DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	11/7/2025-11/24/2025* FEI NUMBER 3014213973

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Joshua A. Butters, Chief Executive Officer

FIRM NAME	STREET ADDRESS
Synergy Spine Solutions, Inc.	357 Mccaslin Blvd , Suite 120
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Louisville, CO 80027-2949	Sponsor

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:
The following observations are associated with the review of protocol #110-00001: A Multi-Center, Prospective, Historically Controlled Pivotal Trial Comparing The Safety And Effectiveness Of The Synergy Disc To Anterior Cervical Discectomy And Fusion In Patients With One-Level Symptomatic Cervical Degenerative Disc Disease (DDD).

OBSERVATION 1
An investigator was not complying with the signed agreement, requirements of the regulations and conditions of approval imposed by the IRB or FDA and compliance of the investigator was not promptly secured.

Specifically,

1. Pregnant subjects or those planning pregnancy during the study were excluded from enrollment. Therefore, pregnancy testing was required on Day 0 (surgery) to determine eligibility for participants of childbearing potential.

   At Site [redacted] five (5) participants of childbearing potential [redacted] refused pregnancy testing (signed waivers) and were enrolled in the study. Monitoring activities were inadequate to assure immediate protocol compliance.

   - IMV 2 (3/29/2022): Pre-surgical pregnancy tests results were missing from subject binder for [redacted] the data was SDV'd
   - IMV 3 (7/21-22/2022): Pregnancy tests from [redacted] and [redacted] were still outstanding, and one additional subject was enrolled without available results [redacted]
   - IMV 4 (11/10/2022): The monitor was informed waivers were signed by these participants which were considered 'standard of care' by the clinical site.

   No protocol deviations have been submitted to the IRB regarding this pregnancy verification risk prior to

AMENDMENT 1

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	Theressa B Smith, Investigator	X Theressa B Smith Investigator Signed By: Theressa B. Smith -S Date Signed: 11-24-2025 15:13:35	11/24/2025

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device implantation to ensure eligibility for enrollment.

OBSERVATION 2

For an investigational study, investigators were not provided with the information they need to conduct an investigation properly, proper monitoring was not ensured, reviewing IRBs were not promptly informed of significant new information about an investigation and FDA was not promptly informed of significant new information about an investigation.

Specifically,

1. The following modifications to Protocol #110-00001 have not been submitted to the FDA through required reporting (i.e. 5-day, or annual progress reports) after implementation.
   - Protocol Addendum version 1.0 (dated 08-03-2021): approved by the central IRB on 9/5/2021
   - Protocol Addendum Letter (dated 10-11-2021): Administrative Clarification approved by the central IRB on 10/22/2021 which included corrections to the schedule of events

   These changes extended visit windows and permitted remote visits when in-person follow-up visits were not feasible. Per documents, these changes were implemented to protect the rights, safety, and welfare of the subjects.

2. Based on the Protocol Addendum (dated 11 Oct 2021), the addendum remains in effect and applies to all protocol amendments until termination. The addendum was never terminated, nor were the changes incorporated into Protocol Version 7.0 (dated 08 Feb 2023) approved by the central IRB on ~~10/22/2021~~ **4/17/2023**.

3. There is no documented evidence the sponsor level approval of the Protocol Addendum (dated 10-11-2021), and approved by the IRB on 10/22/2021 has been provided to clinical Site #07 (b)(6) for submission to their local IRB.

4. No documented evidence exists that the sponsor and/or CRO reviewed and/or approved informed consent modifications for Site #07 (b)(6) in accordance with **MCRA** SOP CA-104 **Informed Consent Documents** (v 8.0, effective 4 March 2020).
   - The IRB approval notice (dated 12/2/2021) documents Site #07 submitted Informed Consent revisions for Protocol Addendum Version 1.0 (dated 30 August 2021) but should have included the administrative clarification (Protocol **Addendum** Letter, dated 10-11-2021) which included

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corrections for the schedule of events.

An interim monitoring visit completed by the monitor from 1/20/2022 – 1/21/2022 failed to identify these issues.

On 10/5/2023, clinical site staff were notified of patient stipend changes requiring modification to the ICF. The revised ICF (dated 11/8/2023) approved by the local IRB was provided to the monitor and CRO but still lacked clarifications outlined in the Protocol Addendum (dated 10-11-2021). These issues remain unresolved at the time of inspection.

5. EDC access was not provided timely to 17 of 20 Investigators to assure adequate oversight, review of study data and resolution of queries. Access was granted no more than 36 days before database lock (6/19/2025). For example,
   - Site #17 [redacted] was activated on 10/1/2021, Investigator access was granted on 6/13/2025
   - Site #22 [redacted] was activated on 9/20/2022; Investigator access was granted on 5/14/2025
   - Site #12 [redacted] was activated on 8/17/2021; Investigator access was granted on 6/11/2025

6. Per the Clinical Monitoring Plan (Section 7.1 – Monitor Training), monitors will receive training throughout the conduct of the study when protocol or other study related procedure changes occur. There is no documented training record regarding Protocol Addendum version 1.0 (dated 08-03-2021) and the Protocol Letter (dated 10-11-2021) for the following [redacted] (Sites# 5,12); [redacted] (Sites# 3, 6, 7) [redacted] (Site 3); [redacted] (Sites #3, 6, 7); and [redacted] (Sites # 3, 6, 7).

7. Verification of GCP training for all study staff is not adequately reviewed during interim monitoring visits. For example, For example, GCP training was not documented as current/ active during the entire period when the following staff participated in the study at Site #12 [redacted]: 1) [redacted] (on study from 8/6/2021 – 5/2/2025); and 2) [redacted] (on study from 8/6/2021 – 12/31/2022).

OBSERVATION 3

Records that FDA requires to be maintained for a particular investigation are not all accurate, complete and current.

Specifically,

1. EDC data is inaccurate for subjects who refused pregnancy testing. No documented evidence of

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sterility/menopause exists for subjects [redacted] No test results are documented for subjects [redacted]

Subject ID	Day 0	How was pregnancy status determined	Result
(b)(6)	19 Jan 2022	Non-childbearing potential (menopausal/surgical sterile)	
	2 Feb 2022	Urine	Negative
	2 Mar 2022	Non-childbearing potential (menopausal/surgical sterile	
	16 Mar 2022		Negative
	6 July 2022		Negative

2. Neck, left and right arm/shoulder pain were assessed using a 100 mm Visual Analog Scale (VAS) at baseline and follow-up visits. Protocol deviations are not reported when VAS source documents were shorter than 100 mm. Since the paper-based surveys are printed, this process has altered the VAS line measurements affecting the validity of the scale. For example,
   - VAS surveys printed from the IRB portal rather than using sponsor-provided worksheets yielded different measurements:
     - Subject [redacted] on 9/16/2021 (Pre-Op) – 100 mm scale
     - Subject [redacted] on 6/8/2022 (6 week) – 97 mm scale

   Source worksheets lack evidence of how clinical staff calculated VAS scores from paper records. This practice has continued through 7/2/2025 (Subject [redacted], 36-month VAS) despite multiple monitoring visits from November 2021 (IMVI) through July 2025 (IMV 9).

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***DATES OF INSPECTION**
11/07/2025(Fri), 11/10/2025(Mon), 11/12/2025(Wed), 11/13/2025(Thu), 11/14/2025(Fri), 11/17/2025(Mon), 11/18/2025(Tue), 11/20/2025(Thu), 11/21/2025(Fri), 11/24/2025(Mon)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."