TABLE OF CONTENTS

SUMMARY [redacted]

The Center for Biologics Evaluation and Research (CBER) requested a High Priority, PDUFA, Surveillance, Domestic, Initial, Comprehensive inspection, Application No: IND # 19736, of Steven H. Reynolds, DO, using Bioresearch Monitoring Compliance Program 7348.811 and Program Assignment Code 45811. This inspection, as part of DBIMO2 (West), LOS-DO FY'21 work plan under MARCS Operation ID: 179325 (no FACTS No assigned), covered Good Clinical Practices (GCPs).

Dr. Reynolds has no prior FDA inspection history and no warnings. CBER issued an assignment memorandum dated October 20, 2020, containing various instructions.

This inspection covered one study protocol, per the table below.

Sponsor	Study Protocol	Study Title	Product	Site
BioNTech RNA Pharmaceuticals GmbH and Pfizer, Inc.	C4591001	A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals	RNA Vaccine Candidates BNT162 & PF-07302048	(b) (4)

This inspection included review of on-site documents noted in the table below.

Regulatory Documents	Source Documents
CV & Financial Records	Concomitant medication logs
eDiary manuals	eDiary entries/reviews
FDA 1572 Statement of Investigator	Eligibility records
IRB approval records	Informed consent forms
Laboratory accreditations	Subject identity records
List of studies	Product accountability
Monitoring records	Product labeling
Signature and delegation Log	Product storage/handling
Site training	Progress notes
Study protocol and amendments	(Serious) adverse event records
Subject screening/enrollment logs	Subject visit reports

This inspection revealed no objectionable findings. We held no significant discussions during the inspection. We noted corrections by the SMO in response to discussions held during a prior inspection (ref: **Additional Information** section). We did not collect any samples and we did not encounter any refusals.

ADMINISTRATIVE DATA (LNL)

Inspected firm:	Steven H. Reynolds, DO
Location and Mailing Address:	Collaborative Neuroscience (CNS) Network, LLC 2600 Redondo Avenue, Suite 415 Long Beach, CA 90806
Phone (no Fax)	562-304-1742
Email:	stevenreynolds@cnstrial.com
Dates of inspection:	11/16/2020, 11/17/2020, 11/18/2020, 11/19/2020, 11/20/2020, 11/23/2020
Days in the facility:	Six (6)
Participants:	(b) (6), (b) (7)(C) CSO [Lead] (b) (6), (b) (7)(C) CSO (b) (6), (b) (7)(C) CSO (present 11/16-17/2020) *Initials next to each section header denote the contributor(s).*
Non-FDA Participants	not applicable

On November 16th, 2020, we presented our credentials and issued Form FDA 482 Notice of Inspection to Steven H. Reynolds, DO, Clinical Investigator and most responsible person.

HISTORY (b) (6), (b) (7)(C)

Steven H. Reynolds, DO, operates as a contracted clinical investigator of Collaborative Neuroscience (CNS) Network, LLC, a site management organization (SMO). His hours of operation vary, but tend to be Monday – Friday, 8:00 am – 5:00 pm. His curriculum vitae (CV) documents his research experience and length of service at the organization (ref: **Exhibit 1**). CSO (b) (6), (b) (7)(C) obtained a list of studies summarizing his FDA-regulated research activities (ref: **Exhibit** (b) (6), (b) (7)(C). We collected a copy of his service contract with CNS (ref: **Exhibit 2**).

The facility is located on the 4th and 5th floors (suites 415 and 500) of the Health Care Partners building at the north east corner of Redondo Avenue and East Willow Street. Dr. Reynolds saw clinical research subjects in suite 415 (located on the 4th floor). Administrative offices and monitoring suites are also located in this suite. Study records are archived at CNS headquarters [12772 Valley View Street, Suite 3, Garden Grove, CA 92845]. We collected the firm's organization chart (ref: **Exhibit 3**).

Dr. Reynolds has no prior FDA inspection history and no warnings.

Please send all FDA correspondence to:

Steven H. Reynolds, DO
Collaborative Neuroscience (CNS) Network, LLC
2600 Redondo Avenue, Suite 415
Long Beach, CA 90806
stevenreynolds@cnstrial.com

INTERSTATE (I.S.) COMMERCE (b) (6), (b) (7)(C)

Records show that investigational products (i.e. BNT vaccine/placebo DB kit) were shipped to CNS [2600 Redondo Avenue, Suite 500, Long Beach, CA 90806] for delivery to the site pharmacy. Shipments originate from (b) (4) indicating interstate commerce.

JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED) (b) (6), (b) (7)(C)

FDA has jurisdiction over investigational products under section 505 of the Food Drug & Cosmetic (FD&C) Act. The study sponsor was responsible to oversee the manufacture and shipment (in interstate commerce) of investigational products to the clinical site for administration to human subjects. The firm is not responsible for product labeling; therefore, such agreements do not apply.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED (b) (6), (b) (7)(C)

Steven H. Reynolds, DO, Clinical Investigator, identified himself as the most responsible and highest ranking person of the firm. He has the duty, power and authority, and responsibility to detect, correct and prevent violations, as demonstrated by his signatures on Form FDA 1572 Statement of Investigator (ref: **Authority and Administration** section) and on all versions of the study protocols (ref: **Protocol** section). He also identified himself as Principal Investigator on the Signature Sheet and Delegation of Duties Log (ref: **Exhibit 4**) bearing each team member's assigned functions.

Personnel present and participating in the inspection are included in the table below.

Name	Title	Experience	Duties	Reports To	Inspection Role
Steven H. Reynolds, DO	Clinical Investigator	11 years	Ref: **Exhibit 4**	Dalia Botros, Executive VP (b) (6), Sr. PM	Received 482, present during opening/closing discussions; answered procedural questions
Dalia R. Botros, MBBS	Executive Vice President	Exec. VP since 2020	Oversees all operations and managers CNS-wide	David P. Walling, CEO	Answered questions, provided records, present during discussions with Dr. Reynolds
(b) (6)	Senior Project Manager	Since 2007; 2 years in current role	Ref: **Exhibit 4**	Dalia Botros, Executive VP	Answered questions, reviewed/provided regulatory/electronic records, present during discussions with Dr. Reynolds
(b) (6)	Pharmacist (unblinded)	Since 2008	Ref: **Exhibit 4**	Dalia Botros, Executive VP	Answered questions, provided pharmacy/IP records, present during discussions with Dr. Reynolds
(b) (6)	Research Assistant	Since 2020	Ref: **Exhibit 4**	(b) (6), Sr. PM	Facilitated requests for records from personnel

Dr. Reynolds provided information on himself, the recruitment/informed consent process and evaluation of concomitant medications. Dr. Botros provided information on herself and on Dr. Reynolds's availability. She also facilitated meetings with (b) (6) for review of electronic records and provided copies of those records. (b) (6) provided information on herself and on regulatory and electronic records. She also provided copies of records.

(b) (6) provided information on herself and access to the Pharmacy and pharmacy/IP accountability records. (b) (6) also described pharmacy-specific procedures. (b) (6) provided information on herself and on the status of requests made during the inspection.

CLINICAL SITE TRAINING (b) (6), (b) (7)(C)

We saw no significant issues that would indicate training deficiencies.

COMPLAINTS (b) (6), (b) (7)(C)

We found no complaints about Dr. Reynolds within FDA's database.

AUTHORITY AND ADMINISTRATION (b) (6), (b) (7)(C)

We collected all signed Form FDA 1572 Statement of Investigator documents (ref: **Exhibit 5**). Dr. Reynolds assumed responsibility for the trial on 07/22/2020, as determined by his signature on Form FDA 1572 Statement of Investigator. CSO (b) (6), (b) (7)(C) determined that the site maintains accreditation records for the clinical laboratories listed on Form FDA 1572 Statement of Investigator, indicating that those facilities are equipped to perform all relevant tests required by the study protocol.

CSO (b) (6), (b) (7)(C) obtained a list of all studies conducted by Dr. Reynolds, including the protocol numbers and titles, names of sponsors, study status, study dates and number of enrolled subjects (ref: **Exhibit** (b) (6), (b) (7)(C) and **History** section). We determined the location where study visits occurred (ref: **History** section and we reviewed site initiation visit (SIV) training documents and determined that the sponsor did not allow the use of satellite sites. We determined that Dr. Reynolds did not stop his participation in the study at any time.

We determined that the sponsor provided information to the clinical site about the investigational product, study protocol, and the obligations of a clinical investigator by way of site visits and reports, emails and sponsor correspondences to the site. We determined that Dr. Reynolds properly delegated authority for the conduct of the trial to ensure he maintained control and knowledge of the study and that there were no changes to the clinical investigator during the study. The study is still active and site closure has not yet occurred.

CSO (b) (6), (b) (7)(C) obtained IRB approval dates, including initial review of the protocol, applicable amendments, informed consent forms, eDiary materials, etc. (ref: **Institutional Review Board** (**IRB**) section).

We determined the requested study dates, as noted below.

First Subject - (b) (6)			Last Subject - (b) (6)		
Screen/ICF	Randomized	First Dose	Randomized	Last Dose	Last Follow-up
5-Aug-20	5-Aug-20		27-Oct-20	not yet occurred*	

*study still in active status for all subjects; 2nd vaccine administration pending for this subject

Regarding recruitment, Dr. Reynolds explained that the site already has a sizable database of subjects to contact, and Pfizer also has an agency (b) (4) for recruiting at all sites.

We saw no materials or methods that appeared to be coercive in nature or that misrepresented the safety, effectiveness, benefits, and/or outcomes of the investigational product (IP). We obtained a copy of the screening and enrollment log (ref: **Exhibit 6**) and we accounted for all noted subjects. The log also identifies those subjects enrolled in the reactogenicity cohort.

CLINICALTRIALS.GOV REQUIREMENTS (b) (6), (b) (7)(C)

The Clinical Investigator was not appointed by the sponsor to be a responsible party to meet CT.gov requirements.

We viewed the webpage associated with BioNTech SE/Pfizer's ClinicalTrials.gov registration [NCT04368728] and verified that the site, Collaborative Neuroscience Research, LLC, is listed on the page.

PROTOCOL (b) (6), (b) (7)(C)

We determined that the site used additional protocol versions compared to what was provided in background materials; therefore, we obtained copies (ref: **Exhibits 7** & **8**). We determined that Dr. Reynolds began screening and enrollment under Protocol Amendment 4 (30 Jun 2020), according to protocol signature pages (ref: **Exhibit 9**). He signed Amendment 4 on 7-22-2020. The IRB approved this version on 07/16/2020.

CSO (b) (6), (b) (7)(C) reviewed protocol deviations that were maintained via hardcopy within sponsor and monitor correspondence files and determined that the site made no planned deviations in procedures and that protocol deviations revealed no violations of FDA regulations.

We determined that Dr. Reynolds and staff followed the protocol with respect to subject selection, number of subjects enrolled, blinding scheme, required procedures/evaluations, and IP handling, storage and administration. As this study is still active and ongoing, we had no data regarding the assessment of the primary endpoint and no sponsor data line listings to compare against on-site records.

INSTITUTIONAL REVIEW BOARD (IRB) (b) (6), (b) (7)(C)

(b) (4) IRB oversees all sites for this study. IRB membership rosters were saved in the regulatory binder. The table below displays key IRB approval dates. There were no stipulations regarding IRB approvals. (b) (4) IRB granted initial approval prior to the first subject's screening, enrollment, and first vaccine dose administration.

(b) (4) IRB

(b) (4)

Chairperson: (b) (6)

Key IRB Approvals	Date of Approval	Expiration Date
Protocol dated 4/15/2020	7/16/2020	4/21/2021
Revised Protocol (5/13/2020) Incorporating Amendment 1	7/16/2020	4/21/2021
Revised Protocol (6/10/2020) Incorporating Amendment 3	7/16/2020	4/21/2021
Revised Protocol (6/30/2020) Incorporating Amendment 4	7/16/2020	4/21/2021
Consent Form – Pregnant Partner [S0]	7/16/2020	4/21/2021
Consent Form – Stage 3 [S2]	7/16/2020	4/21/2021
Electronic Informed Consent – Stage 3 # 27797100.0 (b) (4)	7/16/2020	4/21/2021
Consent Form – Stage 3 [S2]	7/22/2020	4/21/2021
Revised Protocol (7/24/2020) Incorporating Amendment 5		
Consent Form – Phase 2/3 [S3]	7/31/2020	4/21/2021
Consent Form – Phase 2/3 [S3]	8/4/2020	4/21/2021
Revised Protocol (9/8/2020) Incorporating Amendment 6	9/11/2020	4/21/2021
Consent Form – Assent [S0]	9/11/2020	4/21/2021
Consent Form – Parental [S0]	9/11/2020	4/21/2021
Consent Form – Phase 2/3 [S4]	9/11/2020	4/21/2021
Consent Form – Pregnant Partner [S2]	9/11/2020	4/21/2021
Revised Protocol (10/6/2020) Incorporating Amendment 7	10/10/2020	4/21/2021
Consent Form – Assent [S1]	10/10/2020	4/21/2021
Consent Form – Parental [S1]	10/10/2020	4/21/2021
Consent From – Phase 2/3 [S5]	10/10/2020	4/21/2021
Consent Form – Parental [S2]	10/15/2020	4/21/2021
Revised Protocol (10/15/2020) Incorporating Amendment 8	10/16/2020	4/21/2021
Revised Protocol (10/29/2020) Incorporating Amendment 9	11/5/2020	4/21/2021

Per (b) (4) IRB's Note to File sent to the site, effective October 12, 2020, (b) (4) has combined its (b) (4) IRBs into a single IRB called (b) (4) IRB." This includes (b) (4) (b) (4) On October 12, 2020 all new studies (excepting (b) (4) sites) will be managed under (b) (4) IRB's (b) (4) IRB registration number (b) (4) which was previously the registration number for (b) (4) IRB. All ongoing studies at (b) (4) (b) (4) IRB will be transferred to this IRB registration number.

SUBJECT'S RECORDS (b) (6), (b) (7)(C)

Informed Consent Documentation and Process (b) (6), (b) (7)(C)

We reviewed hardcopy and electronic informed consent documents signed by study subjects and we determined that the correct version of the consent document was used for each subject prior to initiation of study procedures and activities. Per (b) (6) the site used driver licenses to determine the identity of each subject. We determined that no pediatric subjects participated in this trial and that the site used no assent forms.

The firm maintains SOPs for obtaining informed consent: the subject receives the California Research Subject's Bill of Rights before any consenting procedures start, then the site presents the IRB-approved informed consent form (ICF) to each prospective subject. The subject has the ability to take the form with them for further review and, when willing, signs and dates the form. The site retains the original form and provides the copy to the study subject. The site describes the process in writing for each subject.

During ICF review, we determined that Dr. Reynolds used the IRB-approved versions in a language understandable to each subject. We determined that the site did not use short-form consents. We copied the most recent IRB-approved, signed and dated, informed consent form (ref: **Exhibit 10** and **Electronic Records and Electronic Signatures** section for description).

Source Records (b) (6), (b) (7)(C)

The subject source documentation was well organized within binders and divided by individual tabs for each subject. According to the site's enrollment log, 344 subjects were screened, eight (8) screened failed, and 13 discontinued the study. There were 323 subjects enrolled and active as of the close of the inspection. We reviewed 20% of subject records and informed consent forms (ICFs) for eligibility, visit assessments and evaluations, AEs and SAEs, IP administration, and concomitant/prohibited medications and procedures.

(b) (6) described the process for obtaining and recording information in source documents and CRFs. All source documents were signed and dated by the individual who recorded them.

Investigator (b) (6), (b) (7)(C) reviewed 77 ICFs and the following subjects' records: (b) (6) (b) (6)

Investigator (b) (6), (b) (7)(C) reviewed the following subjects' records: (b) (6) and (b) (6).

Source documentation consisted of original paper copies of subject visit case report forms (CRFs), notes to file, progress notes, correspondence between the site and subject, and correspondence between the site and monitor/sponsor regarding the subject. Records appeared to be attributable, legible, contemporaneous, original, accurate, complete, and were organized

according to subject number, visit date, activity and/or event. The site had adequate documentation to ensure that all subjects were alive and available for the duration of their stated participation in the study. We reviewed the subjects' records and found that protocol-required study visits and procedures were completed and well-documented. The IP administration data was noted in source records and initialed by unblinded pharmacy staff.

We discussed with Dr. Reynolds and verified how he and other Sub-Is determined which concomitant therapies and medications would exclude the subject from this study since the exclusion criteria for Phase 2/3 are so broad. Dr. Reynolds responded that the study team reviews each subject's concomitant therapies and medications and uses their clinical judgement to assess whether the subject meets eligibility criteria. In instances where the study team is unsure of the subject's eligibility, the site would contact their monitor to seek guidance. Examples of instances in which the site contacted the sponsor for advice include Subject (b) (6) who screen failed because the subject received the flu vaccine less than 14 days prior to their screening visit, and Subject (b) (6) who screen failed because the subject was taking Taltx (ixekizumab) for treatment of an autoimmune disease.

Source documents consist of subject medical records/medical histories, vital statistics, pregnancy results for female subjects, physical and neurological examination reports, progress notes, IP administration records, enrollment status, etc. The site organized documents according to subject number and visit date. The records were organized, legible, and in good condition. Source records include eDiary data submitted by study subjects, which contain information, and data on the condition of each subject at the time of their entry into the trial and their condition throughout the trial. The site also prints eDiary data for review in preparation for a subject's pending site visit. We confirmed that there is adequate documentation to ensure that subjects are alive and available for the duration of their stated participation in the trial.

Interactive response technology (IRT) confirmation printouts and investigational product administration records confirm each subject's enrollment into the trial and exposure to the investigational product (IP). The site documented all adverse events on source records, including severity assessments and relationship to the IP, as well as associated concomitant medications.

We determined that source records document subject eligibility, study visits and procedures, administration of IP, safety monitoring and reporting, and reasons for subject withdrawals. The Signature Sheet and Delegation of Duties Log (ref: **Exhibit 5**) identifies key personnel obtaining and assessing data.

Case Report Forms (b) (6), (b) (7)(C)

Electronic case report forms (eCRFs) were documented by the site though (b) (4) which required a username and password to access and enter data. Data collected during the visit was documented in the subjects' records and later entered in the eCRFs by those listed in the

delegation log. We compared source documents against the eCRFs and found no discrepancies. We asked (b) (6) to show us the audit trails for instances in which data was changed, and found the audit trails and explanation on how to submit a data change form (DCF) and the process to change data in the eCRFs to be satisfactory. We also requested (b) (6) to show us how COVID-19 symptoms and reactogenicity data was documented in (b) (4) and (b) (4) for subjects who were part of the reactogenicity subgroup and those who were not.

We compared source documents against eCRFs for 72 enrolled subjects and had no concerns. We determined that eCRF entries are ongoing as the study still open and active at this site.

Reactogenicity (b) (6), (b) (7)(C)

(b) (6) explained reactogenicity during the inspection: the sponsor provided correspondence to the site stating that the first 6000 participants in the study across all sites were considered part of the reactogenicity subset cohort. These subjects, per (b) (6) were expected to complete the eDiary each day for seven days after receiving each of the vaccines, to communicate the presence or absence of COVID symptoms.

Initially, the first 71 participating subjects at Dr. Reynolds's site (upon enrollment if/when applicable) participated as part of the cohort. The associated study protocol versions used at the site contained instructions for how to manage reactogenicity subjects. The sponsor discontinued recruitment for the reactogenicity subset on August 17, 2020, per site correspondence (ref: **Exhibit 6**, **pages 40-42**).

Protocol amendment 6 shows that the sponsor re-opened the reactogenicity subset for all Phase 3 participants who are (b) (6), as stated in section 8.2.2. Electronic Diary (ref: **Attachments** section). The site enrolled six additional subjects into this cohort (b) (6) (b) (6) The subject's screening and enrollment log identifies all the subjects enrolled under the reactogenicity subset cohort (ref: **Authority and Administration** section and **Exhibit 6**).

OTHER STUDY RECORDS (b) (6), (b) (7)(C)

We determined that Dr. Reynolds maintained other records pertinent to the study, such as protocol deviation reports, sponsor/monitor correspondence files, notes to file regarding study-specific procedures, electronic equipment manuals, etc. We noted no concerns.

ELECTRONIC RECORDS AND ELECTRONIC SIGNATURES (b) (6), (b) (7)(C)

We determined that the site relies on electronic records and signatures to record and transmit data to the study sponsor. The site has retained these records and made them available during the inspection.

Computerized systems and software used during the study are included the table below.

System/Software	Version/Serial Code	Purpose
Android/iPhone smartphone	[subject's own device]	(b) (4) (eDiary) application
(b) (4) eBinder/(b) (4)	(b) (4)	Remote monitoring; manage collection of eICFs and essential documents (b) (4) externally hosted (b) (4) solution with no integration)
(b) (4) tablet		eICF hardware
(b) (4)		eICF software used by Pfizer
(b) (4) cellular phone (model unknown)		eDiary hardware alternate for subjects with no smartphone
(b) (4)		clinical trial data management and storage (eCRF software)
Pfizer (b) (4)		Interactive Response Technology (IRT) for registration of subject enrollment and visit status
(b) (4)		patient reported outcomes (b) (4) (eDiary) application

As the site is currently ongoing, we were able to fully review eDiary and eCRF entries, as well as audit trails, for selected subjects and to obtain copies. The study sponsor determined which records to use for regulatory purposes; and the sponsor provided documentation to the clinical site in the form of correspondences, brochures and instruction manuals, for informing the site regarding appropriate use of and documentation in eCRFs.

The site also provided (b) (4) cellular phones containing the (b) (4) application for subjects who did not possess a smartphone. (b) (6) estimated that 10–12 subjects used this option. Subject source records indicated whether the subject used a personal or site-provided device.

We collected manuals presented to study subjects for the use of eDiary software at the site (ref: **Exhibits 11 – 14**), consisting of the following:

- Participant Guide to Using the (b) (4) App [07APR2020 Version: 2]
- Participant Guide to Using the (b) (4) App for the COVID-19 Illness Diary [19-JUN-2020 Version: 2]
- Participant Guide to Using the (b) (4) App for Vaccination and COVID-19 Illness Diary [19-JUN-2020 Version: 2]
- App Subject Facing Screen Report [22-JUN-2020 Version 2]

The site used electronic informed consent forms (eICFs) during the trial. (b) (6) demonstrated the process for obtaining electronic informed consent for subjects (b) (6) and (b) (6) study subjects operated the eICF device autonomously with site staff available for any questions. The eICF featured a (b) (4) orientation/instructional video on the initial page for the subject to view, if so desired. I viewed the video and I noted no concerns

The subject would indicate understanding of each page of the eICF by swiping the curser at the bottom of the screen to the right. At this point, the cursor would become green and the screen would show the next page. The subject would indicate a question by swiping the cursor left. The

cursor would become red, allowing the subject to touch the paragraph applicable to the concern and indicating to site staff the topic in question. Once the issue was addressed to the subject's satisfaction, the subject may swipe the cursor to the right. The subject would sign the eICF by using a finger to draw a signature. Each page of the eICF contains an audit trail documenting when the subject accessed the page and swiped and/or signed.

We obtained a copy of the manual containing electronic informed consent (eICF) procedures (ref: **Exhibit 15**).

Individuals at the site did not have authority, training or expertise to develop or maintain electronic systems for the study protocols. Individuals had training and instruction to use the systems facilitated by the sponsor and/or vendors, however. We did not cover electronic data security.

INTERVIEWS OF SUBJECTS/PERSONNEL (b) (6), (b) (7)(C)

We did not interview any study subjects or additional site personnel.

FINANCIAL DISCLOSURE (b) (6), (b) (7)(C)

We reviewed the following financial disclosure documents and did not find any discrepancies.

The table below displays the dates that financial disclosure documents were signed by Clinical Investigators.

Study Staff	Role in Study	Date Signed
Steven H. Reynolds, DO	PI	7/22/2020
(b) (6)	Sub-I	7/17/2020
(b) (6)	Sub-I	7/16/2020
(b) (6)	Sub-I	7/16/2020
(b) (6)	Sub-I	7/20/2020
(b) (6)	Sub-I	7/22/2020

CONTROL OF INVESTIGATIONAL PRODUCT (b) (6), (b) (7)(C)

We determined that the Site Signature and Delegation Log (ref: **Exhibit 5**) indicates which study personnel have authorization to prepare and to dispense the test article. Once the site dispensed study drug to subjects, the staff documented the activities on IP accountability logs. Facility tour was not conducted during this inspection; therefore, we could not confirm the condition and storage of the investigational product.

The Site Signature and Delegation Log identifies those with the authority to oversee dispensation of investigational products. Source records show the person performing this activity. We performed a spot-check of investigational product dispensation and accountability

and we noted no discrepancies. Per (b) (6), (b) (4). does all conducts (b) (4) pharmacy equipment calibration (refrigerators, freezers, etc.).

Blinding Procedures (b) (6), (b) (7)(C)

Per Section 6.3.2 of the protocol (Amendment 8), the study staff receiving, storing, dispensing, preparing, and administering the study interventions will be unblinded. All other study and site personnel will be blinded to study intervention assignments.

We reviewed the site's blinding procedures and interviewed blinded and unblinded staff during the pharmacy tour and daily discussions. We determined that the Pharmacy staff was unblinded to which treatment group study subjects were randomized to while study staff were all blinded. The site's blinding procedures (**EXHIBIT** (b) (6), (b) (7)(C) were appropriately followed to maintain the integrity of the trial.

Since the BNT162 COVID-19 vaccine candidate and saline placebo were different in physical appearance, blinding labels were used to cover the viewable area of the intervention syringes prior to it leaving the dispensary and administered to the subjects to keep the blind intact.

RECORDS CUSTODY AND RETENTION (b) (6), (b) (7)(C)

We determined that the site retained study records per the protocol and per applicable regulations. We confirmed that study records in all forms are stored securely to prevent unauthorized access and/or removal from the designated storage location. As this study is still active and ongoing, we could not confirm how the site retains records at study conclusion.

REPORTS TO SPONSOR (b) (6), (b) (7)(C)

We determined that the site submitted an SAE report to the sponsor for subject (b) (6) (ref: **Exhibit 16**), who experienced severe cough resulting in hospitalization on (b) (6). This event was reported to the sponsor on 03 Nov 2020. The subject was tested for COVID-19 with negative results, according to the report. The site alerted the IRB on 11/5/2020, with fax confirmation for the date and time of submission.

We determined that the site submitted other required reports to the sponsor per the protocol and per applicable regulations.

MONITORING (b) (6), (b) (7)(C)

We determined that the sponsor did monitor the progress of the study to assure that the site complied with the protocol and applicable regulations. Regulatory records included site monitoring reports and correspondences regarding follow-up activities with respect to noted deficiencies and recommended changes. Study monitoring was done both remotely and on-site. **Table 1** shows the type, frequency, and responsible party for study monitoring activities. Study

monitoring was conducted by Pfizer's department of Regulatory Quality Assurance and by contract research organizations (CROs)(b) (4)

Pfizer: 235 East 42nd Street New York, NY 10017
(b) (4)

Per the site initiation visit (SIV) training slides, monitoring activities are carried out using a risk-based monitoring (RBM) approach. The sponsor defined RBM as an adaptive approach to clinical trial monitoring which utilizes data and site level information to determine needs for performing on-site, remote and centralized activities and focuses resources on risk that have the most potential to impact subjects' safety and data quality integrity. Both on-site and remote visits will occur throughout the study based on output from centralized monitoring activities designed to detect areas of risk, if any, and that will require additional investigation by the Site Monitor.

Routine monitoring activities included: review of data and documents submitted through Pfizer systems, review of paper informed consent forms (ICFs), review of electronic ICFs, assessment of drug accountability, assessment of compliance with defined safety reporting process, source data verification, and protocol deviations assessments and verifications.

The table below shows study monitoring activities and dates at the site.

Type of Monitoring	Dates	Audit Conducted By
Remote/Virtual Monitoring Visit	August 27-28, 31, 2020	(b) (4)
Remote/Virtual Monitoring Visit	Sept 2-4, 2020	
Remote/Virtual Monitoring Visit	Sept 8-10, 2020	
Remote/Virtual Monitoring Visit	Sept 14-17, 2020	
Remote/Virtual Monitoring Visit	Sept 22-25, 2020	
Remote/Virtual Monitoring Visit	Oct 1-2, 2020	
Onsite	Oct 5-7, 2020	
Remote/Virtual Monitoring Visit	Oct 16, 19-20, 2020	Pfizer Regulatory Quality Assurance
Onsite	Oct 16, 19-20, 2020	(b) (4)
Remote/Virtual Monitoring Visit	Oct 18-20, 2020	
Remote/Virtual Monitoring Visit	Oct 27-30, 2020	
Remote/Virtual Monitoring Visit	Nov 2-6, 2020	

We collected the monitoring site visit log, containing the noted dates (ref: **Exhibit 17**).

REFUSALS (b) (6), (b) (7)(C)

We did not encounter any refusals.

SAMPLES COLLECTED (b) (6), (b) (7)(C)

We did not collect any samples.

GENERAL DISCUSSION WITH MANAGEMENT (b) (6), (b) (7)(C)

The following personnel were present during the discussion with management:

Name	Title
Steven H. Reynolds, DO	Clinical Investigator
Dalia R. Botros, MBBS	CNS Executive Vice President
(b) (6)	CNS Senior Project Manager
(b) (6)	CNS Pharmacist (unblinded)

We did not issue Form FDA 483 Inspectional Observations and we held no significant discussions. We noted corrections by the SMO in response to discussions held during a prior inspection (ref: **Additional Information** section).

ADDITIONAL INFORMATION (b) (6), (b) (7)(C)

The firm required face masks upon check-in, with documentation of name, date and time of entry on the daily visitor log. Each day, prior to allowing entry to restricted areas, the firm instructed us to allow an infrared forehead body temperature to be taken and to complete a COVID questionnaire. This questionnaire included a signature field, which we each left blank. The site provided hand sanitizer for daily use.

Dr. Reynolds has no prior FDA inspection history and no warnings; however, CNS, as a site management organization (SMO), has been involved in numerous FDA site inspections of various clinical investigators. Accordingly, an inspection conducted of a clinical investigator on 09/26/2019 (Op ID: 128618) revealed that CNS had limited prior history with conducting studies using electronic records; therefore, they were unfamiliar with the requirements associated with audit trails. The sponsor for this previous trial used an ERT vendor to provide and manage a database for subject eDiary entries.

During this previous inspection, I discovered that the site's access to audit trails within the ERT database was revoked by the study sponsor at site closure without the site's knowledge. The site did not review audit trails during the trial, nor did they review them when the sponsor provided final study data on CD-R, because they received communications from the sponsor that gave the impression that audit trails would be in the custody of the sponsor, and were not intended for the clinical site, per (b) (6) Subsequent discussions with the study sponsor during the inspection confirmed this impression.

After lengthy discussion with the site (and the clinical investigator), I confirmed that they learned and understood the requirements regarding audit trails for all data generated and

collected electronically during a clinical trial. I informed the firm that subsequent FDA inspections are likely to cover this topic again to determine compliance. (b) (6) Dr. Botros and the clinical investigator acknowledged my comments.

This current inspection revealed that the site met the requirements regarding their access, use and documentation of review with respect to audit trails. During the debriefing at the close of this inspection, the firm stated that they took serious consideration of my previous comments and have incorporated them into their current activities. We noted no deficiencies with respect to audit trails.

We obtained digital copies of subject's eDiary screens, with audit trails, as representative samples (ref: **Exhibits 18 – 19**). We also collected the site's Patient Identification List (ref: **Exhibit 20**).

VOLUNTARY CORRECTIONS (b) (6), (b) (7)(C)

Voluntary corrections do not apply to this assignment.

EXHIBITS COLLECTED (b) (6), (b) (7)(C)

1. Curriculum Vitae (76 pages)
2. CNS Service Contract (1 page)
3. CNS Corporate Organizational Chart (1 page)
4. Signature Sheet and Delegation of Duties Log (14 pages)
5. Form FDA 1572 Statement of Investigator (9 pages)
6. Screening and Enrollment Log and sponsor correspondence (42 pages)
7. C4591001 Clinical Protocol Amendment 7 [06 Oct 2020] (152 pages)
8. C4591001 Clinical Protocol Amendment 9 [29 Oct 2020] (155 pages)
9. Protocol Signatures of Receipt (6 pages)
10. Subject (b) (6) Signed Informed Consent Form (27 pages)
11. Participant Guide to Using the (b) (4) App [Pfizer] [07APR2020 Version: 2] (26 pages)
12. Participant Guide to Using the (b) (4) App for the COVID-19 Illness Diary [Pfizer] [19-JUN-2020 Version: 2] (18 pages)
13. Participant Guide to Using the (b) (4) App for Vaccination and COVID-19 Illness Diary [Pfizer] [19-JUN-2020 Version: 2] (28 pages)
14. App Subject Facing Screen Report [22-JUN-2020 Version 2] (57 pages)
15. Electronic Informed Consent (b) (4) (4 pages)
16. Subject (b) (6) SAE Report (16 pages)
17. Monitoring Site Visit Log (3 pages)
18. Subject vaccination eDiary print screen (sample) (5 pages)
19. Subject vaccination eDiary print screen (sample) (5 pages)
20. C4591001 Patient Identification List (21 pages)

List of Studies (4 pages)
Blinding SOPs (2 pages)

ATTACHMENTS

Form FDA 482 Notice of Inspection, 3 pages
CBER Assignment Memorandum, 5 pages
Background Information, 520 pages
Inspection Correspondence, 4 pages

SIGNATURES

(b) (6), (b) (7)(C)

Consumer Safety Officer

(b) (6), (b) (7)(C)

Consumer Safety Officer

(b) (6), (b) (7)(C)

(b) (6), (b) (7)(C)