TABLE OF CONTENTS



## SUMMARY [redacted]

This FY'21, High Priority, Prescription Drug User Fee (PDUFA) clinical investigator inspection was conducted at the request of the Center for Biologics Evaluation and Research (CBER). The inspection

was completed in accordance with Compliance Program 7348.811, Clinical Investigators and Sponsor-Investigators. The inspection was designated under eNSpect OP ID #180484.

The previous FDA inspection of Dr. Eder was a PDUFA Data Integrity Clinical Investigator inspection conducted 2/1/2016 – 2/4/2016 and it was classified as NAI.

This inspection covered the study conduct of the following protocols:

- mRNA-1273-P301: "A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older" in support of IND 19745.
  - The sponsor for the study is ModernaTX, Inc., Cambridge, MA and the institutional review board (IRB) is (b) (4). The study was approved on (b) (4). The site screened 478 subjects with eight dropped and one screen failure. Three subject numbers were created in error and no subjects were enrolled with those numbers (b) (6). The first subject signed the informed consent form (ICF) on July 27, 2020 and received the first dose on July 27, 2020.

- C4591001: "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 Individuals" in support of IND 19736. This was a limited review of study records covering the e-Diary electronic data capture (EDC) system, monitoring for signs and symptoms, and investigational product (IP).
  - The sponsor for the study is BioNTech/Pfizer and (b) (4) is the IRB. The study was approved on 05/29/2020. The site screened 130 subjects with two withdrew consent and one screened failure. The first subject signed the ICF on August 10, 2020 and received the first dose on August 10, 2020.

Both studies are ongoing but closed to enrollment and the subjects are in the follow-up phase.

This inspection covered study approval, informed consent, subject eligibility, study monitoring, adverse events, concomitant medications, protocol deviations, e-Diary electronic data capture system, IP records, and the training of study staff. Informed consent was obtained from all subjects prior to study activities.

No FDA-483, Inspectional Observations, was issued at the end of the inspection. There was one discussion item for protocol mRNA-1273-P301. The test result reports from (b) (4) for Subjects (b) (6) draw dates state 25 AUG 2020 and the source documentation for the subjects reveals a draw date of 24 AUG 2020.

No samples were collected. No refusals were encountered.

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

| | |
|---|---|
| Inspected firm: | Frank Steven Eder, MD |
| Location: | 1290 Upper Front St<br>Binghamton, NY 13901-1046 |
| Phone: | 607-771-1064 x2 |
| FAX: | 607-771-4656 |
| Mailing address: | 1290 Upper Front St<br>Binghamton, NY 13901-1046 |
| Email address: | feder@mcrmed.com |
| Dates of inspection: | 11/10/2020-11/13/2020, 11/16/2020-11/20/2020, 11/23/2020 |
| Days in the facility: | 10 |
| Participants: | (b) (6), (b) (7)(C), **Investigator**<br>(b) (6), (b) (7)(C), **Supervisory Investigator** |

Non-FDA Participants: None

On 11/03/2020, I, Investigator (b) (6), (b) (7)(C) spoke with Dr. Eder by phone to pre-announce the inspection. We agreed to a start date of 11/10/2020.

On11/10/2020, Supervisory Investigator (b) (6), (b) (7)(C) and I presented our credentials and issued a Form FDA 482, Notice of Inspection **(Attachment 1)** to Frank S. Eder, MD- Clinical Investigator. We explained that the purpose of our visit was to review the study records for protocol mRNA-1273-P301. The assignment memo is attached, **Attachment 2**. The following individuals were also present at the opening meeting:

- Deborah Hubish- Regional Operations Manager (Meridian)
  Unblinded IP Coordinator (Moderna & Pfizer)
- Kathe Olmstead- Site Director
  Lead Unblinded IP Coordinator (Moderna)
  Back-up IP Coordinator (Pfizer)

The inspection was later extended at CBER's request to conduct a limited review of the study records for protocol C4591001 in support of IND 19736.

Post- inspectional correspondence should be sent to:

Frank S. Eder, MD
1290 Upper Front St
Binghamton, NY 103901
feder@mcrmed.com

Deborah Hubish
1290 Upper Front St
Binghamton, NY 13901
dhubish@mcrmed.com

This report was written by Supervisory Investigator (b) (6), (b) (7)(C) and me (b) (6), (b) (7)(C) s indicated by the placement of our respective initials on each report heading.

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

Previous inspection of this Clinical Investigator was conducted on 02/01-04/ 2016 and was classified as NAI.

Dr. Frank S. Eder is a practicing Family Medicine physician and Associate Medical Director within United Health Services (UHS) and principal investigator contracted by Meridian Clinical Research. Dr. Eder has participated in clinical trials for over 20 years.

We reviewed records at the UHS located at 1290 Upper Front Street, Binghamton, New York 13901. The office hours of operations is 8:00 am – 4:30 pm, Monday to Friday. The site operates on (b) (4) if subjects are required to be seen for study procedures.

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

Dr. Eder is the PI for both protocols titled,

- "A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older" conducted under IND 19745, and
- "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 Individuals" conducted under IND 19736.

During our review of study records, we observed the following shipping records documenting the shipment of test articles:

- mRNA-1273, from Moderna Therapeutics located at 320 Bent St, Cambridge, MA 02141, **Exhibit M1**
- BNT162b2, from (b) (4) located at (b) (4), **Exhibit P1, pgs. 1-2,** to Meridian Clinical Research LLC located at 1290 Upper Front Street, Binghamton, NY 13901

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

Dr. Frank Eder is a clinical investigator performing research on human subjects utilizing the investigational products, mRNA-1273 and BNT162b2 (COVID- 19 vaccines). These vaccines are classified as a biologic product used for investigational purposes in support of IND 19745 and IND

19736 under the Food, Drug, and Cosmetic Act and this research is regulated by the Food and Drug Administration.

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

**Frank S. Eder, MD- Principal Investigator**

Dr. Eder identified himself as the principal investigator (PI) of both protocols, but his title is identified as Clinical Investigator on the Form FDA 482. Dr. Eder stated that his study responsibilities included, but not limited to, oversight of staff, answering questions during the consenting process, performing physical exams, determining eligibility, and reviewing subject charts. He stated that he is currently overseeing two COVID-19 vaccine trials. Dr. Eder was present for the opening and closing meetings. He was available to answer questions throughout the inspection. We reviewed Dr. Eder's Curriculum Vitae (CV) and it appeared adequate for his role as PI for the studies, **Exhibit M2**.

(b) (6) **QA Specialist Both Protocols**

(b) (6) monitors the electronic system and charts, regulatory binders (electronic and paper) through a portal called (b) (4) for the Moderna study. For the Pfizer study, (b) (6) participates as an unblinded verifier, completes relevant source documentation, and maintains regulatory information. (b) (6) was available to provide us copies and answered questions in regard to regulatory documentation.

(b) (6) **Moderna's Lead Study Coordinator**

(b) (6) has been the lead study coordinator for the Moderna study from its initiation. (b) (6) is blinded in both studies and is a backup coordinator for the Pfizer study. (b) (6) was available to us everyday of the inspection to answer questions relevant to the Moderna study, provided us with requested copies of subject records, and navigated us through (b) (4), the electronic data capture (EDC) system.

**Kathe Olmstead, RN, BSN- Moderna's Lead Unblinded Vaccinator & Pfizer's Backup**

Ms. Olmstead is unblinded in both studies. She participates in receiving, preparing, and administering the investigational product (IP) to subjects. She gave us a walk-through of the IP administration process and provided us with requested IP documentation and copies.

**Deborah Hubish, LPN-Moderna's Backup Unblinded Vaccinator**

Ms. Hubish is an unblinded backup vaccinator in both studies. She participates in receiving, preparing, and administering the IP to subjects. She was present everyday of the inspection. She gave us a walk-through of the IP administration process and provided us with requested IP documentation and copies.

**(b) (6) - Pfizer's Lead Study Coordinator**

(b) (6) became the lead study coordinator of the Pfizer study in July, after it was transferred from (b) (6). (b) (6) has primary contact with the monitors, oversees data entry, uploads source information, and completes subject illness calls. (b) (6) navigated us through the e-Diary system and the EDC. (b) (6) provided us with subject records and copies.

**(b) (6) - Pfizer's Lead Unblinded Vaccinator**

(b) (6) has been an unblinded vaccinator in the Pfizer study since its initiation. (b) (6) participates in receiving, preparing, and administering the IP to subjects. (b) (6) gave us a walk-through of the IP administration process and provided us with requested IP documentation and copies.

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

Study specific training was provided by the sponsor for each study. Records contained documentation that site personnel received and completed relevant training on the protocol, amendments, IP, e-Diary, and procedures.

Moderna

The site invitation visit (SIV) was on 23 July 2020. See attached **Exhibit M3, pp 6-9** and M**4, pp 1-4** for attendance.

Pfizer

The site invitation visit (SIV) was on 25 June 2020 See attached **P3 pp 4-5** for attendance. See **Exhibit P2** for protocol training procedures.

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

Moderna

Dr. Eder stated that he has been the PI since the study was initiated in July 2020. Dr. Eder signed the Form FDA 1572 on 19 Jun 2020 and 23 Jun 2020, **Exhibit M5**. A listing of clinical trials that Dr. Eder has participated in is attached as **Exhibit M6**.

Subjects study visits were conducted at 1290 Upper Front Street, Binghamton, NY 13901.

The Signature and Delegation of Duties Log for both blinded and unblinded staff was reviewed, **Exhibit M7**. We did not identify any concerns with the delegation of responsibilities. No discrepancies were observed and appeared to be adequate.

IRB approval was obtained on 2 July 2020 for Protocol Amendment 1 (Dated: 26 Jun 2020). As of the inspection, there have been 3 additional IRB approved protocol version amendments all used by study staff.

| Protocol Amendment Number | Letter of IRB Approval |
|---|---|
| 1 **(Exhibit M9, pg.1-2)** | 2 Jul 2020 |
| 2 | 31 Jul 2020 |
| 3 | 20 Aug 2020 |
| 4 | 30 Sep 2020 |

Record review revealed the IRB approved three versions of the ICF, but subjects were consented under two*:

- Version 30 Jun 2020, Revised 2 Jul 2020, approved on 2 Jul 2020
- Version 17 Jul 2020, Revised 21 Jul 2020, approved on 15 Jul 2020* **(Exhibit M12)**
- Version 6 Aug 2020, Revised 6 Aug 2020, approved on 6 Aug 2020* **(Exhibit M13)**

A copy of all IRB approval letters are attached as **Exhibit M9**.

The first subject signed the informed consent form (ICF) on July 27, 2020 and was screened, randomized, and received the first vaccine dose on July 27, 2020. The study is ongoing.

All subject COVID PCR Swabs and phlebotomy samples are shipped to (b) (4) located at (b) (4). The site received results report for COVID PCR swabs, which were inserted in subject folders. The records reviewed revealed samples were collected, stored, and shipped as per the (b) (4), **Exhibit M10.**

Dr. Eder explained subjects were recruited via Meridian's (b) (4) subject database, patients of UHS practice, IRB approved advertisements (social media, printed, and radio) and word of mouth. Subjects were seen and received IP administration on site. The study staff would initiate the consenting process, answer subject questions and if needed call upon Dr. Eder. Once the subject has signed the consent form, Dr Eder or another sub-investigator would initiate the physical exam,

A copy of the Enrollment/ Screening Log is attached as **Exhibit M8**. There were 478 subjects screened at the site, 477 enrolled, 8 subjects dropped (lost to follow up or withdrew consent), and the study is currently ongoing but closed to enrollment.

Pfizer

The record review was limited to e-Diary electronic data capture (EDC) system, monitoring for signs and symptoms, and investigational product (IP). Therefore, the FDA-1572 was not collected.

Subjects study visits were conducted at 1290 Upper Front Street, Binghamton, NY 13901.

The Signature and Delegation of Duties Log for both blinded and unblinded staff was reviewed, **Exhibit P4**. We did not identify any concerns with the delegation of responsibilities. No discrepancies were observed and appeared to be adequate.

IRB approval was obtained on 05/29/2020 for Protocol (04-15-2020) and Revised Protocol (05-13-2020) Incorporating Amendment 1.

| Revised Protocol Incorporating Amendment | Letter of IRB Approval |
|---|---|
| 4 (06-30-2020)<br>**Exhibit P6, pgs. 1-3** | 07/13/2020 |
| 5 (07-24-2020) | 07/31/2020 |
| 6 (09-08-2020) | 09/11/2020 |
| 7 (10-06-2020) | 10/10/2020 |
| 8 (10-15-2020) | 10/16/2020 |
| 9 (10-29-2020) | 11/05/2020 |

Record review revealed the IRB approved several ICF versions for assents, parents, Phase 2/3, and pregnant partner. The site only utilized the Phase 2/3 ICF, subjects were consented under three versions**:

- Consent Form- Phase 3 [S0], approved 05/29/2020
- Consent Form- Phase 3 [S2], approved on 07/13/2020
- Consent Form- Phase 2/3 [S3], approved on 07/31/2020**
- Consent Form- Phase 2/3 [S4], approved on 09/11/2020**
- Consent Form- Phase 2/3 [S5], approved on 10/10/2020**

The first subject signed the ICF on 10 Aug 2020 and was screened, randomized, and received the first vaccine dose on 10 Aug 2020. Study is currently ongoing and is closed to enrollment.

All subject serum and nasal swabs were shipped to (b) (4) located at (b) (4) (b) (4). The site did not receive test results unless the sample test was positive for SARS-CoV-2. The review of records revealed samples were collected, stored, and shipped as per the Study Laboratory Manual, **Exhibit P7.**

Study staff explained that patients were recruited using (b) (4) or by word of mouth. The study staff would initiate the consenting process where subjects had the option of completing an electronic or hardcopy ICF, answer subject questions, and if needed call upon Dr. Eder. Once the subject has signed the consent form, Dr. Eder or another sub-investigator would initiate the physical exam and required screening procedures thereafter would be completed. Subject eligibility checklists were observed to be signed off by Dr. Eder.

A copy of the Enrollment Log is attached as **Exhibit P5**. There were 130 subjects screened at the site, 1 screen failed, and 2 withdrew consent.

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

Moderna

We reviewed the ClinicalTrials.gov website and found the study start date listed as July 27, 2020 and the estimated primary completion date as October 27, 2022. As per website, Moderna TX, Inc. provided the information listed on the website.

Pfizer

We reviewed the ClinicalTrials.gov website and found the study start date listed as April 29, 2020 and the estimated primary completion date as August 1, 2021. As per the website, BioNTech SE provided the information listed on the website.

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

Moderna

Records reviewed revealed the CI followed the IRB approved protocol and amendments procedures throughout the study.

The site maintained a protocol deviation log, **Exhibit M11**. We did not observe any underreporting of deviations.

We reviewed documentation of subject e-Diary entries being reviewed and monitored by study staff for 7 days after each vaccination. If an entry was missed by subjects, the follow up calls performed by study staff were documented in subject records.

Pfizer

The site maintained a protocol deviation log, **Exhibit P8**. We did not observe any underreporting of deviations.

The first 38 subjects were enrolled by study staff to follow the reactogenicity pathway of the protocol. We observed documentation of e-Diary entries for subjects being reviewed and monitored by study staff for 7 days after each vaccine and weekly illness entries thereafter. The study staff followed-up on missing e-Diary entries not submitted by subjects.

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

Moderna

The study site used (b) (4) as their designated IRB. (b) (4) is located at (b) (4) The site received IRB approval on 2 Jul 2020. The IRB approved a variety of subject related documentation such as, subject material, recruitment material, translated documentation, and product information. Our review of protocol procedures revealed that the site received IRB approval prior to initiating any new material. IRB submissions and reports are performed in the database, (b) (4) This is maintained by the designated study staff.

A copy of all IRB approval letters are attached as **Exhibit M9**.

Pfizer

The site uses (b) (4) IRB located in (b) (4) as their designated IRB. The site received IRB approval on 05/29/2020. The IRB approved a variety of subject related material, recruitment material, and product information. Our review of protocol procedures revealed that the site received IRB approval prior to initiating any new material. Regulatory documents are maintained on the electronic database, (b) (4)

A copy of all IRB approval letters are attached as **Exhibit P6**.

Moderna & Pfizer: Elements of Informed Consent

All versions of the ICFs for both studies were reviewed for the 8 required elements and the additional elements. No discrepancies were noted and all appeared to be adequate. The clinical trial statement for applicable studies according to 21 CFR 50.25 (a) was observed in all ICF versions.

## SUBJECTS' RECORDS (b) (6), (b) (7)(C)

Informed Consent

As per (b) (6), lead coordinator, of the Moderna study and Pfizer study at the start the study, potential subjects were explained the study procedures by delegated study personnel and were given the opportunity to ask questions to include being provided with the ICF to review. Some versions of the ICFs for the Pfizer study were electronic. If the electronic version was not available, the potential subjects were given the hard copy version. Subjects were given copies of all signed ICFs. (b) (6) took over the Pfizer study in July and maintained the same procedures.

We reviewed 99 of 478 source records for the Modera and 48 of 130 source records for Pfizer. We found subjects signed the ICF prior to receiving the IP and resigned the ICF on next visit if the revised version was approved by the IRB for both studies.

According to Mrs. Deborah Hubish, regional operations manager, the site received many individuals interested in participating in the COVID-19 vaccine studies. Some of them were from New York City and out of state.

Source Records

We randomly chose 99 of 478 subjects' source records for the Moderna study and 48 of 130 subjects' source records for Pfizer study for review and found the site followed protocol procedures for both studies. Subject study records were maintained in individual folders in reverse chronological order.

We found that each subject file contained a copy of the original ICF, screening and randomization, vaccination visit, convalescent or unplanned visit if needed, concomitant medication, adverse event, laboratory report for nasopharyngeal and saliva samples, and progress notes. These documents contained name, date of birth, gender, medical history, weight, height, vital signs, pregnancy test result, and e-Diary information. The records contained e-Diary training for a personal smartphone or hand-held device and instructions on e-Diary completion. All subjects were given protocol specific quick reference guides for the Apps. The e-Diary was activated on Day 1 during the waiting period after the first vaccination. The records reviewed found subjects were contacted notified when they failed to submit daily or weekly symptom reports.

Moderna

All subjects were monitored for seven days after receiving each vaccination. The 7-day reactogenicity is captured using (b) (4) . The App uses an unique activation code generated by site personnel during (b) (4) subject registration in (b) (4) and links the subject to the e-Diary on a personal smartphone or hand-held device. The activation code is unique for each subject. (b) (4) is an electronic data capture (EDC) system used to capture and manage clinical trial data and the (b) (4) is the e-Diary component of the data management system.

Our review of the subject files found the draw dates on the laboratory result for some COVID PCR swabs did not coincide with the visit date from the source documentation for some subjects. The dates were off by one day and the firm submitted a demographic change form (DCR) requesting (b) (4) to correct the date. See General Discussion with Management.

Pfizer

Only the first 38 subjects were monitored for 7 days after receiving each vaccination. The 7-day reactogenicity is captured using (b) (4) The App uses an unique activation code generated by an

unblinded personnel in (b) (4) using the subject's demographic information, telephone number, and or email address. The activation code is sent to the subject with login details on setting up the e-Diary on a personal smartphone or provisioned device. The activation code is unique for each subject and links (b) (4) to (b) (4) We observed an unique auto measure code unique for each subject.

Subjects were given nasal swab kit with instructions on performing nasal swab, if needed, **Exhibit P9**.

Case Report Forms

Dr. Eder has delegated study personnel to transcribe the information from the hard-copy source records to the electronic case report forms. We did not compare the source data with the electronic case report forms. The study is open and data entry is ongoing.

Adverse Events

Subjects were instructed at each site visit and reminded via voice message as needed to report all adverse events encountered at any time. Adverse events were documented in study records and assessed by qualified study staff. In addition, subjects were asked to report any concomitant medications taken for adverse events or not. The inquiries included vaccines such as the influenza vaccine. For the Pfizer study, we observed one serious adverse event reported to the sponsor.

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

Moderna

The site maintained a master pregnancy test log, master device log, MedWatch forms, and master screening/ enrollment logs. These were all maintained as hardcopies in a protocol labeled binder.

Pfizer

The site maintained a master pregnancy test log, master device log, SAE reporting, and master screening/ enrollment logs. There were all maintained as hardcopies in a protocol labeled binder.

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

We did not observe any objectionable findings that prompted interviews with study subjects for either protocol.

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

Moderna and Pfizer

Dr. Eder and sub-investigator financial disclosures (FD) are maintained in the (b) (4) database. A copy of the FD from the Moderna study was collected and attached as **Exhibit M14**. We did not note any discrepancies amongst them, and they appeared to be adequate.

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

The site uses multiple electronic systems to record regulatory and subject source information.

Subjects are recruited for both studies using Meridian's database (b) (4). Study staff explained to us that subjects are added in the database using their name, date of birth, social security number, and a copy of their driver's license. In the database, subjects' profiles are locked when they are enrolled in a study. After 30 days of study completion, the lock is removed. Each study staff has an unique username and password to access the system.

The regulatory files are maintained in '(b) (4) (b) (6) is responsible for maintaining the database. (b) (6) provided necessary documentation and answered all questions.

Moderna

The electronic data capture system (EDC) used in the study is (b) (4). Subjects are randomized at the screening/baseline visit using (b) (4) and the app for e-Diary entry is downloaded on subject personal devices or site provided devices to (b) (4).

(b) (4) is utilized by the blinded designated staff personnel to randomize subjects. An email is sent to unblinded vaccinators with the treatment number to begin vaccine preparation.

The designated study staff educates the patient about the e-Diary app and assists the patient in setting it up on their personal phone or provided device. We observed in the EDC the unique activation code used for each subject to create the e-Diary, **Exhibit M15**. The EDC entries are managed by two designated study staff personnel with unique username and password. As per (b) (6) anyone with EDC access receives an email if a subject enters 'yes' to any of the questions while completing the eDiary entry.

Pfizer

The electronic data capture system (EDC) used in the study is (b) (4). Subjects are randomized at the screening/ baseline using (b) (4) and the app for e-Diary entry is (b) (4) which is downloaded on subject personal devices or site provided devices.

(b) (4) is utilized by unblinded staff personnel with unique username and password to randomize the subject. Two reports can be accessed and printed by the unblinded staff personnel that details the randomization code and the QR code used for verification during the preparation process.

The designated study staff educates the patient about the e-Diary app and assists the patient in setting it up on their personal device or provided device. We observed in the (b) (4) website, if a patient had multiple app download resets, they will have their initial activation code striked out and a new populated activation code on their subject profile. Their prior illness e-Diary entries will still be linked to their subject number. The EDC entries are managed by delegated study staff. As per Ms. (b) (6) the subject can only select 'yes' or 'no' on the app. The study blinded study coordinators will be notified is 'yes' is selected and will have to initiate a call to gather more information.

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

Moderna

The designated unblinded vaccinators have access to the secure investigational product (IP) and placebo in a key locked research designated room. In the room, the IP is stored in a key locked and labeled vaccine refrigerator within trays labeled with the expiry date. The placebo is stored in a key locked ambient cabinet labeled with the sponsor's name. Both the placebo and IP are prepared in the "MedRoom", this is a secured room that is accessed by unblinded vaccinators using a combination code. Throughout the preparation and administration process, there was one person preparing or administering and another verifying.

Product accountability logs are maintained as hardcopies by unblinded study staff as required by the protocol. IP and placebo specific documents and logs are kept in separate binders. The documents included regulatory documents, shipping records, blinding physician orders, and (b) (4) treatment/randomizing emails.

Pfizer

The designated unblinded vaccinators have stored the IP and placebo in two locked research designated rooms. The placebo is stored in a locked ambient cabinet labeled with the sponsor's name. The IP is stored in a locked freezer in the "MedRoom". Both the IP and placebo are prepared in the MedRoom. During preparation, the boxes of IP and placebo are retained in the MedRoom in a research only labeled cabinet for reconciliation and the boxes are verified prior to preparation using an app, (b) (4) Throughout the preparation and administration process, there was one person preparing or administering and another verifying. A copy of the site's IP blinding plan was collected and attached, **Exhibit P10**.

During our review of Pfizer's shipping records, we found that a temperature excursion of received vaccines upon shipment was brought to the attention of the monitor and the sponsor. The

temperature excursion was deemed acceptable by Pfizer and a copy of the correspondence and related documents was collected and attached, **Exhibit P1, pp. 3-15**.

Product accountability logs are maintained as hardcopies by unblinded study staff as required by the protocol. IP and placebo specified documents and logs are kept in separate binders. The documents include, regulatory documents, shipping records, and (b) (4) treatment/ randomization emails.

No objectionable observations were noted during our review of IP records.

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

Moderna and Pfizer

Both studies are still ongoing. Subject folders and records are kept in the research office. IP related binders are stored with access to unblinded staff only. The clinical site maintains both electronic and paper format study records. All required records were on hand and available for review during the inspection.

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

Moderna

There have been not been any reports sent by the study site to the sponsor for this study.

Pfizer

Thus far, the study site has experienced one serious adverse event (SAE) that has been reported to the sponsor. Subject (b) (6) experienced Sigmoid Diverticulitis, determined to be not related to the study vaccine, and was hospitalized. The site notified the sponsor via fax of the event.

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

Moderna

The monitor for this study is (b) (4) located at (b) (4) (b) (4) Blinded and Unblinded documentation are monitored at different visits by different clinical research associates (CRAs). Monitoring visits have occurred remotely and on site. A copy of the Site Visit Log and the Unblinded Site Visit Log is attached as **Exhibit M16**. The site initiation visit occurred on 23 Jul 2020 for blinded and unblinded activities. The monitoring visit follow-up letters for the unblinded interim visit and blinded SIV and interim visits are attached as **Exhibit M17**.

Pfizer

The monitor for this study is (b) (4) located in (b) (4) Blinded and Unblinded documentation are monitored at different visits by different clinical research associates (CRAs). Monitoring visits have occurred remotely and on site. A copy of the blinded site visit log and unblinded remote monitor visit log is attached as **Exhibit P11**. The monitoring visit follow-up letters for the unblinded interim visit and SIV visit are attached as **Exhibit P12**.

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

There are no complaints reported for this site.

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

No objectionable observations were noted during the review of the source documents. Therefore, no FDA-483 was issued at the closing of the inspection.

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

No refusals were encountered.

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

On November 23, 2020, Supervisory Investigator (b) (6), (b) (7)(C) and I held a close-out meeting with Dr. Frank S. Eder, principal investigator. The following staff was present at the close-out meeting:

- Deborah Hubish- Regional Operations Manager (Meridian)
  Unblinded IP Coordinator (Moderna & Pfizer)
- Kathe Olmstead- Site Director
  Lead Unblinded IP Coordinator (Moderna)
  Back-Up IP Coordinator (Pfizer)
- (b) (6) - Lead Clinical Coordinator (Moderna)
  Back-Up Coordinator (Pfizer)
- (b) (6) Lead Clinical Research Coordinator (Pfizer)
  Back-Up Coordinator (Moderna)
- (b) (6) - Lead Unblinded IP Coordinator (Pfizer)

See **Exhibit M19** for closing meeting attendance list.

We did not issue an FDA 483, Inspectional Observations for this inspection. We discussed with Dr. Eder one item:

- For the Moderna study, we observed the test result reports from (b) (4) for Subjects (b) (6) with draw dates of 25 AUG 2020 but source documentation reveals a draw date of 24 AUG 2020 for each of the subjects.

Dr. Eder acknowledged the discussion item. Study staff submitted Demographic(s) Change Request Forms for each subject, **Exhibit M18**. It was explained by (b) (6) that the staff inadvertently did not change the sample collection dates in the system during shipment for samples collected on the previous day.

We informed Dr. Eder that the report will be reported to the Center for Biologic Evaluation and Research for review and classification. In addition, a copy of the report will be sent to him and Ms. Hubish at the provided email address once the inspection is deemed closed by the agency.

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

Each day we arrived at the facility, our working area was sanitized. Supervisory Investigator (b) (6), (b) (7)(C) and I arrived wearing masks and conducted the inspection in a room where social distancing of six feet was easily maintained. Dr. Eder and the Meridian Clinical Research staff also wore masks throughout the entire facility.

Our assignment was extended to review protocol, C4591001, IND# 19736 at the request of CBER. We compared the enrollment logs for the Moderna and Pfizer studies for duplication.

The site provided the ICFs and protocol amendments electronically via CD for Pfizer. In addition, we received the blank subject visit source documents electronically via CD for Moderna We took pictures of the self-swab kit provided to subjects in the Pfizer study. The officially sealed original copy containing the photographs and documents gathered during the inspection are filed with the unlabeled exhibits and attachments.

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

No samples were collected during the inspection.

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

Not applicable.

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

Moderna

| Exhibit Number | Title | Number of page(s) |
|---|---|---|
| M1 | Vaccine shipping records shipment date (b) (4) | 10 |
| M2 | Dr. Eder's Curriculum Vitae | 11 |
| M3 | Unblinded staff training logs | 9 |
| M4 | Blinded staff training logs | 39 |
| M5 | Signed Form FDA 1572s | 8 |
| M6 | Dr. Eder's list of clinical trials | 3 |
| M7 | Signature delegation of duties log | 8 |
| M8 | Master enrollment/ screening log | 80 |
| M9 | IRB approval letters | 24 |
| M10 | (b) (4) central laboratory manual | 50 |
| M11 | Protocol deviation log | 8 |
| M12 | ICF Version 17 Jul 2020 | 20 |
| M13 | ICF Version 6 Aug 2020 | 20 |
| M14 | Dr. Eder's financial disclosure | 2 |
| M15 | EDC listing of subject activation code screenshot | 2 |
| M16 | Site visit log and the unblinded site visit log | 5 |
| M17 | Unblinded monitoring and blinded SIV/ interim visit follow-up letters | 17 |
| M18 | Demographic(s) change request forms for Subjects (b) (6) (b) (6) | 16 |
| M19 | Closing meeting attendance | 1 |

Pfizer

| Exhibit Number | Title | Number of page(s) |
|---|---|---|
| P1 | Vaccine shipping records date printed (b) (4) and temperature excursion correspondence | 15 |
| P2 | Unblinded staff training logs | 5 |
| P3 | Blinded staff training logs (SIV and nasal swab) | 5 |
| P4 | Signature delegation of duties log | 7 |
| P5 | Master enrollment log | 4 |
| P6 | IRB approval letters | 19 |

| | | |
|---|---|---|
| P7 | Study laboratory manual | 46 |
| P8 | Protocol deviation log | 1 |
| P9 | Pictures taken by investigators of nasal swab kit and instructions given to subjects for at home use, if needed | 1 |
| P10 | Site's IP blinding plan | 8 |
| P11 | Site visit log and the unblinded remote site visit log | 3 |
| P12 | Unblinded monitoring and SIV visit follow-up letters | 10 |

**ATTACHMENTS** (b) (6), (b) (7)(C)

| Attachment Number | Title | Number of Pages |
|---|---|---|
| 1 | Form FDA 482, Notice of Inspection dated 11/10/2020 | 3 |
| 2 | Assignment Memo, eNSpect OP ID 180484 | 6 |

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

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

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

(b) (6), (b) (7)(C) Supervisory Investigator