



Health
Canada

Santé
Canada

Guidance on amendments to the Food and Drug Regulations for drugs for use in relation to COVID-19



Canada 

Date adopted 2021-03-31
Effective date 2021-03-31

Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. Health Canada is committed to improving the lives of all of Canada's people and to making this country's population among the healthiest in the world as measured by longevity, lifestyle and effective use of the public health care system.

Également disponible en français sous le titre :
Lignes directrices sur les modifications apportées au Règlement sur les aliments et drogues pour les médicaments contre la COVID-19

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: hc.publications-publications.sc@canada.ca

© Her Majesty the Queen in Right of Canada, as represented by the Minister of Health, 2021

Publication date: March 2021

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

Cat.: H164-318/2021E-PDF
ISBN: 978-0-660-38328-6
Pub.: 210010

Foreword

Guidance documents provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. They also provide guidance to Health Canada staff on how mandates and objectives should be met fairly, consistently and effectively.

Guidance documents are administrative, not legal, instruments. This means that flexibility can be applied by industry. However, to be acceptable, alternate approaches to the principles and practices described in this document must be supported by adequate justification. They 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 always, Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, to help us adequately assess the safety, efficacy or quality of a therapeutic product. We must make sure 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

Overview	1
Background	1
Scope and application	2
Policy objectives.....	2
Policy statements.....	3
Explanation of key terms	3
Preparing a submission or supplement	5
Submission scenarios.....	5
Modified requirements.....	6
Safety and efficacy: C.08.002(2.1) as an alternative to C.08.002(2)(g) and C.08.002(2)(h)	7
Product labels	7
Rolling submissions.....	7
Regulatory activity and transaction details for designated COVID-19 drugs.....	9
Pre-submission meetings.....	9
Format and structure for filing	9
Content and requirements for filing	10
Non-clinical information and requirements	10
Clinical information and requirements.....	10
Quality (chemistry and manufacturing) information and requirements.....	10
Comparative submissions for subsequent entry drugs	10
Information and requirements for veterinary drugs	11
Risk management plan.....	11
Labelling.....	12
Filing a supplement to an NDS for a COVID-19 drug	13
Notice of compliance (NOC) for a COVID-19 drug	13
Drug identification number (DIN)	13
Terms and conditions on a DIN pertaining to a COVID-19 drug relying on modified requirements in C.08.002(2.1).....	14
Submitting information to fulfill terms and conditions	15
Market notification.....	15
Changes in product ownership, mergers and buyouts or licensing agreements.....	15
Notification of discontinuation of sale	15
Transparency	16
Performance standards	16

Fees.....	16
Submission fees	16
Drug establishment licences and good manufacturing practices.....	18
Drug establishment licences for COVID-19 drugs.....	18
Applying for a new or amended DEL for a COVID-19 drug.....	18
Issuance of a DEL for a COVID-19 drug.....	18
DEL terms and conditions	19
DEL suspension and cancellation	19
DEL performance standards	19
Drug establishment licence fees.....	19
Transitioning of DELs issued or amended under the ISAD IO.....	20
Notification	20
Good manufacturing practices	20
Finished product testing	21
Intellectual property	22
Data protection.....	22
<i>Patented Medicine (Notice of Compliance) Regulations</i>	22
Certificate of supplementary protection	22
Post-market requirements.....	24
Pharmacovigilance reporting requirements	24
Adverse reaction reporting.....	24
Annual summary reporting.....	24
Issue-related summary reports.....	24
Additional good pharmacovigilance practices.....	25
Foreign actions reporting.....	25
Other post-market requirements	25
Record keeping	25
Shortages or discontinuation of sale	25
Compliance and enforcement	25
Pre-positioning of COVID-19 drugs.....	26
Importation and distribution of a pre-positioned drug.....	26
Transition of pre-positioned drugs from the ISAD IO to the <i>Regulations</i>	27

Submission scenarios, reference documents and key contacts	28
Submission scenarios	28
Scenario 1	28
Scenario 2	28
Scenario 3	29
Scenario 4	29
Reference documents.....	30
Key contacts.....	32

Overview

This guidance applies to sponsors of new COVID-19 drug submissions as well as sponsors seeking a Notice of Compliance (NOC) for COVID-19 drugs that received temporary authorization under the [Interim order respecting the importation, sale and advertising of drugs for use in relation to COVID-19](#) (ISAD IO). It also applies to new COVID-19 drug establishment licences under the *Food and Drug Regulations*.

This document will help manufacturers prepare a submission for a Notice of Compliance for a COVID-19 drug under the *Regulations*. It also outlines the process for meeting the post-market regulatory requirements.

Background

The COVID-19 pandemic posed an immediate and significant risk to the health and safety of Canadians. To address the associated public health need in Canada, the Minister of Health made a number of interim orders to expedite and facilitate access to drugs, medical devices and foods for a special dietary purpose. The Minister used the power granted under section 30.1 of the *Food and Drugs Act* to make these interim orders.

The ISAD IO came into effect on September 16, 2020 and provided:

- an optional, expedited authorization pathway for the importation, sale and advertising of drugs to be used in relation to COVID-19
- modified requirements for drug establishment licence (DEL) applications for those drugs
- the introduction of a mechanism for the placement of COVID-19 drugs in Canadian facilities prior to the authorization to sell in Canada (pre-positioning)

The ISAD IO ends 1 year after it came into effect. After this time, drugs authorized through the ISAD IO would no longer have been legally permitted to be sold in Canada, unless transition measures were implemented.

The ISAD IO provided a temporary emergency authorization for COVID-19 drugs to address the pandemic. The authorization was not a Notice of Compliance. In order for drugs to receive an NOC, a submission needs to be made under Division 8 of the *Food and Drug Regulations*.

The *Food and Drug Regulations* have been amended to allow for modified requirements that facilitate the regulatory process for new COVID-19 drugs to receive an NOC through a new drug submission (NDS). The amendments maintain some of the mechanisms introduced through the ISAD IO, thus continuing to provide Canadians with quick access to safe and effective COVID-19 drugs. This guidance document explains the modified requirements provided in these amendments to the *Regulations*.

For more information on these measures and the ISAD IO, refer to the following items:

- [Explanatory note](#)
- [Interim order respecting the importation, sale and advertising of drugs for use in relation to COVID-19](#)
- [Information and application requirements for drugs authorized under the interim order: Guidance document](#)
- [Canada Gazette II of amendments to the Food and Drug Regulations](#)

Scope and application

COVID-19 means the coronavirus disease 2019. This guidance document applies to:

- drug products authorized under the interim order
- manufacturers planning to file a submission for a Notice of Compliance (NOC) for a designated COVID-19 drug as defined in C.08.001.2
- establishments seeking a DEL related to COVID-19 drugs
- pre-positioning mechanism introduced under the ISAD IO

A “designated COVID-19 drug” is a new drug for which the purpose and conditions of use recommended by the manufacturer relate to COVID-19. For the purpose of this document, COVID-19 drugs also include designated COVID-19 drugs.

For guidance on obtaining product authorization for disinfectants, hand sanitizers and veterinary health products, manufacturers should refer to the following guidance documents:

- [Management of drug submissions and applications](#)
- [Management of disinfectant drug applications](#)
- [Human-use antiseptic drugs](#)
- [Veterinary health products: About the VHP notification program](#)

The amendments introduced in Part C, Divisions 1, 1A, 2 and 8 of the *Regulations* are described in this guidance document. The amendments introduce similar provisions found in the ISAD IO with regards to requirements for drug product authorizations, DEL applications and pre-positioning of products prior to authorization. The integration of these measures in the *Regulations* aims to give Canadians continued and timely access to safe and effective COVID-19 drugs.

Policy objectives

The objective of the amended *Regulations* is to allow for a mechanism for continued and timely access to safe and effective COVID-19 drugs. The review, authorization and oversight of these drugs will be conducted under the *Regulations*.

The amendments to the *Regulations* offer the following benefits:

- continues to support access to safe, effective, and high quality COVID-19 drugs
- enables the sale and advertising of COVID-19 drugs that were authorized under the ISAD IO to continue after the IO expires
- enables manufacturers of new COVID-19 drugs for which an authorization was not sought under the ISAD IO to seek authorization under the *Regulations* with similar requirements as those provided under the ISAD IO
- continues the post-market regulatory obligations placed on authorization holders, manufacturers and importers after the ISAD IO expires
- continues to allow the early importation and placement in Canadian facilities (pre-positioning) of a promising COVID-19 drug for which a federal government contract for its procurement is in place, before that drug receives market authorization in Canada
- continues an agile approach for DELs that authorizes regulated activities for COVID-19 drugs

Under the amended *Regulations*:

1. Health Canada only grants an NOC for a COVID-19 drug under the *Regulations* if it's determined that the benefits and risks of the product are supported by evidence of the drug's safety, efficacy and consistent quality.
2. Any uncertainties or risk mitigation measures related to the drug in the context of the public health need due to COVID-19 are managed through the use of terms and conditions.
3. As with all drugs, Health Canada assesses and monitors the safety and effectiveness of all COVID-19 drugs for which an NOC was issued. If required, Health Canada takes immediate action, including compliance and enforcement measures and the suspension or cancellation of an NOC to protect the health and safety of Canadians.

Policy statements

Manufacturers of COVID-19 drugs may be able to obtain an NOC under the *Regulations* by leveraging certain options and modified requirements carried over from the ISAD IO.

These amendments to the *Regulations* allow for a submission for drugs to treat or prevent COVID-19 to be filed earlier through a "rolling submission" process. Manufacturers are responsible for completing the required documentation and providing the necessary evidence to Health Canada. COVID-19 drug submissions will be prioritized based on public health needs.

Licensing decisions are based on the materials submitted in the application. Health Canada will consider the necessity of the drug in addressing urgent COVID-19-related public health needs.

Manufacturers who have a valid authorization issued under the ISAD IO can file a new drug submission (NDS) under the *Regulations*. Sale of the drug may continue while the submission is in review, as long as it was filed within the 90-day period. (See section on "Timelines within which to file a submission under the *Regulations* to obtain a Notice of Compliance.") Where an expanded indication for COVID-19 was authorized under the ISAD IO for a marketed drug, the manufacturer is able to submit an SNDS to add the new COVID-19 indication. Modified requirements, including the ability to file a rolling submission, are not available to these SNDSs.

With this approach, manufacturers who initially obtained an authorization under the ISAD IO may submit an NDS with the same data as was included in their interim order application, along with any necessary updates. Where applicable, newly available data should be included in the NDS. To facilitate an expedited review, the sponsor should provide a summary of the submission package highlighting any changes. COVID-19 drugs are reviewed on an expedited timeline above the usual performance standards. As such, the Priority Review Policy does not apply.

Manufacturers who had their ISAD IO authorization revoked or who have never applied can also file an NDS submission leveraging the modified requirements for COVID-19 drugs in the *Regulations*.

Explanation of key terms

Designated COVID-19 drug: As defined in C.08.001.2, is a "new drug" under C.08.001. As such, it is subject to the requirements in Part C, Division 8 of the *Food and Drug Regulations*, including the:

- existing NDS and supplemental NDS (SNDS) provisions that require an NOC (see C.08.002(1) and C.08.003(1)) to allow a new drug to be sold
- submission outcomes under C.08.004
- suspension provisions under C.08.006

For this document, designated COVID-19 drugs will be collectively referred to as COVID-19 drugs.

Drug: According to the *Food and Drugs Act*, includes any substance or mixture of substances manufactured, sold or represented for use in:

- the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical state or its symptoms in human beings or animals
- restoring, correcting or modifying organic functions in human beings or animals
- disinfection in premises where food is manufactured, prepared or kept

Preparing a submission or supplement

Submission scenarios

The Governor in Council introduced amendments to the *Regulations* to provide a mechanism for COVID-19 drugs to be authorized through the issuance of an NOC, based on modified requirements that have been transferred from the ISAD IO.

Table 1 provides an overview of the modified requirements for COVID-19 drugs in the Regulations.

The “NDS CV” submission type has been created for NDSs that seek approval on the basis of any of the requirements in subsections C.08.002(2.1), C.08.002(2.2) or C.08.002(2.3) of the Regulations. To make use of any of the alternative requirements, the manufacturer must make the statements required by paragraphs C.08.002(2.4)(a) and meet the requirement in C.08.002(2.4)(b). To meet the requirements in subsection C.08.002(2.1), the manufacturer must also make the statement required by paragraph C.08.002(2.1)(a) and meet the requirement in C.08.002(2.1)(b). Manufacturers should ensure that all statements required are made in module 1.2.3, “Certification and Attestation Forms.

For more details, please refer to Submission scenarios. NDS CV submission type means NDS [COVID].

Table 1: Overview of modified requirements for COVID-19 drug submissions

Scenario	Submission type	Available modified requirements	Terms and conditions
New drug with same data as filed under IO (and possible additional data)	NDS	C.08.002(2.1): supportive evidence C.08.002(2.2): draft label C.08.002(2.3): rolling submission	Yes, only if C.08.002(2.1) is used
New COVID-19 drug (not previously filed under the ISAD IO)	NDS	C.08.002(2.1): supportive evidence C.08.002(2.2): draft label C.08.002(2.3): rolling submission	Yes, only if C.08.002(2.1) is used
Marketed drug adding additional indication for COVID-19	SNDS	None	No
Supplemental new drug submissions following authorization of the NDS	SNDS	None	Yes, if carried forward from NDS C.08.002 (2.1) and may include additional (C.01.014.21(1)(b))

Timelines within which to file a submission under the *Regulations* to obtain a Notice of Compliance

The amendments to the *Regulations* provide that an ISAD IO authorization will be revoked unless a submission is filed within:

- 90 days following the coming into force of the amendments, if the drug was authorized under the ISAD IO before the amendments came into force or
- 90 days following the issuance of an authorization under the ISAD IO, if the drug was authorized after the amendments came into force

Where a submission has been filed within these timelines, the COVID-19 drug may continue to be sold under the ISAD IO authorization until the submission has been approved, rejected or withdrawn. This is the case even after the ISAD IO ceases to have effect.

If a manufacturer fails to file a submission under the *Regulations* within the prescribed timelines, the manufacturer will have to wait until the product is authorized under the *Regulations* to resume sale.

Modified requirements

Manufacturers of COVID-19 drugs will have the option to follow similar requirements under the *Regulations* to those under the ISAD IO, as set out in paragraphs C.08.002(2.1) to (2.3). To make use of these alternate requirements, manufacturers must include a statement identifying that the purpose and conditions of use specified in the NDS relate only to COVID-19.

Manufacturers should ensure that all statements required are made in module 1.2.3, “Certification and Attestation Forms.” Manufacturers are also encouraged to identify in a cover letter the modified requirements they intend to follow.

Modified requirements include:

- ability to file a rolling submission(C.08.002(2.3))
- exemption from submitting detailed reports of tests made to establish the safety and clinical effectiveness of the new drug under C.08.002(2)(g) and (h)
 - however, the manufacturer must provide sufficient evidence that the benefits of the drug outweigh the risks, taking into account uncertainties as well as the public health need due to COVID-19 (C.08.002(2.1)(b))
- exemption from being required under C.08.002(2)(j.1) to provide a mock-up label if the manufacturer provides a draft of the label
 - submission must also include any package insert and document provided upon request that sets out supplementary information on use of the drug (C.08.002(2.2))
- exemption from being required under C.08.002(2)(o) to conduct an assessment as to whether there is a likelihood the new drug will be mistaken for another drug due to a resemblance between the brand names
 - commonly referred to as a brand name assessment

The options available in subsections C.08.002(2.1), C.08.002(2.2) and C.08.002(2.3) only apply if the manufacturer has met the requirements outlined in subsection C.08.002(2.4).

Health Canada intends to assess the requirements of subsections C.08.002(2.1), C.08.002(2.2), C.08.002(2.3) and C.08.002(2.4) in screening.

In accordance with C.08.002(2.5), the amended regulations do not apply if the manufacturer is seeking a notice of compliance for a COVID-19 drug on the basis of a direct or indirect comparison between the COVID-19 drug and another COVID-19 drug (for example, a generic or biosimilar submission). Submissions will be assessed under C.08.002(2.5) before a submission receives a filing date.

Safety and efficacy: C.08.002(2.1) as an alternative to C.08.002(2)(g) and C.08.002(2)(h)

The *Regulations* were amended to allow manufacturers who seek approval for a COVID-19 drug to file a submission with an alternative data package where justified based on the urgent public health needs resulting from COVID-19. As more products emerge to address the public health needs brought upon by COVID-19, manufacturers should discuss data requirements with Health Canada prior to filing. A data package based on C.08.002(2.1) may only be appropriate in some circumstances.

Following discussion with Health Canada, a manufacturer may file an NDS for a COVID-19 drug without complying with the requirements set out in paragraphs C.08.002(2)(g) and C.08.002(2)(h). To do so:

- the manufacturer must state that the NDS is for a COVID-19 drug (C.08.002(2)(2.1)(a))
- the NDS must contain sufficient safety, efficacy and quality evidence such that the benefits of the new drug outweigh the risks (C.08.002(2)(2.1)(b))

Manufacturers should make the required statement in module 1.2.3, “Certification and Attestation Forms.” Manufacturers are encouraged to specify in a cover letter that the NDS relies on subsection C.08.002(2.1) of the *Regulations* to facilitate processing.

A manufacturer who relies on C.08.002(2.1) to provide evidence of safety and efficacy will be subject to any terms and conditions that might be imposed on an NOC issued for the COVID-19 drug. (See paragraph C.01.014.21(1)(b).) In the context of the public health need related to COVID-19, the manufacturer is required to include in the NDS sufficient safety, efficacy and quality evidence showing that the drug’s benefits outweigh the risks. Health Canada reviews the NDS and will apply terms and conditions on the authorization to require the manufacturer to address risks and uncertainties after authorization.

If the manufacturer has a full data package to support the NDS, then they may choose not to rely on C.08.002(2.1).

For more information, see the following guidance documents on:

- [Evidence requirements for COVID-19 vaccines](#)

Product labels

C.08.002(2.2) provides for exemption from the requirement in C.08.002(2)(j.1) to provide a mock-up of labels of the drug.

However, the submission must contain a draft of every label to be used with the new drug. This includes any package insert and any document that sets out supplementary information on the use of the new drug.

Manufacturers are encouraged to specify in a cover letter that the NDS relies on subsection C.08.002(2.2) of the *Regulations* to facilitate processing.

Rolling submissions

C.08.002(2.3) carries over a manufacturer’s ability to file a rolling submission, as permitted in the ISAD IO. It is recognized that submissions may not be complete at the time of initial filing. Health Canada will begin its review using the information submitted by the manufacturer and accept new evidence as it becomes available until the submission is deemed complete. A manufacturer may file an NDS for a new COVID-19 drug without including some of the data otherwise required under:

- paragraphs C.08.002(2)(e) to C.08.002(2)(k), C.08.002(2)(m) and C.08.002(2)(n)
- paragraph C.08.002(2.1)(b) or
- subsection C.08.002(2.2)

This rolling review process can reduce the time it takes to authorize these critical new drugs while maintaining appropriate standards of safety, efficacy and quality.

To file a rolling submission, the manufacturer must include all applicable forms and other administrative components. The NDS must also include a plan identifying the missing parts of the submission. This plan must specify how and when the missing information or material will be provided to the Minister during the review period. (See C.08.002(2.3).)

Manufacturers are encouraged to specify in a cover letter that the NDS relies on subsection C.08.002(2.3) of the *Regulations* to facilitate processing. As with other NDSs under Division 8, the filing date refers to the date that:

- the NDS is deemed administratively complete by Health Canada
- all the elements and forms required for processing are completed and submitted to Health Canada

The filing date may differ from the date of original receipt if the submission is considered to be administratively incomplete at that time. Data or information that is subsequently provided in a rolling submission will be considered solicited information under the NDS and will not change the filing date of the submission.

Sufficient information must be submitted within a reasonable timeframe. The Minister reviews the NDS based on the requirements and makes a decision, as per section C.08.004 of the *Regulations*.

The plan should contain:

- a list of the non-clinical, clinical and quality data to be provided (planned and in progress)
- a timeframe for when this clinical and quality data will be available
- a timeframe for when this clinical and quality data will be filed for review

If the missing information outlined in the plan will be submitted as multiple packages, the plan must clearly specify what information will be contained in each data package. For example:

- data package A will be submitted on DD/MM/YYYY and contains results from studies XX, YY and ZZ
- data package B will be submitted on DD/MM/YYYY and contains results from studies MM, NN and OO

Pre-submission meetings provide an opportunity to discuss the plan in detail. These meetings should be used to:

- establish submission content and timelines
- determine the data that will be submitted when the submission is filed
- determine the data that will be provided at a later date

The cover letter should refer to the plan. If changes are required to labelling to reflect the new information, annotated and clean copies of the drug labels should be included.

Health Canada will:

- review the submission to ensure it includes the detailed plan
- assess the information submitted by the manufacturer
- accept new evidence as it becomes available until the review has been completed

Any subsequent data or information sent later is considered solicited information under the NDS if the data or information is provided according to the plan or in response to Health Canada's request. Information or data provided otherwise may be considered unsolicited information.

Health Canada will not issue an NOC until the Minister is satisfied that the NDS complies with the requirements of C.08.002.

Regulatory activity and transaction details for designated COVID-19 drugs

As noted above, modified requirements introduced through amendments to the *Regulations* are only available for an NDS. The “NDS CV” submission type has been created for NDSs that use any of the provisions in subsections C.08.002(2.1), C.08.002(2.2) or C.08.002(2.3) of the *Regulations*. The manufacturer must select the “NDS CV” submission type in the appropriate Regulatory Enrolment Process (REP) regulatory transaction template when submitting their NDS. “NDS CV” submission types are described as “Drug Submission with modified requirements for Designated COVID-19 drugs.”

To file an NDS that does not benefit from any of the modified requirements mentioned in the 3 subsections above, a manufacturer must select the regular NDS submission type when submitting its NDS.

Pre-submission meetings

Manufacturers are encouraged to have regular communications with Health Canada. Early and ongoing consultation(s) with Health Canada help ensure that regulatory requirements are met.

Before filing an NDS, manufacturers are encouraged to request a pre-submission meeting to discuss all aspects of their submission. At this meeting, Health Canada will expect you to describe your submission plan and indicate how and when you will provide the Minister with the missing information or material, if applicable (subsection C.08.002(2.3)).

To request a pre-submission meeting with the appropriate directorate, consult the guidance documents on the:

- [Management of drug submissions and applications](#)
- [Management of regulatory submissions for veterinary drugs](#)

For relevant contact information, please see key contacts.

Format and structure for filing

For general procedures on how to file applications, please also refer to the guidance documents on the:

- [Management of drug submissions and applications](#) or
- [Management of regulatory submissions for veterinary drugs](#)

Submissions for human drugs should be formatted, structured and filed as outlined in the:

- [Guidance document on the preparation of regulatory activities in the eCTD format](#)
- [Organisation and document placement for Canadian module 1](#)
- [Guidance document on the regulatory enrolment process \(REP\)](#)

Manufacturers who cannot comply with the formatting requirements may contact the Office of Submissions and Intellectual Property for further options and guidance. Please send an email to hc.ereview.sc@canada.ca.

Submissions for veterinary drugs should be formatted, structured and filed as outlined in the following guidance documents on the:

- [Preparation of regulatory activities in the non-eCTD format](#)
- [Regulatory enrolment process \(REP\)](#)

Manufacturers who cannot comply with the formatting requirements may contact the Veterinary Drugs Directorate by email at hc.vdd.skmd.so-dgps.dmv.cp.sc@canada.ca.

Submissions made under the *Regulations* must be independent from any ISAD IO application. At a minimum, they must contain the same data that was included in the ISAD IO application, along with any required updates. The sponsor must include all the data they rely on to support their submission in the NDS.

Submissions filed under the *Regulations* for which an application was previously filed under the ISAD IO will receive the same dossier ID as the ISAD IO application. Manufacturers are expected to identify this dossier ID in relevant correspondence.

Content and requirements for filing

For both the non-clinical and clinical information package, you may not need to include as much information as you do for a data package in a typical drug submission. This is balanced by additional information, which is to be provided as part of the rolling submissions as well as the terms and conditions of authorization.

Non-clinical information and requirements

Key non-clinical information may be required to:

- demonstrate the potential for clinical effectiveness under the proposed conditions of use
- support the safety of the COVID-19 drug

All key studies should be conducted in accordance with good laboratory practices.

For more information, consult the following guidance document:

- [Non-clinical laboratory study data supporting drug product applications and submissions: Adherence to good laboratory practice](#)

Clinical information and requirements

A manufacturer may submit an NDS relying on the modified requirements in C.08.002(2.1) to (2.3). All known information should be provided to support the safety and efficacy of the COVID-19 drug. This includes all available clinical trial data and the safety and efficacy summary documents.

For more information, consult the following guidance documents on:

- [Evidence requirements for COVID-19 vaccines](#)

Quality (chemistry and manufacturing) information and requirements

For further guidance on meeting application and information requirements, consult the list of guidance documents. Under section C.08.002(2.3) in the *Regulations*, the manufacturer may provide the information and material normally required under paragraphs (2)(e), (f) and (m) on a rolling basis. The manufacturer must specify in their plan how and when they will provide the missing information to Health Canada.

For more information, consult the following guidance documents on:

- [Evidence requirements for COVID-19 vaccines](#)

Comparative submissions for subsequent entry drugs

Under the Abbreviated New Drug Submissions (ANDS) and NDS pathways of the *Food and Drug Regulations*, manufacturers of subsequent entry drugs (generics and biosimilars) can seek an NOC on the basis of a comparison to a drug that has already received an NOC.

Manufacturers must demonstrate similarity to an authorized reference drug (for example, in the case of generics, a Canadian reference product as defined in section C.08.001.1). This is done by filing a comparative submission that relies, in part, on the previously authorized evidence of safety and effectiveness for the reference drug. The manufacturer may then submit a reduced data package in the submission.

The amendments do not extend the modified requirements provided under new subsections C.08.002(2.1), (2.2) and (2.3) to cases where manufacturers seek an NOC for a COVID-19 drug on the basis of a direct or indirect comparison between that drug and another COVID-19 drug.

The *Regulations* do not allow comparative submissions to be filed while benefitting from any of the modified requirements, even where consent from the reference product manufacturer is provided. Therefore, comparative submissions are expected to be filed as an ANDS or a comparative NDS.

Health Canada will apply subsection C.08.002(2.5) of the *Regulations* in processing and comparative submissions that seek approval on the basis of any of the new subsections C.08.002(2.1), (2.2) and (2.3) will not receive a filing date. When it appears that the filing of a submission is prevented, the manufacturer will be provided with a written preliminary decision and an opportunity to make representations in response. If, following consideration of the representations, Health Canada remains of the view that the submission cannot be filed, the manufacturer will be notified and the submission will not be processed further.

Manufacturers of subsequent entry products are prohibited from filing a submission on the basis of a direct or indirect comparison to a COVID-19 drug for which an authorization was issued under the ISAD IO (C.08.003.01(2)). Note that subsection C.08.003.01(2) is not intended to prevent the filing of a submission that contains new data from clinical trials comparing the efficacy of the new drug to an existing one. Also note that C.08.003.01 does not prevent the filing of a submission or supplement on the basis of a comparison to a COVID-19 drug that has received an NOC (C.08.003.01(3)).

Manufacturers who intend to file a submission seeking an NOC for a COVID-19 drug on the basis of a comparison with another COVID-19 drug are encouraged to contact Health Canada for a pre-submission meeting.

Information and requirements for veterinary drugs

A COVID-19 drug submission should contain all available information to help Health Canada assess the drug's safety, efficacy and quality. Information should include evidence of its efficacy in the target species, animal safety, human safety and quality.

For drugs used in a food-producing animal, information should be provided on the safety of drug residues in meat and other food products from the treated animal intended for human consumption.

Risk management plan

Manufacturers should submit a Risk Management Plan (RMP) for a COVID-19 drug. If an RMP has been filed as part of the ISAD IO application, an updated RMP with the most recent post marketing data, risk minimization measures and pharmacovigilance activities should be submitted.

The RMP should focus on the product's updated safety risks in the context of COVID-19 use to ensure that:

- the benefit-risk profile of the product is managed optimally during its life-cycle
- knowledge gaps at the time of authorization are described and risks are further quantified and characterized over time

It should:

- outline the product's safety risks related to COVID-19 use
- outline the pharmacovigilance activities and risk minimization activities used to identify, characterize, prevent or minimize risks
- contain an evaluation of the effectiveness of such risk minimization measures

For information on the scope of RMPs, please refer to the following guidance document:

- [Submission of risk management plans and follow-up commitments](#)

For COVID-19 drugs submitted for authorization, the RMP should include the following:

- safety specification section on the identified risks, potential risks and missing information for the product (for example, special populations where there is limited information or who were excluded from clinical trials), with a focus on risks in COVID-19 patients, where appropriate
- pharmacovigilance plan on the specific activities to be taken to identify and report safety issues, including expedited adverse reaction reporting, periodic reporting and ongoing/planned studies to quantify and characterize those risks (for example, registries, prospective cohort studies)
- risk minimization plan to manage the safety risks including routine risk minimization measures (for example, labelling) and additional measures beyond those considered routine (such as educational materials for health care professionals or patients, or a restricted access or distribution program), if needed
- plan to measure the effectiveness of additional risk minimization activities

An RMP that has been reviewed and accepted as part of the submission for a COVID-19 drug is expected to be implemented. If the manufacturer filed under the requirement in subsection C.08.002(2.1), any elements of an RMP that are essential for the safe and effective use of the product could be identified as terms or conditions and must be implemented.

A Canadian addendum that demonstrates that the RMP meets Canadian regulatory requirements must accompany the core RMP. Information on these requirements are provided in the following guidance documents and recent notice:

- [Evidence requirements for COVID-19 vaccines](#)
- [Notice of clarification to drug manufacturers and sponsors on Canadian-specific considerations in risk management plans](#)

If you have a question about the type of quality, safety and effectiveness information required, please contact the appropriate directorate within Health Canada. Please refer to the key contacts for relevant contact information.

Labelling

Manufacturers of a COVID-19 drug must comply with all applicable labelling requirements in the *Food and Drugs Act* and parts A and C of the *Regulations*:

- A.01.014
- A.01.015
- A.01.60.1 to A.01.068
- A.01.065
- C.01.004 to C.01.011
- C.01.401
- C.03.202
- C.03.203
- C.03.206 to C.03.209
- C.04.019 and C.04.020

Existing regulatory provisions on the labelling of veterinary drugs also apply.

Manufacturers that file an NDS for a COVID-19 drug using the modified requirements may be asked to include a warning statement on the inner and outer labels. This statement may be displayed on any panel. The data submitted to support the NDS and any associated terms and conditions that the Minister places on the DIN will dictate this.

The plain language labelling requirements for mock-up labels and a brand name assessment package do not apply (C.08.002(2)(j.1) and C.08.002(2)(o)).

While exempt from these requirements, manufacturers are strongly encouraged to complete and submit a brand name assessment package and to provide mock-up labels:

- at the time of NDS filing (if available) or
- at the earliest time after the NDS is filed

Manufacturers may also file these materials after the NOC is granted.

Health Canada may apply labelling terms and conditions as necessary. We will request that the sponsor submit a brand name assessment and final mock-up package labels at an agreed-upon time if the sponsor chooses to use the labelling modified requirements provided by the *Regulations*.

Manufacturers that are unable to provide a complete brand name assessment package at the time of filing or at the earliest time after the NDS is filed, may provide a package where simulation exercises are omitted.

Plain language labelling and Look-alike Sound-alike components are not needed with respect to the labelling of veterinary drugs.

Consult the list of guidance documents for further guidance on labelling.

Filing a supplement to an NDS for a COVID-19 drug

A manufacturer of a COVID-19 drug that holds an authorization for a new drug under the ISAD IO may file an NDS under section C.08.002 of the *Regulations*. Once the manufacturer receives an NOC for the COVID-19 drug, they may file a supplement to that new drug submission (SNDS) for any changes post-NOC. Where applicable, the manufacturer may also be able to incorporate the change as part of its NDS.

Consult the following guidance documents on post-NOC:

- [Framework document for pharmaceutical, biologic and radiopharmaceutical drugs for human use only](#)
- [Safety and efficacy document for pharmaceutical, biologic and radiopharmaceutical drugs for human use only](#)
- [Post-notice of compliance \(NOC\) changes: Quality document](#)

Notice of compliance (NOC) for a COVID-19 drug

For Health Canada to issue an NOC (C.08.004) for the sale of a COVID-19 drug, the NDS must meet the requirements of section C.08.002. For drugs relying on the modified requirements in C.08.002 (2.1), the NDS must contain enough evidence to support the conclusion that the drug's benefits outweigh the risks when used as indicated. The evidence takes into consideration the uncertainties around the drug in the context of the public health need related to COVID-19.

Drug identification number (DIN)

When the manufacturer of a COVID-19 drug that was previously authorized under the ISAD IO submits an NDS to obtain an NOC, the DIN that was assigned under the ISAD IO remains active until the NDS has been approved, rejected or withdrawn. This ensures that all regulatory obligations associated with the DIN continue.

Once an NOC is issued for a COVID-19 drug, Health Canada may assign the same digits for the DIN under C.01.014.2 as were issued under section 7 of the ISAD IO.

If the submission that was submitted under the *Regulations* is rejected or withdrawn, the DIN will be revoked at that time.

Manufacturers should refer to the [Guidance document on the regulatory requirements for drug identification numbers \(DINs\)](#) for more information on DINs.

Terms and conditions on a DIN pertaining to a COVID-19 drug relying on modified requirements in C.08.002(2.1)

Health Canada may at any time impose or amend terms and conditions on a DIN (C.01.014.21(1)(b)) of a COVID-19 drug where the manufacturer relied on C.08.002(2.1) to obtain an NOC. If the manufacturer only used other provisions, then the terms and conditions power does not apply.

This authority allows Health Canada to issue an NOC for a COVID-19 drug while attaching additional conditions that the DIN holder must comply with. These terms or conditions are used to ensure appropriate oversight, manage uncertainties or mitigate risks. However, the terms and conditions on a DIN for a COVID-19 drug using the submission flexibility in C.08.002(2.1) will be based on what's needed when a submission is not able to meet the usual data requirements. Examples of anticipated terms and conditions include:

- specific pharmacovigilance and risk mitigation and management measures
- additional quality information
- confirmation of effectiveness
- drug shortage measures introduced to prevent or alleviate a shortage

The terms and conditions are on the DIN and remain on the DIN regardless of subsequent SNDSs (supplement to a new drug submission). The exception is if the Minister removes the terms and conditions as part of the (SNDS) process.

The terms and conditions may also apply to drugs authorized on the basis of a comparison to a COVID-19 drug, where the NOC of the comparator product had relied on these submission flexibilities (C.01.014.21(1.1)(b)). This ensures that any post-market commitments for a reference product may also be imposed on NOCs issued on the basis of a comparison.

Terms and conditions can be imposed or amended at any time on a DIN for a COVID-19 drug (C.01.014.21(1.1)(a)) that was filed as:

- an NDS under section C.08.002 relying on the data flexibility referred to in C.08.002(2.1)
- a supplement to an NDS for that new drug

They can also be imposed or amended at any time on a DIN for a COVID-19 drug (C.01.014.21(1.1)(b)) authorized on the basis of a direct or indirect comparison to another COVID-19 drug (see C.01.014.21(1.1)(a)) and filed as:

- an NDS filed under C.08.002
- an abbreviated new drug submission (ANDS) filed under C.08.002.1
- a supplement to a new drug submission or an abbreviated new drug submission that is filed under section C.08.003

Health Canada will discuss the terms and conditions with the sponsor prior to imposing them. All terms and conditions are enforceable under section 21.7 of the Act.

Terms and conditions do not apply to any drugs, including COVID-19 drugs, authorized through the existing NDS and SNDS pathway if the manufacturer:

- is able to satisfy the full data requirements (C.08.002(2)(g) and (h))
- has not relied on C.08.002(2.1)

Submitting information to fulfill terms and conditions

Information on the fulfilment of terms and conditions should be submitted as solicited information with an accompanying cover letter. The subject should state “Solicited information, fulfilling Terms and Conditions for COVID-19 drug.” Supporting documentation is to be provided.

Health Canada will review the documentation to determine if the conditions have been met. Once we are satisfied that the manufacturer has complied with all the terms and conditions, we will indicate this in a letter and reference the original file/control number.

Market notification

A market notification for a drug authorized under the ISAD IO does not constitute market notification of a drug under the *Regulations*. This is the case even if the same digits have been issued to the drug as the DIN under both the ISAD IO and the *Regulations*.

The manufacturer of a COVID-19 drug authorized under the *Regulations* must notify Health Canada when they first sell the COVID-19 drug under an NOC. The manufacturer must complete, sign, date and return the Health Canada-issued drug notification form (DNF) within 30 days of the date of the first sale. All pages of the DNF must be returned to Health Canada.

The DIN assigned under the ISAD IO will be revoked once the same DIN is assigned to the drug under the *Regulations*. Our [drug product database](#) will indicate the DIN as “approved” until the manufacturer submits a completed DNF, at which point the DIN will be “marketed.”

If the manufacturer did not file mock-up labels during review, the manufacturer should submit final mock-ups or final printed labels when the COVID-19 drug is marketed or launched.

For more information on market notifications or notifications for the ‘interruption of sale,’ consult the:

- [Guidance document on the regulatory requirements for drug identification numbers \(DINs\)](#)

Changes in product ownership, mergers and buyouts or licensing agreements

Submissions proposing administrative changes should be filed within Administrative (Abbreviated) New Drug Submissions ((A)NDS).

If sponsors are proposing labelling changes along with the proposed administrative changes, they must file these changes within an (A)NDS ‘labelling only’ to obtain Health Canada authorization. They must do so before making any changes to labelling materials on the market.

Refer to the following guidance document for more information:

- [Administrative processing of submissions and applications involving human or disinfectant drugs](#)

Notification of discontinuation of sale

The manufacturer of a COVID-19 drug must submit the notification of discontinuation of sale to Health Canada within 30 days after the COVID-19 drug is permanently discontinued in Canada. The date of discontinuance is when the manufacturer last sells its drug, not when it is last sold at retail.

For information and general procedures on notification of discontinuance, authorization holders should consult the:

- [Guidance document on the regulatory requirements for drug identification numbers \(DINs\)](#)

For more information on additional requirements on how to report a discontinuance of sale, see the section on [shortages or discontinuation of sale](#).

Transparency

Health Canada will continue to communicate up-to-date information about COVID-19 drugs under the amended *Food and Drug Regulations*.

You can find the following information online:

- [COVID-19 vaccines and treatments portal](#)
- submissions for COVID-19 drugs that have been accepted for review in the [lists for drug and health product submissions under review](#)
- [regulatory decision summaries \(RDS\)](#) and [summary basis of decisions](#) documents (SBDs) for COVID-19 drugs in the [drug and health product register](#)
- clinical information used to seek approval of COVID-19 drugs can be viewed on Health Canada's [clinical information portal](#) or the [drug and health product register](#)
- drug inspection outcomes and measures in the [drug and health product inspections database](#)

In addition, Health Canada will continue to provide the most up-to-date approved Risk Management Plans for COVID vaccines in their entirety to external stakeholders upon request.

Please also consult the following guidance documents:

- [Public release of clinical information](#)

Performance standards

Health Canada aims to prioritize submissions for COVID-19 drugs. Drug submissions will be prioritized and reviewed to reflect the public health need.

The time required to review a submission will depend on the submission itself, the volume of data to be assessed and the ability of the manufacturer to submit the data as per the plan, where applicable. Published performance standards will apply to submissions related to COVID-19 drugs, other than rolling submissions, made under the *Regulations*.

Rolling submissions will not be subject to performance standards (in other words, credits to manufacturers due to missed performance standards). This is explained in the Fees section below.

For more information, refer to the following guidance documents on the:

- [Management of drug submissions and applications](#)
- [Management of regulatory submissions for veterinary drugs](#)

Fees

Submission fees

Pre-market evaluation fees will be remitted for submissions filed under the *Food and Drug Regulations* seeking approval for a COVID-19 drug, provided that:

- an application was previously filed under the ISAD IO for the same drug and
- no submission was previously filed under the *Food and Drug Regulations* for that drug

Once a drug has received an NOC under the *Regulations*, the existing Drug Right To Sell (DRTS) fee will apply.

Where an application had not been filed under the ISAD IO, the following fees will apply to COVID-19 drug submissions filed under the *Regulations*:

- existing evaluation fees will be charged for submissions
- existing small business mitigation measures are available for COVID-19 drug submissions, and include
- full waiver of evaluation fee for the company's first drug submission with Health Canada
- a 50% reduction in all other evaluation fees as well as a 25% reduction in DIN and DEL fees

Please consult the guidance document on:

- [Fees for the review of human and disinfectant drug submissions and applications](#)

Submissions with fees have associated performance standards. Penalties may apply:

- Published performance standards will apply, but it's expected that most COVID-19 drug submissions will be managed and reviewed efficiently.
- Rolling submissions will not be subject to performance standards (in other words, the 25% remittance to manufacturers due to missed performance standards will not apply).

Drug establishment licences and good manufacturing practices

Drug establishment licences for COVID-19 drugs

Division 1A of Part C of the *Regulations* applies to COVID-19 drugs. A person must hold a drug establishment licence (DEL) authorizing any activities conducted with respect to COVID-19 drugs.

You can find the following information online:

- how to interpret the *Regulations* for DEL requirements in the [Guidance on drug establishment licences \(GUI-0002\)](#)
- your responsibilities related to the DEL application process and how Health Canada manages DEL applications in the document on the [Management of applications and performance for drug establishment licences \(GUI-0127\)](#)

For more information about drug establishment licences and COVID-19, see our page on [drug establishment licences and COVID-19](#).

If you have questions about the DEL requirements or DEL applications for COVID-19 drugs, please email us at hc.del.questions-leppp.sc@canada.ca. Include the term “COVID-19” in your email subject line for a faster response.

Applying for a new or amended DEL for a COVID-19 drug

New drug establishment licence (DEL) applications (C.01A.005(1)) or amendment applications (C.01A.006(1) (1.1)) for a COVID-19 drug can be submitted under the *Regulations*. Follow the [standard process and use the most current version of the application form \(FRM-0033\)](#).

When applying for a new or amended DEL for a COVID-19 drug, be sure to include the following information:

- the subject line “COVID-19 drug” in the application email, which signals that this is a high-priority application
- a statement in the body of the application email or cover letter that the DEL application is for a COVID-19 drug submitted under C.01A.005(2) or C.01A.006(1.1) of the *Regulations*
- the name of the drug

Submit your completed application form by email to hc.el.applications-le.sc@canada.ca.

For more information on DEL requirements, please consult the following guidance documents on:

- [Drug establishment licences \(GUI-0002\)](#)
- [How to demonstrate foreign building compliance with drug good manufacturing practices \(GUI-0080\)](#)
- [Management of applications and performance for drug establishment licences \(GUI-0127\)](#)

Issuance of a DEL for a COVID-19 drug

Health Canada issues or amends DELs in accordance with Part C, Division 1A of the *Regulations*.

COVID-19-related DEL applications submitted under the *Regulations* are processed in an expedited manner. Timelines for the expedited review are determined on a case-by-case basis. The materials submitted in the application and the volume of information to be assessed are factors in how quickly we can review the application.

For more information on the issuance of a DEL or DEL amendments, please consult the:

- [Guidance on drug establishment licences \(GUI-0002\)](#)

DEL terms and conditions

At any time, Health Canada may impose or amend terms and conditions on DELs for a COVID-19 drug submitted under the *Regulations*. Decisions to impose or amend terms and conditions are based on the need to mitigate or manage additional oversight for risk-based reasons. These reasons include matters related to available evidence, medical necessity and activities conducted.

The ability to impose or amend terms and conditions gives Health Canada the agility to facilitate rapid access to COVID-19 drugs while mitigating risks.

Terms and conditions previously imposed on a DEL issued under the ISAD IO for a COVID-19 drug will continue to apply under the *Regulations* as necessary.

Every person who holds a DEL must conduct the licensable activities in accordance with the licence, and any terms and conditions imposed on it.

DEL holders that do not comply with the terms and conditions imposed on their licence will be subject to compliance and enforcement action for the contravention of s. 21.7 of the Food and Drugs Act. Such actions will align with the legislative framework and the principles outlined in our [compliance and enforcement policy for health products](#) (POL-0001).

DEL suspension and cancellation

Health Canada can suspend or cancel a DEL in full or in part for any of the reasons set out in sections C.01A.016 to C.01A.017.1 in order to prevent a risk to the health and safety of the consumer in relation to a COVID-19 drug. When a DEL is suspended or cancelled, the DEL holder must cease all suspended/cancelled activities.

For more information on DEL suspension and cancellation, consult the:

- [Guidance on drug establishment licences \(GUI-0002\)](#)

DEL performance standards

DEL applications related to COVID-19 drugs will be prioritized and reviewed based on the:

- public health need
- materials submitted in the application
- volume of information to be assessed

For more information on the performance standard, consult the guidance document on the:

- [Management of applications and performance for drug establishment licences \(GUI-0127\)](#)

Drug establishment licence fees

DEL fees will be remitted for applications submitted under the ISAD IO until September 16, 2021. After that time, drug establishment licence fees will apply to the review of DEL applications submitted for a COVID-19 drug.

Please consult the guidance document on:

- [Fees for the review of human and veterinary drug establishment licence applications](#)

Fees apply for the review of the following types of DEL applications:

- an application for a new or reinstated DEL
- an application for an amendment to add a domestic building to a DEL
- an application for the annual licence review of a DEL

The DEL fee is calculated using the following components:

- Domestic component: the fee charged for each building listed on the licence or application based on the most upstream activity at that building
- Foreign building component: the fee charged for each unique foreign building (or building outside Canada) on the licence or application

Fees can be requested to be waived or reduced for applications filed by:

- a small business
- a publicly funded health care institution
- any branch or agency of the Government of Canada or of a province or territory

Transitioning of DELs issued or amended under the ISAD IO

Applications that have been submitted under section 20 of the ISAD IO before it expires but have not been issued will continue to be reviewed as though they were submitted under subsections C.01A.005(2) or C.01A.006(1.1) of the *Food and Drug Regulations*. For such applications, DEL fees do not apply.

Notification

DEL holders who wish to maintain their licence, or part of their licence, for a COVID-19 drug under the *Regulations* must notify Health Canada before the ISAD IO expires. We recommend doing so at least 30 days before the ISAD IO expires.

To maintain a DEL issued under section 20 of the ISAD IO, please submit the following information to Health Canada:

- include “Maintain COVID-19 drug IO DEL” in the subject line of the notification email
- include details indicating the notification is being submitted to maintain a DEL or part of a DEL issued for an application submitted under section 20 of the ISAD IO
- include the application number assigned by the Drug Establishment Licensing Unit

Health Canada will review your notification to maintain and will inform you if additional information is required.

Failure to notify us will result in the DEL being cancelled, in whole or in part by operation of the transitional rule of the *Regulations*.

Good manufacturing practices

For information on the requirements around good manufacturing practices (GMP), consult the:

- [Good manufacturing practices guide for drug products \(GUI-0001\)](#)

Evidence requirements to support GMP compliance of foreign buildings is included in the following guidance:

- [How to demonstrate foreign building compliance with drug good manufacturing practices \(GUI-0080\)](#)

If you're unable to obtain documents outlined in GUI-0080 due to the pandemic, please email us at hc.foreign.site-etranger.sc@canada.ca. You should contact us before you send in your DEL application. Be sure to include “COVID-19” in your subject line.

If you're unable to host a GMP drug inspection at your facility due to the pandemic, please email us at hc.drug.gmp.questions-bpf.medicaments.sc@canada.ca. We may consider operational relief and flexibilities to inspection timelines as set under the current fee regime on a case-by-case basis. To monitor compliance, GMP inspections will be conducted using a risk-based approach for licensable activities.

Extension of certain flexible measures for DEL and GMP compliance, as communicated in DEL bulletins, will continue until further notice.

For more information about good manufacturing practices and COVID-19, see our page on [good manufacturing practices and COVID-19](#).

Finished product testing

DEL holders must meet all product release requirements as outlined in the *Food and Drug Regulations*.

Finished product testing requirements in C.02.019 of the Regulations no longer apply to a distributor or importer of a schedule D (biologic) COVID-19 drug if it's subject to a written request under the lot release program (C.04.015).

Licence holders must comply with testing requirements set out in Division 2 of the *Regulations*. If you are unable to meet these requirements due to the pandemic, contact us at hc.drug.gmp.questions-bpf.medicaments.sc@canada.ca.

For more information on the lot release program requirements, refer to the:

- [Guidance for sponsors on the lot release program for schedule D \(biologic\) drugs](#)
- [Good manufacturing practices guide for drug products \(GUI-0001\)](#)

Intellectual property

As a consequence of the review, authorization and oversight of COVID-19 drugs under the *Regulations*, manufacturers may benefit from intellectual property protections that are available in respect of a submission that results in an NOC. These protections include:

- data protection under section C.08.004.1 of the *Food and Drug Regulations*
- protection under the *Patented Medicines (Notice of Compliance) Regulations (PM (NOC) Regulations)*
- protection under the *Certificate of Supplementary Protection* regime

Data protection

The amendments contain one interpretive provision clarifying the impact of an authorization under the ISAD IO on data protection eligibility, but do not alter these protections.

Subsection C.08.004.1(1) of the *Food and Drug Regulations* provides that an “innovative drug” is one that contains a medicinal ingredient not previously approved in a drug by the Minister and that is not a variation of a previously approved medicinal ingredient. The amendments introduce language to explain that, for the purpose of the definition of “innovative drug” in subsection C.08.004.1(1) of the *Regulations*, a medicinal ingredient is not considered to be approved in a drug by reason of an authorization under the ISAD IO. This provision is not intended to change the scope or current interpretation of “approved” under the existing definition. Rather, it explains the intended application of that definition where a medicinal ingredient was used in a drug authorized under the ISAD IO.

The interpretation of “innovative drug” ensures that an authorization granted under the ISAD IO does not preclude data protection eligibility under the *Regulations*.

Data protection will be assessed in accordance with the existing process, as described in the [Guidance document on data protection under C.08.004.1 of the *Food and Drug Regulations*](#).

Patented Medicine (Notice of Compliance) Regulations

The amendments to the *Food and Drug Regulations* do not disturb the operation of the *Patent Act* or the *Patented Medicine (NOC) Regulations*. Patent lists may be added to the Patent Register at the time the submission or supplement is approved under the *Regulations*, provided the requirements of the *PM(NOC) Regulations* are met.

For a rolling submission, data or information provided after the filing date will not change the filing date of the submission. As with other submissions, patent lists provided after the filing date of the submission must meet the timing requirements of subsection 4(6) of the *PM(NOC) Regulations* to be considered for inclusion on the Patent Register.

The *PM(NOC) Regulations* will continue to be administered in accordance with existing processes. These are described in the [guidance document on Patented Medicines \(Notice of Compliance\) Regulations](#).

Certificate of supplementary protection

The amendments to the *Food and Drug Regulations* do not disturb the operation of the *Patent Act* or the *Certificate of Supplementary Protection Regulations (CSP Regulations)*. Therefore, a certificate of supplementary protection may be issued in respect of a patent to a drug approved under the *Regulations*, provided the requirements of the *CSP Regulations* and *Patent Act* have been met.

Though not introduced for this purpose, the provisions contained in these amendments allow an earlier filing of an NDS, making it easier for manufacturers to file their NDS within the time period specified in paragraph 106(1)(f) under the *Patent Act* and 6(1)(b) established under the *CSP Regulations* to be eligible to obtain a certificate of supplementary protection.

The certificate of supplementary protection scheme will continue to be administered in accordance with existing laws and the process described in the [Guidance document on certificates of supplementary protection](#). Stakeholders are encouraged to consult section 2.2.2 of this document to review Health Canada's continued interpretation respecting an "application for a marketing approval equivalent to an authorization for sale" for the purpose of paragraph 106(1)(f) of the *Patent Act* and paragraph 6(1)(b) of the *CSP Regulations*.

Post-market requirements

The only amendment related to post-market regulation is the Minister's new (continued) authority to impose terms and conditions for a designated COVID-19 drug (C.01.014.21).

To ensure the safe and effective use of a product, additional post-market requirements may be imposed as a term or condition on the authorization. An example of a post-market term or condition on the authorization is the submission and implementation of a risk management plan ((RMP) and/or elements thereof). Otherwise, existing post-market regulations remain the same.

For more information on the scope of RMPs, consult the:

- [Guidance document on the submission of risk management plans and follow-up commitments](#)

Pharmacovigilance reporting requirements

Adverse reaction reporting

Adverse reactions must be reported to the [Canada Vigilance Program](#).

The market authorization holder (MAH) must report within 15 days of receiving the following information (C.01.017):

- domestic serious expected and unexpected adverse drug reactions
- foreign serious unexpected adverse reactions
- unusual failures in efficacy for new drugs (C.08.007, C.08.008)

However, adverse reactions associated with COVID-19 drugs are a priority. MAHs are strongly encouraged to submit reports related to this priority area to Health Canada without delay. MAHs should identify in the report that the drug is a COVID-19 drug.

For information and general procedures on how to report serious adverse drug reactions, consult the guidance document on:

- [reporting adverse reactions to marketed health products](#)

You can also obtain more information on [submitting reports electronically](#).

For details on how to report adverse reactions associated with veterinary drugs, MAHs of veterinary drugs are encouraged to contact the Veterinary Drugs Directorate by email at hc.pv-vet.sc@canada.ca.

Annual summary reporting

Once a year and when requested by the Minister of Health, MAHs must conduct a concise, critical analysis of the adverse reactions and serious adverse reactions to a drug. They must also prepare a summary report relating to the reports received during the previous 12 months (C.01.018).

For information on preparing and submitting an annual summary report, consult the guidance document on:

- [Preparing and submitting summary reports for marketed drugs and natural health products](#)

Issue-related summary reports

Health Canada may request an issue-related summary report (C.01.019) any time. This report is a concise, critical analysis of a specific safety or effectiveness issue.

For information on preparing and submitting an issue-related summary report, consult the guidance document on:

- [Preparing and submitting summary reports for marketed drugs and natural health products](#)

Additional good pharmacovigilance practices

For additional information on good pharmacovigilance requirements, consult the:

- [Good pharmacovigilance practices \(GVP\) guidelines \(GUI-0102\)](#)

Foreign actions reporting

Under section C.01.050 of the *Regulations*, authorization holders must notify Health Canada of foreign regulatory actions. These include serious risk related to recalls, suspension or revocation of manufacturing or market authorizations within one of the specified foreign regulatory jurisdictions.

For information on this reporting requirement, consult the guidance document on:

- [Notifying Health Canada of foreign actions](#)

Other post-market requirements

Record keeping

Under sections C.01.020(1) of the *Regulations*, manufacturers of a COVID-19 drug must maintain records and case reports as they relate to sections C.01.017 to C.01.019.

Under section C.02.020, DEL holders must maintain records for each COVID-19 drug that they fabricate, package/label, distribute or import.

For more information, consult the:

- [Good manufacturing practices guide for drug products \(GUI-0001\)](#)

Shortages or discontinuation of sale

For drugs for human use, authorization holders should consult sections C.01.014.9 and C.01.014.10 and the [guide to reporting drug shortages and discontinuations](#). The guide contains additional information and general procedures on how to report drug shortages and discontinuations of sale.

For details on shortages, see the [Interim order respecting the prevention and alleviation of shortages of drugs in relation to COVID-19](#).

For more information on reporting shortages, authorization holders of veterinary drugs should contact the Veterinary Drugs Directorate by email at hc.vdd.vetdrugs-medsvet.dmv.sc@canada.ca.

Compliance and enforcement

Health Canada monitors compliance, undertakes enforcement activities and works to prevent non-compliance. When taking compliance and enforcement action, Health Canada considers a number of factors while adhering to the legislative framework and principles of our [compliance and enforcement policy for health products](#) (POL-0001).

For further guidance, see the [list of guidance documents](#).

Pre-positioning of COVID-19 drugs

A promising COVID-19 drug may be imported into Canada before it receives a Canadian market authorization. This early importation and placement in Canadian facilities is referred to as “pre-positioning.” It facilitates the immediate distribution of the drug upon authorization, making it available to Canadians as early as possible.

This mechanism may be used to import a promising COVID-19 drug into Canada if the Chief Public Health Officer (CPHO) of the Public Health Agency of Canada has notified the Minister identifying the COVID-19 drug that is to be pre-positioned.

To be eligible to import a COVID-19 drug for pre-positioning, several conditions are required:

- The Government of Canada has entered into a contract for its procurement.
- An authorization for the drug has not been issued.
- The manufacturer has filed a submission for the drug’s authorization.
- The importer of the drug to be pre-positioned has a valid Canadian drug establishment licence.
- The CPHO has provided the Minister with information required under C.08.009.03.
- The DEL holding importer has provided the Minister with information required under C.08.009.03(2), including
- Evidence demonstrating the foreign building(s) for which the COVID-19 drug is fabricated, packaged, labelled or tested meets the applicable requirements of the provisions of Divisions 2 to 4 of Part C of the *Regulations*.

Importation and distribution of a pre-positioned drug

Following the review of the information provided by the CPHO and importer, the Minister of Health issues a letter to the CPHO indicating whether the requirements of pre-positioning have been met. To facilitate importation of the pre-positioned drug into Canada, a copy of this letter should accompany the product across the border.

The person importing a COVID-19 drug for pre-positioning must have a drug establishment licence (DEL), but does not require the activity of importation to be licensed on the DEL. However, the DEL holder responsible for importing the pre-positioned COVID-19 drug will be subject to certain sections in Part C, Divisions 2 to 4 of the *Regulations* concerning storage, distribution, quality control and rapid recall.

A pre-positioned COVID-19 drug cannot be distributed for use until it is authorized in Canada. It can, however, be moved to an alternate storage facility, as long as the Minister has been notified by the CPHO of the civic address of that facility.

Once the drug receives market authorization in Canada, all DEL requirements apply to subsequent importation and distribution.

Pre-positioned COVID-19 drugs that do not receive market authorization under the *Regulations* must be destroyed or returned to the manufacturer.

For guidance on meeting the regulatory requirements for record keeping, storage and distribution of pre-positioned COVID-19 drugs, consult the:

- [Good manufacturing practices guide for drug products \(GUI-0001\)](#)

Evidence requirements to support the GMP compliance is included in the following guidance document:

- [How to demonstrate foreign building compliance with drug good manufacturing practices \(GUI-0080\)](#)

For more information about good manufacturing practices and COVID-19, visit [Good manufacturing practices and COVID-19](#).

Transition of pre-positioned drugs from the ISAD IO to the *Regulations*

COVID-19 drugs that met the requirements under sections 27 to 30 of the ISAD IO are deemed to have been pre-positioned under the *Regulations*.

Any information provided under sections 27 to 30 of the ISAD IO before it expires but has not been deemed to have met all requirements to pre-position will continue to be reviewed under the *Regulations*.

Submission scenarios, reference documents and key contacts

Submission scenarios

Please refer to Table 1 in this guidance document for a summary of submission scenarios.

Scenario 1

COVID-19 drug is authorized under the ISAD IO (authorization was not suspended or revoked) and a submission is subsequently filed under the *Food and Drug Regulations* for that drug

Manufacturers would file an NDS under Division 8 of the Regulations. The submission must include the same data as was included in the ISAD IO application, along with any necessary updates. This can include new evidence that was not available when the application was filed under the ISAD IO. Manufacturers would outline in a summary the changes to the application compared to the ISAD IO filing.

To maintain the ability to sell the COVID-19 drug authorized under the ISAD IO, the NDS must be filed:

- within 90 days following coming into force of the amendments, if the drug was authorized under the ISAD IO before the amendments came into force or
- 90 days following issuance of an authorization under the ISAD IO, if the drug was authorized after the amendments came into force

Manufacturers can continue selling the COVID-19 drug under the ISAD IO authorization until the NDS is approved, rejected or withdrawn. This is the case even after the ISAD IO expires.

Many of the regulatory provisions found in the ISAD IO are available when filing a submission under the Regulations. These are further described in:

- [Rolling submissions](#)
- [Clinical information and requirements](#)
- [Non-clinical information and requirements](#)
- [Quality \(chemistry and manufacturing\) information and requirements](#)
- [Product labels](#)
- [Labelling](#)

An NDS filed under the amended *Regulations* would support the issuance of the notice of compliance (NOC), along with any applicable terms and conditions. Further details are provided in the:

- [Issuance of a notice of compliance for a COVID-19 drug](#)
- [Terms and conditions on a drug identification number relying on modified requirements in C.08.002\(2.1\)](#)

While the NDS is under review, the DIN that was assigned under the ISAD IO remains assigned to the drug authorized under the ISAD IO. This continues to ensure the operation of all regulatory obligations associated with the drug. Sponsors are invited to discuss with Health Canada their plans for packaging and labelling and reuse of a DIN.

Scenario 2

An NDS is filed for a COVID-19 drug for which an application was never filed under the ISAD IO

Manufacturers of new COVID-19 drugs who did not file an application under the ISAD IO may file an NDS seeking approval of the drug on the basis of the modified requirements under the amended NDS pathway in the Regulations.

Many of the regulatory provisions found in the ISAD IO are available when filing a submission under the Regulations. These are further described in:

- [Rolling submissions](#)
- [Clinical information and requirements](#)
- [Non-clinical information and requirements](#)
- [Quality \(chemistry and manufacturing\) information and requirements](#)
- [Product labels](#)
- [Labelling](#)

An NDS filed under the amended *Regulations* would support the issuance of the NOC, along with any applicable terms and conditions. Further details are provided in the:

- [Issuance of a notice of compliance for a COVID-19 drug](#)
- [Terms and conditions on a drug identification number relying on modified requirements in C.08.002\(2.1\)](#)

The manufacturer will have to wait to receive an NOC before marketing its drug.

Scenario 3

An SNDS for a marketed drug is filed where an expanded indication for COVID-19 was authorized under the ISAD IO

Where an expanded indication for COVID-19 was authorized under the ISAD IO for a marketed drug, the manufacturer is able to submit an SNDS to add the new COVID-19 indication. The amended *Regulations*, including the ability to file an incomplete submission (rolling submission), are not available in this scenario.

To maintain the ability to sell the drug for use in relation to COVID-19, the SNDS must be filed:

- within 90 days following coming into force of the amendments, if the drug was authorized before the amendments came into force or
- 90 days following issuance of an authorization under the ISAD IO, if the drug was authorized after the amendments came into force

Manufacturers can continue selling the COVID-19 drug under the ISAD IO authorization until the SNDS is approved, rejected or withdrawn (even after the ISAD IO expires). Manufacturers are encouraged to file the SNDS before the ISAD IO authorization ceases to have effect.

The manufacturer must include all available known information on the use of the approved drug for COVID-19.

Scenario 4

A submission seeking approval for a subsequent entry drug on the basis of a direct or indirect comparison to a COVID-19 drug (i.e. a comparative submission)

Subsequent entry submissions seeking approval for a COVID-19 drug on the basis of a direct or indirect comparison to another COVID-19 drug are not eligible to benefit from the amended *Regulations*. These submissions will be filed as an ANDS or a comparative NDS.

Reference documents

Authorization application guidance documents and webpages:

- [Management of drug submissions and applications](#)
- [Guidance document: Preparation of regulatory activities in the eCTD format](#)
- [Guidance document: Preparation of regulatory activities in the “Non-eCTD electronic-only” format](#)
- [Regulatory enrolment process](#)
- [Common electronic submissions gateway](#)
- [Management of regulatory submissions for veterinary drugs](#)
- [Filing submissions electronically](#)

General guidance documents:

- [Information and submission requirements for biosimilar biologic drugs](#)
- [Drug submissions relying on third-party data \(literature and market experience\)](#)
- [The use of foreign reviews by Health Canada](#)
- [Determining prescription status for human and veterinary drugs](#)
- [Questions and answers: Prescription drug list](#)
- [Regulatory requirements for drug identification numbers \(DINs\)](#)
- [Drug establishment licences and COVID-19](#)
- [Good manufacturing practices and COVID-19](#)
- [Compliance and enforcement policy for health products \(POL-0001\)](#)
- [Drug and medical device databases](#)
- [Regulatory roadmap for biologic \(Schedule D\) drugs in Canada](#)

Safety and efficacy guidance documents:

- [Non-clinical laboratory study data supporting drug product applications and submissions: Adherence to good laboratory practice](#)
- [Preparation of comparative bioavailability information for drug submissions in the CTD format](#)
- [Cochrane Handbook for Systematic Reviews of Interventions](#)
- [Preferred reporting items for systematic reviews and meta-analyses \(PRISMA\) statement](#)

Quality guidance documents:

- [Preparation of quality information for drug submissions in the CTD format: Biotechnological/biological \(biotech\) products](#)
- [Preparation of quality information for drug submissions in the CTD format: Conventional biotherapeutic products](#)
- [Quality \(chemistry and manufacturing\) guidance: New drug submissions \(NDSs\) and abbreviated new drug submissions \(ANDSs\)](#)

Labelling guidance documents:

- [Review of drug brand names: Guidance document for industry](#)
- [Frequently asked questions review of drug brand names](#)
- [Good label and package practices guide for prescription drugs \(GLPPG\)](#)
- [Questions and answers: Plain language labelling regulations for prescription drugs](#)
- [Labelling of special containers policy](#)
- [Labelling of pharmaceutical drugs for human use](#)
- [Product monograph guidance documents and notices](#)

Establishment licensing guidance documents:

- [Guidance on drug establishment licences and drug establishment licensing fees \(GUI-0002\)](#)
- [Management of applications and performance for drug establishment licences \(GUI-0127\)](#)

Good manufacturing practices (GMP) guidance documents:

- [Good manufacturing practices guide for drug products \(GUI-0001\)](#)
- [Annex 2 to the current edition of the good manufacturing practices guidelines schedule D drugs \(biological drugs\) \(GUI-0027\)](#)
- [How to demonstrate foreign building compliance with drug good manufacturing practices \(GUI-0080\)](#)
- [Good manufacturing practices \(GMP\) for Active Pharmaceutical Ingredients \(APIs\) \(GUI-0104\)](#)

Good laboratory practices (GLP) guidance document:

- [Good laboratory practices \(GLP\) guidelines \(Dir-9801\)](#)

Post-market vigilance guidance documents :

- [Reporting adverse reactions to marketed health products \(overview\)](#)
- [Report an adverse reaction to a drug: industry](#)
- [Preparing and submitting summary reports for marketed drugs and natural health products](#)
- [Good pharmacovigilance practices \(GVP\) guidelines \(GUI-0102\)](#)
- [Notifying Health Canada of foreign actions: Guidance document for industry](#)
- [Amendments to the *Food and Drugs Act*: Guide to new authorities \(power to require and disclose information, power to order a label change and power to order a recall\)](#)
- [Format and content for post-market drug benefit-risk assessment in Canada](#)
- [Submission of risk management plans and follow-up commitments](#)
- [Guide to reporting drug shortages and discontinuations](#)
- [Recall policy for health products \(POL-0016\)](#)
- [Drug and natural health products recall guide \(GUI-0039\)](#)

Post-notice of compliance (NOC) changes guidance documents:

- [Framework document \(pharmaceutical, biologic and radiopharmaceutical drugs for human use only\)](#)
- [Quality document](#)
- [Safety and efficacy document \(for pharmaceutical, biologic and radiopharmaceutical drugs for human use only\)](#)

Advertising guidance documents:

- [Marketing of drugs and medical devices](#)

Disinfectants guidance documents and monograph :

- [Management of disinfectant drug applications](#)
- [Safety and efficacy requirements for surface disinfectant drugs](#)
- [Disinfectant drugs](#)
- [Applying for a drug identification number \(DIN\) for a disinfectant drug during the COVID-19 pandemic](#)
- [Hard-surface disinfectants monograph](#)

Non-prescription pharmaceuticals and hand sanitizer (antiseptic skin cleansers) guidance documents and monographs:

- [Human-use antiseptic drugs](#)
- [Management of drug submissions and applications](#)
- [Compendium of monographs](#)

Key contacts

To help ensure that we prioritize your inquiry, please include “COVID-19 drug” in the subject line of your email.

Biologic and Radiopharmaceutical Drugs Directorate
Office of Regulatory Affairs
Email: hc.brdd.ora.sc@canada.ca

Therapeutic Products Directorate
Regulatory Project Management Division
Email: hc.rpmd-dgpr.sc@canada.ca

Veterinary Drugs Directorate
Submission and Knowledge Management Division
Email: hc.vdd.skmd.so-dgps.dmv.cp.sc@canada.ca

Natural and Non-prescription Health Products Directorate
General Enquiries
Email: hc.nnhpd-dpsnso.sc@canada.ca

For intellectual property-related inquiries:

Office of Patented Medicines and Liaison
Email: hc.opml-bmbl.sc@canada.ca

For application format-related inquiries:

Office of Submissions and Intellectual Property
Email: hc.ereview.sc@canada.ca

For adverse reaction reporting-related inquiries:

[Canada Vigilance Program \(CVP\)](#)

For inquiries about good manufacturing practices (GMP) compliance requirements:

Email: GMP_Questions_BPF@hc-sc.gc.ca

For drug establishment licensing (DEL)-related inquiries:

Email: hc.del.questions-leppp.sc@canada.ca