

TERMS AND CONDITIONS**Company: ModernaTx Inc.****Product: Spikevax Bivalent (elasomeran/imelasomeran) mRNA vaccine****Dossier ID: HC6-024-E264986****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 September 1, 2022:**Table: Terms and Conditions**

	Terms and Conditions	Issued	Status
1	As the immunogenicity at Day 91 was the pre-specified primary objective in Study mRNA-1273-P205 Part F (cohort 2) and Part G, and the design of the study including type I error were adjusted accordingly, the results for immunogenicity and safety at Day 91 should be provided and included in the Product Monograph. Please provide these data when they become available.	September 1, 2022	Ongoing
2	Provide the Day 181 immunogenicity and safety data from Study mRNA-1273-P205 Part F (cohort 2) and Part G, as soon as the data become available.	September 1, 2022	Ongoing
3	Provide the full Clinical Study Report (CSR) (interim and final analysis) for study P205 Part G and Part F (cohort 2), as soon as they become available.	September 1, 2022	Ongoing

4	For the Drug Substance (DS) Provide stability updates in a timely manner.	September 1, 2022	Ongoing
5	Provide final validation report related to the mRNA ratio method for the Drug product (DP)	September 1, 2022	Ongoing
6	Provide Final validation to support extrapolation of RNA ratio results, for the DP	September 1, 2022	Ongoing
7	Provide Stability updates in a timely manner, for the DP.	September 1, 2022	Ongoing
8	Provide Final Certificates of Analyses, for the DP	September 1, 2022	Ongoing
9	Provide Stability data updates in a timely manner for the new Drug Product manufacturing facility.	September 1, 2022	Ongoing
10	ModernaTX, Inc. is required to treat adverse reactions associated with Spikevax Bivalent as priority and submit the corresponding reports to Health Canada without delay.	September 1, 2022	Ongoing
11	<p>ModernaTX, Inc. is required to submit Monthly Safety Summary Reports (MSSRs) for Spikevax Bivalent, unless otherwise determined by Health Canada. The MSSR 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:</p> <ul style="list-style-type: none"> 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. Reporting interval and cumulative number of reports per High Level Term (HLT) and System Organ Class (SOC); c. Reporting interval and cumulative number of adverse event reports in Canada and globally stratified by seriousness, age groups, gender, dose and in special populations (e.g. pregnant women). Should specific demographic data not be available, ModernaTX, Inc. shall document this and provide an explanation in the MSSR; d. Estimated exposure and use patterns including doses distributed/administered in the reporting interval/cumulative period, stratified by country, including any available data on age groups, race, ethnicity, on indigenous populations and remote communities. Should specific demographic data not be available, ModernaTX, Inc. shall document this and provide an explanation in the MSSR; 	September 1, 2022	Ongoing

	<p>e. Actions taken in the reporting interval for safety reasons and changes to reference safety information;</p> <p>f. Overview of new/ongoing/closed signals during the reporting interval, and discussion of proposed risk minimization measures (if applicable). Reviews of safety topics identified by Health Canada and/or foreign regulators;</p> <p>g. Updated list of Adverse Events of Special Interest (AESIs) from regulatory authorities, internationally recognized collaborations, and scientific literature, including the Safety Platform for Emergency vaccines (SPEAC) list. Summaries of reported cases of all AESIs and RMP safety concerns (including the additional missing information): numbers and relevant cases for the reporting interval/cumulative period including complete evaluation, time to-onset, observed/expected analyses, and causality assessment (if applicable);</p> <p>h. Fatal reports – reporting interval/cumulative number of reports, including observed/expected analyses and discussion of relevant cases;</p> <p>i. 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;</p> <p>j. Overall risk/benefit assessment.</p>		
12	<p>ModernaTX, Inc. is required to submit Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs) every 6 months for Spikevax Bivalent, unless otherwise determined by Health Canada. The core PSUR/PBRER format should follow international guidance for COVID-19 vaccines.</p>	September 1, 2022	Ongoing
13	<p>ModernaTX, Inc. is required to submit an updated core RMP with the Canadian Addendum in a timely manner if a safety issue is identified that requires immediate regulatory action or as requested by Health Canada. The RMP format should follow the guidance (Guidance Document Submission of Risk Management Plans and Follow-Up Commitments) and should include the following:</p> <p>a. A safety specification that details the identified risks, potential risks, and missing information for Spikevax Bivalent;</p>	September 1, 2022	Ongoing

	<ul style="list-style-type: none"> 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 c. A risk minimization plan, if applicable, to manage risks that may require additional measures beyond those considered standard (for instance, labelling). 		
14	ModernaTX, Inc. to submit final snapshots of all components of the electronic platform (linked to any foreign or Canadian specific labels), containing the approved Canadian-specific information for Spikevax Bivalent in French and English for Health Canada’s review and records, prior to launch of the electronic platform, and for each subsequent update.	September 1, 2022	Ongoing
15	<p>ModernaTX, Inc. 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 ModernaTX, Inc. will delay implementation of Canadian-specific inner/outer labels following NDS-CV approval for Spikevax Bivalent, and that interim inner/outer labels will be used for the short term. Please note the following:</p> <ul style="list-style-type: none"> a. ModernaTX, Inc. should include images and texts of these labels in the HPRC and clearly outline all deviations from Canadian requirements; 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 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 (PM) by mail or fax from ModernaTX, Inc., if they cannot access the internet 	September 1, 2022	Ongoing
16	ModernaTX, Inc. to commit to developing Canadian specific bilingual labelling for SPIKEVAX Bivalent 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.	September 1, 2022	Ongoing

	<p>a. During the period prior to implementation of the Canadian-specific bilingual labeling, Canadian reference labels should be made available to healthcare professionals.</p>		
--	--	--	--