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Kratom Industry GMPs Target Swaying FDA By Exceeding Agency Standards

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Author:

Eileen Frances
eileen.francis@informa.com

Executive Summary

“We want to show that the kratom industry is maturing, that people want to do the right thing,” says AKA Chairman Dave Herman. The standards go “well beyond” FDA's minimum GMP requirements for dietary supplements, AKA says.

The American Kratom Association expects a good manufacturing practices program it developed and a database of compliant firms will demonstrate the industry’s commitment to safety through self-regulation and help end FDA's objections to the herb's use in dietary supplements.

“We want to show that the kratom industry is maturing, that people want to do the right thing,” said AKA Chairman Dave Herman.

The program's roll-out to stakeholders will be complete on Nov. 16, with all the particulars on establishing standards, processes and procedures for compliance in place. It will include manufacturing, labeling and verification requirements for kratom dietary supplements *(see box below)*.

The standards go “well beyond” FDA's minimum GMP requirements for dietary supplements, AKA notes in an Aug. 20 release on the standards.

The program “will send the clear message to the FDA and federal and state legislators that we are committed to removing adulterated or contaminated kratom products from the marketplace, and we will not allow impermissible health claims to be made by any credible kratom vendor,” the association says.

AKA Kratom GMP Standards

AKA’s GMP standards are a “minimum” baseline for manufacturing kratom products. This is an outline of the areas covered in the program:

Standard Operating Procedures

- personnel
- manufacturing facility and equipment
- manufacturing operations

Recordkeeping

- general
- master manufacturing records
- batch production records
- traceability

Adverse Event Reporting System and Recalls

- establish and implement a written adverse event reporting system
- recalls

Marketing

- labeling and advertising

Companies that participate in the program must have facilities audited by independent third parties that will verify compliance with FDA GMPs for supplements, plus additional requirements established under AKA's program, the association says. It will maintain a list of auditors qualified through training and experience to audit against the AKA program criteria as well as conduct dietary supplement GMP audits.

Over roughly the next month, AKA will train auditors on the program, giving vendors time to refine their existing processes or implement new protocols, the association said. It has conducted two training seminars for stakeholders and plans another on Sept. 26.

Supplements that meet the exacting standards of the program will be listed on the association's website and be eligible to bear the “AKA Certified” seal.

To demonstrate how high its GMP standards bar is, AKA says companies participating will need to test every production lot of kratom to assure it is free of any microorganisms of public health concern, as well as disclose the quantity of the mitragynine and 7-hydroxymitragynine alkaloid in the product.

Mitragynine and 7-hydroxymitragynine were the subjects of an FDA public health advisory published in 2017 after the agency found the two kratom compounds are opioids. (Also see "FDA Turns Kratom's Future In US Dietary Supplement Market Into History" - Rose Sheet, 14 Nov, 2017.)

FDA also submitted its findings on kratom's safety and chemical profile to the Drug Enforcement Administration, which is considering scheduling the two constituent ingredients as controlled substances. (Also see "DEA Proposal To Schedule Kratom Stirs Wave Of Opposition" - Rose Sheet, 8 Dec, 2016.)

Scheduling those substances would shut down US sales of products containing kratom, which is extracted from a tropical deciduous and evergreen tree in the same biological family as coffee and native in Southeast Asia and currently is used by 3m to 5m US consumers.

Prior to publishing its findings on mitragynine and 7-hydroxymitragynine, FDA issued an import alert for kratom in 2012 and updated it in 2014 and 2016. FDA advised firms that kratom is a new dietary ingredient that has not been notified to the agency with proof of safety for its intended use in a supplement.

Salmonella contaminations also have heightened scrutiny. In July, FDA reported the link between kratom and salmonella is more widespread than initially thought. (Also see "Salmonella In Kratom, Like Use Of The Herb, Exceeds FDA Expectations" - Rose Sheet, 2 Jul, 2018.)

Gottlieb 'Won't Talk To Us'

Herman says during a leadership summit in May AKA solicited feedback from stakeholders about manufacturing practices. "We then went into analysis mode and decided to bring forward the most reasonable standards that are capable of making the consumer safe," he said.

AKA is interested in feedback from FDA on its standards. In its release on the GMPs, the association says it hopes to work with the agency "to eradicate the unscrupulous bad actors who put dangerous adulterants in the natural plant kratom."

However, Herman says FDA has been unresponsive to its outreach, including requests for a meeting with the National Institutes of Health's National Institute on Drug Abuse. FDA Commissioner Scott Gottlieb has made numerous statements, in tweets as well as news releases, stating the agency's concerns about kratom, but Herman said he "won't talk to us at all."

AKA continuously has expressed frustration with FDA's kratom crackdown, ratcheting up its fight with a white paper published Aug. 14 accusing the agency of manipulating and obscuring data on the botanical to influence "unwarranted" restrictions on the substance. (Also see "Kratom Group Contests FDA's Opioid Finding, Requests Joint Meeting With NIDA" - Rose Sheet, 16 Aug, 2018.)

In the paper, the association criticized FDA's review of adverse event reports and other clinical literature on kratom. The agency concluded that from January 2011 through April this year, 47 deaths "may be kratom-related."

AKA said FDA's report presented "inaccurate, extrapolated and distorted information on adverse events and deaths allegedly associated with the use of kratom" to mislead DEA, the Center for Disease Control and NIDA. The group says FDA did not independently verify or perform any due diligence on the death reports and its own documents indicate that every reported case involved other factors, including adulteration.

AKA says it requested a joint meeting with FDA and NIDA to resolve "significant conflicts in the science" and develop an "appropriate public health policy that allows for consumers to safely use natural kratom" but has had no luck. (Also see "Kratom Experts Seek NIDA As Ally To Show Herb's Safety And Benefits" - Rose Sheet, 27 Nov, 2017.)

FDA Statements: Semantics Or 'Evolution?'

Herman acknowledged FDA's latest kratom statement, by Gottlieb on Sept. 11, omitted any mention of its potential link to deaths identified in adverse event reports. The omission, however, doesn't signal a change in the agency's position on the botanical as much as it does FDA is taking a closer look at the data associated with adverse event reports, he said.

"I don't think they're evolving on openness to kratom but evolving in going after a product and being more careful, because they have been shown that what they were saying was incorrect," Herman added.

Gottlieb's statement also departed from FDA's previous releases in skipping that the agency considers kratom a dietary ingredient that was not part of the US food supply before October 1994, the cutoff date for ingredients allowed for use in supplements without being notified to the agency as NDIs.

The FDA statement directly addressed kratom marketers that received warning letters in early September, an online retailer identified as "Chillin Max Kratom" and North Carolina business Mitra Distributing Inc., for unsubstantiated claims the products could "relieve opium withdrawal" and treat ailments including diarrhea, depression and diabetes. (Also see "Warnings On Kratom Opioid Withdrawal Claims Mark Tip Of FDA Concerns" - Rose Sheet, 11 Sep, 2018.)

Gottlieb characterized the marketers as "unscrupulous" and stressed that despite FDA warnings and regulatory and enforcement actions, the agency continues to find marketers actively selling kratom with unsubstantiated claims. Despite the warning letter, Chillin Max continues to make

the same unsupported claims on its website, though Mitra Distributing appears to have removed the claims from its site.

Chad Landmon, chair of Axinn Veltrop & Harkrider LLP's FDA practice in Hartford, Conn., said the omissions were not notable to him.

Landmon, who focuses his practice on patent litigation and counseling and food and drug law with an emphasis on pharmaceuticals, biologics and human tissue products, said companies continuing to market kratom products with unsupported claims at this point “seem pretty dug in" on continuing to market the items. Those firms, he said, are “arguing their case as to why their kratom products should be considered supplements and be allowed to continue on the market.”

He suggested FDA may get more aggressive in response. “FDA may be working with DEA but also likely won’t be shy in bringing its own enforcement actions if these companies continue with their marketing efforts,” Landmon said.