An official website of the United States government Here's how you know

WARNING LETTER

ByHeart, Inc.

MARCS-CMS 653854 — AUGUST 30, 2023

More Warning Letters

Warning Letters

About Warning and Close-Out Letters

Delivery Method: Via Email
Product: Food & Beverages

Recipient:
Ron Belldegrun
CEO and Co-Founder
ByHeart, Inc.
131 Varick Street, 11th Floor
New York, NY 10013
United States

Ron@byheart.com

Issuing Office:
HUMAN AND ANIMAL FOOD WEST I COMPLIANCE BRANCH (HAFW1-CB)
United States

Content current as of:
08/30/2023

Regulated Product(s)
Food & Beverages

WARNING LETTER

August 30, 2023

Reference #653854

Dear Ron Belldegrun,

The United States Food and Drug Administration ("FDA") inspected your powdered infant formula facility, **(b)(4)**, located at **(b)(4)**, **(b)(4)**, PA 19606 from December 21, 2022, through February 17, 2023. Your **(b)(4)** facility manufactures an infant formula base product that is subsequently blended and packaged at a third-party contract manufacturing facility. Based on the information **(b)(4)** provided to FDA during the inspection, ByHeart, Inc. ("ByHeart") is the owner and parent company of **(b)(4)**. As such, ByHeart is responsible for making all decisions related to your brand of powdered infant formula products, including disposition decisions, and holds contracts with multiple third-party contract manufacturers to produce your powdered infant formula finished product.

During our inspection at the **(b)(4)** facility, FDA investigators found significant violations of Title 21, Code of Federal Regulations, Part 106 (21 C.F.R. Part 106), Infant Formula Requirements Pertaining to Current Good Manufacturing Practice, Quality Control Procedures, Quality Factors, Records and Reports, and Notifications ("the Infant Formula Rule"). At the conclusion of the inspection, the FDA investigators issued a Form FDA-483, Inspectional Observations ("Form FDA-483"), listing the deviations found at the **(b)(4)** facility. Based on the inspectional findings, FDA has determined that your actions have violated the Federal Food, Drug, and Cosmetic Act ("the Act") and the Infant Formula Rule. See Sections 402(a)(4), 412(a)(3), and 301(a) of the Act [21 U.S.C. §§ 342(a)(4), 350a(a)(3), and 331(a)]. You may find the Act and FDA regulations, including 21 C.F.R. Part 106, through links on FDA's website at www.fda.gov.

You submitted corrective action responses to the Form FDA-483, which include descriptions of your firm's ongoing corrective actions. We received corrective action responses from you dated March 10, 2023, April 10, 2023, April 27, 2023, May 10, 2023, June 9, 2023, and July 17, 2023. After thoroughly reviewing your submissions, FDA is issuing you this letter to advise you of the Agency's concerns and bring to your attention areas that still require corrective actions.

1. You did not establish a system of process controls covering all stages of processing that was designed to ensure that infant formula does not become adulterated due to the presence of microorganisms in the formula or in the processing environment, as required by 21 C.F.R. § 106.55(a). Specifically:

a. On October 17, 2022, you notified **(b)(4)** that a batch of ByHeart Whole Nutrition Infant Formula finished product had tested positive for *Cronobacter* spp. and was later confirmed as *Cronobacter sakazakii ("C. sakazakii").* The infant formula base, which was a component of the contaminated finished product, was manufactured during a continuous production campaign at the **(b)(4)** facility from July 13, 2022, through August 23, 2022. The infant formula base from this campaign was then blended and packaged as a finished product at one of your third-party contract manufacturer's facilities from September 15, 2022 through October 7, 2022.

In response to the finished product positive, **(b)(4)** conducted a root cause analysis, which is documented in its "Event Reporting and Investigation Procedure" Event 22138. **(b)(4)** root cause analysis concluded that post-production sample handling by a third-party laboratory was the source of the contamination, essentially resulting in a laboratory error. However, the third-party laboratory provided an "OOS Result Investigational Report for Microbiological Testing" regarding the *C. sakazakii* findings in finished product, which concluded that "Laboratory error was not found or supported." The third-party laboratory reached this conclusion after reviewing its internal protocols and testing conditions, finding no basis to attribute the sample results to laboratory error. Typically, a conclusion of lab error within an RCA is supported with confirmed evidence, such as written confirmation from the third-party laboratory attesting to the error. Here, there is no attestation; there is evidence to the contrary.

Despite the discrepancy between the third-party laboratory and the internal conclusion within **(b)(4)** root cause analysis, neither you nor your subsidiary company, **(b)(4)**, took any additional efforts to evaluate other routes of contamination that may have contributed to this event. Our review of your records obtained during the **(b)(4)** inspection show that you did not work with your third-party contract manufacturer to further investigate the origin(s) or root cause(s) of the finished product positive findings. As the parent company and entity making all product disposition decisions, it is your responsibility to investigate all aspects of the production process for your products, including operations conducted at your **(b)(4)** facility and your third-party contract manufacturer's facility, when evaluating the potential root cause(s) for a product contamination event.

In response to the *C. sakazakii* finished product findings, you directed your third-party contract manufacturer to hold and destroy the lot of product that tested positive for *C. sakazakii* and the first pallet of the subsequent lot in the same production campaign. However, you directed the release of all other ByHeart Whole Nutrition Infant Formula finished product manufactured as part of your third-party contract manufacturer's continuous production campaign. Upon further evaluation of **(b)(4)** sanitation and production records, and following discussions with FDA, your firm subsequently conducted a voluntary recall of the remaining five lots of ByHeart Whole Nutrition Infant Formula, Milk Based Powder with Iron from the same September 15, 2022 – October 7, 2022 campaign that you had previously released into U.S. commerce.

Further, FDA investigators' review of **(b)(4)** "Event Reporting and Investigation Form" Event Number 22107 found that on August 24, 2022, **(b)(4)** manufactured an infant formula base mix that had tested positive for *C. sakazakii.* **(b)(4)** root cause analysis states:

"[the SOP for] Interventions into Product Contact Zones was not followed during the work completed on back pressure valve FCV2700. The exposure of a product contact surface to the environment such as a processing line post heat treatment (DSI) [direct steam injector] is highly risky, particularly when intervention procedures are not followed, and effective cleaning is not completed afterwards. This scenario poses the potential introduction of *Cronobacter* to the product processing stream."

Accordingly, the maintenance work and repair to the valve here was not treated, verified, and recorded as an intervention into a product contact zone, as was required by your SOPs. In response to these findings, your firm rejected and destroyed the entire production campaign, which consisted of one (1) lot of base mix product, produced from August 24, 2022, to August 25, 2022.

FDA's evaluation of the sanitation activities that your **(b)(4)** facility conducted established that on July 13, 2022, and August 25, 2022, **(b)(4)** performed a full clean-in-place (CIP) cycle, which included the application of sanitizer to food contact surfaces. Further on August 24, 2022, prior to starting a production campaign, **(b)(4)** performed a CIP (excluding the dryer). While the Agency acknowledges that you reviewed sanitation records as part of the "Event Reporting and Investigation Form" Event Number 22107, the review did not appear to include an evaluation of the intervening sanitation breaks. Intervening sanitation breaks are a critical factor in assessing how a pathogen finding may impact product within a production campaign. **(b)(4)** "Event Reporting and Investigation Form" Event Number 22107 does not contain an evaluation of the extent of the sanitation conducted and if it was sufficient to mitigate microbiological contamination from the system.

FDA acknowledges that, with your approval, the third-party laboratory provided FDA the whole genome sequencing (WGS) isolate data for the ByHeart Whole Nutrition Infant Formula finished product positive. FDA advised you of the WGS results via a conference call on December 16, 2022. However, you did not conduct WGS analysis on **(b)(4)** August 24, 2022, *C. sakazakii* isolate. In light of the timeframe between the production of the base product that was a component of the finished product you voluntarily recalled and the isolation of *C. sakazakii* in your infant formula base, further isolate analysis would have enabled your firm to have conducted a more comprehensive root cause analysis. Notably, your root cause analysis did not include any investigation of the available environmental isolates.

Further investigation of all these isolates, such as conducting WGS, would have provided more information about the potential role of your facility in contributing to the contamination event by indicating whether the strain of *C. sakazakii* found in finished product matched a strain of *C. sakazakii* previously detected at your **(b)(4)** facility. WGS results could also indicate whether the same strain of *C. sakazakii* may be contributing to multiple contamination events, which would then inform the type of corrective action and verification activities you would need to perform to sufficiently remediate the contamination from your **(b)(4)** facility following an intrusion event. We advised you of the importance of performing WGS on finished product and environmental isolates and comparing these results as part of a thorough root cause analysis via round table discussions on February 6, 2023 and May 9, 2023, as well as in FDA's Letter to Industry on March 8, 2023.

Your corrective actions submitted in response to the Form FDA-483 provided information about the contamination events. Additionally, your corrective actions from your March 10, 2023 letter includes a commitment expressing that:

"All product and environmental positive *Cronobacter*, Listeria, and Salmonella species will be further tested by Whole Genome Sequencing (WGS). WGS data will be used in root cause analysis of positive product samples."

The Agency applauds this commitment, and again urges you to clearly incorporate evaluation of all sanitation activities in the processing environments when making product disposition decisions if future product testing detects a pathogen. We will assess the adequacy of your corrective actions during our next inspection of your facility.

b. From July 25, 2022, through August 27, 2022, **(b)(4)** received multiple notifications from the third-party laboratory of positive *Cronobacter* spp. findings within the **(b)(4)** facility processing environment. Your third-party laboratory later confirmed these *Cronobacter* spp. findings as *C. sakazakii*. The goal of a well-designed environmental monitoring program is to identify environmental pathogens, such as *Cronobacter* spp., and any harborage sites, if present, in your facility and to implement effective corrective actions to eliminate such environmental pathogens and harborage sites. In response to each of these positive samples, **(b)(4)** created an "Event Reporting Investigation Form," which describes the actions **(b)(4)** took, including conducting a root cause analysis, and describing the remediation cleaning, sanitation, and verification swabbing activities. While **(b)(4)** conducted a root cause analysis for these *C. sakazakii* positive environmental swabs, the determination on causation was attributed to isolated events such as facility repairs, using an ineffective sanitizer, or ineffective cleaning frequency. While **(b)(4)** listed possible sources of contamination in the Event Reporting Investigation Form, the root cause analysis did not include further investigation on the available environmental isolates, evaluation of water events in and around the time of the environmental detections, employee practices, material and equipment traffic, and hygienic practices. In addition, the investigation and root cause analysis did not evaluate the potential connection between these environmental positives and **(b)(4)** infant formula base produced on August 24 that tested positive for *Cronobacter* spp. Further, upon learning about the October 17, 2022 finished product positive for *C. sakazakii* at your third-party contract manufacturer's facility, which was blended using the infant formula base produced at the **(b)(4)** facility between July 13 and August 23, neither you nor **(b)(4)** considered these environmental positives as potentially contributing to that contamination event.

Your 483 responses included corrective actions such as using a third-party auditor to determine insufficiencies in the environmental monitoring program at the **(b)(4)** facility and revising the **(b)(4)** SOPs. We will assess the adequacy of your corrective actions during our next inspection of your facility.

c. FDA's review of your "Event Reporting and Investigation Form" found that you identified two (2) water events where water from outside of your **(b)(4)** facility's building leaked into the manufacturing areas.

i. On June 23, 2022, **(b)(4)** identified a leak through a skylight installed on the roof in the **(b)(4)** processing room. An "Event Reporting and Investigation Form" Event #2270 was created, and the root cause analysis determined that heavy rain on June 23, 2022 caused the leak. On July 25, 2022, you were notified by your third-party laboratory that *C. sakazakii* was detected through the environmental monitoring program in the **(b)(4)** facility's **(b)(4)** processing room. Despite having a leak in June and a notification the following month of product testing positive for *C.* sakazakaii, the root cause analysis never considered or evaluated whether the leak may have contributed to the contamination.

ii. On December 15, 2022, **(b)(4)** identified a leak in the sealant around the louver on **(b)(4)** of the Dryer Tower. An "Event Reporting and Investigation Form" Event #22179 was created, and the root cause analysis determined that a worn sealant around the frame of the inlet louver and heavy wind and rain all day on December 15, 2022 caused the leak. During environmental swabbing conducted on December 15, 2022, after identification of the leak, four (4) swabs detected *Cronobacter* spp. in the following locations of the dryer tower: two different swabs from the **(b)(4)** dryer tower diamond plate next to repainted surface; the **(b)(4)** dryer tower left side surface of small stainless-steel table; and the **(b)(4)** dryer tower floor in front of small-stainless steel table. Despite having a leak in December and then detecting *Cronobacter* spp. via environmental swabbing following the leak, the root cause analysis never considered or evaluated whether the leak may have contributed to the contamination.

Wet conditions – such as those areas of a manufacturing plant where water occasionally wets the area, either intentionally as part of wet cleaning, or inadvertently as the result of leaking pipes or valves or roofs – are especially favorable for the growth of *Cronobacter*. An ideal growth and survival environment is one which periodically gets wet even if only once every few months and then takes at least one day or more to fully dry. For example, when equipment is mounted to the floor of the plant, water may seep under the structure of the equipment and then remain wet for many days. Organisms may grow to high numbers during the time the area is wet; when the area dries, the organisms will remain viable and when *Cronobacter* becomes established in a "niche" environment, it may be difficult to locate the organisms. In the niche environment, the organisms grow to very high numbers during periods of nutrient and water availability. The organism may spread to other areas of the food processing plant from this niche environment by various means including employee movement, forklifts and totes, air flow, and water used during sanitation.

We acknowledge that in response to these external water leaks, **(b)(4)** conducted corrective actions, including cleaning, sanitizing, and performing verification swabbing on the impacted areas. However, FDA verbally discussed external water leaks and control of water within the production environment with your firm management during our previous inspection of your **(b)(4)** facility on May 23, 2022, through June 9, 2022. Your 483 corrective action responses indicate that you and **(b)(4)** have taken actions to address

Feedback

these findings, including repositioning the main inlet burner louvers frame, conducting monthly inspections of the burner louvers, installing rain hoods over the louvers, disposing of the existing skylight dome and framing, and revising your leak notification procedures. We will assess the adequacy of your corrective actions during our next inspection of your **(b)(4)** facility.

This letter is not intended to be an all-inclusive statement of violations that may exist in connection with your products. You are responsible for ensuring that your facilities operate in compliance with the Act, the Infant Formula rule, and other applicable laws, and for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations.

You should take prompt action to correct the violations noted in this letter. Failure to do so may result in legal action by the FDA without further notice, including, without limitation, seizure and injunction.

In addition to the above violations, we offer the following comment. To comply with 21 C.F.R. § 106.150, you must promptly notify FDA when infant formula product that may be adulterated leaves your establishment subject to your control as the manufacturer.

As discussed with you during your **(b)(4)** facility inspection, and as set forth in FDA's March 8, 2023 letter to industry, when *Cronobacter* is detected in a finished infant formula product that is part of a continuous production run/campaign, all product prepared, packed, or held under the same insanitary conditions as the positive batch, whereby it may have become contaminated or rendered injurious to health, is deemed adulterated under section 402(a)(4) of the Act [21 U.S.C. § 342(a)(4)]. This would include all product produced before the contaminated lot going back to the last sanitation break unless the outcome of a root cause analysis or investigation can conclusively identify when the production system became contaminated, and that all product produced before this time was not subjected to the insanitary conditions created by the contamination event. Likewise, this would include all product produced after the contaminated lot until the next sanitation break unless some other sanitation/remediation procedures were conducted for which there is adequate information or data to demonstrate that the sanitation/remediation procedure is sufficient to mitigate the insanitary conditions created by the contamination event. As previously discussed, an adequate sanitation break requires either a full CIP cycle or the application of a sanitizing treatment (i.e., heat treatment or chemical treatment) to all food contact surfaces.

Releasing product that may be adulterated into interstate commerce without notifying FDA violates 21 C.F.R. § 106.150 and section 412(e)(1)(B) of the Act [21 U.S.C. § 350a(e)(1)(B)]. Specifically:

On October 15, 2022, you notified your third-party contract manufacturer that ByHeart Whole Nutrition Infant Formula finished product, tested positive for *C. sakazakii*. The campaign for this product was blended at your third-party contract manufacturer's facility between September 15 – 20, 2022 and then packaged between September 30 – October 7, 2022. In response to the positive *C. sakazakii* findings, you directed your third-party contract manufacturer as to which lots of the continuous production campaign should be destroyed and which lots should be released for distribution into interstate commerce. While the lot that tested positive for *C. sakazakii* and the first pallet of the subsequent lot were held and destroyed per your instructions, the other lots manufactured as part of the same September 30 – October 7, 2022 campaign were released. When conducting the root cause analysis for the contamination and making your product disposition decisions, you did not evaluate production records or consider intervening sanitation breaks as a factor. Following FDA's review of your contract manufacturer's records and lack of intervening sanitation breaks, FDA determined that your firm released adulterated powdered infant formula into U.S. commerce. You determined that these lots of adulterated infant formula product could leave control of your third-party contract manufacturer's facility between October 17, 2022, through November 14, 2022, for distribution into interstate commerce, and you failed to notify FDA of this occurrence. Accordingly, your firm subsequently conducted a voluntary recall of the batches previously released from within this production campaign. (Based on recall effectiveness checks, FDA believes that your recall was effective and that you successfully removed these batches from the market.)

Please notify this office within fifteen working days of receipt of this letter as to the specific steps you have taken to correct the stated violations, including an explanation of each step being taken to identify violations and make corrections to ensure that similar violations will not recur. In your response, you should include copies of related documentation and any other useful information that would assist us in evaluating your corrections. If you cannot complete corrective actions within fifteen working days, state the reason for the delay and the time within which you will do so. If you believe that your products are not in violation of the Act, include your reasoning and any supporting information for our consideration. In addition, the Agency would be happy to meet with you, per your request, to discuss your proposed corrective actions.

Please send your written response to the U.S. Food and Drug Administration Compliance Officer Andrew J. Howard, 11155 Dolfield Boulevard, Suite 117, Owings Mills, Maryland 21117. An emailed response is also acceptable. If you have questions regarding this letter, please contact CO Howard by telephone at (410) 779-5125, or by email at Andrew.Howard@fda.hhs.gov.

Sincerely,
/S/
Ann M. Oxenham, JD
Director

Office of Compliance
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration

/S/
Michael Dutcher, DVM
Acting Assistant Commissioner
Office of Human and Animal Food Operations U.S. Food and Drug Administration

1 See also FD&C Act Chapter IV: Food (Mar. 28, 2018), https://www.fda.gov/regulatory-information/federal-food-drug-and-cosmetic-act-fdc-act/fdc-act-chapter-iv-food; CFR - Code of Federal Regulations Title 21 (June 7, 2023), https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=106.

Was this page helpful? *

Yes

No

Submit

An official form of the United States government. Provided by Touchpoints