WARNING LETTER

KDunn and Associates, P.A. dba HealthQuilt

MARCS-CMS 611864 — FEBRUARY 16, 2021

Delivery Method:

VIA UNITED PARCEL SERVICE

Reference #:

21-HFD-45-02-02

Product:

Drugs

Recipient:

Kimberly Dunn, M.D., Ph.D.

President and Chief Medical Officer

KDunn and Associates, P.A. dba HealthQuilt

2504 Elmen Street

Houston, TX 77019-6712

United States

drdunn@healthquilt.com

Issuing Office:

Center for Drug Evaluation and Research | CDER

United States

WARNING LETTER

Ref.: 21-HFD-45-02-02

Dear Dr. Dunn:

This Warning Letter informs you of objectionable conditions observed during the U.S. Food and Drug Administration (FDA) inspection conducted from August 4 to August 13, 2020. Investigator Iris C. MacInnes, representing FDA, reviewed the role of KDunn and Associates, P.A. dba HealthQuilt (hereinafter referred to as HealthQuilt) as the sponsor of the following clinical investigation of the investigational drug **(b)(4)** (also referred to as **(b)(4)**) (hereinafter referred to as **(b)(4)**): "An Open-label Pilot Study to Assess the Efficacy and Safety of **(b)(4)** in Subjects and Their Quarantined Close Contacts Who Test Positive for COVID-19[1]." During the inspection, FDA also reviewed your conduct as a clinical investigator of the clinical investigation referenced above.

This inspection was conducted as a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to help ensure that the rights, safety, and welfare of human subjects have been protected.

At the conclusion of the inspection, Investigator MacInnes presented and discussed with you Form FDA 483, Inspectional Observations. We acknowledge our receipt of HealthQuilt's August 27, 2020, written response to the Form FDA 483.

From our review of the FDA Establishment Inspection Report, the documents submitted with that report, and HealthQuilt's August 27, 2020, written response to the Form FDA 483, we conclude that HealthQuilt, as the sponsor, and you, as the clinical investigator, did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations and the protection of human subjects. We wish to emphasize the following:

1. You failed to submit an IND for the conduct of clinical investigations with an investigational new drug that is subject to 21 CFR 312.2(a) [21 CFR 312.20(a), 312.20(b), and 312.40(a)].

In relevant part, the Federal Food, Drug, and Cosmetic Act (FD&C Act) defines the term *drug* as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals" [21 U.S.C. 321(g)]. HealthQuilt studied the efficacy and safety of **(b)(4)** in subjects who had

tested positive for COVID-19 or who were close contacts of subjects who had tested positive, to determine whether and to what extent **(b)(4)** has antiviral properties, helps patients with COVID-19 recover faster, and prevents transmission of disease. Because the product was intended for the treatment, cure, and prevention of COVID-19, it meets the definition of a drug under the FD&C Act. **(b)(4)** is not generally recognized as safe and effective for the above-referenced uses, and therefore this product is a "new drug" under section 201(p) of the Act [21 U.S.C. 321(p)].

To market a new drug lawfully, with certain exceptions not applicable here, a sponsor must obtain FDA approval of either a new drug application or an abbreviated new drug application under section 505 of the FD&C Act [21 U.S.C. 355]. An Investigational New Drug application (IND) allows a sponsor to obtain an exemption from this requirement in order to distribute an investigational drug [21 U.S.C. 355(i)]. FDA regulations require a sponsor to submit an IND before conducting a clinical investigation of a drug in human subjects, unless the clinical investigation qualifies for an IND exemption under 21 CFR 312.2(b). That regulation provides an exemption from the requirement to obtain an IND before initiating a clinical investigation of a drug if **all** the following exemption criteria are met:

• The drug product is lawfully marketed in the United States.
• The investigation is not intended to be reported to FDA as a well-controlled study in support of a new indication for use, and there is no intent to use the investigation to support any other significant change in the labeling of the drug.
• In the case of a lawfully marketed prescription drug, the investigation is not intended to support a significant change in the advertising for the drug.
• The investigation does not involve a route of administration, dosage level, use in a patient population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.
• The investigation is conducted in compliance with the requirements for institutional review set forth in 21 CFR part 56 and with the requirements for informed consent set forth in 21 CFR part 50.
• The investigation is conducted in compliance with the requirements of 21 CFR 312.7.

This clinical investigation of **(b)(4)** failed to meet at least the first criterion. The investigational drug **(b)(4)** used in the study was an unapproved new drug, administered to human subjects **(b)(4)** for **(b)(4)** to treat, cure, and prevent COVID-19. **(b)(4)** is not a lawfully marketed drug product in the United States and therefore was not exempt from the IND requirements. Before using **(b)(4)** in a clinical investigation, HealthQuilt was required to submit an IND to FDA and to have an IND in effect under 21 CFR 312.40. FDA records indicate that HealthQuilt failed to submit an IND before conducting a clinical investigation, in which **(b)(4)** human subjects were enrolled.

HealthQuilt's August 27, 2020, written response to the Form FDA 483 stated, "[O]ur intent in conducting this study was to evaluate the use of **(b)(4)** as a dietary supplement only." HealthQuilt also stated that, while it acknowledged and deferred to the Center for Drug Evaluation and Research that an IND was required, it did not intend to submit the results of the study in support of the product's approval as a new drug. In addition, HealthQuilt stated that it is in the process of working

with legal counsel to develop new policies and procedures regarding the initiation of future clinical studies, to ensure that such studies are conducted in compliance with 21 CFR part 312. HealthQuilt's response is inadequate because, as discussed above, **(b)(4)** is a drug under section 201(g) of the FD&C Act [21 U.S.C. 321(g)].

Further, **(b)(4)** cannot be a dietary supplement because it does not meet the definition of a dietary supplement under 201(ff) of the FD&C Act [21 U.S.C. 321(ff)]. **(b)(4)**, the investigational product used in your study, contains the **(b)(4)**. Based on available evidence, FDA has concluded that products containing **(b)(4)** are excluded from the dietary supplement definition under section 201(ff)(3)(B)(ii) of the FD&C Act [21 U.S.C. 321(ff)(3)(B)(ii)]. Under this provision, if an article (such as **(b)(4)**) has been authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, then products containing that article are outside the definition of a dietary supplement, unless the article was marketed as a dietary supplement or as a food before it was authorized for investigation as a new drug. **(b)(4)** has been previously authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public.[2] Further, FDA is not aware of any evidence that **(b)(4)** was marketed as a dietary supplement or as a food before being authorized for investigation as a new drug. Therefore, under 21 U.S.C. 321(ff)(3)(B)(ii), **(b)(4)** is excluded from the definition of a dietary supplement and may not be marketed as or in a dietary supplement.[3]

In addition, **(b)(4)** is intended for sublingual administration. The FD&C Act defines the term *dietary supplement* in section 201(ff)(2)(A) [21 U.S.C. 321(ff)(2)(A)] as a product that is "intended for ingestion." Because sublingual products are intended to enter the body directly through the skin or mucosal tissues, they are not intended for ingestion. Therefore, **(b)(4)** does not meet the definition of a dietary supplement under section 201(ff) of the FD&C Act for this additional reason.

Because **(b)(4)** is a drug under section 201(g) of the FD&C Act [21 U.S.C. 321(g)], and because this clinical investigation did not qualify for an exemption under 21 CFR 312.2 from the requirement to submit an IND, HealthQuilt was required to submit an IND for this clinical investigation before initiating the study and before enrolling human subjects, even if it did not intend to submit the results of this study to FDA for approval. There are no FDA records to indicate that HealthQuilt submitted an IND before conducting the clinical investigation of **(b)(4)**. We note that **(b)(4)** human subjects were enrolled at three clinical sites for this study. Subjects were administered **(b)(4)**, an unapproved drug, **(b)(4)** for **(b)(4)** for the treatment, cure, and prevention of COVID-19.

Moreover, HealthQuilt's corrective action plan does not provide sufficient details about how it would determine whether future clinical studies fall under the requirements of 21 CFR part 312. Without these details, we are unable to determine whether HealthQuilt's corrective action plan is adequate to prevent similar violations in the future.

2. You failed to maintain adequate records showing the receipt, shipment, or other

disposition of the investigational drug (21 CFR 312.57(a)).

As a sponsor, HealthQuilt was required to maintain adequate records showing the receipt, shipment, or other disposition of the investigational drug **(b)(4)**. These records were required to include, as appropriate, the name of the investigator to whom the drug is shipped, and the date, quantity, and batch or code mark of each shipment. HealthQuilt failed to maintain adequate records with respect to the investigational drug **(b)(4)**. Specifically, HealthQuilt did not maintain any records showing receipt, shipment, or other disposition of the investigational drug.

HealthQuilt's August 27, 2020, written response indicated that its understanding was that the requirements of 21 CFR part 312 were not applicable. HealthQuilt noted that it did not perceive any significant risk to the security of the product during transport, since it was delivered to HealthQuilt from the manufacturer in a private vehicle. HealthQuilt also indicated that for any future shipments received, records will be maintained as required under 21 CFR 312.57(a) using an inventory management system, and that, for any future studies, it would use a QR code/bar code tracking system.

HealthQuilt's written response is inadequate because it did not provide sufficient details about its plan for implementing additional measures and procedures to address the inspection findings concerning its failure to maintain adequate records. As a result, we are unable to determine whether HealthQuilt's plans appear sufficient to prevent similar violations in the future.

3. You failed to obtain informed consent in accordance with the provisions of 21 CFR part 50 [21 CFR 312.60 and 21 CFR 50.20].

As a clinical investigator, it is your responsibility to obtain informed consent in accordance with 21 CFR part 50. FDA's regulations at 21 CFR 50.20 state that, except as provided in 21 CFR 50.23 and 50.24, no investigator may involve a human being as a subject in research covered by the regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

The informed consent forms for the above-referenced clinical investigation were not in compliance with these regulations because the informed consent forms included the following statement:

"Subject agrees to waive, release, forever discharge and hold harmless the Schull Institute, KDunn and Associates, PA, HealthQuilt, Investigator, **(b)(4)** (maker of the supplement) its owners, principals, shareholders, investors, managers, employees, partners, attorneys, officers, directors, predecessors, successors, and assigns, from and against any and all claims, demands, causes of action or suits arising out of any type of physical, psychological or other financial injury, loss or damage,

including but not limited to illness, paralysis, death, loss of earnings, economic or emotional loss, that may occur as a direct or proximate result of participation in the study."

HealthQuilt's August 27, 2020, written response indicated that the understanding was that the requirements of 21 CFR part 50 did not apply because the study protocol was developed to monitor patients' treatment and not to support any research or marketing application. It was noted that language for the informed consent was provided by the manufacturer, **(b)(4)**. As a corrective action, this written response indicated that, going forward, any language purporting to release an investigator, sponsor, institution, or their agents from liability for negligence will be removed from any informed consent form subject to the requirements of 21 CFR part 50.

We are unable to determine if this written response provides a corrective action plan that, if properly carried out, would prevent this type of violation in the future. Specifically, this written response does not provide sufficient details about how you would determine whether future clinical studies fall under the requirements of 21 CFR part 50. Without these details, we are unable to determine whether your corrective action plan for removing exculpatory language from informed consent forms for studies subject to the requirements of 21 CFR part 50 is adequate to prevent similar violations in the future.

4. You failed to retain records required to be maintained under 21 CFR part 312 for a period of two years following the date a marketing application is approved for the drug for the indication for which the drug is being investigated; or, if no application is filed or if the application is not approved for such indication, until two years after the investigation is discontinued [21 CFR 312.62(c)].

As a clinical investigator, you are required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. You are required to retain these records for a period of two years following the date on which a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or the application is not approved for such an indication, until two years after the investigation is discontinued and FDA is notified.

You failed to adhere to these requirements. You were required to retain case histories, including informed consent forms, for a period of two years following discontinuation of the investigation, which was on July 23, 2020; however, you failed to retain at least eight signed and dated informed consent forms.

HealthQuilt's August 27, 2020, written response indicated that each subject whose original paper informed consent form could not be located was contacted to confirm that consent was obtained before starting the study. As a corrective action, it was indicated that, going forward, informed consent would be archived automatically into the subject's folder.

This written response is inadequate because it did not provide sufficient details about your plans for implementing additional measures and procedures to address the inspection findings regarding failure to retain records. For example, this written response did not address how you will retain study records for the required retention period. As a result, we are unable to determine whether your plan appears sufficient to prevent similar violations in the future.

This letter is not intended to be an all-inclusive list of deficiencies with this clinical study of an investigational drug. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You should address these deficiencies and establish procedures to ensure that any ongoing or future studies comply with FDA regulations.

Within fifteen (15) working days of your receipt of this letter, you should notify this office in writing of the actions you have taken to prevent similar violations in the future. Failure to address the violations noted above adequately and promptly may result in regulatory action without further notice. If you believe you have complied with the FD&C Act and FDA regulations, include your reasoning and any supporting information for our consideration. If you believe that HealthQuilt's written response to the Form FDA 483 dated August 27, 2020, fully explains the actions you have taken to prevent similar violations in the future, please communicate that to us in writing within fifteen (15) business days. You may refer to the written response dated August 27, 2020, in your response to this letter.

If you have any questions, please call Mark S. Miller, Pharm.D., at 301-796-2798. Alternatively, you may e-mail FDA at CDER-OSI-Advisory@fda.hhs.gov. Your written response and any pertinent documentation should be addressed to:

Mark S. Miller, Pharm.D., BCPS, RAC
CAPT, USPHS
Branch Chief
Compliance Enforcement Branch
Division of Enforcement and Postmarketing Safety
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Building 51, Room 5352
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely yours,

/S/

Donald D. Ashley
Director

Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

---

1 Coronavirus Disease 2019 (COVID-19) is the respiratory disease caused by the novel coronavirus called *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2).

2 *See*, for example, **(b)(4)**.

3 *See* FDA's **(b)(4)**, New Dietary Ingredient (NDI) Notification Response: **(b)(4)**.

Content current as of:
03/02/2021

Regulated Product(s)
Drugs

More Warning Letters