U.S. FOOD & DRUG ADMINISTRATION

DIVISION OF
BIORESEARCHMONITORING
OPERATIONS II
Dallas District Office
1201 Main Street, One Main Place,
Suite 7200
Dallas, Texas 75202

05/13/2024

Deirdre C. McMullen, MD
3281 Rocky Creek Dr Ste 500
Missouri City, TX 77459-4756
US

Reference: Inspection Date(s):10/10/2023 - 10/16/2023

Location: Deirdre C. McMullen, MD
3281 Rocky Creek Dr Ste 500
Missouri City, TX 77459-4756
US

Dear Dr. McMullen:

We are enclosing a copy of the establishment inspection report (EIR) for the inspection that was conducted by or on behalf of the U.S. Food and Drug Administration (FDA) at your premises on the referenced locale and date(s). When the Agency concludes that an inspection is "closed" under 21 CFR 20.64(d)(3), it will release a copy of the EIR to the inspected establishment. This procedure is applicable to EIRs for inspections completed on or after April 1, 1997. Visit the FDA website at (www.fda.gov) and search for 'FOIA Request' to submit a FOIA request.

The Agency continually works to make its regulatory process and activities more transparent to the regulated industry. Releasing this EIR to you is part of this effort. The copy being provided to you comprises the narrative portion of the report; it may reflect redactions made by the Agency in accordance with the Freedom of Information Act (FOIA) and 21 CFR Part 20. This, however, does not preclude you from requesting additional information under FOIA.

If you have any questions regarding this letter, you may contact Michelle Hines,Commander, US Public Health Service Commissioned Corps Supervisory Investigator, US Food and Drug Administration; Michelle.Hines@fda.hhs.gov; 301-651-2388

For more information on the U.S. FDA, please visit our website at www.fda.gov.

Sincerely,

Michelle J. Hines -S

Digitally signed by Michelle J. Hines -S
Date: 2024.06.05 12:24:03 -05'00'

FEI:3026791982
Enclosure: Establishment Inspection Report (EIR)

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SUMMARY

This FY' 2023 CBER/OCBQ Directed, "For Cause" Assignment, Prescription Drug User Fee Act (PDUFA), Clinical Investigator Inspection was conducted at the request of Center for Biologics Evaluation and Research (CBER), Office of Compliance and Biologics Quality (OCBQ), Division of Inspections and Surveillance (DIS), Bioresearch Monitoring Branch (BMB) Assignment Memorandum was dated 05/23/2023 and Op ID Assignment #253029. This inspection was conducted in

accordance with the instructions found in CP7348.811, Clinical Investigators (CI) and the instructions found within the Assignment Memorandum.

The current inspection was the first FDA inspection of this Clinical Investigator and covered the following studies: Protocol /Study Number and Title entitled, "**mRNA-1647-P301: A Phase 3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety, and Immunogenicity of m-RNA -1647 Cytomegalovirus (CMV) Vaccine in Healthy Participants 16 to 40 Years of Age.**" This study was sponsored by Moderna-TX, Inc. under [redacted].

The focus of this inspection as requested in the assignment was to determine the Clinical Investigator's conduct of the above studies in response to complaints of serious non-compliance by Advarra IRB to FDA. The CI, Dr. McMullen self-reported a series of site deviations in a response to corrections made upon discovery. The termination of 2 research employees responsible for handling issues self-reported by the CI, Dr. McMullen, served as a significant resolution of the site's CAPA.

This inspection covered the subject records, financial disclosures, investigational product controls, and monitoring of the study.

The inspection included the review of all available relevant records as follows: informed consents, protocols with amendments, signed investigator agreements, financial disclosure statements, IRB submissions and correspondence, adverse event reporting, clinical source data, study test article accountability, concomitant medication, and sponsor monitoring activities.

The following information was gathered for this Assignment:

Total Number of Subjects Screened at the Site: 144
Total Number Enrolled at the site: 22
Total Early Termination (EOT): 23*
Screen Failures: 99, lab value based 100% of the time due to +CMV
*1 subject enrolled, but a + pregnancy test resulted in EOT and no drug was administered,
Proposed Classification: NAI

At the conclusion of this inspection, there were no refusals encountered, there were no samples or photographs taken, there were no additional items for discussion, and there was no FDA 483, Inspectional Observations issued.

ADMINISTRATIVE DATA

Inspected firm:	Deirdre C. McMullen, MD
Location:	3281 Rocky Creek Dr Ste 500 Missouri City, TX 77459-4756
Phone:	
FAX:	
Mailing address:	3281 Rocky Creek Dr Ste 500 Missouri City, TX 77459-4756
Email address:	
Website:	
Dates of inspection:	10/10/2023-10/13/2023, 10/16/2023
Days in the facility:	5
Participants:	**Anya D Lockett-Evans, Investigator**

On the morning of 10/10/2023, I, Investigator Anya D. Lockett-Evans, issued an FDA 482, Notice of Inspection to the Director of Operations, Ms. Shamim Memon. I issued the FDA 482, Notice of Inspection to Ms. Memon, because the CI, Dr. D. McMullen, was booked with patients (the morning of the inspection commenced).

Later the same morning, I was introduced to the Clinical Investigator (CI), Deidre McMullen, MD. Dr. McMullen stated she was the Clinical Investigator for the study.

Because the inspection was unannounced and space was limited, the clinic located an empty examining room to serve as the central location for conducting my inspection.

I explained at the brief opening meeting that included the Director of Operations, Ms. Shamim Memon and the Clinical Investigator, Dr. McMullen that the purpose of the inspection was "For-Cause", and I requested access to the study records.

HISTORY

Dr. McMullen has been involved in research for over 15 years. She has been practicing Medicine for over 20 years.

Her office has been at their present location in Missouri City, Texas since 2008. This study was found by the Director of Operations, Ms. S. Memon, whose responsibility is to scout for studies for the firm.

The clinic staff has expanded in size and now consists of a second physician, 2 nurse practitioners, a registered nurse and an administrative staff with a subset of the clinic staffers and staff.

The firm's hours of operation are Monday through Friday 8 AM to 5 PM, closed weekends, and most holidays.

All FDA Correspondence to include FMD -145 should be addressed to-
Dierdre McMullen, MD
Synergy Groups Medical LLC
3281 Rocky Creek Dr #500
Missouri City, TX 77459

INTERSTATE (I.S.) COMMERCE/JURISDICTION (PRODUCTS MANUFACTURED AND/OR DISTRIBUTED)

Dr. McMullen is the CI for the study and conducts FDA-regulated research in accordance with 21 CFR Parts 50, 56, 58, 11, and 312.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

On 10/10/2023, I issued an FDA-482 Notice of Inspection, to Ms. Shamim Memon, Director of Operations for the clinical investigator, Dr. McMullen, who was booked with patients the morning of the site's unannounced inspection.

Dierdre C. McMullen, MD, **Clinical Investigator**, reported her general responsibilities as an investigator included but were not limited to full and complete oversight of the study, informed consent determining subject eligibility, physical examinations and health assessments, safety report evaluation, review of study related from sponsor, and evaluation/determination of all adverse and serious adverse event reporting. Dr. McMullen's CV is attached as **Exhibit 1**.

The Delegation of Authority Log, **Exhibit 4**, was supplied by the firm.

CLINICAL SITE TRAINING

Initial training on the protocol was conducted by the sponsor. The SIV was conducted 21 May 2022. The training consisted of all aspects of the protocol to include background, protocol assessments, adverse event reporting, site monitoring, vendors, IP dosing/administration, and other study related activities.

All employees are required to have an updated CITI/GCP training. I reviewed the CITI training certificates for the investigators, CRCs, regulatory and quality. I found no issues or observations with their training certifications. I verified the site's training log sign-in sheets (refer to **Exhibit 6**, training documents) that all members of the research team were trained on the protocol as well as its updated versions. Site staff responsible for data management were retrained on source documents, internal SOPs, and GCPs and this retraining was documented.

AUTHORITY AND ADMINISTRATION

Dr. McMullen stated that she accepts the responsibility for every aspect of the study, a review of subject files revealed she reviewed and approved laboratory results, case report forms, and adverse event reports. Dr. McMullen signed the initial FDA form 1572, Statement of Investigator, on 06/24/2021. A signed copy of the 1572 is included as **Exhibit 3.**

Dr. McMullen is Board certified in Family Practice and she's the Clinical Investigator for Synergy Groups Medical, LLC, previously known as Discovery MM Services. I emphasized to Dr. McMullen that I was auditing her as the PI of the study and that she bore all responsibility for the data.

A list of Dr. McMullen's FDA regulated studies conducted by the firm was included as **Exhibit 2.** According to the list of studies provided by the site, Dr. McMullen, CI, did not conduct any opioid-related studies.

I reviewed the Site Signature and Duty Delegation Log; all employee responsibilities were easily identified by the key listing of specific tasks. I found no deviations with the delegation log (**Exhibit 4**).

CLINICALTRIALS.GOV REQUIREMENTS

I documented the registration and submission results information for the study were found on https://ClinicalTrials.gov in accordance with federal regulations. During the inspection, I verified the sponsor was responsible for updating the information on the site.

PROTOCOL

I verified the protocol used was the same one subjects were randomized under. The protocol reviewed on site was the same protocol version that was provided to the Agency as background materials.

Protocol Deviations

The firm used a protocol deviation log during the study (refer to **Exhibit** 5). I reviewed the reportable deviations and verified them with participant subject source documents.

Initially the timeframes for deviation reporting weren't met. However, after corrective actions were implemented, this became a non-issue. There were no discrepancies nor additional deviations noted following the self-reporting of outliers by the CI, Dr. McMullen.

INSTITUTIONAL REVIEW BOARD (IRB)/INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE CONSENT FORMS

The IRB with oversight of the study was Advarra IRB, located at 372 Hollandview Trail, Suite 300, Aurora, Onatrio, Canada. The IRB reviewed the initial study submission. The protocol, and versions of the informed consent form (ICF) were approved prior to any subject being enrolled. An individual tracking log was found in each subject participant's binder that served to reinforce this requirement.

SUBJECT'S RECORDS

Informed Consent

Exhibit 7 is a copy of the Informed Consent Tracking log. There was adequate documentation to show all subjects were alive and available for the duration of their participation in the study. All subject medical records were in paper format. The site provided participant study specific binders. The binders allowed me to confirm that before subjects could participate in the study, the investigator obtained IRB approval of the study protocol, all modifications to the various protocol versions, and human subject.

I reviewed (100%) of all the 22 enrolled subjects Informed Consent Forms. During this inspection Ms. S. Memon who meet the inclusion/exclusion criteria, Director of Operations, explained the process for obtaining informed consent. She stated the study coordinators conduct the ICF process, however the process may also be initiated by the CI. All subjects in this study were selected from the in-house data base by chart review, and pre-identification of patients.

During the study there were 3 versions of the Informed Consent Form used to screen and to enroll all subjects. **Exhibits 8, 9, 10, 11, and 12** included sample informed consent. Subject participant

records included IP dosage, H&P, and other source documents. Source documents were found to be attributable, legible, contemporaneous, organized, and accurate.

There were no subjects enrolled once the hold on enrollment was placed.
Not all visits met the assessment time windows for vaccinations and safety initially, as self-reported by the CI, Dr. McMullen. Several factors were responsible for this deviation to include Covid-19 pandemic, the non-payment of subjects in a timely manner (as promised to subject participants), and staffing changes.

During this inspection I reviewed subject source documentation to include laboratory/x-ray results, conmedications, and related. My review of the various documents found no issues.

Site logs confirmed that the number of subjects listed on the logs accurately reflected the number of subjects screened and enrolled on the treatment arms.

In reference to the incorrect collection of biological samples the CI, Dr. McMullen reports that following the CAPA implementation, the collection of biological samples improved. Biological sample collection is now conducted in accordance with the protocol requirements.

There were no subjects harmed, nor was there any reported compromised data integrity issues resulting from post-CAPA implementation.

There was 1 documented positive pregnancy test. This subject did not receive IP.
Lab reports were reviewed by the CI, Dr. McMullen. Initially blood and urine sample collections were not consistently collected within assessment windows, as self-reported by the CI.

All reportable and non-reportable AEs were captured in the eCRF. Laboratory reports were filed with source documents. Phone calls were made by trained personnel and documented in the respective participant subject's source

Not all subjects completed their e-diaries. The site continued to educate subjects on the importance of e-dairy reporting to their non-compliant subjects. These efforts were documented.

I compared the primary efficacy endpoint data in the source documents with the data line listings provided in the background materials for the study. No discrepancies were noted.

All attributed signatures of site personnel on the source documents corresponded with personnel within the delegation logs, **Exhibit** 4.

Case report forms

The source information was documented on paper, and then entered the electronic case report form by data entry personnel. Access to the electronic systems was granted after training on the system had been completed. No issues were noted.

Adverse Events (AE's)

I reviewed all 22 enrolled subjects for adverse events and/or serious adverse events. There was an individual log for tracking both reportable and non-reportable findings. I found no under-reporting of adverse events.

OTHER STUDY RECORDS

During this inspection, no other records were reviewed outside of the subject records and drug accountability.

ELECTRONIC RECORDS AND ELECTRONIC SIGNATURES

All source and regulatory documents were in paper format. The only electronic system used during the inspection was the eCFR used for uploading of patient source data.

INTERVIEW OF SUBJECTS/PERSONNEL

There were no interviews of study personnel outside of those mentioned in the Individual Responsibility and Persons Interviewed section and those of the research area who supplied information for the report.

FINANCIAL DISCLOSURE

I reviewed signed copies of Dr. McMullen Financial Disclosure forms as well as the sub-investigators . No conflicts of interests were noted.

CONTROL OF INVESTIGATIONAL PRODUCT

During the inspection, Ms. S. Memon, Director of Operations, and Ms. Arsheen Memon, Quality Control, provided access to the investigational drug accountability records for the study. Each drug shipment was documented with receipt, dispensing, and return of investigational product. A copy of the IP log wasn't collected prior to closing, but viewed at the time of walk-through (Day1).

When a shipment was received, the date received, the lot number of each drug, and verifying receipt was recorded. The packing list was also signed and dated. The identification number of the subject that received the drug was recorded on the drug accountability log.

Investigational drug accountability was adequately documented with no discrepancies. The IP was maintained under the storage requirements outlined in the study protocol without issue.

RECORDS CUSTODY AND RETENTION

According to Ms. Asheen Memon, Quality Control (QC), all study records are maintained at the facility per contract and archived at Cube Smart in Richmond, TX. **Exhibit 16** is the archived record storage's full address.

According to the CI, Dr.McCullen, the site previously had a retention plan in place. There is no evidence or cause for a new retention plan to be implemented.

REPORTS TO SPONSOR

There were no additional study related reports reviewed during the inspection.

MONITORING

The sponsor CRO, PPD, was responsible for monitoring the study. Site monitoring was conducted remotely during covid 19, but later resumed. Monitoring activities included review of data entry into eCRFs. The monitor would query the study site via the EDC if there were any issues noted. The study site would respond to the query in the EDC. Monitoring appeared adequate for the study. Monitoring logs were not collected prior to the closing of the inspection.

REFUSALS

There were no refusals encountered.

GENERAL DISCUSSION WITH MANAGEMENT

The closing session was attended by Dr. McMullen, CI, Ms. S. Memon, Director of Operations and Ms.Asheen Memon, Quality Control.

There were problems early in the study, to include staffing changes both with the sponsor and with the site.

Dr. McMullen self-reported a myriad number of issues with the study's CRCs that led to 2 terminations as the site because of the site's CAPA (re). These items were properly addressed and resolved with additional training documented as well.

A sPIP release/closure letter dated 12/23/2022 was received by the site (refer to **Exhibit 13**).

Retention was a big issue, because in part that participating subjects weren't getting paid timely enough. **Exhibit 15** is an email addressing some of the payment issues. Several subjects withdrew from study due to payment related untimeliness. The clinic's credibility with the subject participants was lost.

But, for the most part screen fails due to +CMV laboratory reportings were the primary cause of screen failures (refer to **Exhibit 14**, screening and enrollment log commentary sections).

ADDITIONAL INFORMATION

This inspection was done on paper and files were copied for the sake of exhibits. Not all files/pages collected from the firm were used as exhibits. Some pdf files collected were combined for clarity.

SAMPLES COLLECTED

There were no samples collected during this inspection.

VOLUNTARY CORRECTIONS

There were no voluntary corrections.

EXHIBITS COLLECTED

1. CV of PI, 6 pages
2. CI Active FDA Studies, 4 pages
3. FDA 1572, 3 pages
4. DOA, 3 pages
5. Deviation Log, 12 pages
6. Training Documents, 4 pages
7. ICF Tracking Log, 1 page
8. ICF Sample 1 of 5, 36 pages
9. ICF Sample 2 of 5, 36 pages
10. ICF Sample 3 of 5, 36 pages
11. ICF Sample 4 of 5, 36 pages
12. ICF Sample 5 of 5, 36 pages
13. sPIP Closure Letter, 9 pages
14. Participation and Screening Log, 4 pages
15. Payment issues Email, 4 pages
16. Study Material Archive Location, 1 page
17. CAPA, 1 page

ATTACHMENTS

1 FDA 482 Notice of Inspection, 3 pages
2 Assignment Memo

Anya D. Lockett-evans -S Digitally signed by Anya D. Lockett-evans -S Date: 2023.11.15 20:06:56 -06'00'

Anya D. Lockett-Evans, Investigator
Division of Bioresearch Monitoring Operations II