August 18, 2026

NutraSteward Ltd.
Attention: Elizabeth Lewis, Ph.D.
Scientific and Regulatory Advisor
Frederick House
Johnston, Pembrokeshire SA62 3AQ
United Kingdom

Re: GRAS Notice AGRN 88 – Calcium Salts of Isobutyric Acid and 2-Methylbutyric Acid

Dear Dr. Lewis:

The Food and Drug Administration's (FDA) Center for Veterinary Medicine refers to a generally recognized as safe (GRAS) notice, dated January 10, 2025, and received on August 28, 2025, submitted on behalf of your client, Zinpro Corporation (Zinpro or the notifier). The subject of the notice is calcium isoacids, hereafter referred to as calcium salts of isobutyric acid and 2-methylbutyric acid or the notified substance, to be used as a source of energy in dairy cattle feed at an inclusion rate of up to 80 g/head/day. The submission informs us of the notifier's conclusion that the subject of the submission is GRAS through scientific procedures. You were notified in a letter dated December 9, 2025, that the GRAS notice was acceptable for filing, and the notice was designated as animal GRAS notice number (AGRN) 88. CVM received an amendment, dated April 26, 2026, from the notifier containing additional information. We have completed our evaluation of AGRN 88 and have no questions at this time regarding the conclusion for use of the notified substance as a source of fatty acids in dairy cow and mature dairy bull feed at an inclusion rate of up to 80 g/head/day.

To address identity, method of manufacture, and specifications of the notified substance, the notifier provides the characterization, manufacturing process, specifications, and the analytical methods used to determine the composition of the notified substance. The notified substance is manufactured by neutralizing isobutyric acid and 2-methylbutyric acid followed by drying and milling. The notifier provides specifications for calcium isoacids as follows: color (cream), total fatty acids (min. 65%) with isobutyric acid (min. 44%) and 2-methylbutyric acid (min. 21%), moisture (max. 8%), calcium (min. 18%), arsenic (max. 0.5 mg/kg), lead (max. 0.5 mg/kg), cadmium (max. 0.5 mg/kg), and mercury (max. 0.05 mg/kg). The notifier also provides stability and packaging information for the finished product.

The notifier concludes that information on the physical or other technical effect of the notified substance is not necessary because use of the notified substance for its intended use does not impact target animal safety.

U.S. Food and Drug Administration
Center for Veterinary Medicine
CPK1, Room 1B068
5001 Campus Drive
College Park, MD 20740-3835
www.fda.gov

To address the safety of the notified substance in the target animal, the notifier provides information on potential impurities and contaminants, data and information from published feeding studies conducted in lactating dairy cows and estimated exposure assessments.

However, we have questions regarding Zinpro's conclusion that the notified substance is safe for use in immature dairy cattle, including dairy calves and replacement heifers, under the conditions of its intended use as the notice did not provide substantive data or information to extrapolate the safe use of the notified substance to immature dairy cattle.

To address human food safety associated with use of the notified substance, the notifier provides information on a) the low oral toxicity and known metabolism of branched-chain volatile fatty acids (BCVFAs) including isobutyric acid and 2-methylbutyric acid to innocuous compounds, b) the regulatory status and history of use of a compositionally similar blend of fatty acids (salts of volatile fatty acids), c) the potential impact of the notified substance on the BCVFA content of cow milk, and d) the history of human consumption of isobutyric acid and 2-methylbutyric acid from the background diet. The notifier also included published results of a genotoxicity battery and corroborative unpublished repeated-dose toxicity studies.

Section 403(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Under section 403(a) of the FD&C Act, a food is misbranded if its labeling is false or misleading in any particular. Zinpro did not provide any information to demonstrate that the notified substance functions as intended because the notifier concluded that the intended use would not be expected to impact safety. Therefore, we did not evaluate whether the notified substance would achieve the effect claimed for it. However, please note that if products containing the notified substance bear any claims on the label or in labeling regarding the function of the notified substance, these claims should be supported by appropriate data and information. FDA may take enforcement action if any claims on labels or labeling are found to be false or misleading.

Section 301(ll) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll) (1)-(4) applies. In our evaluation of this notice, concluding that the notified substance is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing the notified substance. Accordingly, our response should not be construed to be a statement that foods containing the notified substance, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusion

Based on the information contained in the notice and amendment submitted by Zinpro Corporation, and other information available to the FDA, we have no questions at this time regarding the notifier's conclusion that calcium salts of isobutyric acid and 2-methylbutyric acid is GRAS under the intended conditions of use in dairy cow and mature dairy bull feed at up to 80 g/head/day. However, the notice does not provide a sufficient basis for a conclusion that calcium salts of isobutyric acid and 2-methylbutyric acid is GRAS under the conditions of its

intended use in immature dairy cattle. The Agency has not made its own determination regarding the GRAS status of the intended use of the notified substance in animal food under 21 CFR 570.35. Unless noted above, our evaluation did not address other provisions of the FD&C Act. As always, it is the continuing responsibility of Zinpro Corporation to ensure that animal food ingredients that the notifier markets are safe and are otherwise in compliance with all applicable legal and regulatory requirements.

In accordance with 21 CFR 570.275(b)(2), the text of this letter responding to AGRN 88 is accessible to the public on our website for the Current Animal Food GRAS Notices Inventory at https://www.fda.gov/animal-veterinary/generally-recognized-safe-gras-notification-program/current-animal-food-gras-notices-inventory.

If you have any questions or comments, please contact Ms. Megan Hall at animalfood-premarket@fda.hhs.gov.

Sincerely,

/s/
Jeanette Murphy, M.S.
Acting Director
Office of Surveillance and Compliance
Center for Veterinary Medicine