Exhibit R25-4 **Regulation SOR/2021-45 which on March 18, 2021, incorporated the provisions of the Interim Order, with some minor changes, into the Food and Drug Regulations**

Regulations Amending the Food and Drug Regulations (Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19): SOR/2021-45

Canada Gazette, Part II, Volume 155, Number 7

Registration

SOR/2021-45 March 18, 2021

FOOD AND DRUGS ACT

P.C. 2021-158 March 17, 2021

His Excellency the Administrator of the Government of Canada in Council, on the recommendation of the Minister of Health, pursuant to section 30 [a] of the *Food and Drugs Act* [b], makes the annexed *Regulations Amending the Food and Drug Regulations (Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19)*.

Regulations Amending the Food and Drug Regulations (Interim Order Respecting the Importation, Sale and Advertising of Drugs

for Use in Relation to COVID-19)

Amendments

1 Subsection C.01.001(1) of the *Food and Drug Regulations* [1] is amended by adding the following in alphabetical order:

COVID-19
means the coronavirus disease 2019; (*COVID-19*)

COVID-19 drug
means a drug, other than a veterinary health product, that is manufactured, sold or represented for use in relation to COVID-19; (*drogue contre la COVID-19*)

ISAD Interim Order
means the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19* made by the Minister on September 16, 2020 and published in Part I of the *Canada Gazette* on October 3, 2020; (*arrêté d'urgence IVPD*)

2 (1) Section C.01.014.21 of the Regulations is amended by adding the following after subsection (1):

(1.1) The Minister may, at any time, impose terms and conditions on a drug identification number assigned for a designated COVID-19 drug, or amend those terms and conditions, if

(a) a notice of compliance was issued under section C.08.004 in respect of

(i) a new drug submission that was filed under section C.08.002 for the designated COVID-19 drug that contains the statement referred to in paragraph C.08.002(2.1)(a), or

(ii) a supplement to a new drug submission referred to in subparagraph (i) that was filed under section C.08.003 for the designated COVID-19 drug; or

(b) a notice of compliance was issued under section C.08.004 in respect of one of the following that was filed for the designated COVID-19 drug on the basis of a direct or indirect comparison to another designated COVID-19 drug referred to in paragraph (a):

(i) a new drug submission under section C.08.002,

(ii) an abbreviated new drug submission under section C.08.002.1, or

(iii) a supplement to a new drug submission or abbreviated new drug submission under section C.08.003.

(2) Subsection C.01.014.21(3) of the Regulations is replaced by the following:

(3) The following definitions apply in this section.

Class B opioid
means a drug set out in Part B of the *List of Opioids*, published by the Government of Canada on its website, as amended from time to time. (*opioïde de catégorie B*)

designated COVID-19 drug
has the same meaning as in section C.08.001.1. (*drogue désignée contre la COVID-19*)

3 Section C.01A.005 of the Regulations is renumbered as subsection C.01A.005(1) and is amended by adding the following:

(2) In addition to the information and documents referred to in subsection (1), a person who submits an application for an establishment

licence that relates to one or more activities set out in Table I to section C.01A.008 to be carried out in respect of a category of drugs set out in Table II to that section that includes a COVID-19 drug may include a statement to that effect in the application.

4 Section C.01A.006 of the Regulations is amended by adding the following after subsection (1):

(1.1) In addition to the information and documents referred to in subsection (1), a person who submits an application to amend an establishment licence that relates to one or more activities set out in Table I to section C.01A.008 to be carried out in respect of a category of drugs set out in Table II to that section that includes a COVID-19 drug may include a statement to that effect in the application.

5 Paragraph C.01A.007(2)(a) of the French version of the Regulations is replaced by the following:

a) qu'une inspection soit effectuée aux heures normales de bureau de tout bâtiment visé aux alinéas C.01A.005(1)g) ou h);

6 (1) Subsection C.01A.008(1) of the Regulations is replaced by the following:

C.01A.008 (1) Subject to subsection (1.1) and section C.01A.010, the Minister shall, on receipt of the information and material referred to in sections C.01A.005 to C.01A.007, issue or amend an establishment licence.

(1.1) The Minister shall, in determining whether he or she has received the information and material referred to in sections C.01A.005 to C.01A.007 in relation to an application referred to in subsection C.01A.005(2) or C.01A.006(1.1) that contains the statement referred to in

the applicable subsection, also take into consideration the public health need related to COVID-19.

(2) Subsection C.01A.008(4) of the Regulations is replaced by the following:

(4) When issuing an establishment licence, the Minister may impose terms and conditions on the establishment licence respecting

(a) the tests to be performed in respect of a drug, and the equipment to be used, to ensure that the drug is not unsafe for use; and

(b) any other matters necessary to prevent injury to the health of consumers, including conditions under which drugs are fabricated, packaged/labelled or tested.

7 Paragraph C.01A.011(1)(a) of the Regulations is replaced by the following:

(a) the requirements of the establishment licence; and

8 Section C.01A.012 of the Regulations is replaced by the following:

C.01A.012 (1) The Minister may amend the terms and conditions of an establishment licence that are imposed under subsection C.01A.008(4) if the Minister believes on reasonable grounds that an amendment is necessary to prevent injury to the health of the consumer.

(2) The Minister shall give at least 15 days notice in writing to the holder of the establishment licence of the proposed amendment, the reasons for it and its effective date.

9 The Regulations are amended by adding the following after section C.01A.012:

C.01A.012.1 (1) Despite subsection C.01A.008(4), the Minister may, at any

time, including when issuing an establishment licence, impose terms and conditions on an establishment licence that is issued or amended under section C.01A.008 on the basis of an application referred to in subsection C.01A.005(2) or C.01A.006(1.1) that contains the statement referred to in the applicable subsection.

(2) For greater certainty, terms and conditions that may be imposed under subsection (1) are not limited to those that may be imposed under subsection C.01A.008(4).

C.01A.012.2 The Minister may, at any time, amend terms or conditions that are imposed on an establishment licence under subsection C.01A.012.1(1).

10 Paragraph C.01A.013(a) of the Regulations is replaced by the following:

(a) there is any change to the information referred to in any of paragraphs C.01A.005(1)(a), (b) and (e) to (i); or

11 The portion of section C.01A.017.1 of the Regulations before paragraph (a) is replaced by the following:

C.01A.017.1 The Minister may suspend an establishment licence in respect of any or all matters indicated in subsection C.01A.008(2) if, after the Minister has, under section 21.31 of the Act, ordered the licensee to conduct an assessment in order to provide evidence establishing that the licensee's buildings, equipment or practices and procedures, as the case may be, continue to meet the requirements referred to in paragraph C.01A.005(1)(l), subparagraph C.01A.005(1)(m)(ii) or (iii) or paragraph C.01A.005(1)(o),

12 Section C.02.019 of the Regulations is amended by adding the

following after subsection (4):

(4.1) Subsections (1) and (2) do not apply to a distributor or importer of a COVID-19 drug if it is the subject of a written request made under section C.04.015.

13 Section C.08.001.1 of the Regulations is amended by adding the following in alphabetical order:

designated COVID-19 drug means a new drug for which the purpose and conditions of use recommended by the manufacturer relate to COVID-19; (*drogue désignée contre la COVID-19*)

14 (1) Paragraph C.08.002(2)(o) of the Regulations is replaced by the following:

(o) in the case of a new drug for human use other than a designated COVID-19 drug, an assessment as to whether there is a likelihood that the new drug will be mistaken for another drug for which a drug identification number has been assigned due to a resemblance between the brand name that is proposed to be used in respect of the new drug and the brand name, common name or proper name of the other drug.

(2) Section C.08.002 of the Regulations is amended by adding the following after subsection (2):

(2.1) A manufacturer may file, for a designated COVID-19 drug, a new drug submission that does not meet the requirements set out in paragraphs (2)(g) and (h) if the submission contains

(a) a statement that the submission contains evidence to establish that the requirement set out in paragraph (b) is met; and

(b) sufficient evidence to support the conclusion that the benefits

associated with the designated COVID-19 drug outweigh the risks for the purpose and under the conditions of use recommended, with consideration given to the uncertainties relating to those benefits and risks as well as the public health need related to COVID-19.

(2.2) A manufacturer may file, for a designated COVID-19 drug for human use, a new drug submission that does not meet the requirements set out in paragraph (2)(j.1) if the submission contains a draft of every label to be used in connection with the designated COVID-19 drug, including any package insert and any document that is provided on request and that sets out supplementary information on the use of the designated COVID-19 drug.

(2.3) If, at the time a new drug submission is filed for a designated COVID-19 drug, the manufacturer is unable to provide the Minister with information or material referred to in any of paragraphs (2)(e) to (k), (m) and (n) or in paragraph (2.1)(b) or subsection (2.2) or that information or material is incomplete, the manufacturer shall provide the Minister, at that time, with a plan that specifies how and when the manufacturer will provide the Minister with the missing information or material.

(2.4) Subsections (2.1) to (2.3) apply if

(a) the new drug submission contains a statement that the submission is for a designated COVID-19 drug; and

(b) the purpose and conditions of use specified in the new drug submission in respect of the designated COVID-19 drug relate only to COVID-19 and the submission contains a statement to that effect.

(2.5) Subsections (2.1) to (2.3) do not apply if the manufacturer is seeking a notice of compliance for a designated COVID-19 drug on the basis of a direct or indirect comparison between the designated COVID-19 drug

and another designated COVID-19 drug.

15 The Regulations are amended by adding the following after section C.08.003:

C.08.003.01 (1) The following definitions apply in this section.

submission

means

(a) a new drug submission that is filed under section C.08.002;

(b) an extraordinary use new drug submission that is filed under section C.08.002.01;

(c) an abbreviated new drug submission that is filed under section C.08.002.1; or

(d) an abbreviated extraordinary use new drug submission that is filed under section C.08.002.1. (*présentation*)

supplement

means a supplement to a submission that is filed under section C.08.003. (*supplément*)

(2) Despite sections C.08.002, C.08.002.01, C.08.002.1 and C.08.003 and subject to subsection (3), the manufacturer of a new drug is not permitted to file a submission or supplement for the new drug on the basis of a direct or indirect comparison to any new drug in respect of which an authorization was issued under the ISAD Interim Order.

(3) Subsection (2) does not prevent the manufacturer of a new drug from filing a submission or supplement for the new drug on the basis of a direct or indirect comparison to another new drug in respect of which an authorization was issued under the ISAD Interim Order if

(a) a notice of compliance is issued under section C.08.004 or

C.08.004.01 in respect of a submission or supplement for that other new drug; and

(b) the comparison is in respect of the matters that were approved by the notice of compliance.

16 Section C.08.004.1 of the Regulations is amended by adding the following after subsection (1):

(1.1) For the purposes of the definition *innovative drug* in subsection (1), a medicinal ingredient is not considered to be approved in a drug by reason of the Minister having issued or amended an authorization under the ISAD Interim Order in respect of a COVID-19 drug that contains the medicinal ingredient.

17 The Regulations are amended by adding the following after section C.08.009:

Pre-positioning of Designated COVID-19 Drugs

C.08.009.01 The following definitions apply in sections C.08.009.03 to C.08.009.05.

Chief Public Health Officer means the Chief Public Health Officer appointed under subsection 6(1) of the *Public Health Agency of Canada Act*. (*administrateur en chef de la santé publique*)

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. (*autorité réglementaire étrangère*)

C.08.009.02 Sections C.08.009.03 to C.08.009.05 apply in respect of a

designated COVID-19 drug if the following conditions are met:

(a) a notice of compliance has not been issued under section C.08.004 or C.08.004.01 in respect of the designated COVID-19 drug; and

(b) Her Majesty in right of Canada has entered into a contract for the procurement of the designated COVID-19 drug.

C.08.009.03 (1) The holder of an establishment licence may import a designated COVID-19 drug if the following conditions are met:

(a) the Chief Public Health Officer provides the Minister with

(i) information indicating that

(A) the designated COVID-19 drug is the subject of a new drug submission that was filed under section C.08.002, or

(B) an application has been submitted to a foreign regulatory authority to authorize the sale of the designated COVID-19 drug,

(ii) the name of the designated COVID-19 drug and a description of it,

(iii) the name and contact information of the designated COVID-19 drug's manufacturer,

(iv) information specifying the quantity of the designated COVID-19 drug to be imported,

(v) the name and contact information of any holder of an establishment licence who is proposed to be an importer of the designated COVID-19 drug, and

(vi) the civic address of the place where the designated COVID-19 drug will be stored after importation;

(b) the holder provides the Minister with

(i) the name and contact information of each fabricator, packager/labeller and tester of the designated COVID-19 drug and the civic address of each building at which the designated COVID-19 drug will be fabricated, packaged/labelled or tested, specifying for each building

(A) the activities referred to in Table I to section C.01A.008 that apply to the designated COVID-19 drug,

(B) the categories referred to in Table II to that section that apply to the designated COVID-19 drug, and

(C) for each category, the dosage form classes, if any, and whether the designated COVID-19 drug will be in a sterile form, and

(ii) a certificate from an inspector indicating that each fabricator's, packager/labeller's and tester's buildings, equipment, practices and procedures meet the applicable requirements of Divisions 2 to 4 or, alternatively, other evidence establishing that those requirements are met; and

(c) the holder is one of those specified in the information that the Chief Public Health Officer provides under subparagraph (a)(v).

(2) Paragraph (1)(b) does not apply to the holder of an establishment licence in respect of a building referred to in subparagraph (1)(b)(i) if

(a) the building is listed in the licence; and

(b) the information referred to in clauses (1)(b)(i)(A) to (C) that the holder submitted in respect of the building in their application for the licence under section C.01A.005 or in an application to amend the

licence under section C.01A.006, has not changed.

(3) If the conditions set out in subsection (1) are met, the Minister shall send a letter to the Chief Public Health Officer to that effect.

C.08.009.04 Sections A.01.040 and C.01.004.1, subsection C.01A.004(1), section C.01A.006 and Divisions 2 to 4, other than the following provisions, do not apply in respect of the importation, under section C.08.009.03, of a designated COVID-19 drug by the holder of an establishment licence:

(a) sections C.02.003.1, C.02.004 and C.02.006, as they apply to the storage of the designated COVID-19 drug by the holder;

(b) subsection C.02.012(1);

(c) sections C.02.013 and C.02.014;

(d) section C.02.015, as it applies to the storage and transportation of the designated COVID-19 drug by the holder;

(e) subsection C.02.021(1), as it applies to the storage of the designated COVID-19 drug by the holder;

(f) subsection C.02.022(1);

(g) section C.02.023;

(h) subsection C.02.024(1);

(i) section C.03.013; and

(j) section C.04.001.1, as it applies to the storage of the designated COVID-19 drug by the holder.

C.08.009.05 Despite anything in these Regulations, the holder of an establishment licence may distribute a designated COVID-19 drug that

they have imported under section C.08.009.03 if the following conditions are met:

(a) the Chief Public Health Officer provides the Minister with the name of the designated COVID-19 drug and the civic address of the place where it will be stored after the distribution; and

(b) the designated COVID-19 drug is distributed to a person who will store it at that place.

Transitional Provisions

Interpretation

18 (1) The following definitions apply in this section and in sections 19 to 30:

authorization
means an authorization that was issued under the ISAD Interim Order in respect of a new drug on the basis of

(a) an application submitted under section 3 of the ISAD Interim Order other than an application that was submitted on the basis of a direct or indirect comparison of the new drug to another drug; or

(b) an application submitted under section 4 of the ISAD Interim Order. (*autorisation*)

supplement
means a supplement to a new drug submission that is filed under section C.08.003 of the *Food and Drug Regulations*. (*supplément*)

(2) Unless the context otherwise requires, words and expressions used in this section and in sections 19 to 30 have the meanings assigned by the *Food and Drug Regulations*.

Authorizations

19 (1) Despite subsection 2(1) of the ISAD Interim Order, the manufacturer of a new drug who is the holder of an authorization in respect of the new drug may file a new drug submission under section C.08.002 of the *Food and Drug Regulations*, or a supplement, for the new drug and subsection C.01.014.1(3) and Division 8 of Part C of those Regulations apply in respect of the submission or supplement.

(2) The authorization is revoked if the manufacturer does not file a new drug submission under section C.08.002 of the *Food and Drug Regulations*, or a supplement, for the new drug within one of the following periods, as applicable:

(a) in the case of an authorization that was issued before the day on which this section comes into force, 90 days after the day on which this section comes into force; or

(b) in the case of an authorization that is issued on or after the day on which this section comes into force, 90 days after the day on which the authorization is issued.

(3) If the manufacturer files a new drug submission under section C.08.002 of the *Food and Drug Regulations*, or a supplement, for the new drug within the applicable period set out in paragraph (2)(a) or (b), the authorization is revoked when one of the following circumstances occurs:

(a) the Minister issues a notice of compliance under section C.08.004 of those Regulations in respect of the submission or supplement;

(b) if the Minister issues a notice to the manufacturer under

paragraph C.08.004(1)(b) of those Regulations in respect of the submission or supplement and the manufacturer does not amend the submission or supplement in accordance with subsection C.08.004(2) of those Regulations, the period referred to in subsection C.08.004(2) expires;

(c) the Minister issues a notice to the manufacturer under paragraph C.08.004(3)(b) of those Regulations in respect of the submission or supplement.

20 The *Food and Drug Regulations* — other than the following provisions — do not apply to a new drug in respect of which an authorization was issued to the manufacturer of the new drug if, immediately before the day on which this section comes into force, the authorization was neither suspended nor revoked:

(a) sections A.01.014, A.01.015, A.01.022 to A.01.043, A.01.050, A.01.051 and A.01.060.1 to A.01.068;

(b) sections C.01.004 to C.01.011, C.01.014.9, C.01.014.10, C.01.017 and C.01.019, subsection C.01.020(1) and sections C.01.020.1, C.01.040.3 to C.01.053, C.01.064 to C.01.069 and C.01.401;

(c) the provisions of Divisions 1A and 2 of Part C;

(d) sections C.03.202, C.03.203 and C.03.206 to C.03.209; and

(e) sections C.04.013 to C.04.016, C.04.019 and C.04.020.

21 (1) The drug identification number that was assigned under subsection 7(1) of the ISAD Interim Order in relation to a new drug that is referred to in section 20 continues to be assigned for the distinct combination of dosage form, strength and route of administration of the new drug.

(2) A reference in Divisions 1 and 1A of Part C of the *Food and Drug Regulations* — other than in sections C.01.050, C.01.052, C.01.053 and C.01A.003 — to a drug identification number is deemed to include a reference to the drug identification number that is referred to in subsection (1).

(3) A reference in section C.01A.003 of the *Food and Drug Regulations* to a distributor who holds a drug identification number is deemed to include a reference to the manufacturer who is referred to in section 20.

22 The manufacturer who is referred to in section 20 shall, within 15 days after the day on which the new drug is first sold in Canada, notify the Minister, in writing, of the date of that first sale, unless the manufacturer has already done so under section 8 of the ISAD Interim Order.

23 The manufacturer who is referred to in section 20 shall, within 15 days after the day on which the manufacturer permanently discontinues the sale in Canada of the new drug, notify the Minister, in writing, of the date on which the sale was permanently discontinued, unless the manufacturer has already done so under section 9 of the ISAD Interim order.

24 Despite the definition *drug* in section C.01.014.8 of the *Food and Drug Regulations*, sections C.01.014.9 and C.01.014.10 of those Regulations apply, with any necessary modifications, to the manufacturer who is referred to in section 20 in respect of the new drug.

25 (1) Subject to subsection (2), sections 20 to 24 cease to apply to a new drug that is referred to in section 20 90 days after the day on

which this section comes into force.

(2) If the manufacturer who is referred to in section 20 files, for the new drug, a new drug submission under section C.08.002 of the *Food and Drug Regulations* or a supplement, within the period referred to in subsection (1) or has filed such a submission or supplement before the day on which this section comes into force, sections 20 to 24 cease to apply to the new drug when one of the circumstances referred to in paragraphs 19(3)(a) to (c) occurs.

26 (1) Despite subsection 1(3) of the ISAD Interim Order, for the purposes of the definition *innovative drug* in subsection C.08.004.1(1) of the *Food and Drug Regulations*, a medicinal ingredient is not considered to be approved in a drug by reason of the Minister having issued or amended an authorization under the ISAD Interim Order in respect of a COVID-19 drug that contains the medicinal ingredient.

(2) Subsection (1) ceases to apply on the day on which the ISAD Interim Order ceases to have effect.

Establishment Licences

27 (1) Any terms and conditions of an establishment licence — other than those that are imposed by the Minister under the ISAD Interim Order — are deemed to be imposed by the Minister under subsection C.01A.008(4) of the *Food and Drug Regulations*.

(2) Any terms and conditions of an establishment licence that are imposed by the Minister under the ISAD Interim Order are deemed to be imposed by the Minister under section C.01A.012.1 of the *Food and Drug Regulations*.

28 (1) Despite subsection 26(1) of the ISAD Interim Order, any

establishment licence that is referred to in that subsection is not cancelled immediately before the ISAD Interim Order ceases to have effect if the holder of the establishment licence notifies the Minister in writing, before the day on which the ISAD Interim Order ceases to have effect, of their intention to continue to conduct activities in respect of the COVID-19 drug under the establishment licence.

(2) Despite subsection 26(2) of the ISAD Interim Order, any amendment that is referred to in that subsection to an establishment licence continues to have effect after the ISAD Interim Order ceases to have effect if the holder of the establishment licence notifies the Minister in writing, before the day on which the ISAD Interim Order ceases to have effect, of their intention to continue to conduct activities in respect of the COVID-19 drug under the amended establishment licence.

Pre-positioning of Designated COVID-19 Drugs

29 Information and material in respect of a designated COVID-19 drug that were provided under paragraphs 28(1)(a) and (b) or 30(a) of the ISAD Interim Order are deemed to have been provided under, as the case may be, paragraphs C.08.009.03(1)(a) and (b) or C.08.009.05(a) of the *Food and Drug Regulations*.

30 Section C.08.009.05 of the *Food and Drug Regulations* applies, with any necessary modifications, in respect of a designated COVID-19 drug that was imported under section 28 of the ISAD Interim Order.

Coming into Force

31 (1) Subject to subsection (2), these Regulations come into force on the day on which they are registered.

(2) Sections 3 to 5, subsection 6(1), sections 9 to 12, 15 to 17 and 20 to 25, subsection 27(2) and sections 29 and 30 come into force on the day on which the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19*, made by the Minister on September 16, 2020 and published in Part I of the *Canada Gazette* on October 3, 2020, ceases to have effect.

REGULATORY IMPACT ANALYSIS STATEMENT

(*This statement is not part of the Regulations*.)

Executive summary

Issues

On September 16, 2020, the Minister of Health made the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19* (the ISAD Interim Order or the Interim Order) to create flexibilities in the drug authorization process, allowing their sale, import and distribution to address the COVID-19 immediate public health risk. The Interim Order will expire one year after being made, however, upon expiry all authorizations and licences issued under the Interim Order will also expire. Unless regulations are brought into place to address this gap, critical access to COVID-19 drugs for Canadians may be interrupted or delayed.

Description

These Regulations introduce amendments to the *Food and Drug Regulations* (FDR) to incorporate some of the elective flexibilities