Health Canada / Santé Canada

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

INTERIM ORDER– TERMS AND CONDITIONS
Company: AstraZeneca Canada Inc.
Product: AstraZeneca Vaccine (ChAdOx1-S)
Dossier ID: HC6-024-E241458

Background:

The Interim Order allows the Minister to impose or amend terms and conditions, and request additional information, in relation to a COVID-19 drug submission, authorization, 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 April 22, 2021:

Total Number: *24*

Ongoing/pending: *16*

Closed: *8*

Table: Terms and Conditions

	Terms and Conditions	Issued	Status
1	Provide available data as soon as possible, from the pooled analyses of COV001/2/3/5. Please note that Health Canada expects related updates in Clinical Overview (Module 2.5) and Clinical Summaries (Module 2.7).	Feb 26, 2021	Pending availability of data
2	Provide available analysed data as soon as possible of the Phase 3 Trial D8110C00001 (US, Chile and Peru). Health Canada considers that this study is important to confirm the benefit and risk of AstraZeneca COVID-19 Vaccine. Please note that Health Canada expects the following documents: • Study Synopsis • Updated Clinical Overview (Module 2.5) and Clinical Summaries (Module 2.7)	Feb 26, 2021	Pending availability of data

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3	Provide all data and narratives for SAEs of nervous system disorders from the Phase 3 trial D8110C00001 as soon as possible following unblinding of these subjects.	Feb 26, 2021	Ongoing
4	Provide clinical study reports for COV001, COV002, COV003 and COV005, when available.	Feb 26, 2021	Pending availability of data
5	Provide data regarding protection against emerging variants, when available (e.g. UK, Brazil, South Africa).	Feb 26, 2021	Ongoing
6	Provide SAE and AESI data from the other trials that are currently underway: COV004-Kenya, D8111C00001-Russia, D8111C00002-Japan, and ICMR/SII COVISHIELD-India.	Feb 26, 2021	Pending availability of data
7	All lots to be sold in Canada should comply with the approved specifications for drug substance (DS) and drug product (DP).The Sponsor will require a lot release letter from the Biologic and Radiopharmaceutical Drugs Directorate (BRDD prior to distribution in the Canadian market. A Lot Release Protocol should be submitted to BRDD for each lot to be distributed in Canada in order to support the issuance of a release letter. A summary of batch disposition should be submitted on a biannual basis from the facilities approved to supply Canada. 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. Health Canada may revisit this requirement at anytime 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.	Feb 26, 2021	Ongoing
8	Post-authorization the following information should be submitted as soon as it is available: • 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. • Comparability of different sites including characterization of DS and DP and enrollment instability studies. • 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. • 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. • Provide all information available to any new facilities relevant to the Canadian supply chain when available.	Feb 26, 2021	Ongoing
9	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.	Feb 26, 2021	Ongoing
10	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.	Feb 26, 2021	Ongoing

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11	Health Canada requests that supporting stability information (real time and/or accelerated) is provided for batches manufactured with Process 4 at the sites relevant to this submission prior to the release of any lots in the Canadian market.	Feb 26, 2021	Ongoing
12	As per the Interim Order authorized drugs, AstraZeneca Canada Inc. will: • Treat adverse reactions associated with AstraZeneca COVID-19 Vaccine as priority and submit the corresponding reports to Health Canada without delay; and • Identify in the report that the Astra-Zeneca COVID-19 Vaccine is an AstraZeneca Canada Inc. product authorized under the Interim Order.	Feb 26, 2021	Ongoing
13	AstraZeneca Canada 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: • Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women); • Interval and cumulative number of reports; Total number of adverse event reports in Canada and Globally; • Exposure data stratified by country, including any available data on age groups, race, ethnicity, on frail elderly, patients with chronic illness, immunocompromised and on indigenous populations and remote communities; • Changes to reference safety information in the interval; • Ongoing and closed signals in the interval; • 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; • Fatal reports–numbers and relevant cases (causality assessment); • Vaccination failure / lack of efficacy (including confirmed and suspected cases) reports and vaccination errors (categories according to preferred terms); • Potential interaction with other vaccines/concomitant treatments-number and relevant cases; • 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 • Overall risk/benefit assessment.	Feb 26, 2021	Ongoing
14	AstraZeneca Canada Inc. is required to provide an updated Canadian Addendum to the Risk Management Plan (RMP) within 2 weeks following authorization. This Canadian addendum should follow Health Canada guidance (1. Guidance Document Submission of Risk Management Plans and Follow-Up Commitments; 2.	Feb 26, 2021	Closed

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	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: A description of the planned pharmacovigilance activities for monitoring of use in pregnant and breastfeeding women in Canada (e.g., inclusion of Canadian women in the pregnancy registry)		
15	AstraZeneca Canada Inc. 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 in the context of the COVID-19 drugs submitted for authorization under the Interim Order: • a safety specification that details the identified risks, potential risks, and missing information for the AstraZeneca COVID-19 Vaccine; • 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 routine(for instance, labelling).	Feb 26, 2021	Ongoing
16	AstraZeneca Canada Inc. to submit final snapshots of all components of the electronic platform (linked to on the foreign and Canadian specific labels), containing Canadian-specific labelling information for AstraZeneca COVID-19 Vaccine in French and English for Health Canada's review and records, prior to launch of the electronic platform.	Feb 26, 2021	Ongoing
17	AstraZeneca Canada 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 AstraZeneca COVID-19 Vaccine under the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19 with foreign labelling (UK-EU and COVAX) for the initial supply, to expedite access of the drug in the context of the pandemic. • 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 AstraZeneca COVID-19 Vaccine until such a time that Canadian specific labelling is implemented. • The letter should specify when the Canadian-specific labels will be implemented.	Feb 26, 2021	Closed
18	AstraZeneca Canada Inc. to implement Canadian-specific bilingual labelling by June 2021. Health Canada should be kept informed of estimated timelines and proposed strategies concerning the implementation of Canadian-specific bilingual labels. • During the period prior to implementation of the Canadian-specific bilingual labeling in June2021, approved mock-ups of the proposed	Feb 26, 2021	Expected Q2 2021

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	Canadian labels should be made available to healthcare professionals as reference.		
19	AstraZeneca Canada Inc. will provide by April 5, 2021, an assessment of the benefits and the risks, stratified by sex and age, for the use of the COVID-19 vaccine in the current Canadian context, taking into consideration disease projections and the epidemiology of circulating variants, and post-market reports of rare thrombotic events, including those associated with thrombocytopenia.	March 29, 2021	Extension granted to April 7 Closed
20	AstraZeneca Canada Inc. will provide an analysis, by March 31, 2021, of the proposed or alternate mechanisms of development of thrombotic events with thrombocytopenia considering available case reports and data.	March 29, 2021	Closed
21	AstraZeneca Canada Inc. will propose additional pharmacovigilance activities, including in the Canadian context, for those individuals who receive(d) the vaccine, to be submitted by March 31,2021.	March 29, 2021	Closed
22	AstraZeneca Canada Inc. will provide an assessment of the need for and propose any additional risk minimization measures that could be applied in the Canadian context, to be submitted by March 31, 2021.	March 29, 2021	Closed
23	Submit the documents requested, related to in-process microbial contamination issues that were identified for some lots. Health Canada requests the investigation report into these microbial contamination issues and any associated corrective/preventative actions. These documents are to be provided no later than April 7, 2021. Additionally, provide confirmation as to whether similar issues were identified during the manufacture of any other drug substance lots at this site.	March 31, 2021	Closed
24	AstraZeneca Canada 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 AstraZeneca COVID-19 Vaccine under the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation toCOVID-19 with foreign labelling (US-labelled supply) for the initial supply, to expedite access of the drug in the context of the pandemic. • 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 AstraZeneca COVID-19 Vaccine until such a time that Canadian specific labelling is implemented. • The letter should specify when the Canadian-specific labels will be implemented.	March 31, 2021	Closed