U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

Joab Trujillo
AB Enzymes, Inc.
8211 W. Broward Blvd., Suite 420
Plantation, FL 33324

Re: GRAS Notice No. GRN 001276

Dear Mr. Trujillo:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001276. We received AB Enzymes Inc. (AB Enzymes)'s notice on May 2, 2025, and filed it on September 9, 2025. AB Enzymes submitted amendments to the notice on February 9, 2026, and March 18, 2026, containing additional information on enzyme identity, manufacturing, specifications, allergenicity, and the safety narrative.

The subject of the notice is cellulase enzyme preparation produced by *Trichoderma reesei* expressing a gene encoding a cellulase from *Aspergillus niger* (cellulase enzyme preparation) for use as an enzyme at up to 19 mg Total Organic Solids (TOS)/kg cereals in the production of baked goods, beer, and malt. The notice informs us of AB Enzymes' view that this use of cellulase 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. AB Enzymes' notice provides information about the components in cellulase enzyme preparation.

Cellulase is identified by the International Union of Biochemistry and Molecular Biology Enzyme Commission Number 3.2.1.4,[1] and the Chemical Abstracts Service Number 9012-54-8. AB Enzymes states that the primary amino acid sequence of the cellulase consists of 223 amino acids with a molecular weight of 24.72 kDa.

AB Enzymes states that the *T. reesei* production organism is a non-pathogenic and non-toxigenic fungus with a history of safe use in food production. AB Enzymes states that the *T. reesei* production strain "AR-852" was constructed from the host strain by

[1] https://iubmb.qmul.ac.uk/enzyme/EC3/2/1/4.html

targeted integration of an expression cassette carrying a gene encoding a cellulase from *A. niger* under control of a promoter and a terminator from *T. reesei* and a selectable marker. AB Enzymes states that whole genome sequencing was used to confirm the sequence integrity of the production strain. AB Enzymes states that the final production strain does not contain any functional or transferable antibiotic resistance genes.

AB Enzymes states that cellulase enzyme preparation is manufactured by controlled fermentation of a pure culture of the *T. reesei* 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 cellulase enzyme concentrate is spray-dried and formulated with sunflower oil and maltodextrin. The final cellulase enzyme preparation is a light beige powder. AB Enzymes states that the entire process is performed in accordance with current Good Manufacturing Practices and with food-grade raw materials.

AB Enzymes has established food-grade specifications including a limit for lead (< 0.1 mg/kg) and states that cellulase enzyme preparation conforms to 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). AB Enzymes provides results from analyses of three non-consecutive batches of cellulase enzyme concentrate to demonstrate that the manufacturing acceptance criteria can be met, including the absence of the production organism in the final product.

AB Enzymes intends to use cellulase enzyme preparation at a maximum level of 19 mg TOS/kg cereals in the production of baked goods, beer, and malt to catalyze the hydrolysis of endo (1,4)-beta-D-glucosidic linkages in beta-D-glucans, resulting in the breakdown of beta-D-glucans into smaller oligosaccharide units. AB Enzymes notes that the cellulase enzyme is inactivated during food production. AB Enzymes estimates a maximum dietary exposure to cellulase enzyme preparation to be 0.099 mg TOS/kg bw/day from the use in food and drinks with the assumption that the added cellulase enzyme preparation remains present in the final food.[2]

In support of the safety of cellulase enzyme preparation, AB Enzymes highlights published information that supports the general safe use of cellulases in food for human consumption. AB Enzymes states that enzymes are generally added at the lowest level to catalyze the desired reaction, and that exposure is generally low. AB Enzymes summarizes data from a literature search through January 2026 that did not identify any information that would contradict a general recognition of safety of cellulase enzyme preparation. Additionally, AB Enzymes summarizes corroborative, unpublished toxicological studies on cellulase enzyme preparation. This includes a bacterial reverse mutation assay, an *in vitro* micronucleus assay, and a 90-day repeated dose oral toxicity

[2] AB Enzymes uses the Budget method to estimate the dietary exposure to cellulase enzyme preparation based on the consumption of 12.5 g of solid foods per kg bw/d and 25 mL of non-milk beverages per kg bw/d (worst case scenario) containing cellulase enzyme preparation at the recommended use level.

study in rats. AB Enzymes states that cellulase 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). AB Enzymes calculates a margin of exposure to be 10152 using the no observed adverse effect level and the estimated dietary exposure for the intended uses of cellulase enzyme preparation.[3] AB Enzymes further relies on published information that discusses the safety of the *T. reesei* production organism, including safe strain lineage and use of the parent strain for production of food ingredients.

AB Enzymes 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 to cellulase. Based on bioinformatic analyses, using criteria recommended by FAO/WHO (FAO/WHO, 2001; Codex Alimentarius, 2009; JECFA, 2016), AB Enzymes reports that no significant sequence homology of their cellulase to known allergens that would raise allergenicity concerns were identified. Based on the totality of information available, AB Enzymes concludes that it is unlikely that oral consumption of cellulase enzyme preparation from the intended uses will result in allergic responses.

Based on the data and information summarized above, AB Enzymes concludes that cellulase enzyme preparation is GRAS for its intended use.

Standards of Identity

In the notice, AB Enzymes states its intention to use cellulase 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.

Allergen Labeling

The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires that the label of a food that is or contains an ingredient that contains a "major food allergen" declare the allergen's presence (section 403(w)). The FD&C Act defines a "major food allergen" as one of nine foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, and sesame) or a food ingredient that contains protein derived from one of those foods. Cellulase enzyme preparation may require labeling under the FD&C Act because it may contain protein derived from wheat. Questions about petitions or notifications for exemptions from the food allergen labeling requirements should be directed to the Division of Food Ingredients in the Office of Pre-Market Additive Safety. Questions related to food labeling in general should be directed to the Office of Nutrition and Food Labeling in the Nutrition Center of Excellence.

[3] FDA notes that the margin of exposure stated by the notifier is based on unpublished safety studies and is corroborative of the published information regarding enzyme preparations used in food processing.

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

Conclusions

Based on the information that AB Enzymes provided, as well as other information available to FDA, we have no questions at this time regarding AB Enzymes' conclusion that cellulase enzyme preparation is GRAS under its intended conditions of use. This letter is not an affirmation that cellulase 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 001276 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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Susan Carlson, Ph.D.
Director
Division of Food Ingredients
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