U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

April 13, 2020

Cathryn W. Sacra
Director, Labeling and Cosmetic Services
EAS Consulting Group, LLC
1700 Diagonal Road, Suite 750
Alexandria, VA 22314

Dear Ms. Sacra:

Thank you for contacting FDA regarding Glanbia Nutritional (Glanbia)'s GRAS notice for the intended use of bovine lactoferrin (bLf). As our December 17, 2020 letter indicates, we declined to file your submission because Glanbia did not identify substantive differences from prior GRAS notices (i.e., GRNs 000465 and 000669) that would warrant a new notice.

In your letter, you request the Office of Food Additive Safety to issue a statement that we do not object to Glanbia's intended use of bLf at 600 mg/L in infant formula. We decline Glanbia's request because, as we previously communicated to Glanbia, the Agency does have safety questions surrounding the intended use of bLf at levels higher than in GRNs 000465 and 000669 (i.e., 150 mg/L). We communicated these concerns on the unsettled science surrounding bioactive ingredients in infant formula on multiple occasions in the context of meetings and emails with Glanbia, as well as in the documents Glanbia received under the Freedom of Information Act that we recommended. We wish to remind Glanbia that:

1. The safe use of ingredients in infant formula that may functionally mimic constituents in human milk is an evolving scientific field.
2. bLf is a bioactive protein and not a toxic chemical; therefore, traditional toxicological endpoints will not necessarily address long-term safety issues related to effects such as immunomodulation and altering iron homeostasis.
3. Anticipated benefits cannot be used as evidence of safety, as these effects cannot compensate for potential risks under FDA's food ingredient safety assessment paradigm.
4. In arriving at a "no questions" conclusion for GRNs 000465 and 000669, FDA considered the widespread and longstanding exposure to roughly comparable quantities of bLf in bovine milk-based infant formulas. However, as the dose-response curve for bLf is moved up and away from historical exposure patterns in infant populations, the potential mechanistic and physiological effects of bLf will have greater impact on the weight-of-evidence approach FDA typically uses to evaluate safety. At the present time, FDA continues to have questions regarding the use of bLf in infant formula at levels higher than 150 mg/L given the unsettled state

of the science.

Regarding other infant formulas, we do not comment on the compliance status of products. We note that we have not evaluated a GRAS notice for the intended use of bLf at 600 mg/L in infant formula. As we previously communicated to Glanbia, GRAS is time-dependent and subject to the currently available science. The current state of the science has raised new questions about the safe use and use level of substances with the potential for effects in the developing infant. Until new data and information become available to address the issues outlined above and previously communicated to you, we would question any GRAS submission for bLf at use levels higher than 150 mg/L in infant formula. We trust this clarifies our position and reasons for declining Glanbia's request.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2020.04.13 14:59:15 -04'00'

Susan Carlson, Ph.D.
Director
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