TERMS AND CONDITIONS
Company: Medicago Inc.
Product: Covifenz (covid-19 vaccine, plant-based virus-like particles [VLP], recombinant, adjuvanted)
Dossier ID: HC6-024-E254598

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 February 24, 2022:

Total Number: 17

Ongoing/pending: 17

Closed: 0

Table: Terms and Conditions

	Terms and Conditions	Issued	Status
1	Provide safety and immunogenicity results for 6 months after the second dose from Study 021, when the data become available.	February 24, 2022	Pending availability of data
2	Provide safety and immunogenicity results for 12 months after the second dose from Study 021, when the data become available.	February 24, 2022	Pending availability of data
3	Provide data regarding immunogenicity/efficacy against current and emerging variants of concern, when available.	February 24, 2022	Pending availability of data
4	Update the Product Monograph with information on the pregnancy registry, when the registry is in effect and the weblink is live.	February 24, 2022	Pending

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5	Three post-authorisation safety studies (PASS) are planned, including two of the PASS studies to assess the effectiveness and safety of Medicago vaccine using electronic health record (EHR) databases (Canada, UK, US, EU and other countries as needed) and one COVID-19 Vaccine Pregnancy Registry. It is required to provide the results when the data are available.	February 24, 2022	Pending availability of data
6	As a sensitivity analysis, provide the results of vaccine efficacy including all cases of COVID-19 occurring before receiving another COVID-19 vaccine, when available.	February 24, 2022	Pending availability of data
7	Provide the final reports for the on-going characterization and validation studies as soon as they are available. Until such time, provide quarterly status updates.	February 24, 2022	Pending availability of data
8	Provide supporting data for transition to the alternative potency assay as soon as they are available. Until such time, provide quarterly status updates. A post-NOC change submission would be required to transition to specifications based on the alternative potency assay if supported by the analysis.	February 24, 2022	Pending availability of data
9	Provide the investigation report of the visual inspection issues following fill and finish activities as soon as they are available. Until such time, provide quarterly status updates.	February 24, 2022	Pending availability of data
10	Provide updates on the stability studies, which should include the following information, as soon as they are available: a. Assessment of potency of the CoVLP component (DS and DP) using both potency assay methods. b. Assessment of polysorbate 80 content. c. Inform BRDD of any out-of-specification results in the stability studies for CoVLP drug substance and drug product as soon as possible. d. Reference standard performance using both potency assay methods. Until such time, provide quarterly status updates.	February 24, 2022	Pending availability of data
11	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.	February 24, 2022	Ongoing
12	A summary of batch disposition should be submitted on a quarterly basis. The summary should include all drug substance and drug product lots produced, failed, or aborted, and a brief description of the issue(s) relevant to the disposition determination. This information should be sent to the following email: vaccines.covid19.vaccins@hc-sc.gc.ca	February 24, 2022	Ongoing
13	Medicago Inc. is required to treat adverse reactions associated with Covifenz as priority and submit the corresponding reports to Health Canada without delay.	February 24, 2022	Ongoing
14	Medicago Inc. is required to submit Monthly Safety Summary Reports (MSSRs) for the first 6-months of marketing in Canada, unless otherwise determined by Health Canada. The MSSR should be submitted within 15 days	February 24, 2022	Ongoing

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	after the last day of a month, beginning after the first full calendar month after authorization. These reports should contain the following: a. Actions taken in the reporting interval for safety reasons and changes to reference safety information; b. Estimated exposure and use patterns including doses distributed/ administered in the reporting interval / cumulative period, stratified by country, age groups, gender and dose. Should specific demographic data not be available, Medicago Inc. shall document this and provide an explanation in the MSSR; 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, Medicago Inc. shall document this and provide an explanation in the MSSR; d. Reporting interval and cumulative number of reports per High Level Term (HLT) and System Organ Class (SOC); e. 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; f. Updated list of Adverse Events of Special Interest (AESIs) from regulatory authorities, internationally recognized collaborations, and scientific literature. Summaries of reported cases of all AESIs and RMP safety concerns: numbers and relevant cases for the reporting interval/ cumulative period including complete evaluation, observed/ expected analyses, and causality assessment (if applicable); g. Fatal reports – reporting interval/ cumulative number of reports, including observed/expected analyses and discussion of relevant cases; h. Vaccination failure / lack of efficacy – reporting interval/ cumulative number of reports including discussion of confirmed and suspected cases, and variants of concern, if available; i. Medication errors – reporting interval and cumulative number of reports and discussion of relevant cases; j. Potential interaction with other vaccines/ concomitant treatments – reporting interval and cumulative number of reports of reports and discussion of relevant cases; and		

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	k. Overall risk/benefit consideration.		
15	Medicago Inc. 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.	February 24, 2022	Ongoing
16	Medicago 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: a. a safety specification that details the identified risks, potential risks, and missing information for Covifenz; 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).	February 24, 2022	Ongoing
17	Medicago 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 Covifenz in French and English for Health Canada's review and records, prior to launch of the electronic platform, and for each subsequent update.	February 24, 2022	Ongoing