U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

Kevin Gillies
Kevin O. Gillies Consulting Services, LLC
1759 Grape St.
Denver, Colorado 80220

Re. GRAS Notice No. GRN 001250

Dear Mr. Gillies:

The Food and Drug Administration (FDA, we) is granting the request that we cease our evaluation of GRN 001250. We received this request on September 19, 2025. We received Advanced Enzymes' notice on January 3, 2025 and filed it on April 28, 2025. Advanced Enzymes submitted an amendment to the notice on August 5, 2025 that provideded additional information about manufacturing, specifications, dietary exposure, and the safety narrative.

The subject of the notice is alternansucrase enzyme preparation produced by *Escherichia coli* expressing the gene encoding alternansucrase from *Leuconostoc mesenteroides* (alternansucrase enzyme preparation) for use as an enzyme in production of maltose oligosaccharides, bread making, and juice production at a level up to 1927 mg total organic solids (TOS)/kg raw material. The notice informs us of Advanced Enzymes' view that these uses of alternansucrase enzyme preparation are GRAS through scientific procedures.

In a meeting on July 23, 2025, we communicated with you as Advanced Enzymes' representative regarding additional information needed to support a GRAS conclusion. We noted that Advanced Enzymes needed to address deficiencies in the notice, including errors in the dietary exposure calculations and absence of critical pieces of the safety narrative, including discussion of potential safety concerns raised by the cited toxicology study for the subject of the notice. Advanced Enzymes requested the opportunity to address our concerns in an amendment, which we received on August 5, 2025. However, the amendment did not sufficiently address the questions related to the toxicology study and contained errors in adjustments made in the dietary exposure calculations.

We have ceased our evaluation of the notice at your request on behalf of Advanced Enzymes. We remind Advanced Enzymes of a manufacturer's responsibility to ensure the safety and regulatory status of the substances that it markets for use in food or that it uses in food. We also remind Advanced Enzymes that the use of a substance in food that is not GRAS (and is not otherwise excluded from the definition of a food additive), must have pre-market approval by FDA for its use in food (21 CFR 170.30(g)). More information about the criteria for GRAS is available in our regulations (21 CFR part 170).

Your request on behalf of Advanced Enzymes does not preclude Advanced Enzymes from submitting a future GRAS notice with respect to the subject of this notice (21 CFR 170.260(b)). We recommend that Advanced Enzymes address the issues raised in this letter to adequately support a GRAS conclusion. Finally, we remind Advanced Enzymes of the signed statements and certification (part 1 of a GRAS notice, 21 CFR 170.225) by which Advanced Enzymes agrees to make all data and information regarding its GRAS conclusion available to FDA upon request.

In accordance with 21 CFR 170.275(b)(3), the text of this letter responding to GRN 001250 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan J. Carlson -S
Date: 2025.09.29 13:58:05 -04'00'

Susan J. Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Pre-Market Additive Safety
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