July 27, 2021

VIA EMAIL [ORAPHARM1_RESPONSES@fda.hhs.gov]

Diana Amador-Toro
Program Division Director
Office of Pharmaceutical Quality Operations Division 1
U.S. Food & Drug Administration, Office of Regulatory Affairs
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Re: Response to Form 483
FEI 3012063246

Dear Ms. Amador-Toro:

Valisure, LLC responds to the Form 483 it received on July 6, 2021. The primary focus of the inspection, and several of the observations in the Form 483, was based on FDA's assumption that Valisure's laboratory testing activities are used for regulatory purposes and thus regulated by FDA and required to meet current good manufacturing practices (cGMP). This assumption is incorrect, and by way of this response Valisure intends to clarify its activities and commit to take actions to make them clearer in the future. As further described below, Valisure's laboratory is accredited to International Organization for Standardization (ISO) 17025 standards and Valisure typically performs analytical "screens" as opposed to product-specific cGMP testing that is required of manufacturers for regulatory purposes.

Valisure's testing activities are intended to provide additional information to manufacturers, pharmacists and others about the characteristics of certain drug products. Valisure's testing is not part of any manufacturer's cGMP quality system. Rather, Valisure provides additional information about certain attributes of a product which complements or supplements the testing that is done by the manufacturer for cGMP compliance. It is essential to understand that Valisure's customers do not use Valisure's testing and certification to determine whether drug products meet FDA specifications. To the extent Valisure's voluntary registration as an Analytical Laboratory unintentionally implicated FDA jurisdiction, Valisure plans to deactivate its FDA registration to clarify that its activities are not subject to cGMP requirements.

Valisure states on its website: "Valisure's mission is to independently check the chemical composition of medications before they reach consumers. Working with

stakeholders throughout healthcare and the pharma supply chain, we deliver enhanced quality assurance to your patients and networks." *See* https://www.valisure.com/. Valisure's testing is independent of the drug manufacturing process (e.g., stability testing, release testing), and the "enhanced" quality assurance Valisure provides to its customers is only for informational and marketing purpose and not for any regulatory purpose. Furthermore, Valisure's testing is not integral to the manufacturer's quality assurance activities regarding cGMP compliance and product release. Passing Valisure testing or obtaining a Valisure certification is not a requirement of drug manufacturing specifications nor FDA approval. In short, Valisure's testing is a voluntary measure that its customers choose as a novel approach to underscore their commitment to quality.

FDA's cGMP regulations apply to "methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a drug to assure that such drug meets the requirements of the act as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess." 21 C.F.R. § 210.1(a). FDA broadly defines "manufacture, processing, packing, or holding of a drug product" to include "packaging and labeling operations, ***testing***, and quality control of drug products." 21 C.F.R. § 210.3(b)(13) (emphasis added). But FDA's authority does not extend to independent laboratories like Valisure, which conducts testing outside the traditional drug cGMP manufacturing and quality control processes. Indeed, none of the laboratory controls required by the cGMP regulations in 21 CFR Parts 210 and 211 is relevant to the Valisure's activities, a point that FDA investigators acknowledged during the close-out meeting of the inspection and is reflected in the absence of any regulation cited in the 483 Valisure received.

FDA guidance further supports Valisure's position that it is not subject to cGMP requirements: "The regulations enable a common understanding of the regulatory process by describing the requirements ***to be followed by drug manufacturers, applicants***, and FDA." *See* FDA Current Good Manufacturing Practice (CGMP) Regulations, at https://www.fda.gov/drugs/pharmaceutical-quality-resources/current-good-manufacturing-practice-cgmp-regulations (emphasis added). Valisure is not a drug manufacturer nor an applicant for a drug product subject to pending FDA review and approval.

Although FDA cites Valisure for not validating its test methods in accordance with cGMP standards, FDA recognizes there are situations "beyond routine quality control tests" in which drug manufacturers can use unvalidated methods (e.g., an "investigation of an atypical impurity or possible contaminant of a drug product or any of its components"). *See* FDA Questions and Answers on Current Good Manufacturing Practices – Laboratory Controls, at https://www.fda.gov/drugs/guidances-drugs/questions-and-answers-current-good-manufacturing-practices-laboratory-

controls#7. Indeed, all testing conducted by Valisure is "beyond routine quality control tests," as its test results are not intended to nor used for any regulatory purpose. Valisure employs the rigorous ISO 17025 quality management system to ensure the testing conducted by Valisure is reliable and accurate. The company is accredited to international ISO/IEC 17025:2017 standards, which demonstrates technical competence for the specific tests it conducts (e.g., dosage test, excipient identification, dissolution test, gluten detection, elemental impurities test, and impurities test), and the operation of a laboratory quality management system. This accreditation was recently renewed in May 2021 by Perry Johnson Laboratory Accreditation, Inc. (Attached as **Exhibit** 1.)

The certification Valisure provides is solely for informational or marketing purposes. Customers choose drug products that bear the Valisure certification because they believe it provides added assurance about the safety of the drug products. Valisure's customers, however, understand that the certification Valisure provides is limited. The Certificate of Analysis states: "The specific medication you received was not analyzed and an analysis of your medication could yield different results. Valisure, LLC does not make, and specifically disclaims, any representations or warranties with regard to these results as they relate to the medication provided to you, including, without limitation, any expressed or implied warranties, warranty of merchantability, warranty of performance, or warranty of fitness for a particular purpose." There is no expectation among recipients of Valisure's certification that the company's testing activities meet the cGMP standards for drug manufacturing or that its certification is based on FDA approved specifications. For example, Valisure's certification program includes a daily intake limit for the drug contaminant N,N-Dimethylformamide that is over one hundred times more strict than current FDA specification.

Pharmaceutical companies, such as (b) (4), who contract with Valisure for these optional testing services acknowledge in Valisure's standard contracts that Valisure's results "are not intended to be a statement, claim or indication of efficacy or suitability of the sample," and "make no claim or indication of the relative efficacy and/or suitability of your pills or the samples as compared with other subsets, batches, lots, brands, formulations, or treatments." ((b) (4) Agreement, attached as **Exhibit** 2.) Pharmaceutical companies also agree that they "have sole responsibility to comply with all relevant federal and state laws, rules and regulations (including without limitation those regulations issued by the Food and Drug Administration)." Furthermore, pharmaceutical companies that sign such contracts as shown in **Exhibit** 2, demonstrate full understanding of these agreements and have specifically made statements that "Valisure analysis and certification services are not used for any regulatory requirement of (b) (4) and that "(b) (4) does not utilize Valisure for the manufacture, processing, packing, or holding of any of (b) (4) products." (b) (4) Statements, attached as **Exhibits** 3 and 4).

Based on feedback during the inspection, Valisure understands that these contractual provisions and the claims on the certification it provides to its customers could be improved to clarify that the testing it performs is not intended for or applicable to any regulatory purpose, including product release. As a corrective action, Valisure will review and revise these claims to further clarify that Valisure's services are not intended for and not appropriate for any regulatory purpose.

The company's voluntary registration with FDA as an Analytical Laboratory establishment is not dispositive of FDA regulation over Valisure. A third-party laboratory is required to register with FDA only if it engages in "control activities for a registered drug establishment (e.g., consulting laboratories)," which Valisure does not. The company's former pharmacy activities do not trigger FDA jurisdiction as pharmacies generally are exempt from FDA registration requirements under 21 C.F.R. § 207.13(a). (Note that the company sold and transferred its pharmacy subsidiary in April 2021.) Even if the company was deemed to "manufacture" or "relabel" drugs due to its testing activities, those activities are exempt from registration under 21 C.F.R. § 207.13(e) because they are for drugs solely for use in "chemical analysis and not for sale." The company did not appreciate the requirements for establishment registration at the time it voluntarily registered as an Analytical Laboratory and it did not anticipate that continued voluntary registration could lead to assumptions by FDA that Valisure's testing is used for regulatory purposes; therefore, it intends to deactivate its establishment registration with FDA.

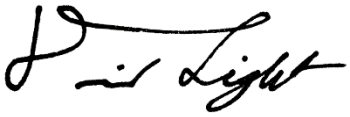
FDA separately cited Valisure for activities conducted by ValisureRx, LLC, a former subsidiary of Valisure, LLC which was sold and transferred to a third party in April 2021, for failing to meet certain verification, recordkeeping and reporting requirements under the Drug Supply Chain Security Act (DSCSA) as a pharmacy or distributor trading partner. These alleged violations related to failing to follow certain procedures for identification and reporting of suspect or illegitimate products. Valisure has maintained a certified drug testing program to identify and detect quality issues with certain drug products. During the relevant time period, all drug products distributed or dispensed by ValisureRx were subject to this certified testing program, and ValisureRx under both its distributor and pharmacy licenses maintained policies and procedures to identify and investigate any products deemed "unfit" and to remove these products from the distribution chain. Thus, Valisure's policies and procedures met the intent of the DSCSA requirement for identifying and investigating suspect and/or illegitimate products. Valisure also maintained procedures to send such products to reverse distributors for destruction. Valisure has also contacted manufacturers of testing results after products were released such that those manufacturers were put on notice about potential issues with the quality of their products. Finally, Valisure has submitted several

Citizen Petitions to FDA to alert the Agency of potential quality issues for certain prescription and OTC drug products.

Although ValisureRx may have been subject to DSCSA requirements previously, Valisure, LLC no longer performs any dispensing or wholesaler operations since the sale and transfer of ValisureRx to Medly Pharmacy in April 2021. The company has a transition services agreement that enables Medly to continue using the Valisure name and the HIPAA-compliant e-commerce pharmacy software that is built into "shop.valisure.com" for a limited period of time. These are operationally difficult and complex systems and are part of the ongoing transition, though entirely operated by and the responsibility of Medly Pharmacy.

We hope this letter and the enclosed exhibits clarify Valisure's status as an independent laboratory not subject to cGMP regulation and without a pharmacy or wholesale business subject to DSCSA regulation. If helpful, we welcome the opportunity to meet with you in person to discuss in further detail Valisure's activities and plans. We also provide in the attachment detailed responses to each of the observations contained in the Form 483.

Very truly yours,



David Y.Y. Light

cc: Robert J. Martin, Investigator

Attachments