Health Canada | Santé Canada

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

TERMS AND CONDITIONS
Company: BioNTech Manufacturing GmbH
Product: Comirnaty (COVID-19 vaccine, mRNA)
Dossier ID: HC6-024-E252736

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 April 4, 2023:

Table: Terms and Conditions

	Terms and Conditions	Issued	Status
1	Provide safety and efficacy data for all participants 12 to 15 years of age in study C4591001 followed up for 6 months after the second dose including the blinded and open-label periods, and immunogenicity data 6 months after the second dose in a subset of participants 12 to 15 years of age, when the data become available.	September 16, 2021	Closed
2	Provide the immunogenicity results 6-month after the second dose from Phase 2 of Study C4591001, when the data become available.	September 16, 2021	Closed
3	Provide study C4591001 report, including safety and efficacy data up to 2 years after the second dose for all participants, and immunogenicity data 6 months after the second dose in a subset of participants, when the data become available.	September 16, 2021	Ongoing

4	Provide a Certified Product Information Document (CPID) by December 31, 2021.	September 16, 2021	Closed
5	In addition to the requirements under the Food and Drug Regulations BioNTech Manufacturing GmbH, commit to the following: BioNTech Manufacturing GmbH is required to treat adverse reactions associated with COMIRNATY as priority and submit the corresponding reports to Health Canada without delay.	September 16, 2021	Ongoing
6	In addition to the requirements under the Food and Drug Regulations BioNTech Manufacturing GmbH, commit to the following: BioNTech Manufacturing GmbH 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: 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 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. Updated list of adverse events of special interest including the Safety Platform for Emergency Vaccines 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 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 Periodic Benefit-Risk Evaluation Report (PBRER), unless a safety signal is identified that requires immediate regulatory action. l. Overall risk/benefit consideration	September 16, 2021	Ongoing

7	In addition to the requirements under the Food and Drug Regulations BioNTech Manufacturing GmbH, commit to the following: BioNTech Manufacturing GmbH 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: a. a safety specification that details the identified risks, potential risks, and missing information for the COMIRNATY; 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).	September 16, 2021	Ongoing
8	BioNTech Manufacturing GmbH to submit final snapshots of all components of the electronic platform (linked to any foreign or Canadian specific labels), containing the approved Canadian-specific labelling information for COMIRNATY in French and English for Health Canada's records, following review and approval by PAAB and for each subsequent update. Vaccine website (COMRINATY.ca and/or CVDVaccine.ca) content only pertaining to drug specific information related to a revision to the approved Product Monograph or vaccine labels will be reviewed by Health Canada for consistency with approved labelling information.	September 16, 2021	Ongoing
9	BioNTech Manufacturing GmbH are 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 BioNTech Manufacturing GmbH will delay implementation of Canadian-specific inner/outer labels following NDS-CV approval for COMIRNATY, and that interim non Canadian inner/outer labels will be used for the short term. Please note the following: a. BioNTech Manufacturing GmbH 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	September 16, 2021	Closed

	Product Monograph by mail or fax from BioNTech Manufacturing GmbH, if they cannot access the internet Finally, BioNTech Manufacturing GmbH should devise an appropriate dissemination strategy to ensure the HPRC reaches the intended audience in a timely manner.		
10	BioNTech Manufacturing GmbH to commit to developing Canadian specific bilingual labelling for COMIRNATY, draft copies to be submitted in Q2 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. a. Once Canadian-specific bilingual labeling, with the approved Brand Name is approved by Health Canada and during the implementation period, Canadian reference labels should be made available to healthcare professionals.	September 16, 2021	Closed
11	Provide immunogenicity and safety data for 6 months after the booster dose from Study C4591001, when the data become available. [1,2]	November 9, 2021	Ongoing
12	Provide immunogenicity and safety data for 18 months after the booster dose from Study C4591001, when the data become available. [1,2]	November 9, 2021	Ongoing
13	Provide the results from Study C4591031, when the data become available. [1,2]	November 9, 2021	Closed
14	Provide the results from the subset of Phase 3 participants receiving the 5 µg or 10 µg booster dose, when the data become available. [1,2]	November 9, 2021	Ongoing
15	BioNTech Manufacturing GmbH is required to submit an updated Core RMP in conjunction with the Canadian Addendum by December 3, 2021 to reflect the use of COMIRNATY as a booster dose in Canada including any changes in the safety concerns, pharmacovigilance and risk minimization activities. [1,2]	November 9, 2021	Closed
16	Provide safety data for all participants 5 to < 12 years of age in study C4591007, 6-month after Dose 2 from both initial and expansion safety cohorts when available. [3]	November 19, 2021	Ongoing
17	Provide the immunogenicity data 6 months after Dose 2 in the subset of participants 5 to < 12 years of age when available. [3]	November 19, 2021	Ongoing
18	Provide the supplemental vaccine efficacy results in participants 5 to < 12 years of age, when the pre-specified/sufficient number of cases have accrued to conduct the analysis. [3]	November 19, 2021	Ongoing

19	Provide study C4591007 report including safety, efficacy and immunogenicity data up to 2 years after Dose 2 in the participants 5 to < 12 years of age, when the study is completed. [3]	November 19, 2021	Ongoing
20	BioNTech Manufacturing GmbH is required to submit an updated Core RMP in conjunction with the RMP Canada Specific Addendum by December 3, 2021 to address any safety concerns and additional pharmacovigilance activities and risk minimization measures related to the use in individuals 5 to 11 years of age. [3]	November 19, 2021	Closed
21	BioNTech Manufacturing GmbH will develop Canadian specific bilingual labelling for Comirnaty. Draft copies will be submitted in sufficient time prior to implementing such labelling and transitioning 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. [3] a. Once Canadian-specific bilingual labeling, with the approved Brand Name is approved by Health Canada and during the implementation period, Canadian reference labels should be made available to healthcare professionals. b. BioNTech Manufacturing GmbH to commit to labelling strategies for the clear differentiation between product formulations, including the use of distinguishing brand names or modifiers.	November 19, 2021	Ongoing
22	Provide safety data, 6-months after a booster dose of Comirnaty for all participants 16 years of age and older in study C4591031, when data becomes available. [1, 2]	June 1, 2022	Ongoing
23	BioNTech Manufacturing GmbH and Pfizer Canada ULC to commit to developing Canadian specific bilingual labelling for Comirnaty presentations (DINs) currently marketed in Canada, to be submitted in Q3 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. [1, 2, 3] a. During the period prior to implementation of the Canadian-specific bilingual labeling, Canadian reference labels should be made available to healthcare professionals.	June 21, 2022	Ongoing
24	Provide immunogenicity and safety data for 6 months after the booster (third) dose for subjects 5 to <12 years of age from Study C4591007 Phase 2/3, when the data become available. [3]	August 19, 2022	Ongoing

25	Provide safety and immunogenicity data 6 months after Dose 3 in Study C4591007 in participants 6 months to < 5 years of age, when the results become available. [4]	September 9, 2022	Ongoing
26	Provide the Vaccine Efficacy (VE) final analysis when the protocol specified number of at least 21 cases for VE analysis post-Dose 3 was reached. [4]	September 9, 2022	Closed
27	Provide the completed Clinical Study Report (CSR) for Study C4591007, when it is available. [4]	September 9, 2022	Ongoing
28	BioNTech Manufacturing GmbH 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. [4]	September 9, 2022	Ongoing
29	BioNTech Manufacturing GmbH to submit final snapshots of all applicable components of the electronic platform (linked to any foreign or Canadian specific Comirnaty labels dispensed in Canada), containing the approved Canadian-specific labelling information for Comirnaty in French and English for Health Canada's records, following review and approval by PAAB and for each subsequent update. Vaccine website (COMRINATY.ca and/or CVDVaccine.ca) content only pertaining to drug specific information related to a revision to the approved Product Monograph or vaccine labels will be reviewed by Health Canada for consistency with approved labelling information. [4]	September 9, 2022	Ongoing
30	BioNTech Manufacturing GmbH are 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 BioNTech Manufacturing GmbH and Pfizer Canada ULC will delay implementation of Canadian-specific inner/outer labels following NDS-CV approval for COMIRNATY, and that interim non-Canadian inner/outer labels will be used for the short term. Please note the following: [4] a. BioNTech Manufacturing GmbH 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	September 9, 2022	Closed

	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 BioNTech Manufacturing GmbH, if they cannot access the internet d. BioNTech Manufacturing GmbH should devise an appropriate dissemination strategy to ensure the HPRC reaches the intended audience in a timely manner.		
31	BioNTech Manufacturing GmbH to commit to developing Canadian specific bilingual labelling for Comirnaty presentations (DINs) currently marketed in Canada, to be submitted in Q3 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. During the period prior to implementation of the Canadian-specific bilingual labeling, Canadian reference labels should be made available to healthcare professionals. [4]	September 9, 2022	Ongoing
32	BioNTech Manufacturing GmbH 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. [1, 2, 3]	November 24, 2022	Ongoing
33	BioNTech Manufacturing GmbH is required to submit monthly safety reports for Comirnaty, unless otherwise determined by Health Canada. The monthly safety report 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: [4] a. Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations; b. Interval and cumulative number of reports per Preferred Term (PT) and System Organ Class (SOC); c. Ad Hoc Summary Tabulations presenting interval data on special populations and vaccine presentations; d. Actions taken in the interval for safety reasons; e. List of ongoing and closed signals in the interval, including a summary of their evaluation; f. Vaccination errors should be included when a pattern of errors leading to safety issue and/or risk minimization activities are considered warranted (e.g. changes of the product labelling, communication to healthcare professional	December 21, 2022	Ongoing

	and the public). Otherwise, data can be presented and discussed in the Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs); g. Summary of all ongoing studies can be included in the six-month scheduled Periodic Benefit-Risk Evaluation Report (PBRER), unless a safety signal is identified that requires immediate regulatory action; h. Overall risk/benefit consideration.		
34	BioNTech Manufacturing GmbH 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 BioNTech Manufacturing GmbH and Pfizer Canada ULC will delay the implementation of Canadian-specific inner/outer labels following NDS-CV approval for Comirnaty (COVID-19 vaccine, mRNA), and that interim inner/outer labels will be used for the short term. Please note the following: [1, 2, 3, 4] a. BioNTech Manufacturing GmbH should consider including images and texts of these labels in the customer communication and clearly outline all deviations from Canadian requirements; 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 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. The company-led customer communication does not require review by Health Canada; however, BioNTech Manufacturing GmbH is welcome to seek courtesy feedback from BRDD. BioNTech Manufacturing GmbH 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

1 Applicable to DIN 02527863 (Gray cap: 16 years and older)

2 Applicable to DIN 02509210 (Purple cap: 16 years and older)

3 Applicable to DIN 02522454 (Orange cap: 5 years to < 12 years)

4 Applicable to DIN 02530325 (Maroon cap: 6 months to < 5 years)