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 Original & Omicron BA.4/BA.5
(COVID-19 mRNA vaccine, Bivalent (Original and Omicron BA.4/BA.5))
Dossier ID: HC6-024-E267502

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 August 31, 2023:

Table: Terms and Conditions

	Terms and Conditions	Issued	Status
1	Provide immunogenicity and safety data after the second booster (fourth) dose in subjects 55 years of age and older from Study C4591031 Phase 3 Substudy E. Please submit the final analysis, when the data become available.	October 7, 2022	Ongoing
2	Provide immunogenicity and safety data after the second booster (fourth) dose in subjects 18 to 54 years of age from Study C4591031 Phase 3 Substudy D. Please submit the final analysis, when the data become available.	October 7, 2022	Ongoing
3	Provide immunogenicity and safety data after the first booster (third) dose of Comirnaty for subjects 12 to 17 years of age from Study C4591031 Phase 3 Substudy C. Please include interim (1 and 6 months) and final analysis, when the data become available.	October 7, 2022	Ongoing

4	Provide safety data after the first booster (third) dose of Comirnaty for subjects 12 to 17 years of age from Study C4591031 Phase 3 Substudy B. Please submit the final analysis, when the data become available.	October 7, 2022	Ongoing
5	Provide immunogenicity and safety data after a booster dose of Bivalent BNT162b RNA-Based Vaccine for subjects ≥ 12 years of age from Study C4591044 Phase 2 (cohorts 2 and 3). Please submit the following data once available: a. 1 month safety and immunogenicity for participants ≥12 years from Cohort 2 b. 1 month safety and immunogenicity for 30 µg recipients ≥18 years from Cohorts 2 & 3 combined c. Final clinical study report, containing safety and immunogenicity data for Cohorts 2 & 3 through 6 months	October 7, 2022	Ongoing
6	Provide updates for ongoing stability studies of the BNT162b2 Omicron BA.4/BA.5 mRNA drug substance. Data for each study can be submitted after the 12 month time-point and at completion.	October 7, 2022	Ongoing
7	Provide updates for ongoing stability studies of the BNT162b2 Bivalent (Original & Omicron BA.4/BA.5) drug product. Data for each study can be submitted after the 12 month time-point and at completion.	October 7, 2022	Ongoing
8	Reassess the proposed drug product specification for the RNA ratio based on data for additional manufactured batches and provide the outcome of this reassessment, including any revision to specification, if applicable, once available.	October 7, 2022	Ongoing
9	Provide a Certified Product Information Document (CPID) by February 28, 2023.	October 7, 2022	Ongoing
10	BioNTech Manufacturing GmbH is required to treat adverse reactions associated with Comirnaty Original & Omicron BA.4/BA.5 (COVID-19 mRNA vaccine, Bivalent (Original and Omicron BA.4/BA.5)), as priority and submit the corresponding reports to Health Canada without delay. [1,2]	October 7, 2022	Closed
11	BioNTech Manufacturing GmbH is required to submit Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs) every 6 months for Comirnaty Original & Omicron BA.4/BA.5 (COVID-19 mRNA vaccine, Bivalent (Original and Omicron BA.4/BA.5)), unless otherwise determined by Health Canada. [1,2,3]	October 7, 2022	Ongoing

12	BioNTech Manufacturing GmbH is required to submit an updated core Risk Management Plan (RMP) with the Canadian Addendum in a timely manner 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: [1,2,3] a. A safety specification that details the identified risks, potential risks, and missing information for Comirnaty Original & Omicron BA.4/BA.5 (COVID-19 mRNA vaccine, Bivalent (Original and Omicron BA.4/BA.5)); 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.	October 7, 2022	Ongoing
13	BioNTech Manufacturing GmbH to provide a summary of the changes made to the website for Health Canada's review with each update. [1,2,3] a. BioNTech Manufacturing GmbH to attest that the content of the website (CVDVaccine.ca) is consistent with the approved Canadian-specific labelling information for Comirnaty Original & Omicron BA.4/BA.5 in French and English. The website content related to the appropriate storage & handling and preparation & administration of Comirnaty Original & Omicron BA.4/BA.5 should be aligned with information in the Product Monograph. b. For revisions to the website design and layout related to updates to the indication, use or presentation of the vaccine, BioNTech Manufacturing GmbH commits to providing final screenshots of relevant components of the electronic platform (linked to any foreign or Canadian specific Comirnaty Original & Omicron BA.4/BA.5 labels dispensed in Canada), containing the approved Canadian-specific labelling information for Comirnaty Original & Omicron BA.4/BA.5 in French and English for Health Canada's records, following review and approval by Pharmaceutical Advertising Advisory Board (PAAB).	October 7, 2022	Ongoing
14	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	October 7, 2022	Closed

	GmbH and Pfizer Canada ULC will delay implementation of Canadian-specific inner/outer labels following NDS-CV approval for Comirnaty Original & Omicron BA.4/BA.5, 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 Product Monograph by mail or fax from BioNTech Manufacturing GmbH, if they cannot access the internet BioNTech Manufacturing GmbH should devise an appropriate dissemination strategy to ensure the HPRC reaches the intended audience in a timely manner.		
15	BioNTech Manufacturing GmbH to commit to developing Canadian specific bilingual labelling for Comirnaty Original & Omicron BA.4/BA.5 presentations Drug Identification Numbers (DINs) currently marketed in Canada, to be submitted in Q1 of 2023, 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. [1,2]	October 7, 2022	Ongoing
16	Provide interim analyses of the immunogenicity (at 1 month) and safety data (at 1 and 6 months) from study C4591048 substudy D pertaining to the primary, secondary, and exploratory immunogenicity and safety objectives, estimands and endpoints as soon as it becomes available. [2]	December 9, 2022	Ongoing
17	Provide the final CSR for study C4591048 substudy D as soon as it becomes available. [2]	December 9, 2022	Ongoing
18	BioNTech Manufacturing GmbH is required to submit monthly safety reports for Comirnaty Original & Omicron BA.4/BA.5 (COVID-19 mRNA vaccine, Bivalent (Original and Omicron BA.4/BA.5)), 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: [1,2]	December 9, 2022	Closed

	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 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.		
19	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 SNDS approval for Comirnaty Original & Omicron BA.4/BA.5 in children 5 to less than 12 years of age, and that interim non-Canadian inner/outer labels will be used for the short term. Please note the following: [2] 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.	December 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.		
20	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 Original & Omicron BA.4/BA.5 (COVID-19 mRNA vaccine, Bivalent (Original and Omicron BA.4/BA.5)), and that interim inner/outer labels will be used for the short term. Please note the following: 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.[1,2,3]	April 4, 2023	Ongoing
21	Provide interim analyses at 1 month of the immunogenicity and safety data from Study C4591048, Substudy A Phase 1 pertaining to the primary, secondary, and exploratory immunogenicity and safety objectives, estimands and endpoints as soon as it becomes available as a Supplement to a New Drug Submission (SNDS)/Level II – Supplement.[1,2,3]	July 6, 2023	Ongoing

22	Provide interim analyses at 1 month of the safety and immunogenicity data from Study C4591048, Substudy A Phase 2/3 pertaining to the primary, secondary, and exploratory safety objectives, estimands and endpoints as soon as it becomes available as a Supplement to a New Drug Submission (SNDS)/ Level II – Supplement.[1,2,3]	July 6, 2023	Ongoing
23	Provide interim analyses at 6 months of the safety and immunogenicity data from Study C4591048, Substudy A Phase 2/3 pertaining to the primary, secondary, and exploratory safety objectives, estimands and endpoints as soon as it becomes available as a Supplement to a New Drug Submission (SNDS)/ Level II – Supplement.[1,2,3]	July 6, 2023	Ongoing
24	Provide the final CSR for Study C4591048, Substudy A as soon as it becomes available.[1,2,3]	July 6, 2023	Ongoing
25	BioNTech Manufacturing GmbH to commit to developing Canadian specific bilingual labelling for Comirnaty Original & Omicron BA.4/BA.5 presentations Drug Identification Numbers (DINs) currently marketed in Canada, to be submitted in Q1 of 2024, 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. [3]	August 31, 2023	Ongoing

1 Applicable to DIN 02531461 (Gray cap: 12 years and older)

2 Applicable to DIN 02533197 (Orange cap: 5 years to < 12 years)

3 Applicable to DIN 02541025 (Maroon cap: 6 months to < 5 years)