Health Canada / Santé Canada

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

**TERMS AND CONDITIONS**

**Company: Moderna Biopharma Canada Corporation**

**Product: Spikevax (elasomeran mRNA vaccine)**

**Dossier ID: HC6-024-E252733**

**Background:**

The Food and Drug Regulations allows the Minister to impose or amend terms and conditions, and request additional information, in relation to a COVID-19 drug submission, Drug Identification Number (DIN), or establishment licence, at any time while it is in effect. In light of the severity of the COVID-19 pandemic, this allows the Minister to act quickly to gather important safety information or mitigate risk in a timely manner.

Depending on the requirement, terms and conditions can be ongoing (e.g., require a monthly report), have a defined time (e.g., a report is due to Health Canada on a specific day) or are to be completed once the data is available (e.g., a clinical trial is completed).

The status of the Terms and Conditions will be updated on a regular basis.

**Status as of October 4, 2023:**

**Table: Terms and Conditions**

| | Terms and Conditions | Issued | Status |
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| 1 | For the indication in adults 18 years of age and older, provide full study report including safety, efficacy and immunogenicity, when available. | September 16, 2021 | Ongoing |
| 2 | For the indication in adults 18 years of age and older, 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. | September 16, 2021 | Closed |
| 3 | For the indication in adults 18 years of age and older, 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. | September 16, 2021 | Ongoing |
| 4 | For the indication in individuals 12 to 17 years of age, provide safety data for all adolescents 12 through 17 years of age in study P203, 6 months after Dose 2, when the data become available. | September 16, 2021 | Ongoing |
| 5 | For the indication in individuals 12 to 17 years of age, provide the report for Study P203 including safety, efficacy and immunogenicity | September 16, 2021 | Ongoing |

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| | data up to 1 year after Dose 2 in adolescents 12 through 17 years of age, when the study is completed. | | |
| 6 | Provide an updated Certified Product Information Document (CPID) that includes the facilities by December 31, 2021. | September 16, 2021 | Closed |
| 7 | Provide final reports for ongoing drug substance (DS) and drug product (DP) PPQ activities at all manufacturing sites/scales as they become available. | September 16, 2021 | Ongoing |
| 8 | Moderna Biopharma Canada Corporation is required to:<br>a. Treat adverse reactions associated with SPIKEVAX as priority and submit the corresponding reports to Health Canada without delay; | September 16, 2021 | Closed |
| 9 | Moderna Biopharma Canada Corporation is required to submit monthly safety reports, 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:<br><br>a. Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women);<br>b. Interval and cumulative number of reports;<br>c. Total number of adverse event reports in Canada and Globally;<br>d. Exposure data stratified by country, including any available data on age groups, race, ethnicity, on indigenous populations and remote communities;<br>e. Changes to reference safety information in the interval;<br>f. Ongoing and closed signals in the interval;<br>g. Updated list of adverse events of special interest including the Safety Platform for Emergency Vaccines (SPEAC) list and Risk Management Plan (RMP) safety concerns (including the additional missing information): reports – numbers and relevant cases, time to-onset and observed/expected analyses including causality assessment;<br>h. Fatal reports – numbers and relevant cases, including observed/expected analyses;<br>i. Vaccination failure / lack of efficacy (including confirmed and suspected cases) reports and vaccination errors (categories according to preferred terms);<br>j. Potential interaction with other vaccines/concomitant treatments-number and relevant cases;<br>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 Periodic Benefit-Risk Evaluation Reports (PBRERs), unless a safety signal is identified that requires immediate regulatory action.; and | September 16, 2021 | Closed |

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| | l. Overall risk/benefit consideration | | |
| 10 | Moderna Biopharma Canada Corporation is required to 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:<br>a. a safety specification that details the identified risks, potential risks, and missing information for the SPIKEVAX;<br>b. 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 a risk minimization plan, if applicable, to manage risks that may require additional measures beyond those considered standard (for instance, labelling). | September 16, 2021 | Ongoing |
| 11 | Moderna Biopharma Canada Corporation to submit final snapshots of all components of the electronic platform (linked to on the any foreign or Canadian specific labels), containing the approved Canadian-specific labelling information for SPIKEVAX in French and English for Health Canada's review and records, prior to launch of the electronic platform, and for each<br>subsequent update. | September 16, 2021 | Ongoing |
| 12 | Moderna Biopharma Canada Corporation is requested to develop and distribute a Health Product Risk Communication (HPRC), in French and English, should a decision be made to import, for Canadian sites, non-Canadian labelled supplies. In this case the HPRC would need to be developed with Health Canada approval and endorsement, to inform healthcare professionals that Moderna Biopharma Canada Corporation will delay implementation of Canadian-specific inner/outer labels following NDS-CV approval for SPIKEVAX, and that interim non-Canadian inner/outer labels will be used for the short term. Please note the following:<br>a. Moderna Biopharma Canada Corporation should include images and texts of these labels in the HPRC and clearly outline all deviations from Canadian requirements<br>b. The HPRC should direct healthcare professionals to the electronic platform where they can find information about the approved Canadian-specific labelling in both official languages<br>c. The HPRC should include an alternative method for the health care professionals to obtain a paper copy of the HPRC and/or Product Monograph by mail or fax from Moderna Biopharma Canada Corporation if they cannot access the internet<br><br>Finally, Moderna Biopharma Canada Corporation should devise an appropriate dissemination strategy to ensure the HPRC reaches the intended audience in a timely manner. | September 16, 2021 | Closed |

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| 13 | Moderna Biopharma Canada Corporation to commit to developing Canadian specific bilingual | September | Closed |
| | labelling for SPIKEVAX, to be submitted in Q1 of 2022, and implementing such labelling once supplies are transitioned to Canadian dedicated supplies. Health Canada should be kept informed of estimated timelines and proposed strategies concerning the development and implementation of Canadian-specific bilingual labels.<br><br>a. During the period prior to implementation of the Canadian-specific bilingual labeling, Canadian reference labels should be made available to healthcare professionals. | 16, 2021 | |
| 14 | Provide immunogenicity and safety data for 6 months following the administration of the booster dose from Study P201, when the data become available. | November 12, 2021 | closed |
| 15 | Provide immunogenicity and safety data for 12 months following the administration of the booster dose from Study P201, when the data become available. | November 12, 2021 | closed |
| 16 | Provide the results from the planned Study P301 Part C, in which a subset of Phase 3 participants will receive a 50 µg booster dose, when the data become available. | November 12, 2021 | Ongoing |
| 17 | Moderna Biopharma Canada Corporation is required to submit an updated Core Risk Management Plan (RMP) in conjunction with the Canadian Addendum by December 10, 2021 to address any safety concerns, pharmacovigilance and risk minimization measures related to the use of a booster dose of Spikevax in Canada. | November 12, 2021 | Closed |
| 18 | Provide safety data for all participants 6-11 years of age in study P204, 6-month after dose 2. | March 17, 2022 | Ongoing |
| 19 | Provide the immunogenicity data 6 months after dose 2 in study P204 Part 2 in participants 6-11 years of age. | March 17, 2022 | Ongoing |
| 20 | Provide the Clinical Study Report (CSR) for study P204 containing safety, immunogenicity and efficacy data 1 year after dose 2, in subjects 6-11 years of age, when the study is completed. | March 17, 2022 | Ongoing |

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| 21 | Moderna Biopharma Canada Corporation is required to submit bi-monthly safety reports, unless otherwise determined by Health Canada - Santé Canada. The bi-monthly safety reports should be submitted within 15 days after the last day of every second month. These reports should contain the following:<br><br>a. Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women);<br>b. Interval and cumulative number of reports;<br>c. Number of reports in Canada and Global;<br>d. Exposure data stratified by country, including any available data on age groups, race, ethnicity, on indigenous populations and remote communities;<br>e. Changes to reference safety information in the interval;<br>f. Ongoing and closed signals in the interval;<br>g. Updated list of adverse events of special interest including the | April 19, 2022 | Closed |
| | Safety Platform for Emergency Vaccines (SPEAC) list and Risk Management Plan (RMP) safety concerns (including the additional missing information): reports – numbers and relevant cases, time-to-onset and observed/expected analyses including causality assessment;<br>h. Fatal reports – numbers and relevant cases, including observed/expected analyses;<br>i. Vaccination failure / lack of efficacy (including confirmed and suspected cases) and vaccination errors (categories according to preferred terms);<br>j. Potential interaction with other vaccines/concomitant treatments-number and relevant cases;<br>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 studies should be included in the six-month scheduled Periodic Benefit-Risk Evaluation Reports (PBRERs), unless a safety signal is identified that requires immediate regulatory action.; and<br>l. Overall risk/benefit consideration. | | |
| 22 | Moderna Biopharma Canada Corporation is required to submit Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs) every 6 months, unless otherwise determined by Health Canada. The core PSUR/PBRER format should follow international guidance for COVID-19 vaccines. | April 19, 2022 | Closed |

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| 23 | Moderna Biopharma Canada Corporation to commit to implementing Canadian specific bilingual labelling for Spikevax once supplies are transitioned to Canadian dedicated supplies. Health Canada should be kept informed of estimated timelines and proposed strategies concerning the implementation of Canadian-specific bilingual labels. | June 1, 2022 | Ongoing |
| 24 | Provide safety data for all participants 6 months to 5 years of age in Study P204, 6-months after Dose 2. | July 14, 2022 | Ongoing |
| 25 | Provide the immunogenicity data 6 months after Dose 2 in Study P204 Part 2 in participants 6 months to 5 years of age | July 14, 2022 | Ongoing |
| 26 | Provide the Clinical Study Report for Study P204, when it is available. | July 14, 2022 | Ongoing |
| 27 | Moderna Biopharma Canada Corporation is required to submit monthly safety reports, unless otherwise determined by Health Canada - Santé Canada. The monthly safety reports should be submitted within 15 days after the last day of every month. These reports should contain the following:<br><br>a. Interval and cumulative number of reports (serious and nonserious), overall and by age groups and in special populations (e.g. pregnant women);<br>b. Interval and cumulative number of reports;<br>c. Number of reports in Canada and Global;<br>d. Exposure data stratified by country, including any available data on age groups, race, ethnicity, on indigenous populations and remote communities;<br>e. Changes to reference safety information in the interval;<br>f. Ongoing and closed signals in the interval;<br>g. Updated list of adverse events of special interest including the Safety Platform for Emergency Vaccines (SPEAC) list and Risk Management Plan (RMP) safety concerns (including the additional missing information): reports – numbers and relevant cases, time-to-onset and observed/expected analyses including causality assessment;<br>h. Fatal reports – numbers and relevant cases, including observed/expected analyses;<br>i. Vaccination failure / lack of efficacy (including confirmed and suspected cases) and vaccination errors (categories according to preferred terms);<br>j. Potential interaction with other vaccines/concomitant treatments-number and relevant cases;<br>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 studies should be included in the six-month scheduled Periodic Benefit-Risk Evaluation Reports (PBRERs), unless a safety | July 14, 2022 | Closed |

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| | signal is identified that requires immediate regulatory action.;<br>l. Overall risk/benefit consideration | | |
| 28 | Provide immunogenicity and safety data (Study P203 Part 1C-1), obtained 6 months after the booster dose, when available. | January 12, 2023 | Ongoing |
| 29 | Provide the final Clinical Study Report for P203 Part 1C-1, when available. | January 12, 2023 | Ongoing |
| 30 | Moderna Biopharma Canada Corporation is requested to develop and distribute a company-led customer communication, in English and French, should a decision be made to import non-Canadian labelled supplies for Canadian sites. The customer communication should aim to inform healthcare professionals that Moderna Biopharma Canada Corporation will delay the implementation of Canadian-specific inner/outer labels following NDS-CV approval for Spikevax Bivalent (Original / Omicron BA. 4/5) (elasomeran/devasomeran) mRNA vaccine, and that interim inner/outer labels will be used for the short term. Please note the following:<br>a) Moderna Biopharma Canada Corporation should consider including images and texts of these labels in the customer communication and clearly outline all deviations from Canadian requirements;<br>b) The customer communication should direct healthcare professionals to the electronic platform where they can find information about the approved Canadian-specific labelling in both official languages<br>c) The customer communication should not resemble a Health Canada-endorsed Health Product Risk Communication and should not reflect a red banner at the top of the document. A company-led risk communication may take the form of a letter carrying the company letterhead, for example.<br>The company-led customer communication does not require review by Health Canada; however, Moderna Biopharma Canada Corporation is welcome to seek courtesy feedback from BRDD. Moderna Biopharma Canada Corporation is expected to exercise due discretion to ensure prompt finalization and dissemination of the customer communication. Please provide a copy of the final, signed customer communication in English and French via eCTD once available. | April 4, 2023 | Ongoing |
| 31 | Moderna Biopharma Canada Corporation is required to submit Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs) every 6 months, unless otherwise determined by Health Canada. | June 7, 2023 | Ongoing |