July 24, 2023

Harita Vasireddi
Managing Director
Vimta Labs Ltd.
142, IDA, Phase II, Cherlapally
Hyderabad 500051, India

Dear Harita Vasireddi,

We are enclosing a copy of the Establishment Inspection Report (EIR) for the inspection conducted at your premises, **Vimta Labs Ltd., 142, IDA, Phase II, Cherlapally, Hyderabad, India,** by the United States Food and Drug Administration (FDA) from **January 9 to January 12, 2023**.

The Agency has concluded that this inspection is closed under 21 CFR 20.64(d)(3). We are therefore releasing a copy of the EIR for the inspected establishment to you. The EIR being provided to you comprises the narrative portion of the report; it reflects redactions made by the Agency in accordance with the Freedom of Information Act (FOIA) and Title 21, Code of Federal Regulations, part 20. However, this does not preclude you from requesting, and possibly obtaining, any additional information provided under FOIA.

The documents provided to you under FDA's FMD-145 Program have not been reviewed for public disclosure, and may contain confidential commercial information (e.g., applicant protocol information) and/or patient information (e.g., patient initials) that you already know in your capacity. FDA would normally redact this type of information before allowing the EIR's public disclosure. **If you were to disclose this information to others, you would be responsible for ensuring that sensitive information is adequately protected.**

If you would like a copy of the EIR that has been reviewed by FDA and redacted for public disclosure, you will need to submit a FOIA request specifically asking for a publicly disclosable version.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

If you have any questions about the released information, please contact me via email at CDER-OSIS-BEQ@FDA.HHS.GOV.

Sincerely,

Sean Kassim -S

Digitally signed by Sean Kassim -S
Date: 2023.07.28 14:08:11 -04'00'

Sean Y. Kassim, Ph.D.
Office Director
Office of Study Integrity and Surveillance
Office of Translational Sciences
Center for Drug Evaluation and Research
Food and Drug Administration
Building 22, Room 1442
10903 New Hampshire Avenue
Silver Spring, MD 20993

Enclosure: Establishment Inspection Report (narrative portion only)

ABBREVIATED NARRATIVE REPORT

This is an abbreviated report of a comprehensive routine, in-vivo bioequivalence inspection of Vimta Labs, Ltd., a biopharmaceutics clinical facility, which was conducted per [redacted] the Division of Generic Drug Bioequivalence Evaluation, Office of Study Integrity and Surveillance, Center for Drug Evaluation and Research (CDER-OSIS). This foreign site inspection was conducted as part of foreign trip [redacted] under Compliance Program 7348.003, In Vivo Bioavailability- Bioequivalence Studies, Clinical.

The previous inspection was conducted 8/12-8/16/19 and [redacted] failure to maintain adequate subject source records related to screening chest x-rays. There was one discussion item regarding lack of details in their written procedures for the selection and retention of reserve samples. This inspection found the discussion item to be corrected. They have since switched to digital x-rays, and all subjects had a legible chest x-ray prior to enrollment.

The current inspection covered the following bioequivalence trial:

[redacted] Protocol #00951/21-22: An open-label, balanced, randomized, single oral dose, two-treatment, three-sequence, three-period, partial replicate crossover bioequivalence study of nisoldipine extended-release tablets, 8.5 mg of Amta Labs Limited, Hongkong (Manufactured by Yichang Humanwell Pharmaceutical Co., Ltd, China) with Sular (nisoldipine) extended-release tablets 8.5 mg, Manufactured for Covis Pharma Zug, 6300 Switzerland, in normal healthy, adult, human study participants under fasting conditions.

Vimta Labs, Ltd., herein referred to as Vimta continues to operate as a clinical site for bioavailability and bioequivalence studies. The Managing Director, Harita Vasireddi, stated there have been no significant operational or administrative changes since the previous inspection.
The current inspection covered the following bioequivalence trial:

> [redacted] **Protocol *#00951/21-22: An open-label, balanced, randomized, single oral dose, two-treatment, three-sequence, three-period, partial replicate crossover bioequivalence study of nisoldipine extended-release tablets, 8.5 mg of Amta Labs Limited, Hongkong (Manufactured by Yichang Humanwell Pharmaceutical Co., Ltd, China) with Sular® (nisoldipine) extended-release tablets 8.5 mg, Manufactured for Covis Pharma Zug, 6300 Switzerland, in normal healthy, adult, human study participants under fasting conditions***

Investigator: Sudershan Vishwanath, M.D. is a medical doctor and pharmacologist. He informed me he started at Vimta as a clinical investigator in 2006 and left to work for another CRO in 2018 and returned in 2019. He stated he does not practice elsewhere and works here Monday through

Friday and every other Saturday and was the principal investigator for the covered trials. Dr. Vishwanath met with me briefly on 1/10/23 to explain his oversight of the covered study, receipt of the investigational products (IP), and the informed consent process.

The study was sponsored by AMTA Labs Limited, of Wanchai, Hong Kong [redacted] Naithika Independent Ethics Committee of Habsiguda, Hyderabad, India approved the trial. I verified the site obtained the ethics committee approval prior to screening any subjects.

On 1/9/23, I presented my credentials and business card to Executive Director, Harriman Vungal and Managing Director, Harita Vasireddi, who identified herself as the most responsible person on site. Associate VP of Quality Assurance, Ms. Anuradha Vadupu, Quality Control Manager, Ms. Madhavi Katragadda, and VP of Clinical Research, Mr. B V Ramakrishna Rao were present during the opening meeting and delegated site staff to answer questions and provide records throughout the inspection. Senior Manager of Process Excellence and Customer Experience Manager, Ms. Sudheshna Vungal was responsible for scribing and preparing scanned records on the USB drive provided to me. I identified the study during the opening meeting. The records were onsite and available after I finished the facility tour.

I reviewed records covering ethics committee approvals, monitoring reports, sample processing, and test article accountability, freezer and IP storage temperature monitoring, and maintenance and calibration of the two deep freezers and two of the four refrigerated centrifuges and ECG machines used during the study and associate written procedures. The site does not currently utilize electronic CRFs but are in the process of testing an electronic records system. All hardcopy documents were scanned upon completion of the study for submission to the sponsor.

I observed general screening, IP dispensing pre-study, and PK sample collection, processing, and transfer to deep freezer storage operations at various times throughout the week.

Table 1 depicts the subject records reviewed for eligibility criteria; protocol required assessments; dosing and pharmacokinetic (PK) sampling and processing; adverse events; and discontinuations. I did not observe any discrepancies between the source and data provided in the background information.

They do mass general screenings to identify subjects that should meet study specific criteria. I verified all 56 enrolled subjects had signed the study specific informed consent form (ICF) and their general screening ICF.

Table 1

# Subjects screened	# Subjects enrolled	# Subjects completing Period I	# Subjects completing Period II	# Subjects completing Period II	30 records reviewed (Subject #s)
56	48	47*	47#	48	2, 4, 5, 6, 8, 10, 12, 13, 14, 16, 18, 20, 21, 22, 24, 26, 28, 29, 30, 32, 34, 36, 37, 38, 40, 42, 44, 45, 46, 48

*Subject 24 discontinued PK sampling after hour 4 due to an episode of vomiting but remained admitted throughout the end of Period I and completed periods II-III (Reference and Test exposure) without further adverse events and was therefore still evaluable per the protocol.

Subject 07 did not come for Period II but completed periods I and III (Reference and Test exposure) and was therefore still evaluable per the protocol.

All subjects were healthy male volunteers who appeared to meet eligibility criteria. Protocol deviations (including late PK sampling times), AEs, and discontinuations were reported accurately by the site and listed in the clinical study report (CSR). I verified the site's randomization schedule to the dosing of 100% of subjects from both studies and did not observe any discrepancies. Test article accountability records were in order and retention samples were selected randomly prior to starting the study.

This was an open label study where only analytical staff were blinded. Samples were identified by study number, subject ID, and timepoint.

Per the assignment memo, I verified retention samples were obtained and stored appropriately, but did not collect them. Lot numbers of the IP retention samples were consistent with those listed in the CSR. [redacted] I randomly selected three other studies to confirm the presence and storage conditions of the retention samples and found no concerns. **Exhibit 1** contains written assurance from both Mr. Vinay Kothapali, Clinical Research Associate in charge of pharmacy and the Executive Director of Operations, Mr. Harriman Vungal that the retention samples are representative of those used in the inspected studies and that they have been stored per label requirements [20-25°C].

Exhibit 2 contains a list of bioavailability and bioequivalence studies conducted by the site since the last inspection. Reserve samples are stored on site. Archived records are either stored onsite or at their other facility in Hyderabad [redacted].

No refusals were encountered during the inspection and there were no complaints reported for the site. Records were provided to me on a white USB with the Vimta Labs, Ltd logo. This USB and a CD containing the retention sample photos were each officially sealed in separate FDA525 envelopes and sent to OSIS for archive as original source records (**Exhibits 3** and **4**).

No FDA 483, Inspectional Observations, was issued at the conclusion of the inspection; however, the following was discussed with the site:

1. It is their procedure to have Clinical Assistants or coordinators explain the informed consent and answer questions before the subjects sign. Then they see one of the clinical investigators to have any further questions answered. When I asked why they signed before speaking to the investigator, they said, they could withdraw consent after speaking with the PI if they learned of something that made them change their mind. I explained, they are not informed, by definition, if all their questions were not answered. They agreed to change the order of the process to signing after speaking with an investigator. On 1/11/23, Mr. Rao showed me the proposed language for updating the consent process in SOP 22/59.

2. The x-rays for subjects 5, 11, 20, 45 and 48 were not taken on full inspiration resulting in less clarity of the lower thoracic region. In addition, they routinely placed the lead ID markers in a position that obscures some of the shoulder anatomy. CI, Dr. Sreeman Narayana Shatagopam stated the films were adequate because the cardiologist had not requested a re-take of the films. I maintained that just because the cardiologist did not reject them, does not necessarily mean they were taken on full inspiration. They provided me an example where the cardiologist had rejected films for lack of full inspiration to demonstrate that it has happened but not with the films in question. Mr. Vungal and Mr. Rao ultimately agreed they will re-train the x-ray techs to assure they are taking the PA chest films upon full inspiration.

3. When the PK sample times are closer together, they explained they put the samples into a cooler with dry ice and a data logger until they can be walked over to the deep freezer storage. They keep the data logger print out, but the records do not indicate which, if any, samples were in the cooler and when. Their records only indicate one time into freezer storage which pertains to when they are put in the long-term storage deep freezer. They agreed to update the form to include columns for the times the samples went in and out of temporary storage.

FDA correspondence should be addressed to Ms. Harita Vasireddi at the site's mailing address or harita@vimta.com.

ADMINISTRATIVE DATA

Inspected firm:	Vimta Labs, Limited
Location:	142, IDA Phase II, Cherlapally Hyderabad, 500051 India

Phone:	(+91)4027264141
FAX:	(+91)4027263657
Mailing address:	142, IDA Phase II, Cherlapally Hyderabad, 500051 India
Email address:	harita@vimta.com
Dates of inspection:	1/9/2023-1/12/2023
Days in the facility:	4
Participants:	**Dawn C Olenjack, Investigator - Dedicated BIMO Cadre**

Non-FDA Participants: Dr. Sachin Kapse, CDSCO Inspector
Agency: CDSCO
Purpose for Being Present: Observation
Dates of Participation: 1/9/2023, 1/10/2023, 1/11/2023, 1/12/2023

EXHIBITS COLLECTED

1	Declaration on IPs Pharmacist_Director 20230112, 1 page
2	List of Studies for Vimta, 1 page
3	USB containing electronic documents collected at the site
4	CD-R containing photos taken of retention samples at the site

[redacted]

Dawn C. Olenjack -S

Digitally signed by Dawn C. Olenjack -S
Date: 2023.01.14 08:47:38 -06'00'