From: melinda.fantene@fda.hhs.gov
To: Cynthia Hansen
Subject: [WARNING: MESSAGE ENCRYPTED]USFDA - FMD 145 EIR - Pace Analytical Life Sciences, LLC - 3001452367
Date: Wednesday, August 14, 2024 9:26:18 AM
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Pace Analytical Life Science EIR_reviewed.pdf

08/06/2024
Cynthia Hansen
Pace Analytical Life Sciences, LLC
1311 Helmo Ave N Oakdale,MN 55128-6023

Dear Cynthia Hansen:

The U.S. Food and Drug Administration (FDA) conducted an inspection at Pace Analytical Life Sciences, LLC, FEI 3001452367, located at 1311 Helmo Ave N, Oakdale, MN 55128-6023, from 07/15/2024 to 07/19/2024. FDA has determined that the inspection classification of this facility is "no action indicated" ("NAI"). Based on this inspection, this facility is considered to be in an acceptable state of compliance with regards to current good manufacturing practice (CGMP).

This letter is not intended as an endorsement or certification of the facility. It remains your responsibility to ensure continued compliance with CGMP.

An inspection classification of NAI for CGMP compliance will not directly negatively impact FDA's assessment of any pending marketing application referencing this facility. Please note, however, that application approval will depend on a product- and application-specific facility assessment conducted by the appropriate CDER or CVM review office. This letter does not address or reflect FDA's decision making with respect to any potential non-CGMP compliance issues.

FDA has concluded that this inspection is ''closed'' under 21 CFR 20.64(d)(3), and we are enclosing a copy of the narrative portion of the Establishment Inspection Report (EIR). It may reflect redactions made by FDA 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 SCSO, Carl Huffman via telephone at 913-495-5190 or email at Carl.Huffman@FDA.HHS.GOV.
Sincerely,

Melinda A Fantene
PROGRAM SUPPORT SPECIALIST
300 River Place, Suite 5900 Detroit, MI 48207-4291 Telephone: (313) 393-8100 Fax: (313) 393-8139/8140


FDA
U.S. FOOD & DRUG
ADMINISTRATION

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SUMMARY

This cGMP surveillance inspection of a contract laboratory was conducted under the FY24 Workplan and was recorded under eNSpect Operation ID# 257920 in accordance with Compliance program 7356.002 "Drug Manufacturing Inspections." The Drug profiles covered on this inspection are Laboratory, Chemical/Physical Testing (LCP), Laboratory, Microbiological Non-Sterility Testing (LMN) and Laboratory Microbiological Sterility Testing (LMS)

The systems covered on this inspection were Quality and Laboratory. The site operates as a testing laboratory only and does not have separate production, facilities and equipment, packaging and labeling or materials systems. We observed the firm's testing, including sterility testing and the microbial testing of [redacted].

The previous inspection resulted in the issuance of a 3-item FDA 483 for inadequate SOPs, change controls, electronic system validations, and risk assessments for workflow, change controls, and electronic systems, electronic systems not qualified for their intended use, and not including suspect test results on certificates of analysis. The previous observations were found to be corrected.

Management was cooperative, there was no refusal, and no samples were collected.

ADMINISTRATIVE DATA

Inspected firm:	Pace Analytical Life Sciences, LLC
Location:	1311 Helmo Ave N Oakdale, MN 55128-6023
Phone:	651-738-2728
FAX:	651-714-9360
Mailing address:	1311 Helmo Ave N Oakdale, MN 55128-6023
Email address:	cynthia.hansen@pacelabs.com
Website:	www.pacelabs.com
Dates of inspection:	7/15/2024-7/19/2024
Days in the facility:	5
Participants:	**Matthew B Casale, Investigator** **Emmanuel T Donyina, Investigator**

At the beginning of the inspection, we showed our credential and issued an FDA 482, Notice of Inspection to Marty E. Shelton, Vice President of GMP Operation, Pace Analytical Life Sciences, LLC, who was the most responsible person for the site during our visit.

This report was written jointly by Lead Investigator Matthew B. Casale and Investigator Emmanuel T. Donyina.

HISTORY

Pace Analytical Services, LLC, headquartered at 2665 Long Lake Road, Suite 300, Roseville, MN 55113 is the parent company of Pace Analytical Life Science, LLC (Pace). Pace Analytical Services is a private contract laboratory which specializes in environmental testing services, while their subsidiary, Pace provides CDMO/CRO support to client throughout the drug development lifecycle. Pace also works with various pharmaceutical, biopharmaceutical, medical devices, and other combination product manufactures. Pace has eight additional sites located in San German, PR, Philadelphia, PA South New Berlin, NY Lebanon, NJ, Salem, NH, Ann Arbor, MI, Boston, MA and San Diego, CA.

Since the last inspection in 2018, the firm has implemented a Master Control Electronic Document System (eDMS). The firm also built a dedicated preparation and instrument room (ICP-MP) for extractable / leachable and trace impurities testing.

Regarding the leadership of the firm, Eric Roman joined in 2019 as the CEO of Pace Analytical Service, Dawn Von Rohr also joined as President of Pace Analytical Life Science, LLC and Marty Edward Shelton, Vice-president of GMP operation and Cynthia Hansen, Formerly Senior Director of Quality moved to IT Program Director and now reports to Kyle Korzenowski, CIO, while Christi Richmond replaced Cynthia Hansen as the Senior Director of Quality and reports to Lou Forcellini, Head of Quality.

INTERSTATE COMMERCE AND JURISDICTION

The firm is a contract laboratory that conducts testing drugs and medical devices under Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP). Most of the products they test are either included in an approved application or awaiting an approval. The firm receives samples from all over the country but does not introduce or received a product they test in interstate commerce for marketing purposes.

INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED

Pace's organizational chart and responsibilities were provided during the inspection (Exhibit 1) which shows hierarchy of management as well as an overview if their responsibilities:
The individuals listed below except for Mr. Shelton were present during the inspection and provided information pertinent to their area of responsibility, answered questions, accompanied us during walkthrough, and or engaged in discussion related to their respective function areas:

Mr. Marty Edward Shelton, Vice President of GMP operation. He is the person we issued the 482 (Notice of inspection) to and identified himself as the most responsible person at the site. Mr. Shelton's role as VP GMP Operations is to provide operational leadership to the GMP Central Laboratory locations, including the Oakdale MN headquarters, San German, Puerto Rico, South New Berlin, New York, and Lebanon, New Jersey.

Ms. Christi Richmond, Senior Director of QA is to lead the quality assurance teams at the GMP Central Labs locations, including the Oakdale, MN headquarters, San German, Puerto Rico, South New Berlin, New York, and Lebanon, New Jersey. Ms. Richmond serves as the Site Head of Quality for the Oakdale MN headquarters.

Ms. Cynthia Hansen, IT Program Director. Ms. Hansen is now a corporate employee (employed by Pace Analytical Services, LLC). She is not employed by the Pace Analytical Life Sciences, LLC division and thus does not have a formal job description in their quality system. Cynthia's current job title is the IT Program Director, and her current role is to provide IT, computer software assurance and data integrity support to the PLS division. Ms. Hansen is the former Senior Director of Quality and said she was participating in the inspection because she felt her expertise would be helpful during our visit.

MANUFACTURING/DESIGN OPERATIONS

The firm is a contract laboratory which conducts testing of identity, purity, quality of excipient and API used in finished product manufacturing. Most of their operations fall under GLP, through there are some GMP testing conducted. This includes chemistry, sterility assurance, bioburden, etc.

Quality System

Management Responsibility

The firm has a defined quality system, with provisions for senior management to have oversight of quality and support for the establishment's quality unit, including policies, planning, resource management, and management review. The quality system provides for coordination and direction of the organization's activities related to conducting sample testing for their

clients, helps establish and maintain a state of control, promotes risk management, and facilitates continual improvement. The firm uses management and quality risk management tools to conduct operations and performs internal audits. No deficiencies were noted.

Investigations, CAPA Activities, and Change Management

The firm utilizes Laboratory Incident Reports (LIRs) to track OOS and Laboratory investigations. The firm also uses a content server for document control. This is handled through the (LIMS). During the inspection, we reviewed a list of LIRs for the past two years for the microbiology and chemistry laboratories. The firm provided a total of 1,159 LIRs. Most of the LIRs are either classified as employee error or the unclear instructions. A review of the firm's corrective action and preventive action (CAPAs) and their effectiveness was performed, and no significant issues were noted. A list of 1,372 deviations for the last two years was provided by the firm. Several were selected at random, and no obvious trends or repeated issues were noted.

Complaints

The firm's provided a list of 17 complaints for the last two years. Because this firm is a contract laboratory, the complaints were from their clients and not from the public. A few were selected randomly and reviewed, no obvious trends or repeated issues were noted.

Training Program

The firm's training program is governed by SOP 4 "Training program" effective October 25, 2023. This program covers the firm's initial general training program for new employees, Good Manufacturing Practices (GMP) and Good Laboratory Practices (GLP), ISO/IEC 17025 on-going training and other external training. The site's QA is responsible for maintaining all training records and auditing them in accordance with SOP 4. For instance, QA is responsible for filling out and maintaining all training records and ensuring that all personal have the appropriate education, training, and experience to perform assigned functions. We reviewed training records of Ms. Maddi Hafner, Associate Scientist II, no deficiencies were observed.

Quality Unit Oversight and Data Integrity

During the inspection, we reviewed and verified raw data for the firm's laboratory. The Electronic data test methods and the equipment qualification were also reviewed. No deficiencies were observed.

Laboratory System

Overall Control of Laboratory Equipment, Facilities, and Environment and Sample Receipt and Accountability

The firm has a large chemistry laboratory divided into different sections. The firm's laboratory and sample handling practices and procedures were reviewed, the reviews were unremarkable. Samples are received in a designated area, where they are entered into LIMS

and IDs are assigned for each sample received. After which, the samples are distributed to the laboratories as required. No issues were noted with the firm's laboratories or sampling receipt and handling practices. The firm uses USP standards for chemical testing, and performs a verification based on USP 1226 "Verification of Compendial Procedures" and EP 5.26 "Implementation of Pharmacopoeia Procedures." Balances are labeled with minimum and maximum weight, and sample and reference standard cabinets are locked and need the sample coordinator to get the sample. The glassware on the floor is segregated so similar sizes are not together.

QC Microbiology Testing
The firm offers a variety of microbial testing, including USP sterility, bioburden, Biological Indicator Test, Antimicrobial Efficacy Test, etc. The firm performs full growth promotion on each batch of media before use. Media is incubated in multiple incubators located throughout the lab. The laboratory has an ISO 7 area with ISO 5 hoods for aseptic testing, and microbial work is also performed in LAF hoods located in various parts of the lab. We observed the firm's sterility and Microbial Limit Test from preparation to testing. No issues were noted with the firm's testing were observed.

QC Analytical Chemistry Testing
This firm uses a Horizon LIMS and Empower 3 software. They offer a wide variety of chemical testing. The site maintains a large variety of chemistry testing equipment, including 70 Agilent and Waters HPLCs (some of which are UPLCs), two Xevo G2-XS QTof units, two Waters Acquity TQ MS units, 20 GCs, a Bio-Rad QX 600 droplet analyzer, a Seq Studio Genetic analyzer, a moisture analyzer, melting point apparatuses, a Malvern Zetasizer, a polarimeter, three ion chromatography units, three TOC units, DSC, AA, ICP, dissolution apparatuses, and various titration and Kf equipment. The firm also has a biopharma laboratory with a calibrated densitometer, a thermo Nanodrop One, a Maurice protein simple, a Sciex PA 800 Plus biologics analysis system, two Spectra Max plate readers, a UV-Vis, and a Thermo QuantStudio5. The site has a yearly in-house qualification for their HPLCs, and the rest of the laboratory equipment is qualified in-house every 6 months or yearly. Each unit has an identification tag and a status tag. The site uses Empower to track chromatography column use, and no issues were noted with the firm's laboratory procedures or practices. This site performed 98,942 tests in 2022, 98,417 tests in 2023, and 46,705 to date in 2024.

Indicators of a Quality System
Quality Unit Oversight (Quality System Indicators)
The firm uses electronic systems to optimize implementation of knowledge management for products, processes, and components and objective performance indicators to identify and drive continual improvement, with monitoring at an appropriate frequency.

Process Parameter and Product Quality Monitoring and Annual Product Review (Quality System Indicators)
The firm has programs in place to identify and mitigate process bottlenecks using risk assessments. They have visuals and signage in laboratory areas to indicate performance status and use recent innovations to improve manufacturing processes.

MANUFACTURING CODES
As a contract testing lab, the firm doesn't have manufacturing codes.

RECALL PROCEDURES
The firm is a testing laboratory only and would not need to conduct recalls; any issues with testing would simply be a customer notification.

OBJECTIONABLE CONDITIONS AND MANAGEMENT'S RESPONSE
No FDA-form 483 was issued for this inspection.

REFUSALS
No refusals were encountered.

GENERAL DISCUSSION WITH MANAGEMENT
At the end of the inspection, we held an informal close-out meeting with the following individuals:

Marty Edward Shelton, Vice President Operations
Christi Richmond, Sr. Director of Quality
Cynthia Hansen, IT Program Director
Six minor issues were found with the firm's investigations:

1. Complaint investigation COMP 075 was opened due to a complaint of a CoA issued for release testing with invalid data. An employee did not record the time out of incubation (but did record the date) for one instance of Microbial Limits testing. The customer approved the deviation but did not accept it and asked for a retest due to the missing time. Pace felt the date justified the use of the data. The root cause investigation drilled down into why the QA people released the report, but the identified root cause was miscoding by the lab; the lab needed to change the "ok" designation in the LIMS to "rw", which didn't happen. The investigation doesn't explain why the code was not changed, or what can be done about it, and doesn't include a discussion of the event or interview to clearly show that the miscoding was human error.

2. Environmental excursion investigation EER 1350 was opened due to a 3-hour and 30-minute excursion on an ultra-low temperature freezer. The investigation was classified minor and was attributed to multiple extended door openings. There was

no discussion of or detail on whether the door openings are acceptable or not and if any action should be taken to improve the issue.

3. Out-of-tolerance investigation OOT 958 was opened due to an incubator/shaker needing to be calibrated early due to suspect readings. The investigation found out of tolerance results at all temperature test points and says they reviewed each test, and none were impacted, but it does not explain how they determined this. According to the firm, they have an independent temperature measurement for the sample, which was in tolerance the entire time; however, the investigation does not document this.

4. Out-of-tolerance investigation OOT 1004 was opened due to the data logger for Room 302 being out of tolerance for humidity. It monitors a general lab with no significant temperature or humidity requirements. The probe is a chamber monitoring probe. The discussion says that none of the other probes were out of tolerance therefore the issue is closed. The investigation does not discuss why the OOT does not impact the location in the chamber, what is at the location, where the location is, or what impact the error could have on the samples.

5. Deviation investigation DEV 6115 was opened due to data sheets being found after an employee left the firm that had not been submitted to QA for review. The investigation record isn't clear if this was work from the end of the employee's time that wasn't finished or if it was earlier work that was never submitted. The investigation showed that there were two unsubmitted worksheets, both were for media testing, and both batches were discarded and not used for testing. The firm felt that the vagueness of the investigation was due to the investigating employees being reluctant to record direct statements that they feel may be blaming other employees, and they stated that they understood that lame is not part of an investigation and would work with the employees to understand this.

6. Deviation investigation DEV 5888 was opened due to found foreign particles found in two of three samples. The investigation found no lab error; however, the root cause is listed as none identified. The firm stated that they understood that they did identify a root cause but are reluctant to say it was due to the sample itself. We informed them that it is acceptable to say that no root cause is needed, or that the root cause is the sample, or the procedures can say not to go to a root cause in the absence of an LIR, but they shouldn't say no root cause was determined when one was.

Marty Edward Shelton, Vice President Operations, promised to correct all items discussed.

SAMPLES COLLECTED
No samples were collected during the inspection.

VOLUNTARY CORRECTIONS
The previous inspection resulted in the issuance of a 3-item FDA 483 for inadequate SOPs, change controls, electronic system validations, and risk assessments for workflow, change controls, and electronic systems, electronic systems not qualified for their intended use, and not including suspect test results on certificates of analysis. The firm made the following corrections to the 483 items:

Observation 1:
The observation was that the responsibilities and procedures applicable to the quality control unit are not in writing and fully followed, and included the following examples:

1. The firm's SOP for Work Order Generation, Work Completion, and Reporting of Results, allowed for two different pathways for investigation: one through the LIR system and one through the Work Order system. The citation centered on the inadequacy of investigations performed through the Work Order system. The firm enhanced the Work Order SOP to include more investigation questions and make the investigations in that system more robust.

2. The firm's "PacePort" and "Validation Package" applications were not managed and tracked under a centralized change management system. These applications compile PDFs from the firm's data systems and put them in a repository for customers to view the compiled data. The system was managed by the firm's corporate site and not the Oakdale site, so changes were handled at the corporate site and not covered by a change control system. The Oakdale site has since added changes to the server to their change control system.

3. The firm did not conduct a full risk assessment when implementing the "PacePort" and "Validation Package" applications. The firm has since performed a new risk assessment for these applications.

4. There was no comprehensive procedure specific to the use, administration, control, tracking, versioning, and validation for custom calculations in the Empower 3. The firm now has a validation SOP for the custom calculations.

5. The firm did not follow their complaint handling SOP when addressing client complaints. They did not initiate full investigations under their LIR system for complaints, but instead used the complaint handling SOP to do these investigations, which were insufficient.

The firm has since removed the investigation procedures in the complaint SOP and now handle them solely in the investigations SOP.

Observation 2:
The observation was that routine checking of electronic equipment is not performed according to a written program designed to assure proper performance, and then specifically mentions the following items:

1. The firm's "Validation Package", an internally developed Oracle Database 10g application, had not been qualified for its intended purpose according to an established protocol and acceptance criteria. This program pulls scanned PDFs from the server and complies them to send to customer. The firm has now qualified the system.

2. The firm's "PacePort" web-based portal had not been qualified for its intended purpose according to an established protocol and acceptance criteria. This is the firm's portal for customers to obtain their testing results and data. The firm has now qualified the system.

3. The firm uses custom calculations (user-defined calculations) in Empower 3 and had not validated them for their intended use according to an established protocol and acceptance criteria. The firm has now validated the custom calculations in Empower 3.

4. The firm's LIMS application for the management, tracking, scheduling, and notification of facilities and equipment qualifications, calibrations and preventative maintenance events had not been qualified for its intended purpose according to an established protocol and acceptance criteria. The firm's equipment scheduling portion was not qualified until 2018 even though the firm started using it in 2013. The system has since been qualified.

5. The firm's automated laboratory glassware washer had not undergone an adequate performance qualification. The firm has since evaluated the issue and written a protocol that includes demonstration of the successfully removal of residues and analytes, which is still ongoing.

Observation 3:
The observation was that the firm excluded failing testing results on the final Certificate of Analysis (CoA) when conducting individual impurities assessments without a valid, documented, scientific justification for its exclusion. The site gives all testing data to all customers, but did not put all results on the CoA, just the final results. The firm now puts any suspect results on the CoA.

EXHIBITS COLLECTED

1 Oakdale Organizational Charts, 7 pages

ATTACHMENTS

1 Issued 482, 3 pages

Matthew B. Casale -S
Digitally signed by Matthew B. Casale -S
Date: 2024.08.02 15:49:20 -04'00'

Matthew Casale
Investigator
U.S. Food and Drug Administration

Emmanuel T. Donyina -S
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Emmanuel Donyina
Investigator
U.S. Food and Drug Administration