U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Celia Martin
Lallemand Inc.
1620 Prefontaine Street
H1W 2N8, Montreal, QC
CANADA

Re: GRAS Notice No. GRN 001290

Dear Dr. Martin:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001290. We received Lallemand Inc. (Lallemand)'s notice on July 23, 2025, and filed it on December 18, 2025. Lallemand submitted an amendment to the notice on March 17, 2026, containing additional information on manufacturing and specifications.

The subject of the notice is glucose oxidase enzyme preparation produced by *Komagataella phaffii* expressing a gene encoding glucose oxidase from *Aspergillus niger* (glucose oxidase enzyme preparation) for use as an enzyme in the production of baked goods at up to 18.2 mg Total Organic Solids (TOS)/kg flour. The notice informs us of Lallemand's view that this use of glucose oxidase enzyme preparation is GRAS through scientific procedures.

Commercial enzyme preparations that are used in food processing typically contain an enzyme component that catalyzes the chemical reaction as well as substances used as stabilizers, preservatives, or diluents. Enzyme preparations may also contain components derived from the production organism and from the manufacturing process, e.g., constituents of the fermentation media or the residues of processing aids. Lallemand's notice provides information about the components in the glucose oxidase enzyme preparation.

Glucose oxidase is identified by the International Union of Biochemistry and Molecular Biology Enzyme Commission Number 1.1.3.4,[1] and the Chemical Abstracts Service Number 9001-37-0. Lallemand states that the primary amino acid sequence of the mature glucose oxidase consists of 589 amino acids with a calculated molecular weight of 64.18 kDa.

Lallemand states that the *K. phaffi* production organism is a non-pathogenic and non-toxigenic yeast with a history of safe use in food production.

[1] https://iubmb.qmul.ac.uk/enzyme/EC1/1/3/4.html

Lallemand states that the *K. phaffi* production strain "LALL-GO2" was constructed from the host strain by targeted integration of a gene encoding a glucose oxidase from *A. niger* under control of a promoter and a terminator from *K. phaffi*. Lallemand states that whole genome sequencing was used to confirm the sequence integrity of the production strain and to verify that the production strain does not contain any functional or transferable antibiotic resistance genes.

Lallemand states that glucose oxidase enzyme preparation is manufactured by controlled fermentation of a pure culture of the *K. phaffi* production strain. The enzyme is secreted into the fermentation medium. After fermentation, the medium containing the enzyme is separated from the biomass, recovered, and concentrated by a series of filtration and ultrafiltration steps. The resulting glucose oxidase enzyme concentrate is spray-dried and formulated with sodium chloride. The final glucose oxidase enzyme preparation is a light beige powder. Lallemand states that the fermentation medium does not contain any major food allergens or components derived from allergenic sources. Lallemand states that the entire process is performed in accordance with current Good Manufacturing Practices and with food-grade raw materials.

Lallemand has established food-grade specifications including a limit for lead (< 0.5 mg/kg) and states that the glucose oxidase enzyme preparation conforms to the specifications established for enzyme preparations in the Food Chemicals Codex (FCC, 14th edition, 2024), and to the General Specifications and Considerations for Enzyme Preparations Used in Food Processing established by the FAO/WHO Joint Expert Committee on Food Additives (JECFA, 2006). Lallemand provides results from analyses of three non-consecutive batches of glucose oxidase enzyme concentrate to demonstrate that the manufacturing acceptance criteria can be met, including the absence of the production organism in the final product.

Lallemand intends to use glucose oxidase enzyme preparation at a maximum level of 18.2 mg TOS/kg flour in the production of baked goods to catalyze the oxidation of ß-D-glucose to D-glucono-1,5-lactone and the reduction of oxygen to hydrogen peroxide. In the presence of water, D-glucono-1,5 -lactone is hydrolyzed to gluconic acid. Lallemand notes that glucose oxidase enzyme is inactivated during food production. Lallemand estimates a maximum dietary exposure to glucose oxidase enzyme preparation to be 0.23 mg TOS/kg body weight (bw)/day from the use in food with the assumption that the added glucose oxidase enzyme preparation remains present in the final food.[2]

In support of the safety of glucose oxidase enzyme preparation, Lallemand highlights published information that supports the general safe use of glucose oxidase in food for human consumption. Lallemand states that enzymes are generally added at the lowest level to catalyze the desired reaction, and that exposure is generally low. Lallemand summarizes data from a literature search through July 2025 that did not identify any information that would contradict a general recognition of safety of glucose oxidase enzyme preparation. Additionally, Lallemand summarizes corroborative, unpublished

[2] Lallemand uses the Budget method to estimate the dietary exposure to glucose oxidase enzyme preparation based on the consumption of 12.5 g of solid foods per kg bw/d (worst case scenario) containing glucose oxidase enzyme preparation at the recommended use level.

toxicological studies on the notified glucose oxidase enzyme preparation. This includes a bacterial reverse mutation assay, an *in vitro* micronucleus assay, and a 90-day repeated dose oral toxicity study in rats. Lallemand states that glucose oxidase enzyme preparation was not mutagenic, and there were no treatment-related adverse effects up to the highest dose tested (1000 mg TOS/kg bw/d). Lallemand further relies on published information that discusses the safety of the *K. phaffi* production organism, including safe strain lineage and use of the parent strain for production of food ingredients.

Lallemand discusses publicly available literature, as well as the conclusions of several organizations and working groups, about the low risk of allergenicity posed by enzymes from their intended use, to address potential allergenicity of glucose oxidase. Based on bioinformatic analyses, using criteria recommended by FAO/WHO (FAO/WHO, 2001; Codex Alimentarius, 2009; JECFA, 2016), Lallemand reports that no significant sequence homology of their glucose oxidase to known allergens that would raise allergenicity concerns were identified. Based on the totality of information available, Lallemand concludes that it is unlikely that oral consumption of glucose oxidase enzyme preparation from the intended uses will result in allergic responses.

Based on the data and information summarized above, Lallemand concludes that glucose oxidase enzyme preparation is GRAS for its intended use.

Standards of Identity

In the notice, Lallemand states its intention to use glucose oxidase enzyme preparation in several food categories, including foods for which standards of identity exist, located in Title 21 of the CFR. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

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 Lallemand's notice concluding that glucose oxidase enzyme preparation 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 glucose oxidase enzyme preparation. Accordingly, our response should not be construed to be a statement that foods containing glucose oxidase enzyme preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Lallemand provided, as well as other information available to FDA, we have no questions at this time regarding Lallemand's conclusion that glucose oxidase enzyme preparation is GRAS under its intended conditions of use. This letter is not an affirmation that glucose oxidase enzyme preparation is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 001290 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

SUSAN J. CARLSON -S

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