Health Canada
Santé Canada

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

Biologic and Radiopharmaceutical Drugs Directorate
100 Eglantine Driveway
LCDC Building,
Tunney's Pasture, A.L. 0601C
Ottawa, Ontario
K1A 0K9

December 9, 2020

Margaret Kanters
Manager - Regulatory Affairs
Pfizer Canada ULC
17300 Trans-Canada Highway
Kirkland, Quebec, Canada H9J 2M5
Fax: 514-426-6824

Dossier ID: HC6-024-E243022
Control #: 244906

INTERIM ORDER AUTHORIZATION – TERMS AND CONDITIONS

Dear Ms. Kanters,

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 Pfizer-BioNTech COVID 19 Vaccine (COVID-19 mRNA Vaccine):

CLINICAL:

1. Provide the 6-month safety update for subjects of the Phase 1, Phase 2 and Phase 2/3 study, when the 6-month safety update will be available for the 6000 study subjects of Phase 2/3 study.

2. The sponsor plans to maintain the participants in the ongoing Phase 3 Study-C4591001 as originally randomized (for as long as possible) to accumulate 6 months of safety follow-up data after Dose 2. The study team responsible for study conduct would remain blinded to individual participant randomization until this time. Provide results obtained during this period of time (up to 6 months after Dose 2) regarding the vaccine efficacy from Phase 3 and immunogenicity data from Phase 2 of Study-C4591001.

3. The pivotal study, C4591001, is designed to follow participants for 2 years after receiving Dose 2. When the study is completed, provide the study report, including safety, efficacy and immunogenicity data up to 2 years after Dose 2.

4. Health Canada would like to be kept informed of the protocol amendment 10 for Study C4591001, when it becomes available.

5. Provide any changes to the plan you have developed to continue collecting efficacy and safety information if the Phase 2/ 3 study cannot continue as planned. 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.

   This information should be sent to the following email:
   hc.vaccines.covid19.vaccins.sc@canada.ca.

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, Pfizer Canada ULC will:
   a. Treat adverse reactions associated with COVID-19 mRNA Vaccine as priority and submit the corresponding reports to Health Canada without delay.
   b. Identify in the report that the COVID-19 mRNA Vaccine is a Pfizer Canada ULC product authorized under the Interim Order.

2. Pfizer Canada ULC 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 per HLT and SOC
   c. Number of reports in Canada and Global
   d. Exposure data, stratified by country, age groups, race and ethnicity
   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 list and RMP safety concerns (including the additional missing information): reports – numbers and relevant cases, including time-to-onset and O/E analyses
h. Fatal reports – numbers and relevant cases, including observed/expected analyses
i. Vaccination failure / lack of efficacy (including confirmed and suspected cases) and errors-number relevant cases
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 studies can be included in the first six-month scheduled PBRER, unless a safety signal is identified that requires immediate regulatory action.
l. Risk/benefit considerations

3. Pfizer Canada ULC is required to provide, prior to distribution, patient information cards to vaccination sites, which will include elements such as manufacturer name, space for recording dates of first and second doses and associated batch/lot numbers.

4. Pfizer Canada ULC is required to:
   a. Provide an updated Core (EU) RMP and a 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) and include the following:
      i. In addition to the missing information already captured in the EU RMP:
         1. Long-term safety
         2. Use in immunocompromised patients and patients with chronic or debilitating conditions
         3. Use in pediatric populations <16 years of age
         4. Interaction with other vaccines

   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 COVID-19 mRNA 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
      iii. a risk minimization plan, if applicable, to manage risks that may require additional measures beyond those considered standard (for instance, labelling)

LABELLING:

1. **BioNTech Manufacturing GmbH** and **Pfizer Canada ULC** to submit final snapshots of all components of the electronic platform (linked to on the Emergency Use Authorization labels), containing the approved Canadian-specific labelling information for ***Pfizer-BioNTech COVID 19 Vaccine*** in French and English for Health Canada's review and records, prior to launch of the electronic platform.

2. **BioNTech Manufacturing GmbH** and **Pfizer Canada ULC** to develop and distribute a Health Product Risk Communication, in French and English, with Health Canada approval and endorsement, to inform healthcare professionals about the authorization of the ***Pfizer- BioNTech 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 the approved Canadian-specific labelling in both official languages and should be issued prior to, and alongside, the distribution of the vaccine.

3. **BioNTech Manufacturing GmbH** and **Pfizer Canada ULC** to commit to developing Canadian-specific bilingual labelling for ***Pfizer-BioNTech COVID-19 Vaccine*** and implementing such labelling once supplies are transitioned to Canadian dedicated supplies. Provide to Health Canada information on the proposed strategies and planned timelines as soon as these are confirmed.

Sincerely,

Celia Lourenco, Ph.D.
Director General