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Yes, Warehouses that Store and Distribute FDA Regulated Products Must Comply with Relevant GMPs



EXPERT
ARTICLE

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In November 2019 FDA issued an unusual warning letter to Greenbrier International Inc (doing business as Dollar Tree). This was based on the outcome of an inspection of their corporate headquarters in Chesapeake, Virginia ending January 18, 2019. It references the inspections of several of their CMO drug product suppliers.

The form-483 identifies four multi-part observations. The second observation of the form-483 identified the lack of quality agreements with their CMOs that manufacture drug products and their contract testing laboratories and a lack of oversight of their contract partners.

The law firm that responded to the form-483 for Greenbrier took the position that “Greenbrier disagrees with the Agency applying the drug manufacturing cGMPs to it...”

FAILURE TO PROVIDE ADEQUATE OVERSIGHT OF SUPPLIERS

In contrast, the warning letter cites failure to comply with the FD&C Act and does not identify failure to comply with the reg-

ulations in 21 CFR 211. This warning letter cites inspections of foreign facilities that manufactured the “Dollar Tree’s Assured Brand drugs,” and were the subject of FDA enforcement action such as warning letters or import alerts. The warning letter focuses on the firm’s use of adulterated products from their suppliers and the use of a problematic testing laboratory recommended by the firm.

[NOTE: They are not alone. Since the November 2019 warning letter was issued to Greenbrier, a quick search in Enforcement Analytics shows that 79 Human Drug GMP facilities were cited for use of a problematic testing laboratory.]

The firm continued to import OTC drugs from firms that were the subject of FDA warning letters and import alerts even after the FDA communicated the warning letters to the Greenbrier COO in three of the four examples provided. FDA notes that they identified rodent feces at the manufacturing facility of one of the suppliers.

Greenbrier was to respond to the warning letter and then contact the FDA to set up a meeting for further discussion. This was clearly not the end of their problems with the FDA.

CONTAMINATED PRODUCTS IN STORES IN SIX STATES

On February 18, 2022, FDA issued a press release warning the public about contaminated products from Family Dollar stores in six states. Dollar Tree acquired the Family Dollar firm in 2015. This recent inspection and action was prompted by a consumer complaint (sent directly to the FDA, I assume).

The products came from a company distribution facility located in West Memphis, Ark., and the action addresses all FDA-regulated products from January 1, 2021, and distributed to stores in:

- Alabama
- Arkansas
- Louisiana
- Mississippi
- Missouri
- Tennessee

Five FDA investigators conducted the inspection over fifteen days between January 11 and February 11, 2022. One of the investigators was a member of the “Dedicated Device Cadre.”

The form-483 from the inspection is twenty-one pages long with twelve often multi-part observations and addresses human food

products (observations 1, 2, and 3), animal food products (observations 4 and 5), and drug products (observations 6 through 12). When FDA investigators count the number of rats running to and fro and “*climbing up rack scaffolding*,” along with identifying gnawed packages of food, it becomes unsettling to read.

[RELATED: As unsettling as this may be to read, sadly, rodent activity is not an unusual finding in Human Drug GMP 483s—we found over 730 primary and secondary citations containing the word “rodent” in the last 12 months alone. See how we found this data, [book a demo](#).]

The FDA press release addressed a wide group of products: *Some examples of these products include:*

- *Human foods (including dietary supplements (vitamin, herbal and mineral supplements))*
- *Cosmetics (skincare products, baby oils, lipsticks, shampoos, baby wipes)*
- *Animal foods (kibble, pet treats, wild bird seed)*
- *Medical devices (feminine hygiene products, surgical masks, contact lens cleaning solutions, bandages, nasal care products)*
- *Over-the-counter (OTC) medications (pain medications, eye drops, dental products, antacids, other medications for both adults and children).*



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ADVICE TO DISCARD PRODUCTS AND WASH HANDS AFTER HANDLING

FDA advises that potentially contaminated products be discarded by consumers and "...Consumers should wash their hands immediately after handling any products from the affected Family Dollar stores."

Note that the communication from FDA does not limit this admonishment to wash hands after handling the FDA regulated product but appears that this extends to any product purchased at Dollar Tree.

FDA states they identified "insanitary conditions" including rodent infestations. *"Conditions observed during the inspection included:*

- *Live rodents*
- *Dead rodents in various states of decay*
- *Rodent feces and urine*
- *Evidence of gnawing, nesting and rodent odors throughout the facility*
- *Dead birds and bird droppings*
- *Products stored in conditions that did not protect against contamination.*

More than 1,100 dead rodents were recovered from the facility following a fumigation at the facility in January 2022. Additionally, a review of the company's internal records also indicated the collection of more than 2,300 rodents between Mar. 29 and Sep. 17, 2021, demonstrating a history of infestation."

Dollar Tree Inc filed a form 8-K on March 2, 2022, that described actions taken by FDA and those taken by the company in response. Note that proposed class action complaints have been filed in the state courts of Arkansas, Mississippi, and Virginia. In these complaints "Plaintiffs seek restitution, damages, interest, punitive damages, attorney fees, costs and expenses, and such further relief (in each case in unspecified amounts), as the Court deems just and equitable."

CONCLUSION

The response to the 483 issued to Greenbrier International explains, for me, why the 2019 warning letter cites only the FD&C Act and not the GMP regulations. The response is interesting reading though it clearly did not adequately address practices

and conditions identified during the inspections of either Greenbrier or their suppliers. I don't think we have seen the last of the enforcement for this firm.

The February 2022 form-483 is unique and it will be interesting to see the company response. At least this time, the firm should understand that the requirements of the FD&C Act do apply to them.

Stay tuned - we will follow up on this.

Two thousand three hundred rodents collected within 5 ½ months in the facility should merit another warning letter, in my opinion. The magnitude of the "pest control" failures is egregious.

All firms should understand they are responsible to monitor the compliance status of their CMOs and take action as warranted based on the warning letter to Greenbrier. Finally, customer complaints provided directly to the FDA are taken seriously and in this case resulted in expensive consequences from a multi product, multi state recall. The 8-K filing of March 2, 2022 notes that this recall has cost approximately \$34 million in the fourth quarter of 2021. It would not be surprising to see follow-on enforcement action from both food and drug Centers of FDA. ■

ABOUT THE AUTHOR

Barbara Unger formed Unger Consulting, Inc. in December 2014 to provide GMP auditing and regulatory intelligence services to the pharmaceutical industry, including general GMP auditing and auditing and remediation in the area of data management and data integrity. Her auditing experience includes leadership of the Amgen corporate GMP audit group for APIs and quality systems.

She also developed, implemented, and maintained a comprehensive GMP regulatory intelligence program for eight years at Amgen. This included surveillance, analysis, and communication of GMP related legislation, regulations, guidance, and industry compliance enforcement trends.

Barbara was the first chairperson of the Rx-360 Monitoring and Reporting workgroup (2009 to 2014) that summarized and published relevant GMP and supply chain related laws, regulations, and guidance. She also served as the chairperson of the Midwest Discussion Group GMP-Intelligence subgroup from 2010 to 2014. Barbara was also the co-lead of the Rx-360 Data Integrity Working Group from 2017 through 2019. She currently serves as a GMP consultant to the Redica Systems team, beginning in 2015, then known as FDAzilla.

Barbara received a bachelor's degree in chemistry from the University of Illinois at Urbana-Champaign. You can contact her at barb.unger@redica.com.