CHANGES TO THE DRUG APPROVAL TEST FOR COVID-19 VACCINES

Permitted Vaccines to be Approved Without Objective Proof of (1) Safety, (2) Efficacy, or (3) the Benefits Outweighing the Risks.

Prepared by Shawn Buckley, LL.B., President of the Natural Health Products Protection Association on February 27, 2023. Latest revision March 17, 2023.

COVID-19 Vaccines were exempted from the normal regulatory requirements requiring objective proof of (1) Safety, (2) Efficacy, and (3) that the benefits of the drug outweigh the risk.

Before being authorized for use, drugs like the COVID-19 vaccines would normally have to be:

1. objectively proven to be safe,
2. objectively proven to be effective, and
3. objectively proven that the benefits of the drug outweigh the risks.

COVID-19 vaccines were exempted from these three objective requirements. Rather, a subjective test that did not require objective proof of safety, efficacy or risk/benefit was applied.

Summary

For COVID-19 vaccines, there were the following major legal changes to deliberately circumvent the normal protections in our drug approval law:

a) The normal drug approval process requires objective proof of:

   i. safety;

   ii. efficacy, and

   iii. benefit outweighing risk.

   COVID-19 vaccines were exempted from this normal drug approval process.

   COVID-19 vaccines were approved under a subjective test which mandated that approval must be granted if the argument could be made that the benefits outweighed the risk. No actual proof of safety, efficacy or benefit outweighing risk was required;

b) the law was changed so that the approval of a COVID-19 vaccine could not be revoked:

   i. due to evidence the vaccine was unsafe or not-effective;

   ii. due to assessments the benefits did not outweigh the risks.

These legal changes were in force from September 16, 2020 to:

i. September 15, 2021, for the Pfizer and Moderna vaccines;

ii. November 18, 2021, for the AstraZeneca vaccine, and

iii. November 22, 2021, for the Johnson & Johnson vaccine, and

c) a classic conflict of interest was created where the Government was allowed to purchase and import unapproved vaccines while the Government waited for itself to approve the vaccines.

Normal new-drug approval process requiring objective evidence of (1) Safety, (2) Efficacy, and (3) that the benefits of the drug outweigh the risk

The new-drug approval process is found in Division 8 of the *Food and Drug Regulations*, C.R.C., c-870 (the "Regulations"). These Regulations apply to any "new drug" which is defined as follows:

> C.08.001 For the purposes of the Act and this Division, **new drug** means a drug, other than a veterinary health product,
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> a) that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use as a drug;
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> b) that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in that combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or
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> c) with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration or duration of action, and that has not been sold for that use or condition of use in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug.

All COVID-19 vaccines are new drugs.

The requirements that must be met in a new drug submission are found in C.08.002(2). Of particular importance are high requirements for proof of both safety and efficacy. These are found as follows:

> C.08.002(2) A new drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug, including the following:
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> g) detailed reports of the tests made to establish the safety of the new drug for the purpose and under the conditions of use recommended;
>
> h) substantial evidence of the clinical effectiveness of the new drug for the purpose and under the conditions of use recommended[.]

The Regulations do not specifically require that the benefits of a new drug outweigh the risk.

The reality is that for new chemical drugs, "safety" often does not mean "safe" to simply take. Rather, they may be "safe" only if managed with restrictions such as requiring a prescription. Similarly, "effectiveness" or "efficacy" may mean the drug only partially works.

The reality of chemical drug licensing is that once the safety and efficacy profiles are known, there is usually a risk-benefit analysis done. The question is asked, do the benefits outweigh the risk?

If the evidence required by C.08.002(2) are met, including proving safety and efficacy (to show the benefits outweigh the risk), the Minister must grant market approval (see C.08.004).

The exemption for COVID-19 vaccines from the requirement to prove safety, efficacy and that the benefits outweigh the risks

September 16, 2020 until March 17, 2021 - Interim Order

Section 30.1 of the *Food and Drugs Act*, R.S.C., 1985, c. F-27, permits the Minister of Health to make an interim order to override normal regulations. The section reads:

> 30.1 (1) The Minister may make an interim order that contains any provision that may be contained in a regulation made under this Act if the Minister believes that immediate action is required to deal with a significant risk, direct or indirect, to health, safety or the environment.

The term "significant risk" is not defined in the Act. Nor is there any proportionality built into this section.

On September 16, 2020 the Minister made an interim order under s. 30.1 to create an approval process that applied only to COVID-19 drugs (which includes vaccines) (the "Interim Order"). The Interim Order was approved by the Governor in Council on September 25, 2020 (see P.C. 2020-682, *Canada Gazette Part I*, Vol. 154, No. 40 p. 2587).

The Interim Order abandoned the C.08.002(2)(g) and (h) requirements for detailed safety evidence and substantial evidence of efficacy. Rather than requiring significant evidence of safety and efficacy as mandatory requirements for approval, the Interim Order only required:

> 3(1) Subject to section 4, an application for an authorization in respect of a COVID-19 drug must be in a form established by the Minister and contain sufficient information and material to enable the Minister to determine whether to issue the authorization, including
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> (o) the known information in relation to the quality, safety and effectiveness of the drug.

The requirement only to provide the "known information" had the following quasi-exemption:

> 3(2) If, at the time an application is initially submitted to the Minister, the applicant is unable to provide information or material referred to in any of paragraphs (1)(g) to (k) and (m) to (o) or that information or material is incomplete, the applicant must include in the initial part of the application a plan as to how and when they will provide the Minister with the missing information or material.

The Interim Order requires the Minister to grant approval for COVID-19 vaccines in the absence of detailed evidence of safety and substantial evidence of efficacy. This is found in s. 5 of the Interim Order which provides:

> 5 The Minister must issue an authorization in respect of a COVID-19 drug if the following requirements are met:
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> a) the applicant has submitted an application to the Minister that meets the requirements set out in subsection 3(1) or 4(2);
>
> b) the applicant has provided the Minister with all information or material, including samples, requested under subsection 13(1) in the time, form and manner specified under subsection 13(2); and
>
> c) the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19.

To ensure there is no misunderstanding, the Minister (i.e. Health Canada) by law had to approve COVID-19 vaccines if:

> the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19 (Interim Order s. 5(c)).

Points to Understand

Point 1: There does not need to be evidence to convince Health Canada the benefits of the vaccine outweigh the risk of the vaccine. The drug company only has to have evidence to argue that the benefits outweigh the risk.

The first part of this test is important to break down. When it reads:

> the Minister has sufficient evidence to **support the conclusion**

this **does not mean the Minister (i.e. Health Canada) has to be convinced and actually reach the conclusion.** If the test was to convince Health Canada, the test would read:

> the Minister has sufficient evidence **to conclude**

However, the test does not require Health Canada be given sufficient evidence "to conclude" that the benefits associated with the vaccine outweigh the risks of the vaccine. Rather the test only requires that there be "sufficient evidence to support the conclusion" that the benefits outweigh the risks.

Evidence "to support" a conclusion is much different than evidence "to prove" a conclusion.

Under the Interim Order there only has to be evidence to support an argument that the benefits outweigh the risk. Under this test, inconclusive evidence can be used to obtain approval. Indeed, under this test, even if the preponderance of the evidence showed the risks outweighed the benefits, the vaccine would have to be approved as long as there was sufficient evidence to support the argument/conclusion that the benefits outweighed the risks.

Point 2: This is a subjective test, rather than the usual test requiring objective evidence of safety and efficacy.

The regular test requires objective evidence of safety and efficacy (see C.08.002(2)(g) and (h) and C.08.004). The test for COVID-19 vaccines is not an objective test, it is subjective.

The Minister only has to have:

> sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks[.]

Point 3: There is no requirement to prove safety.

The regular test requires "detailed reports of the tests made to establish the safety of the new drug" (C.08.002(2)(g)). The test for COVID-19 vaccines has no requirement to prove safety. Rather than having to prove safety, the drug company must provide:

> the known information in relation to the quality, safety and effectiveness of the drug (Interim Order s. 3(1)(o) and 5(a)).

And the following test which does not require proof of safety or even mention safety has to be met:

> the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19 (Interim Order s. 5(c)).

Point 4: There is no requirement to prove efficacy.

The regular test requires "substantial evidence of the clinical effectiveness of the new drug" (C.08.002(2)(h)). The test for COVID-19 vaccines has no requirement to prove efficacy. Rather than having to prove efficacy, the drug company must provide:

> the known information in relation to the quality, safety and effectiveness of the drug (Interim Order s. 3(1)(o) and 5(a)).

And the following test which does not require proof of efficacy or even mention efficacy has to be met:

> the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19 (Interim Order s. 5(c)).

Point 5: Although there is benefit and risk language, there is no requirement to prove the benefits outweigh the risk.

There is no risk-benefit test written into the regular new drug approval regulations. It is simply something that happens as a matter of common sense once the safety and efficacy profiles of a new drug is known.

Put another way, **in the normal course of events, Health Canada will not approve a drug where the risks outweigh the benefits.** In this way, it is a requirement for regular drug approval.

It is important to note that in the regular drug approval process, chances are not taken. If there is uncertainty about either safety or efficacy, the drug is not approved. There must be strict objective evidence of both safety and efficacy. It must also be objectively clear that the benefits outweigh the risks before a new drug is approved. It can only be objectively clear that the benefits of a drug outweigh the risks when the benefits and risks are objectively known.

The test for the COVID-19 vaccines uses benefit and risk language, without actually requiring that it be proven that the benefits outweigh the risks. The test reads:

> the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19 (Interim Order s. 5(c)).

Without the establishment of:

1) the vaccine's safety profile, and

2) the vaccine's efficacy profile,

it is **impossible to assess whether the benefits outweigh the risk.** This is a fallacious test. It is logically unsound.

Point 6: Whenever there is doubt concerning safety, efficacy or whether the benefits outweigh the risks, there is normally no approval - but for the COVID-19 vaccines, the Minister had to approve even if unsure whether the benefits outweighed the risks.

As indicated above, in the regular drug approval process, chances are not taken. If there is uncertainty about either safety or efficacy, the drug is not approved. There must be strict objective evidence of both safety and efficacy. It must also be objectively clear that the benefits outweigh the risks before a new drug is approved. It can only be objectively clear that the benefits of a drug outweigh the risks when the benefits and risks are objectively known.

The test for COVID-19 vaccines abandoned this need for objective certainty. Indeed, it mandated that Health Canada had to approve the vaccines even if unsure about either the benefits, the risks, or both the benefits and the risks. Again, the test reads:

> the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19 (Interim Order s. 5(c)).

Point 7: The "test" for approval is more accurately described as a "direction" to approve.

Although this Discussion Paper uses the word "test", it may be more accurate to describe the "test" in the Interim Order as a "direction" to approve COVID-19 vaccines. **Nothing actually has to be proven.** There simply must be sufficient evidence to support the conclusion/argument that the benefits outweigh the risks. And "sufficient evidence" must be interpreted in light of there being "uncertainties relating to the benefits and risks". Add on the last part of the "test", and Interim Order 5(c) is more accurately described as a direction to approve the vaccines. The last part of the "test" is:

> and the necessity of addressing the urgent public health need related to COVID-19.

In assessing whether there is sufficient evidence to support the conclusion/argument that the benefits outweigh the risks, not only is the Minister allowed to be unsure about the benefits and the risks, but the Minister must take into account "the necessity of addressing the urgent public health need related to COVID-19."

This is not a test to protect the public from unsafe or ineffective vaccines. This is a direction to approve COVID-19 vaccines while specifically and deliberately exempting them from:

1) objective proof of safety;
2) objective proof of efficacy, and
3) objective proof that the benefits outweigh the risks.

It is difficult to conceive of a less-scientific test for drug approval than that found in the Interim Order.

Point 8: Were the COVID-19 vaccines approved under this test without findings they were safe or effective or that the benefits outweighed the risks?

In addition to the Interim Order, and subsequent incorporation of a subjective test for COVID-19 Vaccines into the *Drug Regulations*, Health Canada produced a document called *Guidance for market authorization requirements for COVID-19 vaccines*. This document is intended to provide guidance to pharmaceutical companies applying for market approval. As it must, it follows the new subjective test for the vaccines. For example, the current version includes:

> **About market authorizations for a COVID-19 vaccine**
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> Health Canada will grant authorizations only if we determine that the benefits of the

> vaccine outweigh its potential risks. We will base our decision on the evidence provided on the vaccine's safety, quality and efficacy. For vaccines relying on the modified requirements in C.08.002 (2.1) of the Food and Drug Regulations, the risk-benefit analysis weighs the uncertainties about a potential vaccine against the public health need for a vaccine at the time of the decision.
>
> Modified requirements for COVID-19 drugs make it possible for initial authorization, based on early data, while the manufacturer continues working on developing a vaccine. We will use terms and conditions to manage uncertainties or risk mitigation measures related to the vaccine in the context of public health. (emphasis added).

Celia Lourenco is the Health Canada employee that approved all of the COVID-19 vaccines. She swore an Affidavit for Federal Court File No. T-145-22 in which she outlined the test used for two of the vaccines she approved. For the Pfizer vaccine she stated:

> 98. The interim authorization of the Pfizer.BioNTech COVID.19 Vaccine was based on quality (chemistry and manufacturing), non.clinical (pharmacology and toxicology), and clinical (immunogenicity, safety, and efficacy) information. Following review of the available information, Health Canada concluded that the evidence provided meets the Health Canada standards published in the Guidance for Market Authorization Requirements for COVID-19 Vaccines (a copy of which is attached as Exhibit "K"). The evidence supports the conclusion that the benefits associated with the Pfizer.BioNTech COVID.19 Vaccine outweigh the risks, having regard to a shorter term (median of 2 months) follow up of safety and efficacy at authorization, and the necessity of addressing the urgent public health need related to COVID.19. Based on these considerations, the benefit.risk profile of the Pfizer.BioNTech COVID.19 Vaccine is considered favourable for active immunization to prevent COVID.19 caused by SARS.CoV.2 in individuals 16 years of age and older. Health Canada has also authorized the use of the Pfizer-BioNTech COVID-19 Vaccine in children 5 to 11 years of age, and adolescents 12 years of age and older.

For the Moderna vaccine Celia Lourenco stated:

> 118. The interim authorization of the Moderna COVID.19 Vaccine was based on quality (chemistry and manufacturing), non.clinical (pharmacology and toxicology), and clinical (immunogenicity, safety, and efficacy) information. Following review of the available information, Health Canada concluded that the evidence provided met the Health Canada standards published in the Guidance for Market Authorization Requirements for COVID-19 Vaccines (a copy of which attached as Exhibit "K"). The evidence supported the conclusion that the benefits associated with the Moderna COVID.19 Vaccine outweighed the risks, having regard to a shorter term (median of 2 months) follow up of safety and efficacy at authorization, and the necessity of addressing the urgent public health need related to COVID.19. Based on these considerations, the benefit.risk profile of the Moderna COVID.19 Vaccine was considered favourable for active immunization to prevent against COVID-19 caused by SARS-CoV-2 virus in individuals 18 years
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> (Affidavit of Celia Lourenco sworn April 21, 2022 for Federal Court File T-145-22).

Ms. Lourenco is citing the text of the subjective test in the Interim Order as the basis for the vaccine approvals.

Notably, what is missing from the reasons supporting the vaccine approval is:

1) objective proof of safety;

2) objective proof of efficacy, and

3) objective proof that the benefits outweigh the risks.

Point 9: The medium and long-term risks are unknown.

Some of the COVID-19 vaccines contain novel mRNA technology that is designed to change a person's RNA to get the body to manufacture a spike protein similar to the spike protein in the virus that causes COVID-19.

This is novel technology, of which the medium and long-term effects are unknown.

It is because the medium and long-term effects are unknown, that Health Canada placed further testing and reporting of safety and efficacy data on the vaccine manufacturers. Speaking about conditions placed on Moderna, Celia Lourenco, the Health Canada employee that approved all COVID-19 vaccines testified:

> A. It's to deal with any remaining uncertainties around the vaccine. It could have-- it could be, for example, uncertainties around the longer term efficacy or safety of the vaccine or in additional information that may be needed related to the manufacturing of the vaccine and also to deal with the -- the safety monitoring of the vaccine.
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> (June 6, 2022 cross-examination of Celia Lourenco p. 211 Lines 9-16 Federal Court File T-145-22).

List of COVID-19 vaccines approved under the Interim Order

The following vaccines were approved under the Interim Order:

1) Pfizer-BioNTech on December 9, 2020 for ages 16 and older, and May 5, 2021 for ages 12-15;

2) Moderna on December 23, 2020 for ages 18 and over and August 27, 2021 for ages 12-17;

3) AstraZeneca on February 26, 2021 for ages 18 and older, and

4) Janssen (Johnson & Johnson) on March 5, 2021 for ages 18 and older.

The March 2021 Regulations codifying the subjective test/direction in the Interim Order

An Interim Order approved by the Governor in Council is only valid for a year, or less if replaced by regulations having the same effect as the Interim Order.

On March 17, 2021, regulations came into force to replace the Interim Order with permanent regulations codifying the subjective approval test first found in the Interim Order (see SOR/2021-45).

The following was added to C.08.002:

> C.08.002 (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
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> (a) a statement that the submission contains evidence to establish that the requirement set out in paragraph (b) is met; and
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> (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.

Note that "the requirements set out in paragraphs (2)(g) and (h)" are the normal requirements to prove safety and efficacy. These sections are reproduced earlier in this document but have been included again below for clarity.

> g) detailed reports of the tests made to establish the safety of the new drug for the purpose and under the conditions of use recommended;
>
> h) substantial evidence of the clinical effectiveness of the new drug for the purpose and under the conditions of use recommended[.]

Note that this evidence requirement is **substantially similar** to that in the Interim Order with one significant change. The conclusion in the test changed from:

> having regard to "the necessity of addressing the urgent public health need related to COVID-19" (Interim Order),

to

> consideration given to "the public health need related to COVID-19".

As with the Interim Order, the new Regulations permit the evidence to "support the conclusion" to be delayed or incomplete (see C.08.002(2.3) to (2.5)).

The Interim Order took away the Minister's normal authority to remove market authorization for safety or efficacy concerns

We cannot know if a drug is safe or effective in the general population until it is actually used in the general population. Because of this, the Regulations permit the Minister (i.e. Health Canada) to cancel a market authorization if evidence after the authorization was granted raises a safety or efficacy concern.

This evidence can include:

a) evidence filed in other new drug applications. So, in the normal course of events, if one company was granted an approval for a novel mRNA vaccine, and a later company applied for approval for a similar mRNA vaccine, the information in both applications could be used to revoke an approval (C.08.006(1));

b) clinical or other experience not reported in the submission or supplement or not available to the Minister at the time the notice of compliance was issued (C.08.006(2)(a));

c) tests by new methods or tests by methods not reasonably applicable at the time the notice of compliance was issued (C.08.006(2)(a)).

Normally the market authorization can also be cancelled if there is a material misrepresentation in the new drug application. All of this is found in C.08.006 which includes:

> C.08.006 (1) For the purposes of subsection (2), evidence or new information obtained by the Minister includes any information or material filed by any person under Division 5 or section C.08.002, C.08.002.01, C.08.002.1, C.08.003, C.08.005 or C.08.005.1.
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> C.08.006(2) The Minister may, by notice to a manufacturer, suspend, for a definite or indefinite period, a notice of compliance issued to that manufacturer in respect of a new drug submission, an extraordinary use new drug submission, an abbreviated new drug submission, an abbreviated extraordinary use new drug submission or a supplement to any of those submissions if the Minister considers
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> a) that the drug is not safe for the use represented in the submission or supplement, as shown by evidence obtained from
>
> i. clinical or other experience not reported in the submission or supplement or not available to the Minister at the time the notice of compliance was issued, or
>
> ii. tests by new methods or tests by methods not reasonably applicable at the time the notice of compliance was issued;

b) that, upon the basis of new information obtained after the issuance of the notice of compliance, there is lack of substantial evidence that the drug will have the effect it is represented to have under the conditions of use prescribed, recommended or proposed by the manufacturer;

c) that the submission or supplement contained an untrue statement of material fact;

d) that the manufacturer has failed to establish a system for maintaining required records or has repeatedly or deliberately failed to maintain such records;

e) that, on the basis of new information obtained after the issuance of the notice of compliance, the methods, equipment, plant and controls used in the manufacturing, processing and packaging of the drug are inadequate to assure and preserve the identity, strength, quality or purity of the new drug[.]

<u>It is a fundamental safeguard that the Minister can ordinarily cancel a market authorization if new evidence raises a safety or efficacy concern or if fraud is discovered.</u>

This fundamental safeguard was removed by the Interim Order.

Section 2(1) of the Interim Order sets out that once a COVID-19 vaccine is approved under the Interim Order, most of the *Food and Drug Regulations* do not apply, including C.08.006. Although the COVID-19 vaccines are experimental treatments rushed through approval without requiring proof of safety and efficacy, the Interim Order specifically prevented the Minister from removing the approval due to subsequent safety and/or efficacy concerns. The Interim Order replaces the substantial safeguards found in C.08.006, with limited authority to cancel a market authorization. The only grounds for cancellation under the Interim Order are:

a) if the subjective test in s. 5(c) is no longer met;

b) if it is believed part of the Interim Order, the *Food and Drugs Act* or Regulations have been violated, or

c) for an approval based on an approval from a foreign government (allowed under s. 4 of the Interim Order), if the foreign government cancels their approval.

This is found in section 11 of the Interim Order which reads:

> 11 (1) The Minister may suspend an authorization, in whole or in part, giving reasons, if
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> a) the Minister determines that the requirement set out in paragraph 5(c) is no longer met;

b) the Minister has reasonable grounds to believe that the holder of the authorization has contravened, in relation to the COVID-19 drug to which the authorization relates, any provision of this Interim Order, the Regulations or the Food and Drugs Act or any order made under that Act; or

c) in the case of an authorization that was issued on the basis of an application submitted under section 4, the Minister becomes aware that the foreign regulatory authority has revoked or suspended the authorization to sell the foreign drug.

11(2) The Minister must reinstate a suspended authorization if the holder provides to the Minister, in the time, form and manner specified by the Minister, information or material that demonstrates that the situation giving rise to the suspension did not exist or has been corrected.

This non-applicability of C.08.006 was in force from September 16, 2020 to:

1) September 15, 2021, for the Pfizer and Moderna vaccines;

2) November 18, 2021, for the AstraZeneca vaccine, and

3) November 22, 2021, for the Johnson & Johnson vaccine.

(SOR/2021-45 s. 25).

The Interim Order removed the Minister's normal ability to cancel a market authorization following further assessments

Under s. 21.31 of the *Food and Drugs Act*, the Minister can order a company to conduct further assessments after a market authorization is issued. If the assessment reveals that the benefits of the new drug do not outweigh the risks of the new drug C.08.006(3) authorizes the Minister to suspend the market authorization.

This is found as follows:

C.08.006(3) The Minister may, by notice to a manufacturer, suspend for a definite or indefinite period a notice of compliance issued to that manufacturer in respect of a new drug submission, an extraordinary use new drug submission, an abbreviated new drug submission, an abbreviated extraordinary use new drug submission or a supplement to any of those submissions, if, after the Minister has, under section 21.31 of the Act, ordered the holder of a therapeutic product authorization referred to in subparagraph C.01.052(1)(b)(iii) to conduct an assessment of the new drug in order to provide evidence establishing that the benefits associated with the drug outweigh the risks of injury to health,

a) the holder fails to comply with the order; or

b) the holder complies with the order but the Minister determines that the results of the assessment are not sufficient to establish that the benefits associated with the drug outweigh the risks of injury to health.

Section 2 of the Interim Order takes away the application of C.08.006 for COVID-19 vaccines approved under the Interim Order. If subsequent testing ordered by the Minister showed that the benefits of the vaccine no longer exceeded the risks, the Minister could not use the C.08.006 authority to cancel the market authorization. Because the subjective test in s. 5 of the Interim Order does not require proof that the benefits outweigh the risks, the Minister may not have had the authority to cancel under s. 11 of the Interim Order even if the Minister believed the benefits did not outweigh the risks. This is because the s. 5 test only requires evidence to "support the conclusion" that the benefits outweigh the risks, having regard to the uncertainties in the evidence and the need of addressing the urgent public health need related to COVID-19. As a reminder the Interim Order test is:

5(c) the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19.

This non-applicability of C.08.006 was in force from September 16, 2020 to:

1) September 15, 2021, for the Pfizer and Moderna vaccines;

2) November 18, 2021, for the AstraZeneca vaccine, and

3) November 22, 2021, for the Johnson & Johnson vaccine.

Creating deliberate conflict of interests for the approval of experimental vaccines

Our Regulations prevent finished drugs for human use to be imported into Canada if they have not been approved by Health Canada for use in humans.

The Interim Order allowed unapproved COVID-19 vaccines to be imported into Canada as long as the Canadian Government was the purchaser. This was called pre-positioning in the Interim Order, and later in the Regulations codifying the Interim Order (SOR/2021-45). The rational is to deal with the COVID-19 crisis, by purchasing and distributing the vaccines so that we have them if/when they are approved for use.

This creates a tremendous conflict of interest.

The Government of Canada can purchase, import and distribute for later use unapproved vaccines, while the same Government waits for itself to approve the vaccines. What could go wrong?

Timing of the Interim Order

The September 16, 2020 Interim Order was made just before some of the approval applications were filed with Health Canada. For example, AstraZeneca filed on September 30, 2020. Pfizer filed on October 8, 2020.

The approval applications were made under the Interim Order, and would have been structured to meet the requirements of the Interim Order.

It is unlikely that the applications could have been filed so quickly to comply with the subjective test, unless they had been told of the test in advance, or participated in arriving at the test.

Concluding thoughts

The purpose of this Discussion Paper is simply to explain changes made to the drug regulation requirements concerning approval of the COVID-19 vaccines. In preparing this Discussion Paper, there appeared to be a disconnect between Health Canada messaging concerning vaccine approval and the modified test for actual approval. As indicated above, safety, efficacy and whether the benefits of the vaccines outweighed the risks did not need to be proven.

Despite this new test for the vaccines, the pharmaceutical companies did not have to use the new test. They still had the option to apply for approval under the regular test which required objective proof of safety, efficacy and cost/benefit. The pharmaceutical companies did not choose to objectively prove safety, efficacy and cost/benefit. They choose to apply under the Interim Order test.

Considering this, it is curious that for each COVID-19 vaccine approved of by Health Canada, that Health Canada messages to the public were that the regular requirement were met. For example, at the top of Health Canada's website page for the Pfizer vaccine, Health Canada states:

> All COVID-19 vaccines authorized in Canada **are proven safe, effective and of high quality.**
>
> (emphasis in the original)

This Discussion Paper is the opinion of the author, Shawn Buckley, and does not necessarily reflect the position of the NHPPA.

Primary Sources

Food and Drugs Act, R.S.C. 1985, c. F-27

Food and Drug Regulations, C.R.C., c. 870

September 16, 2020 Interim Order by the Minister of Health under s. 30.1 of the *Food and Drugs Act*

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

Health Canada document - *Guidance for market authorization requirments for COVID-19 vaccines*.

Affidavit of Celia Lourenco sworn April 21, 2022 for Federal Court File T-145-22.

June 3 and 6, 2022 Cross-examination transcripts of Celia Lourenco in Federal Court File T-145-22.

Appendix

Table comparing different approval standards concerning COVID-19 drugs

C.08.002(2) regular new drug submission requirements	Sept 16/20 Interim Order requirements s. 3(1) confirmed by OIC P.C. 2020-682	C.08.002(2.1) COVID-19 drug requirements in force March 17, 2021 SOR/2021-45
(a) a description of the new drug and a statement of its proper name or its common name if there is no proper name;	(b) a description of the drug and a statement of its proper name or its common name if there is no proper name;	same as C.08.002(2)
(b) a statement of the brand name of the new drug or the identifying name or code proposed for the new drug;	(c) a statement of the brand name of the new drug or the identifying name or code proposed for the new drug;	same as C.08.002(2)
(c) a list of the ingredients of the new drug, stated quantitatively, and the specifications for each of those ingredients;	(d) a list of the ingredients of the new drug, stated quantitatively; (e) the specifications for each of the drug's ingredients	same as C.08.002(2)
(d) a description of the plant and equipment to be used in the manufacture, preparation and packaging of the new drug;	(f) a description of the facilities and equipment to be used in the manufacture, preparation and packaging of the drug;	same as C.08.002(2)
(e) details of the method of manufacture and the controls to be used in the manufacture, preparation and packaging of the new drug;	(g) details of the method of manufacture and the controls to be used in the manufacture, preparation and packaging of the drug;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(f) details of the tests to be applied to control the potency, purity, stability and safety of the new drug;	(h) details of the tests to be applied to control the potency, purity, stability and safety of the drug;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(g) detailed reports of the tests made to establish the safety of the new drug for the purpose and under the conditions of use recommended; (h) substantial evidence of the clinical effectiveness of the new drug for the purpose and under the conditions of use recommended;	(o) the known information in relation to the quality, safety and effectiveness of the drug. 5 The Minister must issue an authorization in respect of a COVID-19 drug if the following requirements are met: (a) the applicant has submitted an application to the Minister that meets the requirements set out in subsection 3(1) or 4(2); (b) the applicant has provided the Minister with all information or material, including samples, requested under subsection 13(1) in the time, form and manner specified under subsection 13(2); and (c) the Minister has sufficient evidence to support the conclusion that the benefits associated with the drug outweigh the risks, having regard to the uncertainties relating to the benefits and risks and the necessity of addressing the urgent public health need related to COVID-19.	(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. **[Note (2.1)(b) can be delayed or incomplete as per (2.3-2.5)]**

(i) a statement of the names and qualifications of all the investigators to whom the new drug has been sold;	(i) a statement of the names and qualifications of all the investigators to whom the drug has been sold;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(j) in the case of a new drug for veterinary use, a draft of every label to be used in connection with the new drug, including any package insert and any document that is provided on request and that sets out supplementary information on the use of the new drug;	(j) a draft of every label to be used in connection with the drug, including any package insert and any document that is provided on request and that sets out supplementary information on the use of the drug;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(j.1) in the case of a new drug for human use, mockups of every label to be used in connection with the new drug — including any package insert and any document that is provided on request and that sets out supplementary information on the use of the new drug— and mock-ups of the new drug's packages;		C.08.002(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. **[Note (2.2) can be delayed or incomplete as per (2.3-2.5)]**
(k) a statement of all the representations to be made for the promotion of the new drug respecting (i) the recommended route of administration of the new drug, (ii) the proposed dosage of the new drug, (iii) the claims to be made for the new drug, and (iv) the contra-indications and side effects of the new drug;	(k) a statement of all the representations to be made for the promotion of the drug respecting (i) the recommended route of administration of the drug, (ii) the proposed dosage of the drug, (iii) the drug's indications, and (iv) the contra-indications and side effects of the drug;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(l) a description of the dosage form in which it is proposed that the new drug be sold;	(l) a description of the dosage form that is proposed for the sale of the drug;	same as C.08.002(2)
(m) evidence that all test batches of the new drug used in any studies conducted in connection with the submission were manufactured and controlled in a manner that is representative of market production;	(m) evidence that all test batches of the drug used in any studies conducted in connection with the application were manufactured and controlled in a manner that is representative of market production;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(n) in the case of a new drug intended for administration to food-producing animals, the withdrawal period of the new drug; and	(n) in the case of a drug intended for administration to food-producing animals, the withdrawal period of the drug;	same as C.08.002(2) but can circumvent C.08.002(2.3-2.5)
(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.		**Does not apply**
	(a) the applicant's name and contact information and, in the case of a foreign applicant, the name and contact information of their representative in Canada;	