DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

July 23, 2014

Mr. Michael McGuffin
President
American Herbal Products Association
8630 Fenton Street
Suite 918
Silver Spring, MD 20910

Mr. Anthony L. Young
Mr. James W. Woodlee
Kleinfeld, Kaplan and Becker, LLP
General Counsel
American Herbal Products Association
1140 Nineteenth Street, NW
Suite 900
Washington, DC 20036

Re: Docket No. FDA-2013-P-1291

Dear Messrs. McGuffin, Young, and Woodlee:

This letter responds to the Citizen Petition (FDA-2013-P-1291) you submitted to the Food and Drug Administration ("FDA" or "the Agency") on October 17, 2013, on behalf of the American Herbal Products Association (AHPA).

The petition requests that FDA:

- "formally rescind FDA's policy of prohibiting Agency investigators from quoting or citing the cGMP [current Good Manufacturing Practices] regulations upon which they base their inspectional observations within 483s issued to conventional food and dietary supplement facilities; and

- "revise the IOM [Investigations Operations Manual] to expressly require that 483s issued to conventional food and dietary supplement facilities reference each cGMP regulation to which the Agency investigator's listed observations relate" (Petition at 2).

You cite to section 704 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA regulations (21 CFR Parts 110 and 111), the Investigations Operations Manual (IOM), and the Regulatory Procedures Manual (RPM) in support of these requests.

We have carefully considered your petition. We are denying your petition under 21 CFR § 10.30, for the reasons explained below.

BACKGROUND

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) requires an investigator, upon completing an inspection, to provide the establishment's owner, operator, or agent in charge a written report setting forth any conditions or practices observed which, in the investigator's judgment, indicate that any FDA-regulated product "(1) consists in whole or in part of any filthy, putrid, or decomposed substance, (2) or 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" (21 U.S.C. § 374(b)). The IOM[1] directs investigators to report significant objectionable conditions that relate to products and/or processes or other violations of the laws and regulations FDA enforces on a "Form 483—Inspectional Observations" (FDA 483) (IOM 5.1.1.4, 5.2.3).

FDA recognizes that inspectional observations on FDA 483s are of critical importance to both the Agency and regulated industry. An FDA investigator must ensure that the observations included on the FDA 483 are "significant and correlate to the regulated products or processes being inspected" (IOM 5.2.3). In other words, the observations must be factual and must correspond to the laws and regulations FDA enforces (IOM 5.2.3.2). In preparing the FDA 483, investigators generally use an automated report generating system called Turbo EIR, which allows the investigators to generate FDA 483s that document specific observations and include standardized paraphrases from the Code of Federal Regulations (CFR) to record how investigators believe their observations are associated with relevant regulatory requirements.

FDA investigators prepare FDA 483s during the course of the inspection and provide the report to the highest management official available during closeout discussions with management (IOM 5.1.1.4, 5.2.3.1). In most circumstances, FDA 483s are provided before the investigator leaves the premises, except where the FDA 483 is complex and requires additional time to be prepared (IOM 5.2.3.1). In those instances, FDA investigators will advise the firm that the inspection has not been completed and will return to issue the FDA 483 and discuss inspectional findings at a later date with the understanding that there should be no unreasonable or unwarranted delays in issuing and discussing the FDA 483 (IOM 5.2.3.1).

During the closeout discussion, Agency investigators will review all findings recorded on the FDA 483. At this time, investigators may discuss certain non-reportable observations with the firm's highest management officials (IOM 5.2.3.3, 5.2.7). Investigators are instructed to explain the significance of each listed observation and are encouraged to "relate each listed condition to the applicable sections of law and regulations administered by the FDA" (IOM 5.2.7). Investigators may also discuss certain "objectionable conditions" with management (IOM 5.2.3.3). These conditions include observations of "significant deviations from specific [l]aws and/or regulations" and observations of "questionable significance" and "deemed not to merit inclusion on the FDA 483" (IOM 5.2.3.3, 5.2.7). At that time, the firm's management may ask questions about the observations, request clarification, and inform the inspection team what corrections have been or will be made (IOM 5.2.3). During the closeout meeting, the firm also has the opportunity to provide input or insight into the observations on the FDA 483, which may lead to the determination between the firm and the FDA investigator that errors exist on the FDA 483. In such circumstances, FDA investigators have been trained to make corrections to the FDA 483 (IOM 5.2.3.1.6).

[1] The IOM is the primary guidance document regarding FDA inspection policy and procedures for field investigators. See http://www.fda.gov/iceci/inspections/iom/default.htm.

ANALYSIS

I. Request to Rescind FDA Policy

Your petition requests that FDA "formally rescind FDA's policy of prohibiting Agency investigators from quoting or citing the cGMP regulations upon which they base their inspectional observations within FDA 483s issued to conventional food and dietary supplement facilities" (Petition at 2). Contrary to the assertions in your petition (Petition at 1-2), there is no such policy. As discussed above, investigators are generally limited to describing their factual observations in the FDA 483. Investigator opinions or conclusions, quotations from regulations, or characterizations of conditions as "violative" are not "factual observations" and thus do not appear in FDA 483s (IOM 5.2.3.3).[2] Also, certain investigator observations are classified as "non-reportable" and excluded from FDA 483s.[3] While investigators are limited to recording their factual observations on FDA 483s, investigators are encouraged to "relate each listed condition to the applicable sections of law and regulations administered by the FDA" in their discussions with firm management (IOM 5.2.7). Moreover, FDA understands that the regular practice of its investigators is to include this topic in their discussions with firm management, consistent with the IOM's direction. While you asserted that FDA investigators "decline to orally identify the specific regulations that the listed conditions or practices purportedly violate" (Petition at 4), you provided no evidence in support of this statement and FDA has identified no reason to conclude that investigators are declining to discuss relevant regulations in discussions with firm management.

In that there is no general FDA policy "prohibiting Agency investigators from quoting or citing the cGMP regulations" for FDA to rescind, we are denying your request to rescind FDA policy.

II. Request to Revise the IOM

Your petition states that observations on the FDA 483 "do not normally inform recipients of the specific FDA regulation or regulations relevant to each observation" (Petition at 1) and that they "do not cite to, or use specific wording from, FDA regulations" (Petition at 1). Your petition requests that FDA "revise the IOM to expressly require that 483s issued to conventional food and dietary supplement facilities reference each cGMP regulation to which the Agency investigator's listed observations relate" (Petition at 2). In support of this request, your petition asserts that citing cGMP regulations in 483s will further agency interests; promote understanding, compliance, and transparency; and harmonize the IOM with the RPM. We deny your request for revision of the IOM for the following reasons.

A. FDA's current practice furthers the Agency's interests

Depending on the inspectional findings, additional Agency vetting may be required to determine the appropriate Agency action. FDA's practice is to inform firms of violations and provide written citations after appropriate Agency vetting has taken place. In most cases, the observations in the FDA 483 will not have been reviewed within the Agency until the inspection has been closed out with the firm. Therefore, as discussed above, the IOM advises investigators to limit their observations in 483s to factual observations. The FDA Form 483 itself makes clear that it represents only factual observations and not determinations

---

[2] The determination of whether a condition is violative is an Agency decision made after considering the circumstances, facts, and evidence involved (IOM 5.2.3.3).

[3] Non-reportable observations include: factual observations that require concurrence within the Agency (IOM 5.2.3.2); or, for the foods program, observations pertaining to promotional materials, the lack of required food facility registration, or the use of an unsafe food additive or color additive (IOM 5.2.3.3). Corrective actions are reported in the Establishment Inspection Report (EIR) and not on the FDA 483 (IOM 5.2.3.3).

regarding compliance. The form states: "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" (FDA Form 483 (9/08)).

The process of agency vetting can involve multiple layers of review. After FDA investigators present FDA 483s to firm management and close out the inspections, Agency personnel review the results of the inspections to make compliance determinations. The vetting process may involve review from Office of Regulatory Affairs (ORA) headquarters managerial staff, applicable product Center components, and the Office of Chief Counsel, as necessary. Once input from these offices is obtained, the Agency will take appropriate action, which may include informing a firm of violations, referencing corresponding regulations. FDA provides written communication of this information in Warning Letters and other documents as appropriate.

It is important for FDA to have an opportunity to perform this review process, because it helps ensure the Agency's actions are consistent, reasonable, and fair. Therefore, FDA concludes that limiting FDA Form 483 to factual observations advances the Agency's interests.

Your petition argues that FDA's practice contrasts with the approach of the US Department of Agriculture's (USDA) Food Safety Inspection Service (FSIS) on FSIS Form 5400-4, Noncompliance Record (Petition at 4, fn 8). FDA recognizes that FSIS directs its inspection program personnel to notify firms of specific regulations with which the firm has failed to comply (FSIS Directive 5000-1, V.II.C). However, the role of FSIS inspection program personnel completing FSIS Form 5400-4 is different than the role of FDA investigators completing FDA Form 483. FSIS inspection program personnel verify compliance with specific USDA regulations and make determinations about whether plants are in compliance with the regulations (FSIS Directive 5000-1, V.I.E.2). FSIS Form 5400-4 is titled "Noncompliance Record" and specifies "[t]his document serves as written notification that your failure to comply with regulatory requirement(s) could result in additional regulatory or administrative action" (FSIS Form 5400-4). It represents an agency determination of noncompliance, and includes information about associated appeal rights ("You are hereby advised of your right to appeal this decision…") (FSIS Form 5400-4). By contrast, FDA inspectors are trained to make observations and record a narrative "so that others may take the appropriate action" (IOM, 5.10). As discussed above, the FDA Form 483 explains that it lists inspectional observations and does not represent an agency determination regarding a firm's compliance. The different roles of FDA investigators and FSIS inspection program personnel, and FSIS Form 5400-4 and FDA Form 483, reflect the different needs of their respective agencies. FDA believes that its practice suits its interests.

B. The IOM's procedures promote understanding, compliance, and transparency

The FDA 483 is not the only means by which FDA investigators communicate with inspected firms. We believe it imperative that channels of communication are used effectively. In fact, FDA investigators' engagement with firm representation begins well before an investigator presents an FDA 483 to the firm.

Investigators are trained to interact daily with firm representation throughout the course of an inspection to discuss and exchange information to aid in our efforts towards achieving compliance with Agency regulations. This interaction may include firm representation guiding FDA investigators through a facility at the start of the inspection and traditionally includes a direct communication channel that is often used throughout the course of the inspection. FDA investigators directly interact with firm representation, asking applicable questions based on FDA observations and obtaining real time responses from the firm. The firm can ask questions directly to the FDA investigators, who can respond by providing insight on FDA regulations and answering questions related to what the investigators are observing at certain points in the inspection.

If an inspection is to last more than one day, FDA investigators are trained to have meetings with firm representation at the close of each day. These meetings allow for an additional direct line of communication between the investigators and the firm, providing an opportunity for the firm to ask questions pertaining to the day's activities. Investigators should make every reasonable effort to discuss all observations with management on an ongoing basis, to minimize surprises, errors, and misunderstandings when the FDA 483 is issued (IOM 5.2.3). The FDA investigator may inform the firm what has been accomplished thus far, what the investigator intends to cover the next day, and when the investigator expects the inspection to end. Industry may use this opportunity to ask questions about the observations, request clarification, and inform the inspection team what corrections have been made or will be made during the inspection process (IOM 5.2.3). FDA has found these daily meetings to be of great benefit to both firms and the inspection team. They give firms notice of the inspection team's activities, allowing management to anticipate what aspects of their firm's business may be impacted. They also allow firms to make preparations for the inspection team's activities, thereby enabling the inspection team to be more efficient on future days of the inspection.

Finally, as discussed above, investigators hold a closeout discussion with firm management in which they review the observations on the FDA 483, discuss other observations as applicable, and explain how their observations relate to applicable laws and regulations (IOM 5.2.3.3, 5.2.7). During this meeting, firm management may ask questions and provide input (IOM 5.2.3).

In your petition, you suggest that a firm may not know what regulation is relevant to applicable factual observations on the FDA 483, even after the closeout meeting between the firm and the investigator. FDA concludes, however, that its current practices provide sufficient information to regulated firms and allow multiple opportunities for dialogue and clarification in the event that a firm has questions.

In addition, FDA notes that the IOM instructs investigators to "[u]se Turbo EIR to generate the FDA 483 where applicable cite modules exist" (IOM 5.2.3). References for 21 CFR Part 110 (cGMPs for human foods) and Part 111 (dietary supplement cGMPs) are already included in Turbo EIR's citation database.[4] Investigators generating FDA 483s using Turbo EIR document specific observations using standard paraphrases from the CFR to inform the firm how the investigator believes the observations relate to relevant regulations. Moreover, FDA has published data from Turbo EIR's system that identifies specific numerical citations from the relevant regulations and links them to the language used on FDA Form 483s constructed using Turbo EIR.[5] FDA publishes this information to improve the public's understanding of how the FDA works to protect the public health, to provide the public with a rationale for the Agency's enforcement actions, and to helps inform public and industry decision-making, allowing them to make more informed marketplace choices and help to encourage compliance. In short, the inspection citations and inspectional observation summaries are intended to improve transparency and understanding.

C. The IOM is consistent with the RPM's "prior notice" policy

Your petition also asserts that the IOM conflicts with the RPM's "prior notice" policy (Petition at 6-7).[6] The "prior notice" policy is intended "to afford individuals and firms an opportunity to voluntarily take appropriate and prompt corrective action prior to the initiation of enforcement action" (RPM, 10-2-3). The

---

[4] See. FDA Inspection Observations, http://www.fda.gov/iceci/EnforcementActions/ucm250720.htm (last updated Jan. 15, 2014). Although Turbo EIR's citation database contains citations to Part 110 (cGMPs for human food) and Part 111 (dietary supplement cGMPs), it does not contain citations for all areas of the law enforced by FDA.

[5] See. e.g., FY 2013 Inspectional Observation Summaries, http://www.fda.gov/ICECI/Inspections/ucm381526.htm (last updated May 15, 2014); Inspection Citation Data Sets, http://www.fda.gov/ICECI/Inspections/ucm346077.htm (last updated Mar. 31, 2014).

[6] Section 10-2 of the RPM defines "prior notice" and establishes uniform criteria to determine if adequate prior notice has been provided (RPM, 10-2-1).

RPM makes clear that "[e]xcept in a few specifically defined areas, the Food and Drug Administration (FDA) has no legal obligation to warn firms or individuals that they, their practices, or their products are in violation of the law prior to taking formal enforcement action" (RPM 10-2-2). FDA understands that providing firms with an opportunity to take corrective action before initiating an enforcement action is often beneficial to firms and the Agency, and therefore, FDA's typical practice is to provide firms with prior notice.

The RPM lists five criteria for evaluating the adequacy of prior notice (RPM, 10-2-3). None of these criteria includes notification of regulatory citations. Furthermore, the RPM describes several means by which prior notice may be given: warning letters, civil suits, administrative action, or other "less formal ways" (RPM, 10-2-4). FDA 483s are only one of these "less formal ways." Prior notice may also be given in regulatory meetings and during investigators' discussions with management. The RPM's "prior notice" policy is not restricted to written communications. "Prior Notice may be provided orally or in writing" (RPM, 10-2-4). Consistent with the IOM's provisions, the RPM states that notice "may well be the Investigator's discussion of objectionable conditions with responsible management at the conclusion of the inspection." Finally, the RPM does not indicate any preference for notification via FDA 483s; rather it recognizes that "Warning Letters are the principal means by which the agency provides prior notice of violations and of achieving voluntary compliance" (RPM, 10-2-4). This is also consistent with the IOM and FDA's current practice.

Thus, FDA does not agree that FDA 483s must include regulatory citations in order to provide adequate prior notice of noncompliance or that the RPM's "prior notice" policy is inconsistent with the IOM.

CONCLUSION

For the reasons explained above, we are denying your petition under 21 CFR § 10.30.

Sincerely,

Melinda K. Plaisier
Associate Commissioner for Regulatory Affairs