drug; or the expiration date of the drug, or its stability testing or retesting date.

As per the proposed subsection C.11.007(3), any person who is notified of new information in respect of the drug and who has possession of the drug, must ensure the label or package inserts are updated without delay.

2.1.7 Reporting serious adverse drug reactions

As proposed in section C.11.008, the PHO named in an authorization shall notify the Minister and the manufacturer named in the authorization, of any serious adverse drug reaction. The information to be provided to both parties includes the nature of the reaction, the lot numbers involved, if known, the circumstances under which the reaction occurred, and any corrective action taken. The Minister must be provided this information in the following manner and within the following times:

(a) if the reaction is fatal or life-threatening, the Minister and the manufacturer are to be notified within 24 hours of the PHO becoming aware of the reaction. Within 24 hours of notifying the Minister and the manufacturer of the reaction, the PHO must submit a written report to Health Canada, and

(b) in any other case, the PHO must submit a written report to Health Canada within 15 days after the day on which the PHO becomes aware of the reaction.

2.1.8 Reporting on the results of the use of the drug

Section C.11.009 (1) proposes the PHO must report to the Minister, in writing, on the results of the use of the drug in the public or military health emergency one year following the day of beginning to use the quantity of the drug specified in the letter of authorization and annually until that quantity is used up. Individual patient reports are not necessary. The report shall contain a summary of the number of patients treated, the response of patients to treatment with the drug and outcomes including any adverse events encountered related to the use of the drug, and whether or not the drug continues to be safe and effective.

New information concerning the safety, efficacy or quality of the drug for the authorized use that has not been included in the annual reporting and that could affect the benefit/risk profile of the drug, or that would warrant communication to the impacted population, must be provided to the Minister in writing within 30 days after the day the PHO becomes aware of it (proposed requirement in section C.11.009(2)).

2.1.9 Maintaining information about distribution and use of the drug

As proposed in section C.11.010, the PHO shall maintain all information about the distribution and use of the drug in a way that would allow: (a) the PHO to submit information and reports to the Minister as required in the proposed sections C.11.008 and C.11.009 (refer to section 2.1.7 and 2.1.8 of this guidance), and (b) communication with persons who have been administered the drug, if their health may be endangered by its use.

2.1.10 Annual reporting of remaining stock

PHOs are required to file an annual report of any unused stock (as proposed in section C.11.012). Health Canada needs to know how much drug product has been distributed to ensure the appropriate management and oversight of drugs that are otherwise unauthorized for sale to the general public in Canada. Furthermore, it allows the Department to know how much stock is available in Canada should there be a need for the drug in a specific jurisdiction other than the jurisdiction holding the stock. The SAP may inform a PHO requesting authorization for immediate use of a drug, that they may wish to contact a PHO who has the drug in their stockpile rather than making arrangements with a foreign manufacturer which may involve longer shipping time before a drug is actually in Canada.

2.1.11 Record retention

The proposed section C.11.011 requires PHOs maintain the information on serious adverse drug reactions, reports on the results of the use of the drug in the health emergency, any new information concerning the safety, efficacy or quality of the drug, and information about the distribution and use of the drug (including records of patients who were administered the drug) for a period of 25 years. This time period is similar to requirements that are under Division 5 of the FDR, entitled Drugs for Clinical Trials Involving Human Subjects. Through record retention, the PHO would have the ability to communicate new safety information to those individuals to whom the drug was administered.

Health Canada has adopted this approach since data on drugs authorized under this framework have not undergone extensive review in Canada for safety, efficacy and quality as is the case for a drug receiving a general market authorization.

2.1.12 Cancellation of an authorization

Section C.11.013 proposes authorities that would allow the Minister to cancel an authorization if he or she believes the drug presents a serious or imminent risk of injury to health, whether or not it is to the patient or anyone who is in possession of the drug.

Cancellation may occur as a result of new information that becomes available to the Minister, which was not available at the time of the request. Also, if serious adverse reactions are fatal or life-threatening, or a serious adverse reaction is repeatedly occurring, the Minister may cancel an authorization.

Once an authorization is cancelled the quantity of drug identified in the Letter of Authorization is no longer exempt from the FDR. This means that any remaining stock of the drug cannot be sold or distributed. However unused stock may be returned to the manufacturer or destroyed.

3. Guidance for implementation: Process for filing a request, refusals and issuance, amendment or cancellation of a Letter of Authorization

3.1 PHO filing a drug request

The PHO may file a request for a drug under the proposed block release regulations through Health Canada's SAP by completing the "Block Release Form" and submitting it to the SAP.

The PHO is to specify the health emergency, incident or event for which the request is filed and whether the request is for immediate use of the drug or for stockpiling purposes.

When submitting a request, PHOs must provide a description of the population health event, incident or emergency they are dealing with, or anticipate, and an explanation of why the event requires a drug that is not authorized for sale in Canada. Based on a risk/threat assessment conducted by the PHO, the PHO must provide an explanation to the Minister of what serious condition or injury could arise from the event or exposure to a substance. The PHO must also provide information to support the safety and efficacy of the requested drug for the specific use. PHOs are required to demonstrate in the application that the conditions outlined in section 2.1.1 of this guidance have been met.

Prior to filing a request, PHOs are encouraged to contact individual manufacturers to confirm the availability of a drug and obtain the most up-to-date drug information such as prescribing information and other data that supports the use of the drug. PHOs should:

- assess the risks and benefits associated with bringing the drug into their jurisdiction in light of available evidence, and
- identify and contact the manufacturer to obtain the necessary information (e.g. prescribing information, chemical information about the drug, drug's approval in foreign countries, etc.)

and to identify conditions of sale (e.g. mandatory health professional training, controlled distribution, etc.) set forth by the manufacturer, or the foreign regulator to determine whether these conditions can be fulfilled within their jurisdiction

- for drugs that have been requested, obtain information from the manufacturer about the status of the drug and its market authorization, or if under development, the status of its development. PHOs should obtain as much information as possible from the foreign manufacturer to further inform their decision to choose that particular drug for the identified emergency

A manufacturer is under no obligation to sell an unauthorized drug to a PHO and Health Canada cannot compel a manufacturer to do so. The manufacturer makes the decision as to whether or not the drug will be supplied. The manufacturer can also impose certain restrictions or conditions on the release of the drug to ensure that it is used in accordance with the latest information available. For instance, the manufacturer may restrict the amount of drug released or the indications for which the drug is released. Questions concerning the shipping, cost and/or payment should be directed to the manufacturer of the drug.

3.1.1 Information about the drug to support the requested use

When requesting a drug through the SAP for a public or military health emergency, the PHO must submit information that supports their decision to prescribe the drug. The PHO must meet the conditions set out in the proposed provisions by explaining how the event, incident or emergency is likely to result in a disease, disorder or abnormal physical state that is life-threatening or serious, or affect organic functions in humans and justifies that action is necessary to protect public health from significant harm. Any information or documents available to the PHO must be submitted. This includes, but is not limited to, information published in medical or scientific journals, evidence available from the manufacturer in the form of an investigator's brochure or prescribing information from another jurisdiction.

3.1.2 “Indication” and “recommended conditions for use”

In filing a request, the form requires the PHO to include the indication and the recommended conditions of use. The term “indication” is the specific condition for which the drug has been studied and authorized by a regulatory body. The label of a foreign authorized drug will state the indication or use for which the drug was approved (i.e., for the diagnosis, mitigation, treatment or prevention of a disease or condition). The requested use must be for the authorized or studied indication of that foreign regulatory authority. If the requested use of a foreign authorized drug is different than its authorized indication, the PHO must provide a rationale as to why that foreign authorized drug is the preferred drug to be used in the emergency and provide evidence of safety and efficacy for that specified use.

Recommended conditions of use may include the authorized or studied indication of the drug taking the following factors into consideration: contraindications, warnings, precautions, etc. Additional information to be provided by the PHO may include specific monitoring that is required for a certain medical condition.

3.1.3 Regulatory status of the foreign drug

The PHO is responsible to inform himself/herself regarding the regulatory status of the drug he/she is requesting if it is coming from a foreign country. If the requested drug has been approved by a foreign regulatory authority, all approved indications for use are to be provided in the form submitted to Health Canada. In addition, the medicinal ingredient(s) of the drug; the strength; recommended dosage(s); route(s) of administration; contra-indications; and known side-effects are to be provided. While, it is recognized that a drug in development may not have an "approved" indication, the PHO is to provide the indication for which the drug is in development for and the intended use for which authorization has been requested.

If known, the PHO is to provide the countries that have authorized the sale of the drug for the requested use, (i.e. the country that has approved the drug for that indication). If the drug has not received a foreign market authorization, the PHO is to identify the countries in which a regulatory submission may have been filed. If a drug received a negative regulatory decision from a foreign regulatory authority, this is to be communicated to the Department as well.

3.1.4 Quantity of drug requested and keeping track of drug use and distribution

PHOs are to provide the quantity of drug required to address the emergency, such as the precise number of tablets, vials, etc.

Drugs authorized under the proposed block release regulations are to be accounted for by the PHO, since they are only approved for the specific use identified in the Letter of Authorization and are otherwise unauthorized for sale to the general public in Canada. PHOs should ensure they have procedures in place to track stock that has been distributed or that remains in a stockpile and to report on drug usage. Such procedures are important as they ensure appropriate oversight by the responsible PHO.

3.1.5 Address of manufacturer, PHO and shipping address

PHOs are to specify the name and address of the principal place of business of the foreign manufacturer that will sell the drug, and of the establishment in which the drug was manufactured. The address to where the drug is to be initially shipped by the manufacturer is also to be included, as well as the address of the PHO.

3.1.6 Sending request forms to Health Canada

Completed forms should be faxed, to:

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

Tel: 613-941-2108
Fax: 613-941-3194
E-mail: hc.sapd-pasm.sc@canada.ca

A cover sheet is not required for forms sent by facsimile. Telephone requests should be reserved for life-threatening situations requiring immediate attention. By telephone, PHOs

should be prepared to provide all of the required information using the form as a guide. A written request must follow.

3.2 Health Canada's Special Access Program

Health Canada's Special Access Program (SAP) is responsible for administering the proposed Division 11, in Part C of the FDR.

Most requests to SAP are currently 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 urgent matters take precedence over less urgent matters. For example, requests for immediate emergencies are given priority over requests for stockpiling.

3.2.1 Receipt of request by SAP

Upon receipt of a request, the SAP will send an acknowledgement of receipt to the PHO and proceed to assess the information that has been submitted to support the need for a drug to be used in a public or military health emergency. The form is reviewed to ensure that all sections are complete, the information provided is legible, and the request is signed and dated.

3.2.1.1 SAP review of Block Special Access request and supporting information

In deciding whether or not to issue an authorization, the Department considers if the data supporting the request is credible and supportive of the need for the requested drug for the identified emergency. Health Canada relies on the facts provided by the PHOs in pursuing their mandate under their respective emergency acts. The Department understands that PHOs perform risk threat assessments as the planning premise for determining a potential emergency and what drug is necessary to respond to the emergency. When assessing the information provided, the SAP may, at any time prior to making a decision, request additional information from the PHO regarding the drug and its use, to allow appropriate consideration of the request. The SAP may further consult within the Department to seek additional information and may further confirm as needed, the Canadian and international development and regulatory status of the drug.

The SAP verifies there are no marketed alternatives in Canada. In assessing the information provided with the request, the SAP determines if additional information is needed prior to considering the issuance of a Letter of Authorization.

3.2.2 Issuance of an authorization

Should the Minister be satisfied with the information provided by the PHO, the Minister will issue a Letter of Authorization to a manufacturer allowing the sale of the requested drug and quantity to the named PHO. Authorizations are based on: the PHO meeting the conditions specified in the proposed regulations (please refer to section 2.1.1 of this guidance); the rationale and information provided to support the need for, and the safe use of, the drug, and any other information available to the Minister at the time of the request; or additional information requested from the PHO prior to a final decision.

An authorization will be issued if:

- all conditions have been met as described in section 2.1.1

- the SAP has no reason to disagree with the PHO's assessment that the known and potential benefits outweigh the known and potential risks associated with the uses of the drug, based on all available information, and
- information in or referenced by the application is complete, accurate, and not false or misleading

The Letter of Authorization will be sent by facsimile to the manufacturer and a copy to the PHO.

3.2.3 Refusal to issue a Letter of Authorization

Requests that are denied will be returned promptly by fax to the PHO with an explanation. The SAP would (as per section 2.1.3) also contact the PHO to discuss the reasons for denial and if the PHO has any recourse such as submitting a new request with additional information.

3.2.4 Amendments to a Letter of Authorization

The SAP should be contacted immediately if errors are found on a Letter of Authorization to ensure the Letter is amended and the information is accurate for the purposes of importing the drug into Canada.

Corrections and amendments can be done administratively, such as typographical errors in the spelling of the drug name, manufacturer name, etc. The SAP should be made aware of such errors within a reasonable time frame. Other types of errors such as a new or different route of administration; a different indication, or quantity, require the filing of a new request form.

3.2.5 Cancellation of an authorization

As with all public health emergency preparedness and response activities, Health Canada expects PHOs to have a plan in place for managing the stock they have purchased in the event of an authorization being cancelled. This may be done through contract negotiations with the manufacturer, or the PHO may wish to destroy any remaining stock of the drug product if deemed unsafe.

3.3 Manufacturers receiving a Letter of Authorization

The SAP issues a Letter of Authorization to both the manufacturer and to the PHO. The manufacturer is authorized to sell the identified quantity of drug for the specified use as per the authorization.

Manufacturers may impose conditions on the sale of a drug to ensure that it is used in accordance with the latest information available. For instance, the manufacturer may restrict the amount of drug sold, 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 or Prescribing Information, to requesting PHOs.

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. In the case of a drug to which the Controlled Drugs and Substances Act (CDSA) and its regulations apply, the manufacturer also requires an import permit from Health Canada's Office of Controlled Substances[9]. This permit allows the drug supplies to be shipped into Canada without contravening the CDSA.

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

Manufacturers should also maintain complete and accurate records of all transactions in a manner that permits rapid response to requests from either Health Canada or the PHO.

3.4 Expired stock and replenishing stockpile

Authorizations are valid as long as there is remaining stock from the initial quantity of the drug, or the product has not expired.

Products that have expired are to be returned to the manufacturer or destroyed by the PHO. To replenish stock, the PHO must file another request.

3.5 Return of unused stock

Following the cancellation of an authorization, it is expected that remaining unused stock will be returned to the foreign manufacturer or destroyed by the PHO.

An authorization that has been cancelled results in the quantity of unused stock being subject to the FDR, i.e., the drug is no longer exempt from the FDR and is prohibited from further sale or distribution. Section 37 of the FDA allows the drug to be exported for return to the manufacturer as long as it is not for consumption or use in Canada and all other requirements of section 37 are met. Therefore, remaining stock may be returned to the foreign manufacturer without violating the Act.

As a general rule, unused supply of a drug should be returned to the manufacturer. Some manufacturers require and enforce this as their policy.

4. PHO Obligations - reporting, record-keeping, providing information and labelling

The PHO shall maintain all records for a period of 25 years. These records include serious adverse drug reactions, reports on the results of the use of the drug, information about the distribution and use of the drug (including records of patients who were administered the drug), and any new information concerning the safety, efficacy or quality of the drug, for the authorized use or purpose, that was not captured in any reports.

4.1 PHO reporting serious Adverse Drug Reactions

PHOs must report to the manufacturer and to the SAP on any serious adverse drug reactions (SADRs) encountered (refer to regulatory requirements in section 2.1.7 of this guidance).

The SAP has adopted the International Conference of Harmonization (ICH) guidelines for ADR reporting in regards to what should be reported and the associated timeframes. Specifically, the PHO shall inform the SAP of any serious adverse drug reaction within 15 days after becoming aware of the information if the reaction is neither fatal nor life threatening, and within 24 hours after becoming aware of the information if it is fatal or life threatening. ADRs

should be reported using the Council for International Organizations of Medical Sciences (CIOMS) forms and sent by facsimile to the SAP (refer to section 3.1.6 for contact information).

4.2 PHO reporting - annual outcome summary reports, new information and annual reporting of unused stock

4.2.1 Annual reporting - results on the use of the drug

One year following the day of beginning to use the quantity of the drug specified in the letter of authorization and annually until that quantity is used up, the PHO is required to provide Health Canada with a summary report on the outcome of the use of the drug.

Reporting on the outcome of use of the drug includes information about the number of patients treated, patient response, safety, efficacy and quality information, and whether or not the PHO determines the drug is safe and effective from the results of its use. PHOs may use the follow-up report template entitled: "Public Health Emergencies/Canadian Armed Forces Health Emergencies Annual Reporting Form – Outcome of Use and Quantity of Drug" found on the Health Canada Website.

4.2.2 Reporting of new information regarding safety, efficacy or quality of the drug

In addition, the PHO is further responsible to submit in writing any new information he/she may be aware of concerning the safety, efficacy, or quality of the drug for the authorized use, within 30 days after the day of becoming aware of it, using the form entitled "New information: safety, efficacy or quality". New information may be new contraindications, change in conditions of use, change in the safety profile of the drug, a recall of the drug in another country, or any other safety changes resulting from the actual use of the drug.

Such monitoring allows PHOs to reassess the need and use of the drug. It also allows Health Canada to receive updated information about the drug and its use which will help inform decision-making for subsequent requests received.

4.2.3 Annual reporting of unused stock

PHOs are to report to Health Canada, on a yearly basis how much of the stockpiled product is unused using the form "Public Health Emergencies/Canadian Armed Forces Health Emergencies Annual Reporting Form – Outcome of Use and Quantity of Drug". The PHO is to reference the original request filed, including the quantity of drug requested and indicate the quantity of stock initially received, amount unused and where the stock is situated (i.e., if it has been distributed to different provinces, this must also be specified).

4.3 PHO - providing information on the drug

As the drug may be labelled in a language other than English or French, PHOs are responsible to ensure that information about the drug is provided in English and French to patients to whom the drug is being administered and to whoever is handling and/or administering the drug. Refer to section 2.1.5 of this guidance for information requirements.

Prescribing information should be provided including conditions for storage of the drug as well as any relevant information that will help to ensure the safety of a patient receiving the drug, such as warnings and precautions.

While not a requirement within the proposed regulations, it is recommended that PHOs ensure those responsible for administering the drug to the patients seek informed consent from recipients of the drug. Informed patient consent is the ethical foundation for any treatment or research with human subjects and is an integral part of access to experimental or unapproved therapies. Health Canada recognizes that in an actual public or military health emergency, decisions must be made from a population-based approach and individualized informed consent may not always be feasible.

4.4 Labelling of stockpiled drugs

Any person in possession of a stockpiled drug is responsible to ensure the container holding the stockpiled drug bears a label or is accompanied by a leaflet which has the information set out in section 2.1.6 of this guidance. While not every single drug must be labelled, the PHO, or any person distributing the drug, must ensure that the labelling information or leaflet would accompany each drug that is distributed.

Should the stockpiled drug be used, information about appropriate use of the drug is to be provided to patients and anyone who is administering the drug to ensure the health and safety of these individuals. This includes information about: the medicinal ingredients; the strength of the drug; the dosage form; the recommended dosage and route of administration; all warnings and precautions in respect of the use of the drug, if any; and the recommended storage conditions for the drug. As well, contact information for the reporting of any adverse events should be provided.

Labels and leaflets must be updated should there be changes to the labelled information that would impact the safe use of the drug, or if there is a change in the manufacturer of the drug. Refer to section 2.1.6.1 of this guidance.

5. 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 holidays, an On Call service is available at 613-941-2108.

6. Advertising

In accordance with section 3 of the FDA and section C.08.002 of the FDR, advertising of unauthorized drugs accessed through this framework is strictly prohibited.

Appendices

Appendix A - Definitions

Brand name:
as defined in subsection C.01.001(1) of the FDR, means with reference to a drug, the name, whether or not including the name of any manufacturer, corporation, partnership or individual, in English or French, (a) that is assigned to the drug by its manufacturer, (b) under which the drug is sold or advertised, and (c) that is used to distinguish the drug.

Common name:
as defined in subsection C.01.001(1) of the FDR, means with reference to a drug, the name in English or French by which the drug is (a) commonly known; and (b) as designated in scientific or technical journals.

Conventional therapy:
treatment that is widely accepted and used by most health care professionals using an authorized drug that has been approved for an indication in Canada either through a new drug submission or an extraordinary use new drug submission. Treatment with a medical device is also considered a conventional therapy when widely accepted and used by most health care professionals as well as a procedure that is not subject to Health Canada approval (for example: surgery, radiotherapy, etc.).

Drug:
as defined in section 2 of the FDA, includes any substance or mixture of substances manufactured, sold or represented for use in (a) the diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in human beings, (b) restoring, correcting or modifying organic functions in human beings.

Expiration date:
as defined in subsection C.01.001(1) of the FDR, means (a) in the case of a drug in dosage form, the earlier of the following dates, expressed at minimum as a year and month: (i) the date up to and including which the drug maintains its labelled potency, purity and physical characteristics, and (ii) the date after which the manufacturer recommends that the drug not be used; and (b) in the case of an active ingredient, whichever of the following dates is applicable, expressed at minimum as a year and month: (i) the retest date, or (ii) the date after which the manufacturer recommends that the active ingredient not be used.

Foreign regulatory authority:
s proposed in section C.11.001 of this proposed regulatory framework, a government agency or other entity outside Canada that has a legal right to control the manufacturing, use or sale of drugs within its jurisdiction and that may take enforcement action to ensure that drugs marketed within its jurisdiction comply with the applicable legal requirements.

Proper name:
the name assigned to the drug as specified in a manufacturer's licence.

Public Health Official:

In accordance with the proposed section C.11.002 of the proposed regulations, a Public Health Official (PHO) means: (a) the Chief Public Health Officer appointed under subsection 6(1) of the Public Health Agency of Canada Act; (b) the Chief Medical Officer of Health, or equivalent, of a province; (c) the Medical Officer of Health, or equivalent, of a municipality; (d) the Surgeon General of the Canadian Armed Forces; or (e) the Chief Medical Officer of Public Health for the Department of Indigenous Services Canada.

Adverse Drug Reaction:

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.

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.

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[1] "Municipal government" includes cities, regions, towns, villages.

[2] The Natural Health Products (NHPs) finds its authority under the Natural Health Products Regulations, however it is proposed that section 103.1 of the Natural Health Products Regulations be renumbered as subsection 103.1(1) and amended by adding the following: (2) Division 11 of the Food and Drug Regulations applies in respect of natural health products except that (a) a reference to section C.08.004 or C.08.004.01 shall be read as a reference to section 7 of these Regulations; and (b) a reference to section C.01.014.2(1) shall be read as a reference to section 8(1) of these Regulations.

[3] The term "unauthorized" drug used throughout the document is a drug for human use in dosage form for which a drug identification number has not been assigned under subsection C.01.014.2(1), or for which a notice of compliance has not been issued under section C.08.004 or C.08.004.01. Furthermore, for drugs in development in Canada it implies that sale of the drug has not commenced, pursuant to C.01.014. "Unauthorized" is also the term used fora product has been discontinued or removed from the market pursuant to C.01.014.6 and C.08.006 of the Food and Drug Regulations.

[4] An extraordinary use new drug (EUND) is a drug that was reviewed and approved by Health Canada based on non-clinical and limited clinical information. EUNDs are intended for emergency use in situations where persons have been exposed to a chemical, biological, radiological or nuclear substance and action is required to treat, mitigate or prevent a life-threatening or other serious disease, disorder or abnormal physical state, or its symptoms, that results, or is likely to result, from that exposure, or preventative use in persons who are at risk of exposure to a chemical, biological, radiological or nuclear substance that is potentially lethal or permanently disabling. EUNDs can only be sold to the Government of Canada or the government of a province for the use of a department or agency of that government, on receipt of a written order signed by the minister responsible for the department or by the person in charge of the agency, or by their duly authorized representative; or to a municipal government, or an institution of such a government, on receipt of a written order signed by a senior official of the government or institution or by his or her duly authorized representative (https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/submission-information-requirements-extraordinary-drugs-eunds.html)

[5] Military health emergencies are emergencies specific to Canadian Armed Forces members who require drugs in carrying out their military operations.

[6] "foreign regulatory authority" means a government agency or other entity outside Canada that has a legal right to control the manufacturing, use or sale of drugs within its jurisdiction and that may take enforcement action to ensure that drugs marketed within its jurisdiction comply with the applicable legal requirements.

[7] Refer to section 2.1.4.

[8] Refer to: Health Canada's Guidance Document - Submission and Information Requirements for Extraordinary Use New Drugs (EUNDs) (https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/submission-information-requirements-extraordinary-drugs-eunds.html)

[9] Controlled Substances (https://www.canada.ca/en/health-canada/services/health-concerns/controlled-substances-precursor-chemicals/controlled-substances.html)