



EXTERNAL DATA MONITORING COMMITTEE

C459

Investigational BNT162 Vaccine Program

PF-07302048

Version: 5.0

Date: 04-Nov-2020

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 1 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015467



EXTERNAL DATA MONITORING COMMITTEE

TABLE OF CONTENTS

APPENDICES3

1. INTRODUCTION5

 1.1. Study Design5

 1.2. Purpose of the Committee5

 1.3. Committee Close-Out.....6

2. COMMITTEE MEMBERSHIP6

 2.1. Conflicts of Interest6

 2.2. Confidentiality Agreement/Contract6

 2.3. Authorship6

3. ROLES AND RESPONSIBILITIES7

 3.1. Committee Members7

 3.2. Committee Chairperson.....7

 3.3. Committee Liaison7

 3.4. Reporting Team.....8

 3.5. Study Team9

4. COMMITTEE MEETINGS.....10

 4.1. Meeting Schedule/Frequency10

 4.2. Start-up Meeting.....10

 4.3. Review Meetings11

 4.4. Review Meeting Format.....12

 4.4.1. Open Session12

 4.4.2. Closed Session.....12

 4.5. Voting Procedure.....12

 4.6. *AD HOC* Meetings for Emergent Safety Data13

 4.7. Meeting Minutes13

5. DATA PROVIDED TO THE COMMITTEE AND PARAMETERS TO BE MONITORED/REVIEWED BY THE COMMITTEE.....13

 5.1. C4591001 Study Only13

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 2 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015468



EXTERNAL DATA MONITORING COMMITTEE

5.1.1. Serious Adverse Events 14

5.1.2. Other Safety 14

5.1.3. Surveillance of Events That Could Represent Enhanced COVID-19
Disease 14

5.1.4. Immunogenicity 15

5.1.5. Efficacy 15

5.2. All Other Studies 15

5.2.1. Serious Adverse Events 15

5.2.2. Other Safety 16

5.2.3. Immunogenicity 16

5.2.4. Efficacy 16

5.3. Provision of Study Data to the Committee 16

5.3.1. Open Session Data 16

5.3.2. Closed Session Data 17

5.4. Database Information 17

6. COMMUNICATION PLAN BETWEEN THE PFIZER AND THE COMMITTEE 18

6.1. Recommendations 19

6.2. Communication of Recommendations 19

6.3. External Pfizer Communication 19

6.4. Pfizer Internal Safety Review Committee 20

7. WRITTEN RECORDS 21

7.1. Deliverables to Pfizer 21

7.2. General Project File 21

7.3. Unblinded data in SAS® Datasets 22

8. CHARTER HISTORY 22

APPENDICES

Appendix 1. Committee Membership Log 23

Appendix 2. Plan to Control Dissemination of Results 26

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 3 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015469



EXTERNAL DATA MONITORING COMMITTEE

Appendix 3. Key Contacts27
Appendix 4. List of Studies (if committee is to oversee multiple studies).....34

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 4 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015470



EXTERNAL DATA MONITORING COMMITTEE

1. INTRODUCTION

This External Data Monitoring Committee (E-DMC) (hereafter referred to as “the committee”) is a single, external, independent, expert advisory group established to oversee safety and efficacy data from the BNT162 Vaccine Program. The primary rationale for establishing the committee is to make certain that appropriate external safeguards are in place to help ensure the safety of subjects and to maintain scientific rigor and study integrity while the trial is on-going.

Pfizer is responsible for conducting this study. BioNTech is the regulatory sponsor of this study.

1.1. Study Design

The COVID-19 program is being developed to address the pandemic crisis which has spread globally at high speed. There are currently no vaccines to prevent infection with SARS-CoV-2 or antiviral drugs to treat COVID-19.

Given the rapid transmission of COVID-19 and incidence of disease in the United States and elsewhere, the rapid development of a safe and effective vaccine is of utmost importance. In the COVID-19 vaccine program, the safety and tolerability of the BNT162 vaccine candidates will be evaluated by assessing prompted local injection-site reactions and systemic events, as well as adverse events and serious adverse events. Predefined stopping rules may be used to ensure safety of study subjects and guide dose escalation and participants may also undergo hematological and chemistry evaluation as defined per protocol. These procedures are described in detail in each study protocol where relevant. The background of the COVID-19 vaccine candidates and pre-clinical development is described in the BNT162 COVID-19 Investigator Brochure (IB). The updated IB will be provided to the committee when available.

Please refer to [the current study protocols](#) for details of the study design.

1.2. Purpose of the Committee

The committee will review accumulating safety data across all studies, as well as efficacy data in the Phase 2/3 portion of the C4591001 study. The committee will advise Pfizer regarding the safety of current participants and those yet to be recruited, as well as the continuing scientific validity of the trial. In addition to safety review by the committee, qualified Pfizer personnel will review safety data as specified in the safety surveillance review plan and will inform the committee of significant findings. Efficacy data from the C4591001 study will be available to the committee when there is a planned interim analysis of efficacy or if this is considered necessary to conduct a risk-benefit assessment.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 5 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015471



EXTERNAL DATA MONITORING COMMITTEE

1.3. Committee Close-Out

The committee will have completed its work and been dissolved when it has reviewed final safety data from the last study within the scope of this charter.

2. COMMITTEE MEMBERSHIP

The committee consists of a chairperson and 2-4 additional members, as indicated in the list of members in [Appendix 1 Committee Membership Log](#) including at least one with medical qualifications and at least one other who is a statistician.

During the conduct of the study, membership of the committee may change based on expertise needed, availability, and new conflicts of interest that warrant a change. A dated log must be maintained in [Appendix 1](#) reflecting any changes in membership. Committee membership is to be for the duration specified in each member's contract. If any member leaves the committee, Pfizer will promptly appoint a replacement in consultation with the committee chairperson, if needed.

2.1. Conflicts of Interest

The committee members will complete a CT22-GSOP-RF01 *Independent Oversight Committee Member Conflict of Interest Form*. Committee members should be free of apparent significant conflicts of interest. Any potential conflict of interest that develops during a member's tenure on the committee must be disclosed by the committee member. Pfizer will determine if any potential conflict requires termination of committee membership.

Each time the committee meets, the study team will ask the committee members to consider whether or not any changes in their conflict of interest status have emerged. Status must be recorded in the committee open meeting minutes and any potential conflicts must be reported using CT22-GSOP-RF01.

2.2. Confidentiality Agreement/Contract

A written agreement (i.e., contract, including confidentiality agreement) must be in place for each external committee member before any services are rendered. No communication, either written or verbal, concerning the deliberations or recommendations of the committee will be made outside of the committee without approval of Pfizer, except as provided for in this charter (refer to [Section 6 Communication Plan Between Pfizer and the Committee](#)).

2.3. Authorship

A committee member must not be an author of a publication emanating from any study on the BNT162 vaccine program for which they are a member.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 6 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015472



EXTERNAL DATA MONITORING COMMITTEE

3. ROLES AND RESPONSIBILITIES

3.1. Committee Members

The primary responsibilities of the committee members are:

- Review, endorse, and implement the charter.
- Assess the safety data from the study on a regular basis (refer to [Section 4.1 Meeting/Schedule Frequency](#)) throughout the duration of the trial.
- Assess efficacy data for efficacy and/or futility during Phase 2/3.
- Provide an informed risk-benefit assessment and advise Pfizer regarding the continuation of the trial based on the reviewed data.
- Provide guidance, where appropriate, on additional questions presented by the study team prior to review meetings.
- Adhere to agreements related to potential conflicts of interest.

3.2. Committee Chairperson

The primary responsibilities of the committee chairperson are:

- Review and approve the charter on behalf of the committee members.
- Facilitate discussion by integrating differing points of view and moving the committee towards recommendations to be provided to Pfizer in a timely fashion.
- Prepare closed session meeting minutes (or via a designee).
- Complete CT22-GSOP-RF11 *Brief Recommendation Form* and submit to the study team, according to the communication plan (refer to [Section 6 Communication Plan Between Pfizer and the Committee](#)).
- Communicate with the study team according to the communication plan on behalf of the committee (refer to [Section 6 Communication Plan Between Pfizer and the Committee](#)).
- Provide all written records to the study team for archiving.

3.3. Committee Liaison

The committee liaison is not a member of the study team for any study being reviewed by the committee. The committee liaison is designated by Pfizer and will maintain independence

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.

CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 7 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015473



EXTERNAL DATA MONITORING COMMITTEE

from the study team for the duration of the trial. The primary responsibilities of the committee liaison are:

- Serve as the primary liaison between the committee and Pfizer management.
- Receive and distribute, according to the communication plan, the committee recommendations from the committee chairperson.
- Ensure the committee has access to timely information about the study.
- Handle and maintain a record of communications between the committee and Pfizer.
- Manage written records (e.g., closed session meeting minutes and CT22-GSOP-RF11) between the committee and Pfizer throughout study conduct.

3.4. Reporting Team

The reporting team is designated by Pfizer and is comprised of a reporting statistician and reporting programmer(s). For the Phase 2/3 portion of C4591001 study a medical monitor and clinical scientist is also part of the reporting team. The reporting team are not members of the study team for any of the studies being reviewed by the committee and who will maintain independence from the study team for the duration of the trial. The primary responsibilities of the reporting team are:

- Compile and provide unblinded output to the committee for review.
- Write the closed committee report, including a textual summary of unblinded findings.
- Coordinate appropriate operational support activities from a dedicated team, including a reporting programmer(s).
- Maintain copies of the review meeting materials for each meeting in a secure area with restricted access.
- Serve as the primary contact for all data-related issues. If the committee requires additional data, the request and supporting rationale will be made via email to the reporting statistician (who may elect to consult with the designated Pfizer management). Once the request is agreed, the reporting statistician will provide the data/output to the committee.
- During the Phase 2/3 portion of the C4591001 study the unblinded medical monitor will conduct ongoing review of COVID-19 illness cases.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 8 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015474



EXTERNAL DATA MONITORING COMMITTEE

3.5. Study Team

The study team includes clinician, clinical lead, study statistician, and safety risk lead, and other team members as appropriate. The primary responsibilities of the study team are:

- Ensure qualified study team personnel are available to review blinded (if applicable) safety data per the safety surveillance review plan for the duration of the trial in order to complement the committee's safety role and fulfill Pfizer's obligation to monitor patient safety.
- Select the committee chairperson and members.
- Ensure appropriate study conduct and preservation of the study blind (if applicable) to ensure overall study integrity is maintained.
- Document in a written agreement (e.g., contract) the terms of each committee member's participation and indemnifying all committee members.
- Appoint the committee liaison.
- Appoint the reporting team (including statistician, reporting programmer[s] and medical monitor) not associated with the study team.
- Prepare open session meeting minutes.
- Ensure that all written records are filed appropriately in the Trial Master File (TMF).
- Prepare and implement the committee charter.
- Provide to the committee the study protocol (and any subsequent protocol amendments).
- Notify the committee of any significant new safety information (e.g., toxicology information, potential safety signal, and data from other clinical trials).
- Implement the committee recommendations once endorsed by Pfizer management.
- Promptly review and respond to all committee recommendations and provide the committee with a summary of actions taken in response to its recommendations (as described in [Section 6.2 Communication of Recommendations](#)).
- Maintain committee records other than closed session meeting minutes and CT22-GSOP-RF11 throughout study conduct.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 9 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015475



EXTERNAL DATA MONITORING COMMITTEE

- Archive all records at the end of the study.
- Submit the committee charter to the Food and Drug Administration (FDA) and other regulatory authorities (RA) when appropriate.
- Organize and facilitate committee meetings, including logistical support such as identifying meeting dates and locations and providing assistance with travel arrangements.

4. COMMITTEE MEETINGS

4.1. Meeting Schedule/Frequency

A start-up meeting (refer to Section 4.2 *Start-up Meeting*) will be scheduled with the committee and members of the study team.

The first committee meeting to review study data will be scheduled no later than within the first month of the first participant dosed with BNT162 vaccine candidates and sooner if needed.

Thereafter, the committee will meet in person or via teleconference as required by the protocol to review cumulative safety data, efficacy data at the time of interim analyses and to make risk-benefit assessments until the study in the program is complete or at intervals determined based on availability of key study data. It is anticipated that regular scheduled meetings will occur approximately monthly. The frequency of DMC meetings may decrease (with agreement between Pfizer and the DMC) as the COVID vaccine program matures however no fewer than two meetings per year will be scheduled.

During Phase 2/3 portion of the C4591001 study, the meeting frequency for cumulative data review will be determined based on availability of key study data. DMC meetings may occur weekly and DMC members will be expected to convene at short notice due to the accelerated pace and critical need of the study if required. The chairperson and Pfizer have the discretion to change the meeting frequency (e.g. if enrollment is slow) or request additional *ad hoc* meetings with the rationale documented appropriately.

4.2. Start-up Meeting

As soon as possible after the committee is formed the committee members, the reporting statistician, and members of the study team will meet to discuss the operational details of the committee and the C4591001 protocol. The committee will review and provide input on Pfizer's proposals for data to be monitored, frequency of reviews, methods for review, and criteria for making recommendations to Pfizer.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 10 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015476



EXTERNAL DATA MONITORING COMMITTEE

The committee members, the reporting team, and members of the study team will meet initially to agree on:

- Data and frequency of data outputs to be provided to committee members outside of planned meetings
- Study conduct issues of interest during review meetings,
- Data elements and statistical methods to be included in safety and efficacy review(s),
- List of tables, listings, and figures and mock-ups,
- Procedural issues such as meeting frequency and format, timing of data receipt and format (including table layouts), definition of a “quorum” (comprising of the Chair, Statistician and one Clinician) and handling of meeting documentation, and
- Criteria and process for unblinding the data and maintaining confidentiality of unblinded results (in the case of a blinded trial or an open-label trial in which the dissemination of such information is restricted).

For E-DMCs established for safety monitoring, the charter must be approved before first subject first visit (FSFV). (It is permissible to meet this requirement with approval of a *preliminary* version of the charter; in this situation, the subsequent version of the charter must be approved before the first scheduled time the committee views unblinded data from the trial.)

For all other E-DMCs the charter will be finalized and approved prior to the first review meeting.

4.3. Review Meetings

The committee will convene to review study conduct and safety data at determined intervals after the start-up and initial safety review meetings. The frequency of meetings will be dependent upon availability and nature of data to be reviewed and will be agreed between Pfizer and the Chair. Additionally, the committee will convene to review data on an as-needed basis (e.g., a stopping rule is met, to review reports of COVID-19-like illnesses, unexpected potential safety signal or study conduct concerns). Data listings and summaries will be supplied to committee members by the reporting statistician via secure electronic means at least 24 hours prior to the meeting but may be up to 5 days prior if possible. The study team will present relevant information on new studies prior to the delivery of the first dataset for these studies.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 11 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015477



EXTERNAL DATA MONITORING COMMITTEE

4.4. Review Meeting Format

Each review meeting will consist of an open and a closed session (when needed). The committee and study team will be unblinded during Phase 1 of the C4591001 study (to identify preferred vaccine candidate(s), dose level(s), number of doses and schedule of administration) but not during Phase 2/3 (expanded cohort and efficacy part). No separate open and closed sessions will be required until the study reaches Phase 2/3 (expanded cohort and efficacy part) including other studies in the program.

These sessions will correspond with the type of briefing materials the committee will receive.

4.4.1. Open Session

The open session provides an opportunity for the committee to interact with members of the study team as applicable, for example to review study status, to discuss dose-escalation decisions made by the IRC, and to discuss AEs that met the stopping rule criteria as applicable. In addition, issues relating to the conduct of the study/studies, potential impact of external data on the study/studies, or other topics defined in the open session of the briefing materials can be discussed.

4.4.2. Closed Session

The closed session is the portion of the meeting where the committee discusses any unblinded results, deliberates over any issues, and votes on recommendations to Pfizer. Only committee members attend the closed-session meeting; however, the reporting statistician and/or the committee liaison may attend all or part of the closed-session meetings with concurrence of the committee chairperson.

Debriefing session

Following the closed session, the committee will meet again with Pfizer representatives to relay comments made by the committee.

4.5. Voting Procedure

All committee members are voting members and are expected to participate in all meetings and voting forums. Every effort should be made in scheduling meetings to ensure that all members can participate. If all members are unable to participate in a meeting, the chairperson and at least one additional clinician must participate in voting. Discussions and decisions requiring expert statistical interpretation of study data require that every effort be made to include the committee statistician. Discussions and decisions regarding pause or termination of study vaccination require that every effort be made to include all committee members. In the event of a split vote, the chairperson will make the final decision concerning the committee's

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 12 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015478



EXTERNAL DATA MONITORING COMMITTEE

recommendation. If the chair cannot participate, he/she will delegate his/her role to another member of the committee.

At each meeting, the committee members will vote and provide one of the recommendations listed in [Section 6.1 Recommendations](#).

The recommendations regarding the primary endpoint should be in accordance with the guidance provided in this charter, the protocol, or the SAP (or other document, as appropriate, e.g., interim analysis plan).

4.6. *AD HOC* Meetings for Emergent Safety Data

In the event that the committee is convened for an *ad hoc* meeting to evaluate emergent data, processes other than those outlined in this charter may be undertaken on the recommendation of and/or with the express consent of the committee chairperson in order to ensure patient safety within the trial. Any alternative processes will be documented and justified in the committee meeting minutes. In some instances, when not all committee members are able to attend at short notice, it is expected that a minimum of 3 members will meet. At each meeting, the committee members will vote and provide one of the recommendations listed in [Section 6.1 Recommendations](#).

4.7. Meeting Minutes

The committee chair is accountable for closed session meeting minutes and may delegate the act of recording minutes during the meeting. Committee members will review and agree to the minutes before they are finalized. At a minimum the minutes should record the following information:

- Who attended the meeting;
- Action items created during the meeting including who is responsible for the action;
- Any resolution of action items from a previous meeting;
- Any issues or concerns identified during the review of the data with brief rationale for the concern; and

5. DATA PROVIDED TO THE COMMITTEE AND PARAMETERS TO BE MONITORED/REVIEWED BY THE COMMITTEE

5.1. C4591001 Study Only

The committee will review all data on a regular basis (see [Section 4.1](#) and below) and during Phase 1 will also review data from the BioNTech German study as it becomes available. Committee reviews will allow early detection of signs of efficacy or disease enhancement

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 13 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015479

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)



EXTERNAL DATA MONITORING COMMITTEE

with corresponding early expansion of testing of vaccine candidates, doses, or regimens to larger numbers of subject or, conversely, curtailment of testing for other candidates, doses, or regimens. Immunogenicity data may also be reviewed. The committee chairperson will communicate any required action according to the communication plan (refer to [Section 6 Communication Plan Between Pfizer and the Committee](#)).

5.1.1. Serious Adverse Events

All SAEs deemed unexpected and related to BNT162 SARS-CoV-2 RNA vaccines, either by the investigator or Pfizer (also known as SUSARs [suspected unexpected serious adverse reactions]), will be forwarded to the committee at the same time as they are reported to the RAs, investigators, and institutional review boards (IRBs)/ethics committees (ECs). The term “unexpected” refers to an event that is either not listed in the Investigator’s Brochure (IB) Reference Safety Information section or is of greater severity or specificity than that listed in the IB Reference Safety Information section.

All SAEs collected through 6 months after the vaccination schedule is completed will be reviewed contemporaneously. Additionally, SAE data from the ongoing BioNTech clinical trial (BNT162-01) will be provided to the committee for information during the Phase 1 portion of the C4591001 study as it becomes available to ensure a comprehensive overview of information of the BNT162 vaccines is available.

5.1.2. Other Safety

Cumulative data of reactogenicity events and unsolicited adverse events (including that from the ongoing BioNTech clinical trial as it becomes available in Phase 1) will be reviewed on a regular basis during scheduled committee meetings. Contemporaneous review of related AEs up to 1 month after completion of the vaccination schedule will be performed. In addition, during Phase 2/3 the committee will review all AEs on a weekly basis until safety data through 7 days after dose 2 from the first 360 participants has been submitted to regulatory authorities. The committee will schedule an adhoc meeting if deemed necessary.

The committee will meet as soon as possible to review all available relevant-data when any stopping rule is met. Please refer to [sections 8.2.3](#) and [10.7 of the C4591001 protocol](#) for stopping rules.

5.1.3. Surveillance of Events That Could Represent Enhanced COVID-19 Disease

Because within the course of COVID-19, the illness caused by SARS-CoV-2 infection, the onset of an exaggerated adaptive immune response and containment of viral replication in some instances is associated with a “cytokine storm” that accompanies clinical deterioration,

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 14 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015480



EXTERNAL DATA MONITORING COMMITTEE

patient profiles of all nucleic acid amplification test (NAAT)-confirmed cases will be reviewed contemporaneously by the committee during Phase 1 of the study.

In Phase 2/3, there will be planned reviews of the vaccine/placebo split of protocol-defined severe COVID-19 cases at the time of efficacy/futility analyses. The DMC will review this data and make recommendations based on the guidance outlined in [Section 10.7 of the protocol](#): Stopping and alert rules for severe disease defined.

Additionally, in Phase 2/3, the unblinded team supporting the DMC, including an unblinded medical monitor, will review cases of severe COVID-19 as they are received and will review AEs at least weekly for additional potential cases of severe COVID-19. At any point, the unblinded team may discuss with the DMC chair whether the DMC should review cases for an adverse imbalance of cases of COVID-19 and/or severe COVID-19 between the vaccine and placebo groups. If so, the DMC will then meet to review available severe COVID-19 cases to determine whether the observed imbalance should result in modifications to the study. Please refer to [section 8.2.4 of the protocol](#) for details.

In addition to the above, data regarding COVID-19 confirmed illnesses reported in the BioNTech study will be reviewed by the committee when information is available.

The purpose of these reviews will be to identify whether any features of each case appear unusual, greater in severity, compared to available information at the time of review. Indicators of severity may include accelerated deterioration, need for hospitalization, need for ventilation, death. Observed rates of these indicators will be compared with what could be expected in a similar population to the study participants based upon available information at the time of review (for Phase 1 and 2/3) and to compare cases in active vaccine and placebo recipients in Phase 2/3 (when Pfizer staff will be blinded).

5.1.4. Immunogenicity

The DMC may review safety and immunogenicity data prior to expansion into Phase 2/3.

5.1.5. Efficacy

The DMC will assess efficacy data for efficacy and/or futility during the Phase 2/3 portion of the C4591001 study as defined in the protocol.

5.2. All Other Studies

5.2.1. Serious Adverse Events

All SAEs deemed unexpected and related to BNT162 SARS-CoV-2 RNA vaccines, either by the investigator or Pfizer (also known as SUSARs [suspected unexpected serious adverse reactions]), will be forwarded to the committee at the same time as they are reported to the RAs, investigators, and institutional review boards (IRBs)/ethics committees (ECs). The

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.

CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 15 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015481

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)



EXTERNAL DATA MONITORING COMMITTEE

term “unexpected” refers to an event that is either not listed in the Investigator’s Brochure (IB) Reference Safety Information section or is of greater severity or specificity than that listed in the IB Reference Safety Information section.

All SAEs collected through 6 months after the last dose will be reviewed. Studies in which SAEs are followed for longer timepoints may also be reviewed by the committee.

5.2.2. Other Safety

Cumulative data of reactogenicity events, unsolicited adverse events, and clinical laboratory assessments (if applicable) from other studies in the program will be reviewed on a regular basis during scheduled committee meetings, as described in [Section 5.1.2](#). Data may be blinded or unblinded depending on study design.

5.2.3. Immunogenicity

The DMC may review immunogenicity data.

5.2.4. Efficacy

The DMC will assess efficacy and/or futility for all other studies if appropriate.

5.3. Provision of Study Data to the Committee

The reporting statistician is the primary channel for providing output/reports to the committee. Approximately 24 hours to up to 5 calendar days prior to each review meeting the reporting statistician will transmit all appropriate study data (as described in [Section 5 Data Provided to the Committee and Parameters to be Monitored/Reviewed by the Committee](#)) via secure electronic means to the committee members.

Committee members must handle all study data in accordance with the confidentiality agreement in their contract. Any queries on the data are to be made to reporting statistician and any requests for additional data must be communicated in writing (e.g., meeting minutes) via secure electronic means to the reporting statistician with supporting rationale for such requests. The reporting statistician may consult with the Vaccine Research & Development Clinical and Statistical Heads (or the IRC if applicable) prior to acting upon the request. If the study is blinded, the nature and content of the query requests may not be shared with the study team(s).

5.3.1. Open Session Data

Prior to each review meeting, the committee will receive the following summary data combined across or summarized by the vaccine groups, depending on study phase, regarding the progress of the trials.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 16 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015482

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)



EXTERNAL DATA MONITORING COMMITTEE

- Study conduct issues (e.g., enrollment status, eligibility violations).
- Demographic and other baseline characteristics.
- Dose-escalation decisions made by the IRC as applicable.
- Actions taken by the IRC in response to events that met the stopping rule criteria as applicable.

5.3.2. Closed Session Data

Prior to review meetings, the committee will receive the safety data indicated below summarized/analyzed by vaccine group. Additionally, the committee will receive relevant subject data listings. Closed sessions will be conducted during the blinded stage (Phase 2/3) of the C4591001 study.

- Study status.
- Demographics.
- Reactogenicity data (up to 7 days post vaccination).
- AEs and SAEs.
- AEs associated with withdrawal.
- Laboratory data when available.
- Significant findings identified by the clinician/clinical lead, who will review blinded (during C4591001 blinded Phase 2/3 portion but will be unblinded during Phase 1) safety data as specified in the safety surveillance review plan.
- Significant findings identified by the IRC, who will review unblinded safety data as specified in the IRC charter.
- Data from interim analyses of safety, efficacy, and immunogenicity as defined in the statistical analysis plan.

5.4. Database Information

All data provided to the committee will be from a dynamic database that is continually updated or revised as new information becomes available. A copy of the database snapshot used for the reports will be maintained. Tables, listings, and figures will be annotated with the date on which they were generated.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 17 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015483

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)



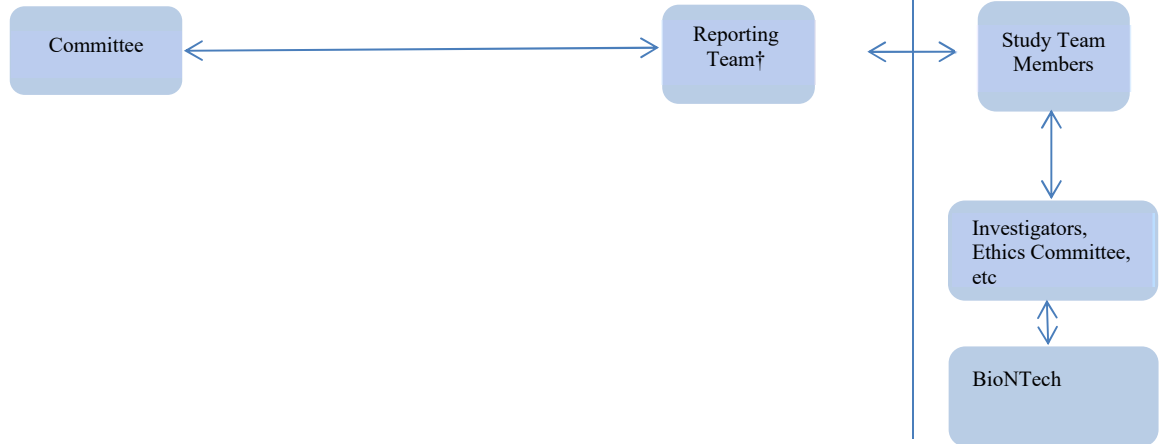
EXTERNAL DATA MONITORING COMMITTEE

6. COMMUNICATION PLAN BETWEEN THE PFIZER AND THE COMMITTEE

The expected flow of information and recommendations are depicted in Figure 1.:

Figure 1:

Other Communication (blinded)*:



* For example, open session meetings, blinded SAE reports, additional analysis/data requests, committee meeting logistics
 † Committee liaison is part of the Reporting Team; During the Phase 2/3 portion of the C4591001 study, an unblinded medical monitor and unblinded Clinical Scientist will be included as part of the Reporting Team. Communication between the DMC and study team occurs through the committee liaison during Phase 2/3.
 NB. C4591005 is sponsor unblinded throughout

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 18 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015484



EXTERNAL DATA MONITORING COMMITTEE

6.1. Recommendations

After each meeting, the committee will provide one of the following recommendations (for each study reviewed) to Pfizer via CT22-GSOP-RF11:

- Withhold final recommendation until further information/data is provided.
- Continue the study or studies as designed.
- Modify the study or studies and continue.
- Stop the study or studies.

Additionally, the committee may be asked to answer study related questions (e.g., concerning operational challenges, impact of findings from Pfizer's safety data review or impact of emerging external information) provided by the study team. The answers to the questions will be provided with the committee recommendation to Pfizer management via the committee liaison.

The recommendations should be in accordance with the guidance provided in this charter, the protocol, or the SAP (or other document, as appropriate, e.g., interim analysis plan).

6.2. Communication of Recommendations

For each review meeting, once a committee recommendation has been finalized the committee chairperson will convey the recommendation in writing within the timelines listed on CT22-GSOP-RF11. The written communication will consist of the CT22-GSOP-RF11 indicating the committee's recommendation and sufficient information to explain the rationale for any recommendation will be transmitted by secure electronic means to the committee liaison.

The final decision to accept or reject the committee's recommendation resides with Pfizer management and will be communicated to the committee chairperson in writing. Review of committee recommendation will be conducted in accordance with CT22-GSOP-RF11.

6.3. External Pfizer Communication

The committee's recommendation, together with Pfizer's response, will be summarized by the study team who will be responsible for communicating to all active investigators participating in the trial and to BioNTech representatives. The investigators and BioNTech will be informed about the decision to continue the trial, to stop the trial, or to implement modifications to trial procedures, on a monthly basis.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 19 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015485

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)



EXTERNAL DATA MONITORING COMMITTEE

6.4. Pfizer Internal Safety Review Committee

Pfizer has established several ad hoc Internal Safety Review Committees (ISRCs), one for each BU/RU. The ISRC for a BU is properly firewalled from all study teams conducting trials sponsored by that unit. The primary objective of an ISRC is to assess specific events that may constitute a safety concern in an unblinded manner. The assessment could result in expedited reports to regulators as required in FDA Final Rule (2010) and EU CT-3 (2011). The assessment may also lead to safety-related protocol changes. When necessary, an ISRC could look at the occurrence of the specific events across multiple studies in a development program.

The activities of an ISRC are intended to be complementary and supplemental to existing Pfizer safety and risk management processes, including this committee. There is a charter for the ISRC describing in detail the purpose, composition, and operations of an ISRC. The charter is available upon request.

There may be several interactions between an ISRC and this committee, including:

- When the ISRC accepts a request from the signal management lead to review specific events, the ISRC chair will notify the committee chairperson that a request has been made and that a review is to be conducted with a target date (typically within 30 calendar days of the request).
- The committee liaison will supply the ISRC chair a copy of the current committee charter, open meeting minutes and correspondences from the committee regarding issues for which the ISRC is currently being consulted.
- ISRC chair will communicate review findings with the committee chairperson.
- If no safety concern is identified, the ISRC will communicate this conclusion to the signal management lead with a copy to the committee.
- If a safety concern is identified, the ISRC chair will communicate its findings to the committee chairperson by an appropriately secure means. The written communication contains the ISRC's rationale and final assessment. (As the findings are typically based on unblinded data, they must not be shared with the study team at this stage.)
- The committee chairperson is requested to acknowledge receipt of the ISRC communication as soon as possible. The committee considers the findings identified by the ISRC but is not obligated to act on them.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 20 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015486



EXTERNAL DATA MONITORING COMMITTEE

- Where disagreement exists between the recommendations of the ISRC and the committee, the two committees attempt to reach consensus through additional communication.
- The final decision to accept or reject the committee's and/or ISRC's recommendation resides with Pfizer management.
- The safety data (tables, listings, and reports, etc.) received by the ISRC for review are kept confidential and will be disclosed to the committee upon request from the committee chairperson.

7. WRITTEN RECORDS

The committee liaison will maintain written records of all closed session meeting minutes, CT22-GSOP-RF11, and materials reviewed by the committee, and communications between the committee and Pfizer. These documents are considered proprietary and confidential and must be available for inspection upon request from RAs. Upon completion of the committee's responsibilities, the study team will obtain all written records for archiving.

7.1. Deliverables to Pfizer

The following are the deliverables from the committee chairperson to the committee liaison.

After each committee review meeting:

- CT22-GSOP-RF11.
- Closed session meeting minutes.

7.2. General Project File

The study team will compile and maintain the following documents and correspondence throughout study conduct.

- Any relevant correspondence between the committee and Pfizer.
- Committee charter and any amendments.
- Current IB.
- Protocol and protocol amendments.
- Curriculum vitae for each committee member.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 21 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015487



EXTERNAL DATA MONITORING COMMITTEE

- CT22-GSOP-RF01 for each committee member.
- Minutes from each open session meeting.

7.3. Unblinded data in SAS® Datasets

The treatment assignment blind will not be broken in the project database **for Phase 2/3 of the study**. The unblinded treatment assignment information will be merged programmatically with the study datasets using SAS®. Unblinded SAS® datasets and program files will be stored and managed in an area that is separate from the general project area and inaccessible except to members of the reporting team.

8. CHARTER HISTORY

Version	Date (dd-Mmm-yyyy)	Summary of Changes
1	29-Apr-2020	N/A
2	10-Jul-2020	Updated to reflect Protocol Amendment 4
3	17-Aug-2020	Updated to reflect Protocol Amendment 5
4	22-Oct-2020	Updated to include C4591005 Japan Study
5	04-Nov-2020	Updated to include 3 additional Programmers and an unblinded Clinical Scientist to the Reporting Team

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 22 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015488



EXTERNAL DATA MONITORING COMMITTEE

Appendix 1. Committee Membership Log

The following outlines the key selection criteria for membership into the E-DMC:

- Relevant clinical, region and/or drug development expertise
- Expert in the field of Infectious Diseases and/or Statistics
- Experience serving on a DMC
- Required time commitment based on the scope of responsibilities

The committee consists of the following members (past and present).

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 23 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015489

**EXTERNAL DATA MONITORING COMMITTEE**

Member	Affiliation/Address	Role	*Dates of Membership	Biography
Jonathan Zenilman, MD	Infectious Diseases Division Johns Hopkins Bayview Medical Center Baltimore, MD, US Tel: +1 410 440 9729	Chair	03-April-2020	Infectious Diseases
Kathryn Edwards, MD	Vanderbilt University School of Medicine 1300 Falkirk Court, Nashville, TN 37221 Tel: +1 615-429-3226	E-DMC member	07-April-2020	Pediatric infectious Diseases
Robert Belshe, MD	Division of Infectious Diseases & Immunology Saint Louis University Medical Center 714 Schiele Ave, San Jose, CA 95126 Tel: +1 314 496 1033	E-DMC member	03-April-2020	Infectious Diseases and Immunology
Lawrence Stanberry, MD	Columbia University 456 Riverside Drive, Apt 8A, New York, NY, 10027 Tel: +1 646-330-8329	E-DMC member	07-April-2020	Pediatric Infectious Diseases
Steve Self, PhD	Fred Hutchinson Cancer Research Center Vaccine and Infectious Disease Division 1100 Fairview Avenue North, M2- C200, Seattle, WA 98109, USA Tel: +1 206-915-9617	E-DMC Biostatistician	02-April-2020	Professor Emeritus, Biostatistics

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 24 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015490



EXTERNAL DATA MONITORING COMMITTEE

* Initial date of membership is the date the effective date of the contract signed by the committee member.

Note: Curriculum vitae are on-file at Pfizer and may be accessed by contacting the Study Team.

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 25 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015491



EXTERNAL DATA MONITORING COMMITTEE

Appendix 2. Plan to Control Dissemination of Results

For studies that require such a plan, this will be documented in a study-level document that will be filed in the TMF.

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 26 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015492



EXTERNAL DATA MONITORING COMMITTEE

Appendix 3. Key Contacts

Vaccine Research & Development Clinical and Statistical Heads	
<i>Name*</i>	<i>Contact Information</i>
William Gruber, MD	Senior Vice President, Vaccine Clinical Research & Development 401 N Middletown Road Pearl River, NY 10965 USA Tel: +1 845-602-3484 Bill.Gruber@Pfizer.com
Stephen Lockhart MD	Vice President Head of Europe and Asia-Pacific, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel: +44 1628 515538 Stephen.P.Lockhart@pfizer.com
Kenneth Koury, PhD	Head of Statistics and Modeling, Vaccine Clinical Research & Development 401 N Middletown Road Pearl River, NY 10965 USA Tel: +1 845-602-2547 Kenneth.Koury@Pfizer.com
Dina Tresnan DVM, PhD	Safety Surveillance and Risk Management 280 Shennecossett Rd, Groton, CT 06340, USA

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 27 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015493



EXTERNAL DATA MONITORING COMMITTEE

	Tel: +1 (860) 581-0880 dina.b.tresnan@pfizer.com
--	---

Committee Liaison	
Name*	Contact Information
Xia Xu (Phase 1 of study only)	Director Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA Tel: +1 484-865-7762 Xia.Xu3@pfizer.com
Satrajit Roychoudhury, PhD (Phase 2/3 of the study)	Senior Director Pfizer, Inc USA Tel : +1 908-901-8106 Cell: +1 862-216-5181 satrajit.roychoudhury@pfizer.com

Reporting Team Members (Unblinded)		
Name*	Contact Information	Role
Satrajit Roychoudhury, PhD	Senior Director Pfizer, Inc USA Tel : +1 908-901-8106 Cell: +1 862-216-5181 satrajit.roychoudhury@pfizer.com	Biostatistician
WeiWei Xiong	Senior Associate Pfizer, Inc 500 Arcola Road	Statistical Programming

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 28 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015494



EXTERNAL DATA MONITORING COMMITTEE

	Collegeville PA 19426 USA Tel: +1 905-818-6801 Weiwei.Xiong@pfizer.com	
Sridhar Guduru	Statistical Programming Lead Manager Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA Sridhar.Guduru@pfizer.com	Statistical Programming
Rong Zhang	Senior Statistical Programming Lead 4/F, Building 3, Lotus Business Park, Lane 60, Naxian Road, Pudong ZhangJiang Hi-tech. Park, Shanghai, China, 201203 Rong.Zhang@pfizer.com	Statistical Programming
Chen Xu*	Senior Statistical Programmer 4/F, Building 3, Lotus Business Park, Lane 60, Naxian Road, Pudong ZhangJiang Hi-tech. Park, Shanghai, China, 201203 Chen.Xu4@pfizer.com	Statistical Programming
Huan Liu*	Senior Statistical Programmer 4/F, Building 3, Lotus Business Park, Lane 60, Naxian Road, Pudong ZhangJiang Hi-tech. Park, Shanghai, China, 201203 Huan.Liu@pfizer.com	Statistical Programming
Jiyang Chen*	Senior Statistical Programmer 4/F, Building 3, Lotus Business Park, Lane 60, Naxian Road,	Statistical Programming

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 29 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015495



EXTERNAL DATA MONITORING COMMITTEE

	Pudong ZhangJiang Hi-tech. Park, Shanghai, China, 201203 Jiyang.Chen@pfizer.com	
Bochen Zhu*	Senior Statistical Programmer 4/F, Building 3, Lotus Business Park, Lane 60, Naxian Road, Pudong ZhangJiang Hi-tech. Park, Shanghai, China, 201203 Bochen.Zhu@pfizer.com	Statistical Programming
Ran Xiong*	Senior Statistical Programmer 4/F, Building 3, Lotus Business Park, Lane 60, Naxian Road, Pudong ZhangJiang Hi-tech. Park, Shanghai, China, 201203 Ran.Xiong@pfizer.com	Statistical Programming
Shon Remich MD	Senior Director Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA Tel: +1 215-872-3633 +1 301-642-6809 shon.remich@pfizer.com	Unblinded Medical Monitor
Lisa Moyer**	Senior Manager Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA Tel: +1 (484) 8658348 Lisa.L.Moyer@pfizer.com	Unblinded Clinical Scientist

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 30 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015496



EXTERNAL DATA MONITORING COMMITTEE

* Due to the volume and frequency of the unblinded tables, figures and listings (TLFs) that would need to be generated and undergo quality checks during Phase 2/3 of the study, additional statistical programming support is required. These members will be involved with providing support for the unblinded TLFs for safety and immunogenicity only. They will be restricted from efficacy at the Interim Analyses.

** The unblinded Clinical Scientist (CS) will assist with responding to subject level queries using relevant data systems during DMC closed sessions, whilst the unblinded medical monitor (MM) is required to address medical questions and interpretation. The MM and CS are complimentary and the paring mimics how Pfizer typically conduct safety reviews for clinical trials for all studies.

Study Team Members		
<i>Name*</i>	<i>Contact Information</i>	<i>Role</i>
Nicholas Kitchin, MD	Senior Director, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel : +44 7557 202435 nicholas.kitchin@pfizer.com	Clinical Study Lead
Judith Absalon, MD, MPH	Senior Director, Vaccine Clinical Research and Development 401 N Middletown Rd Pearl River, NY 10965 USA Tel: +1 845-602-1685 Judith.Absalon@pfizer.com	DMC responsible Clinician
Alejandra Gurtman, MD	Vice President Pfizer Vaccine Clinical Research and Development 401 N Middletown Rd Pearl River, NY 10965	Study Clinician

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 31 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015497



EXTERNAL DATA MONITORING COMMITTEE

	<p>USA</p> <p>Tel: +1 845-602-2842 Cell 201-290-0489 Fax: +1 845 474 3219 alejandra.gurtman@pfizer.com</p>	
Susan Mather, MD	<p>Senior Director, Safety Surveillance and Risk Management 500 Arcola Road Collegeville, PA 19426 USA</p> <p>Tel: +1 (484) 8652514 Susan.Mather@pfizer.com</p>	Safety Risk Lead
Ruth Bailey	<p>Director, Clinical Scientist Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom</p> <p>Tel: +44 1628 515654 ruth.bailey@pfizer.com</p>	Lead Clinical Scientist
Harpreet Seehra	<p>Senior Manager, Clinical Scientist Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom</p> <p>Tel: +44 7901788821 harpreet.seehra@pfizer.com</p>	DMC Responsible Clinical Scientist
Xia Xu	<p>Director Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA</p>	Xia Xu (Study Biostatistician)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 32 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015498



EXTERNAL DATA MONITORING COMMITTEE

	Tel: +1 484-865-7762 Xia.Xu3@pfizer.com	
James Baber MBChB, MPH	Director, Clinician, Global Medical Monitor Level 15-18, 151 Clarence St Sydney NSW 2000 Australia Tel: +61 419410413 james.baber@pfizer.com	Study Clinician C4591005 Study

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*

01-Nov-2019

Page 33 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015499



EXTERNAL DATA MONITORING COMMITTEE

Appendix 4. List of Studies (if committee is to oversee multiple studies)

Study	Date Added (dd-Mmm-yyyy)
C4591001	29-Apr-2020
C4591005	22-Oct-2020

Please refer to [the current C4591001](#) and C4591005 protocols for details of the study designs.

090177e19574a416\Approved\Approved On: 06-Nov-2020 15:39 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 34 of 34

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015500



INTERNAL REVIEW COMMITTEE CHARTER

C4591001

Investigational BNT162 Vaccine Program

PF-07302048

Version: 2.0

Date: 11-June-2020

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 1 of 26

TMF Doc ID: 64.05 and 713.02

FDA-CBER-2021-5683-0015501



INTERNAL REVIEW COMMITTEE CHARTER

TABLE OF CONTENTS

1. INTRODUCTION	4
1.1. Study Design	4
1.2. Purpose of the Committee	4
1.3. Committee Close-Out.....	4
2. COMMITTEE MEMBERSHIP.....	5
2.1. Conflicts of Interest.....	5
2.2. Confidentiality Agreement/Contract	5
2.3. Authorship.....	5
3. ROLES AND RESPONSIBILITIES	5
3.1. Committee Members	5
3.2. Committee Chairperson.....	6
3.3. Committee Liaison	6
3.4. Study Team	7
4. COMMITTEE MEETINGS.....	8
4.1. Meeting Schedule/Frequency	8
4.2. Start-up Meeting.....	9
4.3. Review Meetings	10
4.4. Review Meeting Format.....	10
4.5. Voting Procedure.....	10
4.6. AD HOC Meetings for Emergent Safety Data	11
4.7. Meeting Minutes	11
5. DATA PROVIDED TO THE COMMITTEE AND PARAMETERS TO BE MONITORED/REVIEWED BY THE COMMITTEE.....	12
5.1. Provision of Study Data to the Committee.....	12
5.2. Data for Review Meetings.....	12

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.

CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template

01-Nov-2019

Page 2 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

5.2.1. Open Session Data12

5.2.2. Safety Review for Stopping Rules for Sentinel Cohort.....13

5.3. Database Information14

6. COMMUNICATION PLAN BETWEEN PFIZER AND THE COMMITTEE.....14

6.1. Overview of the Communication Plan14

6.2. Recommendations15

6.3. Communication of Recommendations16

6.4. External Pfizer Communication16

6.5. Pfizer Internal Safety Review Committee.....17

7. WRITTEN RECORDS18

7.1. Deliverables18

7.2. General Project File.....19

7.3. Unblinded data in SAS® Datasets19

8. CHARTER HISTORY19

APPENDICES

Appendix 1. Committee Membership Log20

Appendix 2. Plan to Control Dissemination of Results23

Appendix 3. Key Contacts24

Appendix 4. List of Studies (if committee is to oversee multiple studies).....26

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
 CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
 01-Nov-2019
 Page 3 of 26
 TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

1. INTRODUCTION

This internal review committee (IRC) (hereafter referred to as “the committee”) is a single, expert advisory group including one or more Pfizer colleagues (who are not directly involved in the conduct of this study) established to oversee this Pfizer-managed trial (C4591001). The primary rationale for establishing the committee is to make certain that appropriate safeguards are in place to help ensure the safety of participants. The IRC will be responsible for reviewing safety and immunogenicity data at multiple planned timepoints in the C4591001 study, as well as in the event a stopping rule is met.

Pfizer is responsible for conducting this study. BioNTech is the regulatory sponsor of this study.

1.1. Study Design

C4591001: A Phase 1/2, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study To Describe The Safety, Tolerability, Immunogenicity, And Potential Efficacy Of SARS COV-2-RNA Vaccine Candidates Against COVID 19 In Healthy Adults

Please refer to [the current C4591001 protocol](#) for details of the study design

1.2. Purpose of the Committee

The committee will review accumulating safety and immunogenicity data from the above-mentioned study during Stage 1 and 2. The committee will advise the study team(s) and senior management regarding the safety of current participants, as well as the continuing scientific validity and progress of the trial. The committee will review safety data which may contribute to stopping rules at *ad hoc* meetings and all available safety data at regular meetings (Refer to [Section 5](#) for details).

In addition to safety review by the committee, qualified Pfizer personnel will review safety data as specified in the Safety Surveillance Review Plan and will inform the committee of significant findings.

1.3. Committee Close-Out

The committee will have completed its work and be dissolved when final data from this study under the scope of the IRC Charter has been reviewed.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.

CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 4 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

FDA-CBER-2021-5683-0015504



INTERNAL REVIEW COMMITTEE CHARTER

2. COMMITTEE MEMBERSHIP.

The committee consists of a chairperson and at least 2 additional members, as indicated in the list of members in [Appendix 1 Committee Membership Log](#) including at least one with medical qualifications and at least one other who is a statistician. IRC members are colleagues who are not directly involved in the conduct of these studies.

During the conduct of the study, membership of the committee may change based on expertise needed, availability, and new conflicts of interest that warrant a change. A dated log must be maintained in Appendix 1 reflecting any changes in membership. If any member leaves the committee, the Pfizer will promptly appoint a replacement in consultation with the committee chairperson, if needed.

2.1. Conflicts of Interest

Not applicable. All committee members are Pfizer employees.

2.2. Confidentiality Agreement/Contract

Not applicable. All committee members are Pfizer employees.

2.3. Authorship

Not applicable. All committee members are Pfizer employees.

3. ROLES AND RESPONSIBILITIES

3.1. Committee Members

The primary responsibilities of the committee members are:

- Review, endorse, and implement the charter.
- Review safety data from in scope studies on a regular basis (refer to [section 4.1 Meeting/Schedule Frequency](#)) throughout the duration of the trial.
- Provide an informed risk-benefit assessment and advise the study team regarding the continuation of the trial based on the reviewed data.
- Provide guidance, where appropriate, on additional questions presented by the study team prior to review meetings.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 5 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

3.2. Committee Chairperson

The primary responsibilities of the committee chairperson are:

- Review and approve the charter on behalf of the committee members.
- Facilitate discussion by integrating differing points of view and moving the committee towards recommendations to be provided to Pfizer in a timely fashion.
- Prepare closed session meeting minutes (or prepare via a designee).
- Complete CT22-GSOP-RF11 *Brief Recommendation Form* and submit to the senior management team according to the communication plan (refer to [section 6 Communication Plan Between Pfizer and the Committee](#))
- Communicate with the senior management team according to the communication plan on behalf of the committee (refer to section 6 *Communication Plan Between Pfizer and the Committee*).
- Provide all unblinded written records to the study team for archiving.

3.3. Committee Liaison

The committee liaison is not a member of the study team for any study being reviewed by the committee. The committee liaison is designated by Pfizer and will maintain independence from the study team for the duration of the trial. The primary responsibilities of the committee liaison are:

- Serve as the primary liaison between the committee and Pfizer management.
- Receive and distribute, according to the communication plan, the committee recommendations from the committee chairperson.
- Ensure the committee has access to timely information about the study
- Handle and maintain a record of communications between the committee and Pfizer management.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 6 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

Manage written records (e.g., closed session meeting minutes and CT22-GSOP-RF11) between the committee and Pfizer throughout study conduct.

3.4. Study Team

The study team includes program clinical lead, lead study clinician, clinical scientist, study statistician and other team members as appropriate. The primary responsibilities of the study team are:

- Ensure qualified study team personnel are available to review safety data (unblinded or blinded according to the study stage) per the safety surveillance review plan for the duration of the trial in order to complement the committee's safety role and fulfill Pfizer's obligation to monitor patient safety.
- Select the committee chairperson and members.
- Ensure appropriate study conduct and preservation of the study blind (if applicable) to ensure overall study integrity is maintained.
- Appoint the reporting team (including statistician and reporting programmer[s]) not associated with the study team.
- Prepare open session meeting minutes.
- Ensure that all written records are filed appropriately in the Trial Master File (TMF).
- Prepare and implement the committee charter.
- Provide the study protocol (and any subsequent protocol amendments) to the committee.
- Notify the committee of any significant new safety information (e.g., toxicology information, potential safety signal, and data from other clinical trials).
- Implement the committee recommendations once endorsed by Pfizer management.
- Promptly review and respond to all committee recommendations and provide the committee with a summary of actions taken in response to its recommendations (as described in [section 6.3](#) *Communication of Recommendations*).

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 7 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

- Maintain committee records throughout study conduct.
- Archive all records at the end of the study.
- Submit the committee charter to the Food and Drug Administration (FDA) and other regulatory authorities (RA) when appropriate.
- Organize and facilitate committee meetings, including logistical support such as identifying meeting dates and locations and providing assistance with travel arrangements.

4. COMMITTEE MEETINGS

4.1. Meeting Schedule/Frequency

Prior to the start of enrollment in the C4591001 study, a start-up meeting (refer to [section 4.2 Start-up Meeting](#)) will be scheduled with the committee and members of the study team to review the draft charter, discuss roles, scope of reviews and logistics. The committee will then meet to review safety data from C4591001.

For each vaccine candidate/dose level/dose schedules the IRC will meet to:

- Review safety data to inform and permit dosing decisions in the 18-to 55-year age cohort (Stage 1)
 - Decisions on dosing will be based on IRC review of at least 7-day post-Dose 1 safety data in this study and/or the BioNTech study conducted in Germany (BNT162-01).
 - Note that, for candidates based upon the same RNA platform (eg, BNT162b1, BNT162b2), dose escalation for the second or subsequent candidates studied may be based upon the safety profile of the first candidate studied being deemed acceptable at the same, or a higher, dose level by the IRC.
- Review of safety data in the case of a stopping rule being met
- Review of safety and/or immunogenicity data to:
 - Allow groups of participants of 65 to 85 years of age to proceed

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 8 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

- Groups of participants 65 to 85 years of age will not be started until safety data for the RNA platform have been deemed acceptable at the same, or a higher, dose level in the 18- to 55-year age cohort by the IRC.
- Select vaccine candidate(s)/dose level(s), and schedule(s) to proceed into Stage 2 (as appropriate).
- Select vaccine candidate(s)/dose level(s), and schedule(s) to proceed into Stage 3.
- Review of any available safety and/or immunogenicity data generated during the course of this study, or the BioNTech study conducted in Germany, to determine:
 - Whether groups may be started at the next highest dose
 - Whether any groups may not be started
 - Whether any groups may be terminated early
- Whether any groups may be added with dose levels below the lowest stated dose or intermediate between the lowest and highest stated doses
- Contemporaneous review of all NAAT-confirmed COVID-19 illnesses

4.2. Start-up Meeting

As soon as possible after the committee is formed, the committee members, the reporting statistician, and members of the study team will meet to discuss the operational details of the committee and the protocol.

The committee members and members of the study team will meet initially to agree on:

- Study conduct issues of interest during review meetings,
- Data elements and statistical methods to be included in safety and efficacy review(s),
- List and/or mock-ups of tables, listings, figures and/or data summaries,

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 9 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

FDA-CBER-2021-5683-0015509



INTERNAL REVIEW COMMITTEE CHARTER

- Procedural issues such as meeting frequency and format, timing of data receipt and format (including table layouts), definition of a “quorum” and handling of meeting documentation, and
- Criteria and process for unblinding the data and maintaining confidentiality of unblinded results (in the case of a blinded trial or an open-label trial in which the dissemination of such information is restricted).

The charter will be finalized and approved prior to the first subject first dose.

4.3. Review Meetings

The committee will convene to review study conduct and safety data at determined intervals after the start-up and initial safety review meetings. Additionally, the committee will convene to review data on an as-needed basis (e.g., a stopping rule is met, to review reports of COVID-19-like illnesses, unexpected safety or study conduct concerns, when a stopping rule is met). Committee members will be required to be available at very short notice to allow dose escalation or changes to continuation of specific groups. Data listings and summaries may be supplied to committee members prior to the meeting.

4.4. Review Meeting Format

Each review meeting will consist of an open session during Stages 1 and 2 of the study. The committee and study team will be unblinded during Stage 1 of the study (to identify preferred vaccine candidate(s), dose level(s), number of doses and schedule of administration) and Stage 2 (expanded cohort stage). The IRC will not be required to meet during Stage 3 of the study.

No separate open and closed sessions will be required.

4.5. Voting Procedure

All committee members are voting members and are expected to participate in all meetings and voting forums. Every effort should be made in scheduling meetings to ensure that all members can participate. In the unlikely event that not all members are able to participate in a meeting, a quorum requires the participation of a majority of members, one of whom must be the Chair, one of whom must be medically qualified and the committee statistician. A majority vote is required to make any of the above recommendations. In the event of a split vote, the chairperson will make the final decision concerning the committee’s

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.

CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 10 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

recommendation. If the chair cannot participate, he/she will delegate his/her role to another member of the committee.

At each meeting, the committee members will vote and provide one of the recommendations listed in [section 6.2 Recommendations](#).

4.6. AD HOC Meetings for Emergent Safety Data

In the event that the committee is convened for an *ad hoc* meeting to evaluate emergent data, processes other than those outlined in this charter may be undertaken on the recommendation of and/or with the express consent of the committee chairperson in order to ensure patient safety within the trial. Any alternative processes will be documented and justified in the committee meeting minutes.

4.7. Meeting Minutes

The committee chair is accountable for open session meeting minutes and may delegate the act of recording minutes during the meeting. Committee members will review and agree to the minutes before they are finalized. At a minimum the minutes should record the following information:

- Who attended the meeting;
- Action items created during the meeting including who is responsible for the action;
- Any resolution of action items from a previous meeting;
- Any issues or concerns identified during the review of the data with brief rationale for the concern;
- CT22-GSOP-RF11 *Brief Recommendation Form*.

The study team will work with the committee to prepare open-session meeting minutes that describe the meeting proceedings. The study team is responsible for filing the open-session minutes in the trial master file (TMF).

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 11 of 26
TMF Doc ID: 64.05 and 713.02



INTERNAL REVIEW COMMITTEE CHARTER

5. DATA PROVIDED TO THE COMMITTEE AND PARAMETERS TO BE MONITORED/REVIEWED BY THE COMMITTEE

The committee will review all data from the US study on a regular basis (see [section 4.1](#) and below) and data from the BioNTech German study as they become available.

5.1. Provision of Study Data to the Committee

The study team is the primary channel for providing output/reports to the committee.

5.2. Data for Review Meetings

5.2.1. Open Session Data

Prior to each review meeting, the committee will receive summary data combined across the vaccine groups regarding the progress of the trial. The committee and study team will be unblinded during Stage 1 of the study (to identify preferred vaccine candidate(s), dose level(s), number of doses and schedule of administration) and Stage 2 (expanded cohort stage). No closed sessions will be required.

The committee and study team will review all available listings and summary tables of participants enrolled into BNT162 vaccine candidates/dose level/age group/number of doses to allow for review of the following.

- Demographic and other baseline characteristics.
- BNT162 investigational vaccine candidate randomization assignments and study discontinuations
- 7-day reactogenicity data.
- Discontinuation due to adverse events (AEs)
- AEs and SAEs
- Laboratory data when available.
- Patient profiles of COVID-19 unplanned illness visits
- Immunogenicity data post-dose 1 when available

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 12 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

- Immunogenicity data post-dose 2 when available
- Deaths

If the safety profile is acceptable in the younger age group, a decision will be made to move into next dose level in that age group for each vaccine candidate in Stage 1. Review of safety and/or immunogenicity after dose 1 or 2 data will be required to move into the older age group and dose escalate for each vaccine candidate in Stage 1. The study team will be informed and recommendations will be documented using the *Brief Recommendation Form* (CT22-GSOP-RF11 Brief Recommendation Form).

Cumulative safety and immunogenicity (when available) data will be reviewed from all participants enrolled into the study at each dose level. A recommendation will be made on further dose-escalation. The study team will be informed.

If recommendations are other than to continue the study as planned, the Joint Safety Review Team (JSRT) will make the final decision on study progress (CT22-GSOP-RF11 Brief Recommendation Form). Please see the JSRT charter for further information.

5.2.2. Safety Review for Stopping Rules for Sentinel Cohort

The study team physician/designee will have access to randomization lists to unblind participants (during Stage 1 and 2) with suspected related events in order to select BNT162 RNA platform related events for review by the committee, which may have met the study stopping rules.

- At the open session the committee will review all available data associated with each participant who has met a stopping rule including demographics, medical history, reactogenicity, and AE data.

The committee will recommend further actions required. Study team will be informed. Note that if a stopping rule is met the DMC must meet to review all available and relevant data and also make a recommendation about continuation of the study.

- If recommendations are other than to continue the study as planned, the Joint Safety Review Team (JSRT) will make the final decision on study progress (CT22-GSOP-RF11 Brief Recommendation Form). Please see the JSRT charter for further information.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 13 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

5.3. Database Information

All data provided to the committee will be from a dynamic database that is continually updated or revised as new information becomes available. Tables, listings, and figures will be annotated with the date on which they were generated.

6. COMMUNICATION PLAN BETWEEN PFIZER AND THE COMMITTEE

6.1. Overview of the Communication Plan

The expected flow of unblinded information and recommendations is depicted in [Figure 1](#):

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.

CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 14 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

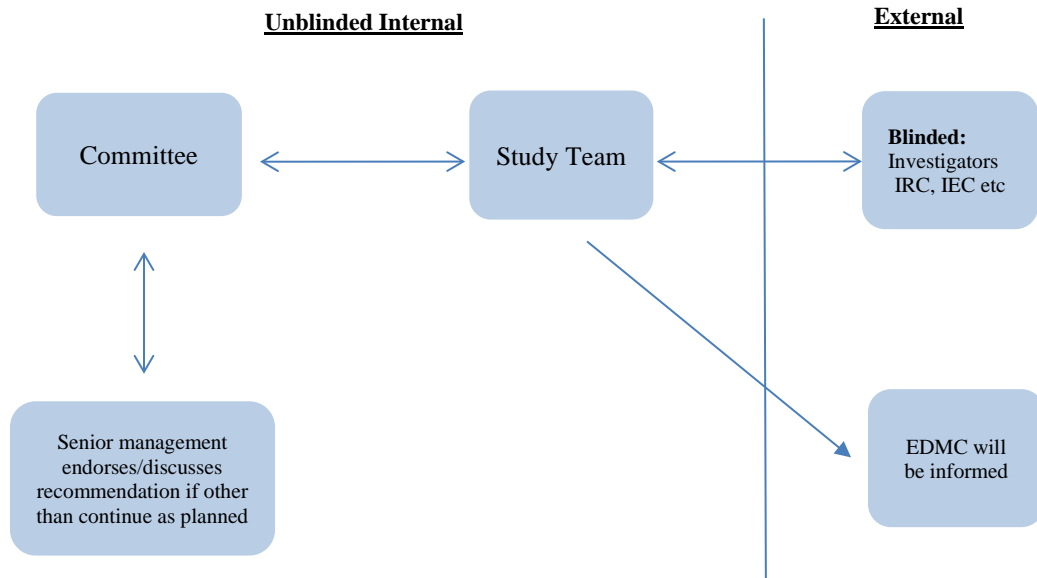
FDA-CBER-2021-5683-0015514



INTERNAL REVIEW COMMITTEE CHARTER

Figure 1

Unblinded Results and Recommendations



6.2. Recommendations

After each meeting, the committee will provide one of the following recommendations to Pfizer via CT22-GSOP-RF11:

- Dose escalation in the younger age group
- Initiate dosing in the older age group
- Dose escalation in the older age group
- Expansion in non-sentinel cohort and expanded cohort
- Continue specific dose levels/vaccine candidate
- Discontinue specific dose level/vaccine candidate

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 15 of 26

TMF Doc ID: 64.05 and 713.02



INTERNAL REVIEW COMMITTEE CHARTER

- Select final vaccine candidate and dose level
- Withhold final recommendation until further information/data is provided.
- Continue the study as designed.
- Modify the study and continue.
- Stop the study.

Additionally, the committee may be asked to answer study related questions (e.g., concerning operational challenges, impact of findings from Pfizer's safety data review or impact of emerging external information) provided by the study team. The answers to the questions will be provided with the committee recommendation to Pfizer management via the committee liaison (role is done by the study team for this study).

The recommendations should be in accordance with the guidance provided in this charter, the protocol, or the SAP (or other document, as appropriate, e.g., interim analysis plan).

6.3. Communication of Recommendations

For each review meeting, once a committee recommendation has been finalized the committee chairperson will convey the recommendation in writing within the timelines listed on CT22-GSOP-RF11. The written communication will consist of the CT22-GSOP-RF11 indicating the committee's recommendation and sufficient information to explain the rationale for any recommendation will be transmitted by secure electronic means to the study team. A copy of the committee recommendations will be forwarded to the JSRT by a member of the study team.

Review of committee recommendation will be conducted in accordance with CT22-GSOP-RF11.

6.4. External Pfizer Communication

The committee's recommendation, together with the senior management's decision, will be summarized by the study team who will be responsible for communicating to all active investigators participating in the trial within 2 business days if the recommendation is other than to continue the trial as planned. The investigators and EDMC will be informed about

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 16 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

the decision to stop the trial, or to implement modifications to trial procedures, as appropriate.

As required, the investigators will be instructed to submit this communication to their respective IRB/EC. The committee's recommendations and senior management endorsement will also be communicated to regulatory authorities (in accordance with local regulations).

6.5. Pfizer Internal Safety Review Committee

Pfizer has established several ad hoc Internal Safety Review Committees (ISRCs), one for each BU/RU. The ISRC for a BU is properly firewalled from all study teams conducting trials sponsored by that unit. The primary objective of an ISRC is to assess specific events that may constitute a safety concern in an unblinded manner. The assessment could result in expedited reports to regulators as required in FDA Final Rule (2010) and EU CT-3 (2011). The assessment may also lead to safety-related protocol changes. When necessary, an ISRC could look at the occurrence of the specific events across multiple studies in a development program.

The activities of an ISRC are intended to be complementary and supplemental to existing Pfizer safety and risk management processes, including this committee. There is a charter for the ISRC describing in detail the purpose, composition, and operations of an ISRC. The charter is available upon request.

There may be several interactions between an ISRC and this committee, including:

- When the ISRC accepts a request from the signal management lead to review specific events, the ISRC chair will notify the committee chairperson that a request has been made and that a review is to be conducted with a target date (typically within 30 calendar days of the request).
- The committee liaison will supply the ISRC chair a copy of the current committee charter, open meeting minutes and correspondences from the committee regarding issues for which the ISRC is currently being consulted.
- ISRC chair will communicate review findings with the committee chairperson.
- If no safety concern is identified, the ISRC will communicate this conclusion to the signal management lead with a copy to the committee.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019

Page 17 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

- If a safety concern is identified, the ISRC chair will communicate its findings to the committee chairperson by an appropriately secure means. The written communication contains the ISRC's rationale and final assessment.
- The committee chairperson is requested to acknowledge receipt of the ISRC communication as soon as possible. The committee considers the findings identified by the ISRC but is not obligated to act on them.
 - Where disagreement exists between the recommendations of the ISRC and the committee, the two committees attempt to reach consensus through additional communication.
 - The final decision to accept or reject the committee's and/or ISRC's recommendation resides with sponsor management.
 - The safety data (tables, listings, and reports, etc.) received by the ISRC for review are kept confidential and will be disclosed to the committee upon request from the committee chairperson.

7. WRITTEN RECORDS

The study team will maintain written records of all open session meeting minutes, CT22-GSOP-RF11, and materials reviewed by the committee, and communications between the committee and the Pfizer. These documents are considered proprietary and confidential and must be available for inspection upon request from RAs. Upon completion of the committee's responsibilities, the study team will obtain all written records for archiving. Closed session minutes are not appropriate to file in the TMF until the last study is complete.

7.1. Deliverables

The following are the deliverables from the committee chairperson to the study team.

After each committee review meeting:

- CT22-GSOP-RF11.
- IRC session meeting minutes.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 18 of 26
TMF Doc ID: 64.05 and 713.02



INTERNAL REVIEW COMMITTEE CHARTER

7.2. General Project File

The study team will compile and maintain the following documents and correspondence throughout study conduct.

- Any relevant correspondence between the committee and Pfizer.
- Committee charter and any amendments.
- Current IB.
- Protocol and protocol amendments.
- Curriculum vitae for each committee member.
- CT22-GSOP-RF01 for each committee member.
- Minutes from each open session meeting.

7.3. Unblinded data in SAS® Datasets

The unblinded treatment assignment information will be merged programmatically with the study datasets using SAS®.

8. CHARTER HISTORY

Version	Date (dd-Mmm-yyyy)	Summary of Changes
1	29-Apr-2020	N/A
2	11-Jun-2020	<ul style="list-style-type: none"> • Amended that IRC decision to progress group(s) into Stages 2 and 3 can be based upon safety and immunogenicity data after dose 1 or 2 • Clarified safety data requirements to permit dose escalation

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
 CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
 01-Nov-2019
 Page 19 of 26
 TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

		<ul style="list-style-type: none"> • Amended that progression to participants 65 to 85 years of age can be based upon data from the same RNA platform • Amended that stopping rules apply to an RNA platform rather than a specific vaccine candidate • Modified the criteria required for the IRC to determine dose escalation in the 18- to 55-year age cohort and advancement to groups of participants 65 to 85 years of age • To permit individual and group dosing alterations for the second dose of study intervention
--	--	--

Appendix 1. Committee Membership Log

The committee consists of the following members (past and present).

Member	Affiliation/Address	Role	Dates of Membership*
Kathrin Jansen, PhD	Senior Vice President, Head of Vaccine Research and Development Tel: +1 845 602 5450 kathrin.jansen@pfizer.com	Committee member	29-April-2020
Philip Dormitzer MD PhD	VP & CSO, Viral Vaccines 401 N Middletown Rd Pearl River, NY 10965 Tel: +1 (845) 6027742	Committee member	29-April-2020

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template
01-Nov-2019

Page 20 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

	Philip.Dormitzer@pfizer.com		
William Gruber MD	Senior Vice President, Vaccine Clinical Research and Development, Pfizer Inc. 401 N Middletown Rd Pearl River, NY 10965 Tel: +1 845 602 3484 bill.gruber@pfizer.com	Chairperson	29-April-2020
Rob Maroko MD	Senior Director, Safety Surveillance and Risk Management 500 Arcola Road Collegeville PA 19426 USA Tel: +1 (484) 8658566 Robert.Maroko@pfizer.com	Committee member	29-April-2020
Stephen Lockhart MD	Vice President Head of Europe and Asia-Pacific, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel: +44 1628 515538 Stephen.P.Lockhart@pfizer.com	Committee member	29-April-2020
Kenneth Koury, PhD	Executive Director Biostatistics, Vaccine Clinical Research and Development, Pfizer Inc.	Statistician	29-April-2020

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 21 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

	401 N Middletown Rd Pearl River, NY 10965 Tel: +1 (845) 602 2547 Kenneth.Koury@pfizer.com		
--	--	--	--

* Initial date of membership is the date the effective date of the contract signed by the committee member.

Note: Curriculum vitae are on-file at Pfizer and may be accessed by contacting the Study Team.

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 22 of 26
TMF Doc ID: 64.05 and 713.02



INTERNAL REVIEW COMMITTEE CHARTER

Appendix 2. Plan to Control Dissemination of Results

This is an observer-blinded study as the physical appearance of the BNT162 vaccine candidates and placebo differ.

At the study site: The participant, investigator, study coordinator, and other site staff will be blinded. The dispenser(s)/administrator(s) and those study site team members who are involved in ensuring that protocol requirements for investigational product handling, allocation, and administration are fulfilled at the site (e.g. study manager, clinical research associates) will be unblinded for the duration of the study.

Breaking the blind by the Investigator: Blinding codes should be broken by the investigator only when knowledge of the actual treatment code is absolutely essential for further management of the participant. The method will be an electronic process via Impala.

Pfizer: For Stage 1 (dose-finding) and Stage 2 (expanded cohort): Pfizer study team members are unblinded to the vaccine assigned/received by all participants.

Pfizer: Laboratory personnel performing the immunologic assays will remain blinded to vaccine assigned/received throughout the study.

Unblinded Pfizer personnel: Randomization codes will be released to reporting team (unblinded reporting statistician and unblinded programmer) who need access to the codes to generate the summaries and participant data listings for the review by the unblinded committee members during Stages 1 and 2 the study. Randomization codes will be available to the committee via the reporting team.

Release of the randomization codes to designated personnel will only be performed upon completion of the Randomization Code Release Request Form in GRAABS. Randomization codes and unblinded data will be maintained in a secure location.

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 23 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

Appendix 3. Key Contacts

Study Team Members		
<i>Name*</i>	<i>Contact Information</i>	<i>Role</i>
Nicholas Kitchin	Senior Director, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel : +44 7557 202435 nicholas.kitchin@pfizer.com	Study Clinician
Ruth Bailey	Director, Clinical Scientist, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel: +44 1628 515654 ruth.bailey@pfizer.com	Lead Clinical Scientist
Judith Absalon, MD, MPH	Senior Director, Vaccine Clinical Research and Development 401 N Middletown Rd Pearl River, NY 10965 Tel: +1 845 602 1685 Judith.Absalon@pfizer.com	Independent Clinician

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 External Data Monitoring Committee and Internal Review Committee Charter Template
01-Nov-2019

Page 24 of 26

TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

FDA-CBER-2021-5683-0015524



INTERNAL REVIEW COMMITTEE CHARTER

Alejandra Gurtman	Vice President Pfizer Vaccine Clinical Research and Development Tel +1 845-602-2842 Cell 201-290-0489 Fax +1 845 474 3219 alejandra.gurtman@pfizer.com	Independent Clinician
Ping Li	Senior Director 500 Arcola Road Collegeville PA 19426 USA Tel: +1 484 8652138 Ping.Li4@pfizer.com	Program Biostatistician

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 25 of 26
TMF Doc ID: 64.05 and 713.02

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)



INTERNAL REVIEW COMMITTEE CHARTER

Appendix 4. List of Studies (if committee is to oversee multiple studies)

Study	Date Added (dd-Mmm-yyyy)
C4591001: A Phase 1/2, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study To Describe The Safety, Tolerability, Immunogenicity, And Potential Efficacy Of SARS COV-2-RNA Vaccine Candidates Against COVID 19 In Healthy Adults	29-Apr-2020

090177e1945bf925\Approved\Approved On: 14-Jul-2020 13:56 (GMT)

PFIZER INTERNAL USE ONLY

The official version of this form is located in the electronic document management system.
CT22-GSOP-RF02 6.0 *External Data Monitoring Committee and Internal Review Committee Charter Template*
01-Nov-2019
Page 26 of 26
TMF Doc ID: 64.05 and 713.02