Health Canada
Santé Canada

Health Products and Food Branch
Direction générale des produits de santé et des aliments

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INTERIM ORDER AUTHORIZATION – TERMS AND CONDITIONS

In accordance with section 10 of the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to Covid-19*, the following Terms and Conditions are imposed on the authorization issued in respect of Moderna COVID-19 Vaccine (mRNA-1273 SARS-CoV-2):

CLINICAL:

1. The next database lock will be determined following changes to the protocol to address the crossing over of placebo recipients to the vaccine group. Please provide the amendment, including how you will try to keep patients in the study and the new data lock points as soon as possible. Based on the new data lock points, provide the following:

    a. An overall safety summary within two weeks after the database lock; and

    b. Full study report including safety, efficacy and immunogenicity when available.

2. Please provide a safety update for subjects in the Phase 3 study (mRNA- 1273-P301) at the 6-month safety follow up when available for at least 3000 vaccinated subjects as well as for available and relevant data from placebo subjects.

3. Also, to fill data gaps, for various sub-populations for example, provide results, when available, of all ongoing studies, or studies to come, conducted with the vaccine.

CHEMISTRY AND MANUFACTURING:

1. All lots to be sold in Canada should comply with the approved specifications for drug substance (DS) and drug product (DP). A certificate of analysis (CoA) should be submitted for each lot distributed in Canada. Certificates of Analysis for lots distributed to the United States should be submitted on a quarterly basis, and a summary of batch disposition should be submitted on a biannual basis. The summary should include all DS and DP lots produced, failed, or aborted and a brief description of the issue(s) where this is relevant. Please note that issuance of a lot release letter prior to distribution of lots in Canada is not required at this time. Health Canada may revisit this requirement at any time based on the risk profile of the product. The email address where this information should be sent will be provided to the Sponsor in an additional correspondence.

2. Post-authorization, the following information should be submitted as soon as it is available:

    a. Updates on process validations at full commercial scale including all additional PPQ batches, comparability data for all facilities included in authorization and in subsequent amendments.

    b. Comparability of different sites including characterization of DS and DP and enrollment in stability studies.

    c. Updates on all assay validation studies completed post-authorization, including assay performance and comparability of all laboratory testing sites. Please note, all analytical assays must be validated prior to New Drug Submission.

    d. Any critical changes to the manufacturing process, the specifications for critical quality attributes or to the key analytical assays should be submitted promptly as amendments to the authorization.

    e. Provide all information available to any new facilities relevant to the Canadian supply chain when available.

3. Provide stability information in a timely manner to support extension of the expiry date. Once approved, relevant databases should be updated with the new expiry date.

4. Provide notification of changes in GMP status for any of the facilities included in the authorization as well as any new facilities relevant to the Canadian supply chain when available.

RISK MANAGEMENT PLAN:

1. As per the Interim Order authorized drugs, Moderna Therapeutics Inc. will:

    a. Treat adverse reactions associated with Moderna COVID-19 Vaccine as priority and submit the corresponding reports to Health Canada without delay; and

    b. Identify in the report that the Moderna COVID-19 Vaccine is a Moderna Therapeutics Inc. product authorized under the Interim Order.

2. Moderna Therapeutics Inc. is required to submit monthly safety reports for the period of the Interim Order authorization, unless otherwise determined by Health Canada. The monthly safety reports should be submitted within 15 days after the last day of a month, beginning after the first full calendar month after authorization. These reports should contain the following:

    a. Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women);

    b. Interval and cumulative number of reports;

    c. Total number of adverse event reports in Canada and Globally;

    d. Exposure data stratified by country, including any available data on age groups, race, ethnicity, on indigenous populations and remote communities;

    e. Changes to reference safety information in the interval;

f. Ongoing and closed signals in the interval;

g. List of adverse events of special interest including the Safety Platform for Emergency vACcines (SPEAC) list and RMP safety concerns (including the additional missing information): reports – numbers and relevant cases, including time-to-onset and observed/expected analyses;

h. Fatal reports – numbers and relevant cases, including observed/expected analyses;

i. Vaccination failure / lack of efficacy (including confirmed and suspected cases) reports and vaccination errors (categories according to preferred terms);

j. Potential interaction with other vaccines/concomitant treatments-number and relevant cases;

k. Summary outcomes of some of the routine pharmacovigilance activities (as presented in the EU RMP Part III and applied in the Canadian context) should be included for the purpose of rapid signal detection and communication activities. Summary of all ongoing registries and studies should be included in the six-month scheduled PBRERs, unless a safety signal is identified that requires immediate regulatory action.; and

l. Overall risk/benefit assessment.

3. Moderna Therapeutics Inc. is required to provide, prior to distribution, patient information cards to support traceability, where required, which will include elements such as manufacturer name, name of vaccinee, space for recording dates of first and second doses and associated batch/lot numbers, and information on how to report any adverse events.

4. Moderna Therapeutics Inc. is required to:

    a. Provide an updated Canadian Addendum to the Risk Management Plan (RMP) following authorization. This Canadian addendum should follow Health Canada guidance (1. Guidance Document Submission of Risk Management Plans and Follow-Up Commitments; 2. Guidance for market authorization requirements for COVID-19 vaccines; 3. Notice of clarification to drug manufacturers and sponsors: Canadian-specific considerations in risk management plans) and include the following:

        i. In addition to the important potential risks in the EU RMP, the following should be included:
            1. Vaccine-associated enhanced disease (VAED)

        ii. In addition to the missing information in the EU RMP, the following should be included:
            1. To specify "<18 years of age" in the "Use in pediatric populations"

    b. Provide an updated Core RMP and Canadian Addendum in a timely manner if a signal of safety issue is observed in post-authorization surveillance. The RMP format should follow the guidance (Guidance Document Submission of Risk Management Plans and Follow-Up Commitments) and should include the following in the context of the COVID-19 drugs submitted for authorization under the Interim Order:

i. a safety specification that details the identified risks, potential risks, and missing information for the Moderna COVID-19 Vaccine;

ii. a pharmacovigilance plan that details specific measures to be taken to identify and report safety issues in COVID-19 patients, including adverse reaction reporting, periodic reporting, and ongoing/planned studies; and

iii. a risk minimization plan, if applicable, to manage risks that may require additional measures beyond those considered standard (for instance, labelling).

LABELLING:

1. Moderna Therapeutics Inc. to submit final snapshots of all components of the electronic platform (linked to on international "pandemic" labels), containing Canadian-specific labelling information for *Moderna COVID-19 Vaccine* in French and English for Health Canada's review and records, prior to launch of the electronic platform.

2. Moderna Therapeutics Inc. to develop and distribute a Health Product Risk Communication (HPRC), in French and English, with Health Canada approval and endorsement, to inform healthcare professionals about the authorization of the *Moderna COVID-19 Vaccine* under the *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19* with English-only vial and carton labels for the initial supply, to expedite global access of the drug in the context of the pandemic.

    a. The letter should direct healthcare professionals to the electronic platform where they can find information about Canadian-specific labelling in both official languages and should be issued prior to and alongside the distribution of the vaccine; and

    b. The letter should specify when the Canadian-specific labels will be implemented.

3. Moderna Therapeutics Inc. to commit to developing Canadian-specific bilingual labelling for *Moderna COVID-19 Vaccine* and implementing such labelling at a point when the global supply and pandemic situation will allow. Health Canada should be kept informed of estimated timelines and proposed strategies concerning the development and implementation of Canadian-specific bilingual labels.

    a. During the period prior to implementation of the Canadian-specific bilingual labeling, authorized interim version of the proposed Canadian labels should be made available to healthcare professionals as reference.