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

This FY21 comprehensive, for cause, PDUFA user fee inspection of a Clinical Investigator was conducted in response to a high priority assignment. The inspection was conducted as requested by the Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality, per assignment memo dated 10/28/2020 **(Attachment 2)** under eNSpect OP ID 180602. The assignment requested to conduct an inspection according to Compliance Program 7348.811, Bioresearch Monitoring Clinical Investigators and Sponsor-Investigators for the following two protocols:

- Protocol C4591001, entitled; "A Phase 1/2/3 Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals," sponsored by BioNTech RNA Pharmaceuticals GmbH/Pfizer, Inc. located at 500 Arcola Road, Collegeville, PA 19436, under IND 19736.
- Protocol mRNA-1273-P301, entitled; "A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARSCoV-2 Vaccine in Adults Aged 18 Years and Older," sponsored by ModernaTX, Inc. located at 200 Technology Drive, Cambridge, MA 02139, under IND 19745.

The product name for Protocol C4591001 is COVID-19 vaccine BNT162, PF-07302048, and the product name for Protocol mRNA-1273-P301 is mRNA-1273.

This is Bruce G. Rankin, DO, Principal Investigator's seventh FDA inspection. The most recent FDA inspection was requested by the Center for Drug Evaluation and Research (CDER) and was performed between 05/04/2015 and 05/08/2015. That FDA inspection was classified as Voluntary Action Indicated (VAI). A Form FDA 483, Inspectional Observations, was issued on 05/08/2015 stating that the investigation was not conducted in accordance with the signed statement of the investigational plan. CDER reviewed Dr. Rankin's response on 05/22/2015 and issued a letter to acknowledge that Dr. Rankin implemented corrective actions to prevent the recurrence of the inspectional findings presented in Form FDA 483.

The current FDA inspection covered the authority and administration of Protocol C4591001 and Protocol mRNA-1273-P301, the IRB documentation, subject records, financial disclosures, investigational product controls, and the monitoring of the study. The inspection included the review of all available relevant records as follows: informed consents, protocols, signed investigator agreements, financial disclosure statements, IRB submissions and correspondence, adverse event reporting, clinical source data, study test article accountability, concomitant medication, subject diaries, and sponsor monitoring activities. We compared the enrollment logs for both studies to determine whether there were dual enrollments between studies. We did not identify any dual enrollments.

We reviewed the following documentation for the C4591001 (Pfizer) and the mRNA-1273-P301 (Moderna) studies:

- Protocols and amendments, and protocol deviations,

- adherence to and documentation of protocol-required visits,
- delegation of study responsibilities and financial disclosure reports,
- informed consent forms and subject medical records,
- source documents and case report forms, and Form FDA 1572s Statement of Investigator,
- subject randomization and subject discontinuation of clinical research studies,
- adverse events, serious adverse events, and deaths,
- Dr. Rankin, Principal Investigator's oversight of the study,
- site training activities and implementation of study procedures,
- site signature and responsibility logs, and site training documentation,
- administration of the investigational product as required by the protocol,
- monitoring visits and correspondence between monitors and the Principal Investigator,
- institutional review board approval letters and correspondence,
- notifications and correspondence between the sponsor and the Principal Investigator,
- drug accountability records, investigational product control, and storage.

The current inspection was conducted from 11/17/2020 to 11/24/2020. Both studies are still ongoing.

Number of subjects in the C4591001 and the mRNA-1273-P301 studies as of the inspection date:

Protocols	C4591001	mRNA-1273-P301
Total number of screened subjects	560	655
Total number of enrolled subjects	555	647
Total number of screen-failed subjects	5	8
Total number of subjects completed the study	N/A	N/A
Total number of subjects discontinued the study	15	18
Total number of serious adverse events	7	9
Total number of deaths	0	0

Initial IRB approval of Protocol C4591001 (Pfizer) was on 6/19/2020.
Initial IRB approval of Protocol mRNA-1273-P301 (Moderna) was on 7/08/2020.

The Site Initiation Visit of Protocol C4591001 (Pfizer) took place on 7/14/2020.
The Site Initiation Visit of Protocol mRNA-1273-P301 (Moderna) took place on 7/29/2020.

The first subject of Protocol C4591001 (Pfizer) signed the ICF on 7/29/20 and the last on 10/06/2020.
The first subject of Protocol mRNA-1273-P301 signed the ICF on 8/6/2020 and the last on 10/06/2020.

For Protocol C4591001 out of 555 enrolled and randomized subjects, 40 subjects' source documents were reviewed, and for Protocol mRNA-1273-P301 (Moderna) out of 647 enrolled and randomized subjects, 40 source documents were reviewed. There were a few instances of under-reporting of

Adverse Events for Protocol C4591001 (Pfizer). There was no evidence of under-reporting of Adverse Events for Protocol mRNA-1273-P301 (Moderna) study. There were 7 Serious Adverse Events for Protocol C4591001 (Pfizer) and 9 Serious Adverse Events for Protocol mRNA-1273-P301 (Moderna) with no deaths in either study.

CBER received a report raising concerns about the operations of clinical studies at the clinical site Deland Clinical Research Unit (CRU), a subsidiary of Accel Clinical Services and part of Accel Research Sites network, where Dr. Bruce Rankin is the Principal Investigator, alleging:

- Inadequacies in subject follow-up safety calls.
- Inappropriate delegation of study tasks.
- Inadequacy in subject safety during the pandemic.

We could not confirm any of the concerns raised in the report. According to the reviewed study records and available source records, study staff were properly trained and delegated, subjects were protected during the pandemic, and follow-up safety calls were assessed by a site manager. Discussion items presented during the exit meeting include:

1. Failure to complete the investigation in accordance with the investigational plan for Protocol C4591001 (Pfizer). Specifically, Dr. Rankin failed to perform FSH tests on subjects as required by protocol. We did not determine the exact number of subjects affected.

2. Failure to maintain accurate and complete case histories with respect to observations and data pertinent to the investigation Protocol C4591001 (Pfizer). Specifically, Dr. Rankin did not document all emergency phone calls made by subjects to the site. We did not determine the exact number of subjects affected.

3. Failure to report non-serious adverse events to the sponsor and IRB in a timely manner. Specifically, non-serious adverse events for four subjects out of forty subjects reviewed were not reported to the sponsor or IRB for Protocol C4591001 (Pfizer).

4. Failure to consent a subject with the most current informed consent form. Specifically, Subject (b) (6) was not consented using Version 4.0 of the informed consent form on the next visit after it was approved by the IRB and implemented at the site for Protocol C4591001 (Pfizer). Subject (b) (6) was the only subject out of forty subjects reviewed not consented with the correct version of ICF.

The current inspection found no objectionable conditions and no FDA - 483, Inspectional Observations was issued. We summarized all areas of the inspection during the exit meeting.

We informed Dr. Rankin that the inspection's final classification would be determined by the FDA's Center for Biologics Evaluation and Research. Dr. Rankin agreed with all discussion items and assured prompt correction.

No samples were collected, and there were no refusals.

ADMINISTRATIVE DATA (b) (6), (b) (7)(C)

Inspected firm:	Bruce G. Rankin, DO
Location:	860 Peachwood Drive DeLand, FL 32720
Phone:	386-785-2400
Email:	brankin@accelclinical.com
Mailing address:	Bruce G. Rankin, DO; Accel Research Sites 860 Peachwood Drive, DeLand, FL 32720
Dates of inspection:	11/17/2020, 11/18/2020, 11/19/2020, 11/20/2020, 11/24/2024
Days in the facility:	5
Participants:	(b) (6), (b) (7)(C) **Investigator** **Investigator**

Non-FDA Participants: N/A

On 11/17/2020, we, (b) (6), (b) (7)(C) FDA Investigators, arrived at Accel Research Sites. We were met by Bruce G. Rankin, DO; Principal Investigator, Melissa Hodges, Vice President, Quality and Compliance, and (b) (6), Regulatory Coordinator. We presented our credentials and issued a signed Form FDA 482, Notice of Inspection, **(Attachment 1)** to Dr. Bruce G. Rankin, Principal Investigator, who identified himself as the Principal Investigator and most responsible person for the conduct of the Pfizer C4591001 and Moderna mRNA-1273-P301 clinical research studies. We stated the purpose of the inspection and requested records for Protocol these two protocols.

Dr. Rankin stated that he conducted these two clinical research studies at Accel Research Sites located at 860 Peachwood Drive, DeLand, FL 32720. Dr. Rankin stated that all subjects for both studies were seen at this location only. Dr. Rankin's site used paper source forms to record study data. The site transcribed paper source to the electronic case report forms, which were then forwarded to the studies sponsors.

All information contained in this report was provided by Bruce G. Rankin, DO, Principal Investigator, and Melissa Hodges, VP Quality and Compliance. Ms. Melissa Hodges was present during the entire duration of the inspection.

On 11/24/2020, we held a close-out meeting with Bruce G. Rankin, DO; Principal Investigator, and Ms. Melissa Hodges, Vice President, Quality and Compliance. We summarized all areas of review during the inspection. A Form FDA 483, Inspectional Observations was not issued. We informed Dr. Rankin that the inspection's final classification would be determined by the FDA's Center for Biologics Evaluation and Research.

This report was written by (b) (6), (b) (7)(C) Sections are labeled with the initials of the writer(s). Both investigators were present on all days of the inspection, and FDA Investigator (b) (6), (b) (7)(C) was the lead on the assignment.

Post-inspectional correspondence should be sent to:

Accel Research Sites
Attn: Bruce G. Rankin, DO; Principal Investigator
860 Peachwood Drive
DeLand, FL 32720
Bruce G. Rankin, DO; Principal Investigator's email is: BRankin@accelclinical.com

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

Bruce G. Rankin, DO, earned his Doctor of Osteopathic Medicine from the Nova Southeastern College of Osteopathic Medicine, North Miami Beach, Florida, in 1985. He then completed his internship at the Doctors General Hospital, Plantation, FL in 1986, and his residency at the Family Medicine, Southeastern Medicine Center, North Miami Beach, FL, in 1987. Dr. Rankin is board certified by the American College of Family Practitioners in Osteopathic Medicine and Surgery. He is licensed to practice medicine in the State of Florida. Dr. Rankin's CV is included as **Exhibit 1**.

Dr. Rankin, Principal Investigator, has been an employee of Accel Research Sites since 1998 as Medical Director. Dr. Rankin said that he has no financial interest or ownership in Accel Research Sites. With Accel Research Sites, he has been the principal investigator on several clinical trials. He has worked with many different sponsors and CROs. Dr. Rankin stated that he devotes (b) (4), (b) (6) of his time to research and (b) (4), (b) (6) to his private practice, which is located a mile away from the Accel research Sites at the Family Practice of West Volusia, 999 W. Plymouth Avenue, DeLand, FL 32720. Dr. Rankin stated that delegated Sub-Investigators were available during his private practice hours. Dr. Rankin' List of Studies is included as **Exhibit 2**.

Accel Research Sites' regular business hours are 7:00 am to 4:00 pm Monday thru Friday. The Accel Research Sites is closed on Saturdays and Sundays. Dr. Rankin stated that the Accel Research Sites added additional hours and days to complete Protocol C4591001 and Protocol mRNA-1273-P301 study visits. The organization chart is included as **Exhibit 3**, and the site's floorplan as **Exhibit 4**.

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

Dr. Rankin is a Principal Investigator and, as such, is not involved in the distribution and marketing of regulated products.

For Protocol C4591001 (Pfizer), Dr. Rankin received a total of (b) (4) shipments of Investigational Product (IP) as of this inspection date on the following dates: (b) (4) The investigational product was shipped to the clinical site from (b) (4) (b) (4) on behalf of the sponsor BioNTech RNA Pharmaceuticals GmbH/Pfizer, Inc.

For Protocol mRNA-1273-P301 (Moderna), Dr. Rankin received a total of (b) (4) shipments of Investigational Product as of this inspection date on the following dates: (b) (4) . The investigational product was shipped to the clinical site from (b) (4) on behalf of the sponsor ModernaTX, Inc.

Dr. Rankin stated that all IP shipments arrived with no temperature excursions, and no quarantine of IP was needed. We randomly checked temperature logs for both studies and did not note any temperature excursions.

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

Dr. Rankin is the clinical investigator for Protocol C4591001 and Protocol mRNA-1273-P301 that are both FDA regulated human clinical trials involving an investigational product, conducted under IND 19736 for the C4591001 study and IND 19745 for the mRNA-1273-P301 study.

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

Bruce G. Rankin, DO, Principal Investigator – Dr. Rankin stated that he was the Principal Investigator and remained blinded during both studies. He stated that he was the most responsible person for C4591001 and mRNA-1273-P301 clinical research studies and signed the Form FDA 1572s. According to Dr. Rankin, he was responsible for all safety and oversight of both clinical research trials. Dr. Rankin said that he devotes seventy percent of his time to research and thirty percent to private medical practice. Dr. Rankin said that he had always had a medical professional, such as a medical doctor or a nurse practitioner, on-site when he was in his private practice to cover all medical aspects of participation in clinical trials, including grading of COVID 19 symptoms, safety assessments, ECG interpretations, review laboratory test results, adverse and serious adverse events, physical examinations, and medical-related exclusions. We confirmed that the Principal Investigator was trained in both protocols before the first subjects were screened. Dr. Rankin was available to answer any questions throughout the inspection.

Ms. Melissa Hodges, Vice President of Quality and Compliance – Ms. Hodges stated that she was trained in study-related activities, such as overseeing study-related procedures to ensure they were

carried out in accordance with the requirements of study protocols. She said that she helped Dr. Rankin with all scheduled study events and remained blinded during both studies. She said that she obtained Informed Consent Forms, completed case report forms, discussed concomitant medications with subjects, obtained nasopharyngeal swabs, drew and processed lab specimens, reviewed, subjects' charts, and made COVID illness safety calls. Ms. Hodges was our main point of contact throughout the inspection and provided us with copies of requested documents. Ms. Hodges was present during the entire duration of the inspection.

(b) (6) – (b) (6) stated that (b) (6) remained blinded during both studies. (b) (6) said that she obtained Informed Consent Forms, discussed medical history and concomitant medications with subjects, drew and processed lab specimens, completed case report forms, obtained nasopharyngeal swabs, reviewed, subjects' charts, and made COVID illness safety calls.

(b) (6) – (b) (6) said that (b) (6) and remained blinded during both studies. (b) (6) stated that she obtained Informed Consent Forms, completed case report forms, discussed concomitant medications with subjects, obtained nasopharyngeal swabs, drew and processed lab specimens, reviewed, subjects' charts, and made COVID illness safety calls.

Dr. Rankin stated that only the pharmacy personnel were the unblinded staff for both studies. Dr. Rankin said that no subject had to be unblinded as of the inspection date in either studies.

The following unblinded personnel took part in the Pfizer C4591001 clinical research study:

(b) (6)

The following blinded Sub-Investigators took part in the Pfizer C4591001 clinical research study:

(b) (6)

The following unblinded personnel took part in the Moderna mRNA-1273-P301 clinical research stu :

(b) (6)

(b) (6)

The following blinded Sub-Investigators took part in the Moderna mRNA-1273-P301 clinical research study:

(b) (6)

Dr. Rankin stated that the sub-investigators had the following delegated responsibilities: discussed informed consent form with subjects as needed, assesses eligibility criteria and contraindications to vaccinations, conducted physical exams, obtained subjects' medical information such as demographics data, medical history and concomitant medication, evaluated continuous eligibility of subjects, assessed adverse and serious adverse events, reviewed laboratory results, and reviewed charts and enrollment logs.

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

Pfizer Protocol C4591001:
The Site Initiation Visit (SIV) for Protocol C4591001 took place virtually on 7/14/20. It was conducted by (b) (6) a monitor from (b) (4) the Contract Research Organization (CRO) hired by the sponsor.

According to the training documents, (b) (6) covered the following topics during the SIV:

- Protocol and compliance,
- Subject population and compliance,
- Informed consent and essential documents,
- Investigator and staff qualifications and responsibilities,
- Source data/documentation including case report forms,
- Safety reporting and equipment,
- Investigational product and study supplies,
- Institutional Review Board, audits, and regulatory authority inspections.

Moderna Protocol mRNA-1273-P301:
The SIV for Protocol mRNA-1273-P301 was on 7/29/2020 and was conducted by (b) (6), a monitor from (b) (4) Clinical Research Organization.

According to the training documents, (b) (6) covered the following topics during the SIV:

- Protocol and compliance,
- Informed consent and Institutional Review Board,
- Investigational product and study supplies,
- Safety reporting and regulatory authority inspections,
- Investigator and staff qualifications and responsibilities,
- Source data and documentation including case report forms,
- Safety reporting and subject population and compliance.

Dr. Rankin stated he provided training throughout the study on topics such as the protocol and amendments, Informed Consent Form (ICF), adverse events (AE) and serious adverse event (SAE) procedures, and other clinical procedures for both studies. Dr. Rankin said that the monitors also trained him and the staff throughout both studies. We reviewed the training records for the research personnel involved in the protocol's conduct and found no observations.

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

Dr. Rankin was aware of the investigational product's status, the nature of the Pfizer Protocol C4591001 and Moderna Protocol mRNA-1273-P301, and his obligations as the clinical investigator. The authority for the conduct of both studies' various aspects was delegated appropriately per the Site Delegation Log. We confirmed that the delegated research staff had the education and training for such tasks. Site Delegation Logs for Pfizer Protocol C4591001 are included as **Exhibit 9**, and for Moderna Protocol mRNA-1273-P301 as **Exhibit 10**.

Ms. Hodges provided a list of studies Dr. Rankin had conducted over the past five years **(Exhibit #2)**

Pfizer Protocol C4591001:
We confirmed that the site maintained the Form FDA 1572 forms on file. The initial FDA 1572 for the study was signed and dated by Dr. Rankin on 6/14/20. Additional FDA 1572s were signed on 6/23/20, 7/14/20, 7/21/20, 7/24/20, 7/29/20, 8/11/20, 8/19/20, 8/24/20, 9/3/20, 9/11/20, 9/13/20, 9/18/20, 10/13/20, and 10/29/20, to update study personnel. All Form FDA1572s are included as **Exhibit 7**.

The first subject was screened, signed the informed consent form (ICF), and randomized on 7/29/20. The first and last subjects were randomized and received the investigational product on 7/29/20 and 10/6/20 respectively. The study is still ongoing.

According to Dr. Rankin, subjects were screened and seen for both clinical research studies only at Accel Research Sites at 860 Peachwood Drive, DeLand, FL 32720. Dr. Rankin said that subjects for both studies were recruited from Accel Research Sites' database. The Principal Investigator stated that the IRB approved advertisements and social media, but they were not used for this study. The Screening and Enrollment Log for the study was collected as **Exhibit 5**. The log accurately reflects the number of subjects screened and randomized in the study.

Dr. Rankin said that for both studies only the urine pregnancy test for women of childbearing potential was done at the Accel Clinical Sites' local laboratory. We checked the Accel Clinical Sites' Clinical Laboratory Improvements Act (CLIA) certificate which was posted inside the laboratory.

The regulatory files for both studies contained the Certification for the Clinical Laboratory Improvement Act (CLIA) and reference ranges on file.

The central clinical laboratory's name and addresses for Protocol C5491001 were listed on Form FDA 1572 as follows:

(b) (4)

Moderna Protocol mRNA-1273-P301:
We confirmed that the site maintained the Form FDA 1572 forms on file. The initial FDA 1572 for the study was signed and dated by Dr. Rankin on 6/23/2020. Additional FDA 1572s were signed on 7/14/2020, 7/21/2020, 7/24/2020, 8/03/2020, 8/05/2020, 8/10/2020, 8/20/2020, 8/24/2020, 8/28/2020, 9/03/2020, 9/08/2020, 9/11/2020, 9/13/2020, 9/18/2020, 10/13/2020, and 10/22/2020 either to add a Sub-Investigator or to remove a Sub-Investigator. All Form FDA1572s are included as **Exhibit 8**.

According to Dr. Rankin, subjects were screened and seen for the mRNA-1273-P301 clinical research study at 860 Peachwood Drive, DeLand, FL 32720. Dr. Rankin said that subjects for this study were recruited from Accel Research Sites' database. He stated that advertisements and social media were approved by the IRB, but not used for this study. The Screening and Enrollment Log for the study was collected as **Exhibit 6**. The log accurately reflects the number of subjects screened and randomized in the study.

The central clinical laboratory's name and address for Protocol mRNA-1273-P301 were listed on Form FDA 1572 as follows:

(b) (4)

We compared the enrollment logs for both studies to determine whether there were dual enrollments between studies. We did not identify any dual enrollments.

In speaking with Dr. Rankin and reviewing selected study records, it was clear that he maintained control for both clinical research studies and provided oversight for the C4591001 and mRNA-1273-P301 clinical research studies. There was no evidence that Dr. Rankin used any coercive methods or procedures to recruit subjects. Dr. Rankin did not appear to promote the investigational products as being safe and effective for its intended use.

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

We reviewed the ClinicaTrials.gov database to ensure that both the Pfizer C4591001 and the Moderna mRNA-1273-P301 clinical research studies have been registered on the ClinicalTrials.gov website.

We confirmed that both clinical research studies had been registered on the website with no posted results. Dr. Rankin stated that he has no agreement with these two studies' sponsors to update any information on the ClinicaTrial.gov website.

The statement "The description of this clinical trial will be available on the www.ClinicalTrials.gov, as required by U.S. Law" was included in the Informed Consent Forms for both clinical research studies.

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

Pfizer
Protocol C4591001 entitled, "A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, And Efficacy Of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 In Healthy Adults," was conducted with the following objectives:

Primary Efficacy Objectives for Phase 2/3:

- To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 in participants without evidence of infection before vaccination.
- To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 in participants with and without evidence of infection before vaccination.

Primary Safety Objective for Phase 2/3:

- To define the safety profile of prophylactic BNT162b2 in all participants randomized in Phase 2/3.

Ms. Hodges stated that multiple protocol amendments were used for the study's conduct, beginning with Amendment 5 dated 6/24/20. According to the regulatory binder, Amendment 9, dated 10/29/20, is currently being utilized. Numerous changes spanning the protocol amendments included: adding secondary phase 2/3 endpoints, clarifying endpoint and interim analyses, expanding the age range of subjects to include subjects as young as 12 and as old as 85, and clarifying protocol definitions. We determined that all protocols and amendments were approved by the IRB prior to initiation of any study related procedures and prior to implementing any changes at the clinical sites.

The protocols onsite matched the protocols provided in the background materials, except for Amendment 9, which is included in this report as **Exhibit #21.** All protocol amendments were approved by the IRB prior to implementation.

We reviewed the protocol deviation log provided and noted that protocol deviations were reported to the IRB and Monitor as necessary. There were four discrepancies between the site's records and the monitoring letters regarding protocol deviation reporting for Protocol C4591001 **(Exhibit 11)**. Please see the source documentation and item number three of the General Discussion with Management Section for more details.

No other discrepancies were discovered regarding the investigator following study related procedures to include: subjects meeting inclusion/exclusion criteria, number of subjects enrolled, blinding procedures, required study procedures, storage of investigational product, administration of investigational product, and data collection.

Moderna

Protocol mRNA-1273-P301, entitled; "A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARSCoV-2 Vaccine in Adults Aged 18 Years and Older," was conducted with the following objectives:

Primary Efficacy Endpoints - To demonstrate the efficacy of mRNA-1273 to prevent COVID-19. Vaccine efficacy of mRNA-1273 to prevent the first occurrence of COVID-19 starting 14 days after the second dose of the investigational product (IP), where COVID-19 is defined as a symptomatic disease based on the following criteria:

- The participant must have experienced at least two of the following systemic symptoms: Fever (≥ 38°C), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR
- The participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and
- The participant must have at least one nasopharyngeal (NP) swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR).

Primary Safety Endpoint - To evaluate the safety and reactogenicity of 2 injections of the mRNA-1273 vaccine given 28 days apart:

- Solicited local and systemic Adverse Reactions (ARs) through 7 days after each dose of IP.
- Unsolicited AEs through 28 days after each dose of IP.
- Medically attended adverse events (MAAEs) or AEs, leading to withdrawal through the entire study period.
- SAEs throughout the entire study period.

We reviewed the regulatory binder and found that, multiple protocol amendments were used for the conduct of the study at Dr. Rankin's site. Dr. Rankin said that the site began with Amendment 1. The following Protocol amendments were present in the regulatory binder:
IRB approval on 8/08/2020 – Protocol Amendment 1, (Dated 26 June 2020),
IRB approval on 8/12/2020 – Protocol Amendment 2, (Dated 31 Jul 2020),
IRB approval on 8/24/2020 – Protocol Amendment 3, (Dated 20 Aug 2020),
IRB approval on 10/01/2020 – Protocol Amendment 4 (Dated 30 Sep 2020),
IRB approval on 11/13/2020 – Protocol Amendment 5 (Dated 11 Nov 2020).

The protocols for the Moderna study found onsite matched the protocols provided in the background materials. The IRB approved all protocol amendments prior to implementation.

A protocol deviation log provided by the monitor was reviewed **(Exhibit 12)**, and protocol deviations were reported to the IRB and Monitor as necessary. Our review of the source documents did not discover discrepancies regarding study-related procedures for Protocol mRNA-1273-P301.

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

Pfizer Protocol C4591001:
The Institutional Review Board (IRB) used was (b) (4) IRB located at (b) (4) (b) (4). The IRB was chaired by (b) (6)
(b) (4) IRB approval and closure dates:

IRB approval and closure
Approval: 6/19/20
Closure: N/A

Our review of the ICFs found that they contained all the required basic elements. Our review of the ICFs also found that they had the required ClinicalTrials.gov statement.

According to Dr. Rankin, the IRB-approved advertisement was not used to recruit subjects. Regulatory binders were well maintained with the required regulatory correspondence, including the study's initial review and approval. Dr. Rankin stated that required communications were reported promptly to the IRB.

The Initial IRB approval of Protocol C4591001was on 6/19/2020, and the (b) (4) IRB approved the following documentation:

- Principal Investigator,
- Protocol (Date: 15 Jun 2020),
- Main Informed Consent Form (English), dated 7/29/2020,
- Advertisement,
- (b) (4) Directions.

(b) (4) IRB approved the following documents with these approval dates:
6/19/2020 - Investigator, Protocol dated 4/15/20, ICF English dated 7/29/20, advertisements, (b) (4) Directions),
7/31/2020 - IRB approval (amendment 5 dated 7/24/20, ICF English Version 3),
9/11/2020 - IRB approval (amendment 6 dated 9/8/20, ICF Spanish/English Version 4),
10/10/2020 - IRB approval (amendment 7 dated 10/6/20, ICF English Version 5),
10/16/2020 - IRB approval (amendment 8 dated 10/15/20),
11/05/2020 - IRB approval (amendment 9 dated 10/29/20).
Sample IRB approval letters for Protocol C4591001 and Amendment 9 of the protocol are included as **Exhibit 21**.

The ICFs were approved by the IRB and contained all the basic elements, including the ClinicalTrials.gov statement as required by 21 CFR 50.25 (b)(c).

Moderna Protocol mRNA-1273-P301:
The Institutional Review Board (IRB) used was (b) (4) IRB, located at (b) (4) (b) (4). The chair for (b) (4) IRB was (b) (6) (b) (6) Regulatory binders were well maintained with the required regulatory correspondence.

(b) (4) IRB approval and closure dates:

IRB approval and closure
Approval: 7/08/2020
Closure: N/A

Our review of the ICFs found that they contained all the required basic elements. Our review of the ICFs also found that they had the required ClinicalTrials.gov statement.

The Initial IRB approval of Protocol mRNA-1273-P301 was on 7/08/2020, and the (b) (4) IRB approved the following documentation:

- Protocol Amendment 1 (Date: 26 Jun 2020),
- Main Informed Consent Form, Version 30 Jun 2020, Revised 8 Jul 2020),
- Investigator Brochure for mRNA-1273-P301 (Version 3.0, Dated 15 June 2020),
- Telephone Script (Dated: 19 June 2020),

- Item Specifications, Digital Thermometer (Not Dated),
- Item Specifications, paper (b) (4) , (Generated 06/03/2020).

(b) (4) IRB approved the following documents with these approval dates:

7/09/2020 Instructions for home saliva collection (V0.3, ed 29 Jun 20),
7/13/2020 Poster, flyer, bulletin board ad (V1, Dated 6 July 2020),
7/16/2020 PowerPoint presentation, Outreach Letter Visit guide, Study fact Sheet,
7/15/2020 Main ICF (Version 1 Jul 2020, Revised 17 Jul 2020),
7/20/2020 Automated Patient email, Browser login page and screen, Mobile Application Login,
7/22/2020 mRNA-1273-P301screening tool for Sars-CoV-2 exposure risk,
7/23/2020 Investigator Brochure,
7/29/2020 US Spanish mRNA-1273-P301screening tool Sars-CoV-2 exposure risk,
7/30/2020 Community Information PowerPoint, Outreach letter, Media Relation Content,
7/31/2020 Spanish Item Specifications and Instructions, Spanish PowerPoint and Visit Guide,
8/03/2020 Spanish Internet Webpage, Visit guide, Outreach letter,
8/04/2020 Spanish translations, fact sheets, and appointment reminders,
8/06/2020 Spanish illness packet,
8/06/2020 Protocol Amendment 2, (Dated 31Jul2020),
8/12/2020 Mass print publication, Internet webpage,
8/19/2020 Spanish Mass distributed print publication,
8/21/2020 Spanish community outreach PPT and Letter,
8/24/2020 Protocol Amendment 3, (Dated 20 Aug 2020),
9/8 & 10/2020 Internet Participant Protocol Summary and Study Brochure (Dated 08 Sep 2020),
9/11/2020 Internet Participant Prescreened, Social Media Post, Facebook Post,
9/14/2020 Safety Call Script (V2.0 Dated 09 Sep 2020),
9/17/2020 Webpage Banner, (b) (4) Post,
9/24/2020 Internet (b) (4) Email, and Submission letter,
9/28/2020 Email Text "Final Reminder: COVID Vaccine Trial in Your Area",
10/01/2020 Protocol Amendment 4 (Dated 30 Sep 2020),
10/28/2020 Addendum # 1 for Investigator Brochure Dated 01 Oct 2020),
11/02/2020 Telephone Screening script Safety call script (Version 3, dated 31 Oct 2020),
11/13/2020 Protocol Amendment 5 (Dated 11 Nov 2020).

According to Dr. Rankin, the IRB approved advertisement was not used to recruit subjects. Required communications were reported promptly to the IRB. Sample IRB approval letters for Protocol mRNA-1273-P301 are included as **Exhibit 22**.

SUBJECT RECORDS

INFORMED CONSENT FORM (b) (6), (b) (7)(C)

We reviewed the signed informed consent forms (ICFs) for 40 subjects enrolled for Pfizer Protocol C4591001 and 40 subjects enrolled for Moderna Protocol mRNA-1273-P301 and found that the ICFs were obtained by delegated study personnel.

According to Dr. Rankin, he performed the consenting procedure for each subject in a private exam room, giving the subject time to read the ICF and ask him questions. Delegated Study Coordinators were responsible for obtaining informed consent forms. Dr. Rankin stated that he was available to answer subjects' questions. Subjects were provided with a copy of the signed ICF for their records, per source documentation. No study procedures were performed before the ICF being obtained. Accel Research Sites has standard operating procedures (SOPs) related to the informed consent process. Our review of the ICF process found the site followed its SOPs. One deficiency was identified for Pfizer Protocol C4591001. Subject (b) (6) was consented with the wrong consent at study enrollment. At study visit #1, which took place on 10/6/20, subject (b) (6) was consented with version 3.0 of the ICF, which was IRB approved on 7/31/20.

Version 3.0 was obsolete at the time of subject (b) (6) enrollment and version 4.0 of the ICF was the most recent ICF at the time as it was IRB approved on 9/11/20. At Study Visit #2, which took place on 10/29/2020, subject (b) (6) was not reconsented with version 4.0 of the ICF.

Pfizer Protocol C4591001:

No.	Type of Consent	Version No.	IRB Approval Date	Implementation Date
1.	ICF and Authorization to Use and Disclose Protected Health Information	1	6/19/20	6/19/20
2.	ICF and Authorization to Use and Disclose Protected Health Information Corrected	1.0	6/25/20	6/25/20
3.	ICF and Authorization to Use and Disclose Protected Health Information As Modified	1.0	7/6/20	7/7/20
4.	ICF and Authorization to Use and Disclose Protected Health Information	2.0	7/13/20	7/17/20
5.	ICF and Authorization to Use and Disclose Protected Health Information	3.0	7/31/20	8/3/20
6.	ICF and Authorization to Use and Disclose Protected Health Information	4.0	9/11/20	9/14/20

7.	ICF and Authorization to Use and Disclose Protected Health Information	5.0	10/10/20	10/12/20

A signed and dated copy of ICF for the first subject enrolled in Protocol C4591001 is included as **Exhibit 13**.

Moderna Protocol mRNA-1273-P301:

No.	Type of Consent	Version No.	IRB Approval Date	Implementation Date
1.	ICF and Authorization to Use and Disclose Protected Health Information Revised 08Jul2020	8-Jul-20	7/08/2020	7/08/2020
2.	ICF and Authorization to Use and Disclose Protected Health Information Revised 17Jul2020	17-Jul-20	7/17/2020	7/21/2020
3.	ICF and Authorization to Use and Disclose Protected Health Information Revised 06Aug2020	6-Aug-20	8/06/2020	8/13/2020
4.	ICF and Authorization to Use and Disclose Protected Health Information Revised 06Aug2020	6-Aug-20	8/17/2020	8/17/2020

A signed and dated copy of ICF for the first subject enrolled in Protocol mRNA-1273-P301 is included as **Exhibit 14**.

SOURCE DOCUMENTATION (b) (6), (b) (7)(C)

The source documents for the two studies covered during tis inspection consisted of a binder for each study subject containing case report forms created by the site. All source documents were in paper form. The records were attributable, legible, contemporaneous, original, accurate, and well organized. There was adequate documentation to infer that all subjects were alive and available for the duration of their stated participation in both clinical research studies. Our review of the records and staff practices found that Dr. Rankin, was knowledgeable about subjects' conditions and study procedures. We confirmed that he maintained control over the study and the investigational product.

We reviewed source records for completeness, accuracy, and compliance with applicable regulations. This inspection did not involve data audits because these two studies were ongoing at the time of the inspection.

Number of subjects in the Pfizer C4591001 and the Moderna mRNA-1273-P301 studies as of the inspection date:

Protocols	C4591001 Pfizer	mRNA-1273-P301 Moderna
Total number of screened subjects	560	655
Total number of enrolled subjects	555	647
Total number of screen-failed subjects	5	8
Total number of subjects completed the study	N/A	N/A
Total number of subjects discontinued the study	15	18
Total number of serious adverse events	7	9
Total number of deaths	0	0

Source Reviewed for Protocol C4591001: 40 of 555 Enrolled Subjects.
Informed Consent Forms reviewed for Protocol C4591001: 40 of 560 Screened Subjects.
The Enrollment Log for the C4591001 study is included as **Exhibit 5**.

Source Reviewed for Protocol mRNA-1273-P301: 40 of 647 Enrolled Subjects.
Informed Consent Forms reviewed for Protocol mRNA-1273-P301: 40 of 655 Screened Subjects.
The Enrollment Log for the mRNA-1273-P301 study is included as **Exhibit 6**.

We evaluated the site's protocol adherence, and we reviewed randomly selected protocol deviations documented in the deviation logs and adverse events documented in the adverse events logs and compared to the subjects' source documents, and they matched. We also confirmed that Accel Research Sites has standard operating procedures regarding subject follow-ups.

Dr. Rankin stated that for both studies, all deviations were promptly reported to the sponsors. The Deviation Log for the Pfizer C4591001 study is included as **Exhibit 11** and for the Moderna mRNA-1273-P301 study as **Exhibit 12**. Refer to the PROTOCOL section of this report for additional information. The index of Accel Research Sites' SOP is included as **Exhibit 27**.

Pfizer Protocol C4591001:
Our review of study records found that Dr. Rankin did not perform the FSH test as required per Protocol C4591001 Section10.4.3 for postmenopausal females less than 60 years of age, without either alternative medical cause/ permanent infertility or with 12 months of no menses. We did not determine the exact number of subjects affected. Please refer to discussion item number one in the General Discussion with Management section for further discussion.

Dr. Rankin did not document emergency phone calls, which had come into the former receptionist's phone after putting her phone on DND (Do not Disturb) mode for Protocol C4591001. Please refer to discussion item number two in the General Discussion with Management section for further discussion.

There were four discrepancies between the site's records and the electronic case report forms (CRFs) for Protocol C4591001 **(Exhibit 25)**.

a. Subject (b) (6) had one unreported AE for headache on 7/30/2020.
b. Subject (b) (6) had one unreported AE for injection site tenderness on 7/29/2020.
c. Subject (b) (6) had one unreported AE for urticaria (hives) on 9/14/2020.
d. Subject (b) (6) had three unreported AEs for diarrhea on 8/21/2020, fatigue and generalized joint pain on 8/22/2020.

Please refer to discussion item number three in the General Discussion with Management section for further discussion.

Subject (b) (6) was not reconsented for Protocol C4591001 with the newer, Version 4.0, of the Informed Consent Form (ICF). At study visit #1, which took place on 10/6/20, subject (b) (6) was consented with version 3.0 of the ICF, which was IRB approved on 7/31/20. Version 3.0 was obsolete at the time of subject (b) (6)'s enrollment and version 4.0 of the ICF was the most recent ICF at the time as it was IRB approved on 9/11/20. At Study Visit #2, which took place on 10/29/2020, subject (b) (6) was not reconsented with version 4.0 of the ICF. This incident was documented as a deviation but not submitted to the IRB until (b) (6), (b) (7)(C) FDA Investigator, pointed this oversight out to the Study Coordinator. The Deviation Log for the C4591001 study is included as **Exhibit 11**. The site regulatory coordinator, (b) (6), then submitted this as a deviation to the IRB **(Exhibit 26)**. Please refer to discussion item number four in the General Discussion with Management section for further discussion.

According to Dr. Rankin, there were seven serious adverse events and none of them were related to the study medication. There were no deaths in the C4591001 clinical research study. The Serious Adverse Events Log is included as **Exhibit 11**. A sample Adverse Event form is included as **Exhibit 15**.

Moderna Protocol mRNA-1273-P301:
According to Dr. Rankin, there were nine serious adverse events and none of them were related to the study medication. There were no deaths in this clinical research study. There was no evidence of under-reporting of Adverse Events in the mRNA-1273-P301 clinical research study. The Serious Adverse Events Log is included as **Exhibit 12**.

The source documents consisted of a binder for each study subject containing case report forms created by the study site. All source documents were in paper form. The records were attributable, legible, contemporaneous, original, accurate, and well organized. There was adequate documentation to infer that all the subjects were alive and available for the duration of their stated participation in the studies. Our review of the records and staff practices found that Dr. Rankin was knowledgeable about the subject's conditions and study procedures. We confirmed that he maintained control over the study and the investigational product.

We evaluated the site's protocol adherence, and we compared randomly selected protocol deviations documented in the deviation logs to the subjects' source documentation and found that they were

recorded accurately. We also confirmed that Accel Research Sites has standard operating procedures (SOPs) regarding subject follow-ups. All deviations reported to the sponsor were verified against source documents. Our review found no discrepancies between the source documents and the deviation reported to the sponsor. The Deviation Log for the mRNA-1273-P301 study is included as **Exhibit 12**. The index of Accel Research Sites' SOPs is included as **Exhibit 27**.

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

All study records were made available during the inspection, including regulatory binders and subjects' source records for Protocol C4591001 and Protocol mRNA-1273-P301. Dr. Rankin stated that no other study records were used at the site.

Bruce G. Rankin, Principal Investigator, signed the Independent Contractor's Agreement with University Clinical Research Deland, LLC doing business as Accel Research Sites on 05/21/2007. The Independent Contractor's Agreement between Dr. Rankin and University Clinical Research is included as **Exhibit 28**. This agreement states that Dr. Rankin was hired as an independent contractor to perform human clinical research for the company to provide examinations, treatment, procedures, consulting, monitoring, and other professional medical services to patients as required under the Protocols.

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

No subjects were interviewed during this inspection. Please refer to the INDIVIDUAL RESPONSIBILITIES AND PERSONS INTERVIEWED section of this report for the personnel that was interviewed.

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

The financial disclosure forms were available for Dr. Rankin and all Sub -Investigators in the studies' regulatory binders for Pfizer Protocol C4591001 and Moderna Protocol mRNA-1273-P301. We verified that Dr. Rankin and all other Sub-Investigators participating in the C4591001 and mRNA-1273-P301 clinical research studies signed the financial disclosure forms and had no financial interests to declare.

Dr. Rankin stated that financial disclosure information was not updated since there have not been any relevant changes since they were originally completed. We found all financial disclosure forms for Protocol C4591001 and mRNA-1273-P301 to be appropriately completed and signed by the Principal Investigators and Sub-Investigators.

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

The source documents used at the site for Protocol mRNA-1273-P3901 and Protocol C4591001 were paper records. According to Ms. Hodges, there were no electronic medical records used at the site. Data was transcribed from the source records into the EDC by delegated Study Coordinators at the Accel Research Sites. Dr. Rankin stated that access was controlled by user name and password

Access to electronic case report forms was provided to Dr. Rankin by the sponsors after the initiation of the study. All users of this system had unique login/password access. There was an audit trail which recorded all activity. I confirmed that electronic case report forms contained valid audit trails.Dr. Rankin stated that he reviewed the EDC for both studies and placed his electronic signature confirming the information entered was correct. All queries were answered by Dr. Rankin or delegated Sub-Investigators. An audit trail was available in the EDC system.

Dr. Rankin said that subjects were required to complete a reactogenicity e-diary through the (b) (4) App application as per Pfizer Protocol C4591001. Ms. Hodges stated that subjects recorded events that occurred in the seven days after administration of the study intervention.

We reviewed random (b) (4) App Subject reports for the e-diary and compared findings to the deviation logs and monitoring reports. There were no available data listings provided with the assignment.

For Moderna Protocol mRNA-1273-P3901, at each dosing visit, subjects were instructed to report adverse reactions in their eDiary. Dr. Rankin stated that adverse reactions were assessed for seven days after each IP dose, and unsolicited adverse events were assessed for twenty-eight days after each IP dose as per the protocol throughout the study. Ms. Hodges stated that the mRNA-1273-P3901 study has been using the (b) (4) Application as the eDiary to record any COVID-19 symptoms. We did not observe any discrepancies between the deviation logs and monitoring reports for this study.

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

Dr. Rankin said that for Protocol mRNA-1273-P3901 and Protocol C4591001staff was delegated duties relating to investigational product according to their training and experience.

According to Dr. Rankin, in both studies, all investigational products (IPs) were dispensed to subjects by delegated unblinded study staff. We confirmed that IP accountability for both studies was conducted by an unblinded clinical research pharmacist and verified by an unblinded contract research associate as per both protocols. The Master IP accountability log for protocol Pfizer C4591001 is included as **Exhibit 23,** and for protocol Moderna mRNA-1273-P301 as **Exhibit 24**.

Ms. Melissa Hodges, VP of Quality Compliance, stated that Accel Research Sites' front double doors were locked after hours. Subjects and outside visitors can only enter the clinic from the lobby, with the site staff granting them access.

Ms. Hodges said that delegated unblinded pharmacists assessed investigational products (IPs) upon receipt to ensure that the shipments were received within the temperature range required by both protocols. Upon receipt, Ms. Hodges said that all IPs were immediately reconciled against the packing list and confirmed into the IWRS system.

According to Ms. Hodges, IPs were stored in the temperature-controlled IP storage room inside a locked freezer. The IP storage room was always locked and had a scanner to allow entry. Only unblinded delegated pharmacists had access to the IP storage room. The IP was stored in a double locked room with temperature controls. There were no temperature excursions noted.

Ms. Hodges stated that the preparation and administration of the investigational drug products required an aseptic technique. Dr. Rankin said that delegated employees were gowned, wore a face shield and hand gloves during the preparation of the IPs. Dr. Rankin stated that all handling and preparation of the drug products were carried out in a laminar airflow hood as per the sponsors' recommendations.

Ms. Hodges stated that IP would be returned to the sponsors' for destruction at the end of these two studies. The unblinded monitor will initiate the IP return during the last onsite visits, and he/she will prepare both IP shipments for return.

We spot-checked unblinded monitoring reports, and we confirmed that monitoring of investigational products was performed by the study monitors for the C4591001 and the mRNA-1273-P301 studies.

We performed IP reconciliation for the Pfizer C4591001 and the Moderna mRNA-1273-P301 studies. We confirmed that IP accountability and disposition were adequately documented in the IP Accountability logbooks for both studies. We reviewed the amount of IP received, dispensed, and held on-site. Ms. Hodges stated that once the studies close, the unblinded monitor will ship unused IP back to study sponsors. We reviewed compliance for dispensed vaccines in the source documentation, compared it to the protocol requirements, and found it matched both studies' protocol requirements. We verified that unblinded IP accountability logs were correct, and the received vaccine vials matched the dispensed and on-site left-over amount.

We also reviewed all IP shipment receipts and dispensing forms for the accuracy and completeness of received, stored, administered, and vaccine vials kept on-site for Protocol C4591001 and Protocol mRNA-1273-P301, and we found no inconsistencies. We reviewed the product labeling for both studies but did not collect copies. We reviewed IP storage temperature log books for both studies and did not observe any temperature excursions during storage.

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

Ms. Melissa Hodges, VP of Quality and Compliance, stated that all paper study records for the C4591001 and mRNA-1273-P301 clinical trials are stored on-site. All requested study records were available for inspection.

Ms. Hodges said that once these two studies close, the long-term storage of archived clinical research documents would be at the following contracted independent storage facility:

(b) (4)

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

The sponsor for Protocol C4591001 was BioNTech RNA Pharmaceuticals GmbH/Pfizer, Inc., located at 500 Arcola Road, Collegeville, PA 19436, and for Protocol mRNA-1273-P3901 was ModernaTX, Inc., located at 200 Technology Drive, Cambridge, MA 02139. Dr. Rankin stated, and we verified that the required reports were submitted to both sponsors. Communication between Dr. Rankin and both sponsors were conducted via e-mail and newsletters.

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

Pfizer Protocol C4591001:
The sponsor contracted with (b) (4) Clinical Research Organization (CRO) to monitor this study. The CRO is located at (b) (4)
27709. The sponsor of this study, BioNTech RNA Pharmaceuticals GmbH/Pfizer, Inc., signed the Clinical Study Agreement between Pfizer Inc., and University Clinical Research-DeLand, LLC d/b/a Accel Research Sites for Pfizer Protocol # C4591001 on 5/22/2020. Dr. Rankin, Principal Investigator, signed this agreement on 5/22/2020. Dr. Rankin stated the following: "I have read and understand this agreement and accept the terms as they relate to my activities as Principal Investigator". We did not collect this agreement.

The Site Initiation Visit of Protocol C4591001 took place on 7/14/20. Training for the C4591001 study was conducted at the site initiation visit. Monitoring was (b) (4) for Protocol C4591001, with a combination in person and remote monitoring visits. We did not collect the monitoring visits and copies of monitoring reports.

The monitor identified several discrepancies, such as out of window visits and treatment deviations. The Training Signature Log and Site Initiation Report by Pfizer's representative, (b) (6), for the C4591001 study is included as **Exhibit 31**.

For Pfizer Protocol C4591001, (b) (6), (b) (7)(C) FDA Investigator, noted discrepancies between the Site's records and the monitoring letters. Please refer to discussion item number three in the General Discussion with Management section for further discussion.

According to Dr. Rankin, the sponsor of Protocol C4591001, Pfizer completed an audit of its study in October 2020. The letter sent by Pfizer for Regulatory Quality Assurance Audit of Protocol C4591001 dated 13 October 2020 is included as **Exhibit 19**. The letter states that Pfizer conducts Good Clinical Practice compliance audits to ensure that the study protocol, ICH GCP guidelines, and all applicable regulatory requirements are being followed. This letter was signed by Cheryl Oprisko, Director (Robert N. Cutler, Director on behalf of Cheryl Oprisko), Senior Quality Assurance Lead, Pfizer Regulatory Quality Assurance.

Moderna Protocol mRNA-1273-P3901:
The sponsor contracted with (b) (4) Clinical Research Organization (CRO), to monitor this study. The CRO is located at (b) (4) The CRO and the sponsor of this study, ModernaTX, Inc., signed a contract with Dr. Rankin, Principal Investigator, on 7/13/2020. The contract is included as **Exhibit 30**, with the timestamp on page 20.

The Site Initiation Visit of Protocol mRNA-1273-P3901 took place on 7/29/2020. Training for the mRNA-1273-P3901 study was conducted at the site initiation visit. The monitor identified several discrepancies, such as test articles not being returned by subjects, out of window visits, and treatment deviations. The Site Visit Log for the mRNA-1273-P3901study is included as **Exhibit 18**. Monitoring was (b) (4) for this study, with of combination in-person and remote monitoring visits.

We reviewed monitoring follow-up letters, e-mailed communications, and study newsletters located in the site files for both clinical research studies. The monitoring follow-up letters for the visits were filed chronologically in the regulatory documents. Our review of the source documents, monitoring reports, and data listings found all deviations were documented correctly. It appeared that Dr. Rankin took corrective actions when the monitor found deficiencies or recommended changes. No discrepancies were identified.

Dr. Rankin stated that the sponsor of Protocol mRNA-1273-P301, ModernaTX completed an audit of its study in October 2020. The letter sent by Moderna specified audit dates as 22-23 October 2020. The letter stated that the purpose of this audit is to assure confidence in the quality of the data and to identify opportunities for process improvement. The letter was signed by Alex McCord, Associate Director, Research and Development Quality, Moderna, and it is included as **Exhibit 17**.

Sample monitoring letters for the Protocol mRNA-1273-P3901 are included as **Exhibit 20**.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE (b) (6), (b) (7)(C)

No FORM FDA 483, Inspectional Observations was issued. I did not find any significant objectionable practice, and there were no warnings given based on this inspection.

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

The Center for Biologics Evaluation and Research (CBER) received a report raising concerns about the operations of clinical studies at the Accel Research Sites, specifically, inadequacies in subject follow-up safety phones, an inappropriate delegation of study tasks, and inadequacies in subject safety during the pandemic **(Attachment 2, page 3)**.

According to the reviewed study records and available source records, including Investigator Progress Notes, we determined the following:

- Approximately (b)(4) Accel Research Sites' staff were delegated to manage Protocol C4591001 and Protocol mRNA-1273-P301 clinical research studies.
- Dr. Rankin said that he has been practicing medicine for 30 years and has been a Principal Investigator on numerous clinical research studies.
- Our review of source documents found that the delegated clinical research staff has been maintaining similar source data for both ongoing studies.
- The Accel Research Sites has been managing only these two COVID 19 vaccine trials currently.
- On August 24, 2020, Accel Research Sites' former receptionist put her phone on Do not Disturb (DND) mode, causing the calls to go directly to a voicemail. Dr. Rankin stated that Pfizer Protocol C4591001 was affected by the phone being on DND mode. The Vice President of Clinical Operations at Accel Research Sites identified the issue as part of a routine check-up of the front-desk station on August 24, 2020. The Senior Site Manager was immediately made aware, and the employee was scheduled for a counseling session with the Human Resources (HR) manager. According to Dr. Rankin, subjects had access to a 24-hour emergency cellphone and the Clinical Research Coordinator's direct extension from the main phone line. Dr. Rankin stated in an Affidavit **(Attachment 3)** that all safety calls were managed as per protocol with Adverse Events and Serious Adverse Events documentation as applicable. The receptionist was terminated on September 8, 2020, due to her phone being on DND and additional performance issues documented by the HR manager in a summary letter. Accel Research Sites implemented a new shared voicemail box on August 27, 2020. The new system simultaneously directs all voicemails and missed calls to the receptionist's extension and to a shared email inbox. According to Dr. Rankin, four clinical staff members were assigned to retrieve, follow-up, and archive voicemails. Accel Research Sites has hired four dedicated receptionists using the shared mailbox. Training of new clinical research staff has been performed and documented on the call routing to allow transparent tracking and follow-

up of incoming calls and voicemails. Additional phone extensions have been added to the process with a ticket tracking system and a third-party answering service vendor.

We reviewed all delegation and training logs and confirmed that all delegated staff were properly trained. Based on the reviewed original source records for Protocol C4591001 and Protocol mRNA-1273-P301, we could not confirm the allegations in the report received by CBER.

We obtained an Affidavit from Bruce G. Rankin, DO, on 11/24/2020. The Principal Investigator stated in the Affidavit that some of the clinical trials' requirements had been delegated to staff under Dr. Rankin's supervision. Dr. Rankin also stated that the Accel Research Sites implemented a corrective action plan regarding incoming telephone calls. He also stated that all clinical research staff was qualified to conduct the study. Dr. Rankin's Affidavit is included as **Attachment 3**.

According to Dr. Rankin, there were no complaints received by the site or himself to date.

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

No refusals were encountered.

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

On 11/24/2020, we, (b) (6), (b) (7)(C), FDA Investigators, held a close-out meeting with:

- Dr. Bruce Rankin, Principal Investigator,
- Ms. Melissa Hodges, Vice President of Quality and Compliance.

We summarized all review areas during the inspection. A Form FDA 483, Inspectional Observations was not issued. The following four discussion items were discussed during the close-out meeting:

1. Dr. Rankin did not perform the FSH test as required per Pfizer Protocol C4591001 Section10.4.3 for postmenopausal females less than 60 years of age, without either alternative medical cause or permanent infertility or 12 months of no menses. We did not determine the exact number of subjects affected.

   Response: Dr. Rankin stated that he will contact Pfizer to suggest amending Protocol C4591001 Section 10.4.3. According to Dr. Rankin, the current standard medical practice is to perform the urine pregnancy test and not to draw blood for the FSH test. The result of the processed blood sample would not have been available for a couple of days. The urine pregnancy test was done during visit 1 before the first dose of vaccine was administered. Additionally, Pfizer did not provide any blood collection supplies for this testing.

2. Dr. Rankin did not document emergency phone calls for Pfizer Protocol C4591001, which had come into the former receptionist's phone on August 24, 2020 after she put the phone on Do not Disturb mode **(Attachment 3)**.

Response: Dr. Rankin said that they had already reviewed all calls but did not document them. The site would review them again, and document all calls. Dr. Rankin stated that neither Serious Adverse Events (SAEs) nor Adverse Events (AEs) were reported to that emergency line on August 24, 2020.

3. There were four discrepancies between the site's records and the electronic case report forms (CRFs) for Pfizer Protocol C4591001 **(Exhibit 25)**.
   a. Subject (b) (6) had one unreported AE for headache on 7/30/2020. We did not collect a copy of the un orted AE.
   b. Subject (b) (6) had one unreported AE for injection site tenderness on 7/29/2020. We did not collect a copy of the unreported AE.
   c. Subject (b) (6) had one unreported AE for urticaria (hives) on 9/14/2020. We did not collect a copy of the unreported AE.
   d. Subject (b) (6) had three unreported AEs for diarrhea on 8/21/2020, fatigue and generalized joint pain on 8/22/2020 **(Exhibit 25**, pages 34 - 51**)**.

Response: Dr. Rankin stated that the protocol didn't give a specific timeframe for reporting nonserious AEs only stated that the investigator is to record on the CRF all directly observed and all spontaneously reported AEs. Dr. Rankin stated that he will report all future nonserious AEs to the IRBs and the research studies' sponsors. Dr. Rankin stated that all SAEs were reported to the sponsor promptly. Dr. Rankin specified promptly as 72 hrs. Dr. Rankin stated and we confirmed that there were no issues reporting SAEs to the IRB.

4. For the Pfizer Protocol C4591001, at study visit #1, which took place on 10/6/20, subject (b) (6) was consented with version 3.0 of the ICF, which was IRB approved on 7/31/20. Version 3.0 was obsolete at the time of subject (b) (6)'s enrollment and version 4.0 of the ICF was the most recent ICF at the time as it was IRB approved on 9/11/20. At Study Visit #2, which took place on 10/29/2020, subject (b) (6) was not reconsented with version 4.0 of the ICF. Subject should have been reconsented with the correct version of the ICF at the next visit, on October 29th, 2020. This was only an administrative error and the ICF did not contain any new safety information. The Study Coordinator did not reconsent this subject. This incident was documented as a deviation but not submitted to the IRB until (b) (6), (b) (7)(C) FDA Investigator, pointed this oversight out to the Study Coordinator. The site regulatory coordinator, (b) (6) , then submitted this as a deviation to the IRB **(Exhibit 26)**.

Response: Dr. Rankin said that the site would submit Deviations to the IRB within five days after the deviation has occurred.

We informed Dr. Rankin, Principal Investigator, that the FDA's Center for Biologics Evaluation and Research determines the final classification of the inspection. I explained that future actions could be taken at their recommendation and that mine was not the final decision. Dr. Rankin expressed understanding.

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

Ms. Melissa Hodges, VP of Quality and Compliance, stated that the Accel Research Sites hired uniformed security guards to enforce COVID 19 protection guidelines. She said that subjects were instructed of safety requirements of mask-wearing and social distancing. Security guards from (b) (4) were stationed in the waiting room, ensuring subjects' safety as they entered the facility with or without a protective face mask. Ms. Hodges said that if any subjects forgot their own mask, they were provided with a free PPE mask and a face shield upon entering the facility.

Ms. Hodges said that the front desk personnel performed temperature checks and COVID 19 illness questioning during the check-in process in the waiting room before the subject could enter the main facility. According to Ms. Hodges, as per the Center for Disease Control and Prevention guidelines, social distancing has been complied with by all subjects and staff during all study visits. She said that Accel Research Sites' staff were required to wear masks, gowns, face shields, and gloves during study visits. Ms. Hodges stated that all surfaces in the exam and waiting rooms were sanitized between each subject with (b) (4) The Accel Research Sites COVID 19 Pandemic Preparedness Guidance and Plan is included as **Exhibit 16**.

We noted that all Accel Research Sites' staff practiced social distancing and wore a PPE mask during this FDA inspection. We reviewed the Standard Operating Procedure and the Accel Research Sites' COVID 19 pandemic preparedness guidance/plan regarding COVID safety practices. According to Ms. Hodges, all staff closely followed the implemented necessary infection prevention measures before, during, and after study visits. We noted that signage was posted in the waiting room and on the exterior doors of exam rooms reiterating restrictions. The contract between (b) (4) (b) (4) and Accel Research Sites to provide property protection during study visits is included as **Exhibit 29**.

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

No samples were collected during the current inspection.

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

No voluntary corrections were done during the current inspection.

EXHIBITS COLLECTED

1 Exhibit 1 - Dr. Rankin's CV, 34 pages
2 Exhibit 2 - List of Studies - Dr. Rankin - November 18, 2015 - November 18, 2020, 4 pages

3 Exhibit 3 - Accel Research Sites Organizational Chart, 6 pages
4 Exhibit 4 - Accel Research Sites' Floor Plan, 1 page
5 Exhibit 5 - Screening and Enrollment Log Protocol ID C4591001, 62 pages
6 Exhibit 6 - Subject Screening and Enrollment Log Protocol mRNA-1273-P301, 111 pages
7 Exhibit 7 - Form FDA 1572 - Statement of Investigator for Protocol C4591001, 60 pages
8 Exhibit 8 - Form FDA 1572 - Statement of Investigator for mRNA-1273-P301, 102 pages
9 Exhibit 9 - Pfizer - Signature Sheet and Delegation of Duties Log for C4591001, 17 pages
10 Exhibit 10 - Vaccine Therapy Area and Team Delegation Log mRNA-1273-P301, 23 pages
11 Exhibit 11 - Protocol Deviation and SAE Report Pfizer C4591001, 3 pages
12 Exhibit 12 - Protocol Deviation and SAE Moderna mRNA- 1273-P301, 2 pages
13 Exhibit 13 - C4591001 - ICF and HIPAA Authorization (Phase 2-3), 30 pages
14 Exhibit 14 - Moderna mRNA-1273-P301 - Sample Informed Consent Form, 20 pages
15 Exhibit 15 -Accel Research Sites Adverse Event Form for Pfizer C45910001 study, 19 pages
16 Exhibit 16 - Accel Research Sites COVID Pandemic Preparedness Guidance/Plan, 3 pages
17 Exhibit 17 - Moderna Audit Letter from October 2020, 2 pages
18 Exhibit 18 - Site Visit Log for Protocol Number mRNA-1273-P301, 4 pages
19 Exhibit 19 - Pfizer Regulatory Quality Audit of C4591001 - Letter 13 October 2020, 3 pages
20 Exhibit 20 - Sample monitoring letters for Protocol mRNA-1273-P301, 30 pages
21 Exhibit 21 - IRB Approval List Pfizer C5591001, 160 pages
22 Exhibit 22 - (b) (4) IRB Approval Letters for Moderna - mRNA-1273-P301 study, 34 pages
23 Exhibit 23 - Investigational Product Accountability Log for Protocol C4591001, 75 pages
24 Exhibit 24 - Investigational Product Accountability Log for mRNA1273-P301, 39 pages
25 Exhibit 25 - Adverse Event reporting discrepancies for C4591001 study, 55 pages
26 Exhibit 26 - Deviation Log C4591001 - Subject signed wrong Version of ICF, 7 Pages
27 Exhibit 27 - Accel Research Sites' Standard Operating Procedures Index, 5 pages
28 Exhibit 28 - Accel Research Sites and Dr. Rankin, Independent Agreement, 13 pages
29 Exhibit 29 - Contract between Licensed Security services and Accel Research Sites, 3 pages
30 Exhibit 30 - Trial Agreement between (b) (4) and University Clinical Research - 24 pages
31 Exhibit 31- Training Signature Log and Site Initiation Visit - Pfizer C4591001, 8 pages

ATTACHMENTS

1 Attachment 1 - Form FDA 482, Notice of Inspection, dated 11/17/2020, 3 pages
2 Attachment 2 - Assignment Memorandum - Dr. Bruce Rankin, 7 pages

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

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