Enzymes
Handling/Processing

Identification of Petitioned Substance

Chemical Names:
Various enzymes from plant, animal and microbial sources are used in organic food handling and processing.

Enzymes can be identified in general groups based on the reactions they catalyze, such as protease, amylase, lipase and lactase.

Some prevalent enzymes used include lipase, pectinase, pepsin, trypsin cellulase, bromelain, rennet and egg white lysozyme.

Summary of Current Use

This is a limited scope Technical Report for the review of ancillary[1] substances contained in formulated enzyme products that are used in the processing and handling of certified organic food. Accordingly, only a subset of the evaluation questions are addressed below.

Enzymes currently appear on §206.605(a) of the National List under three separate listings:

- Animal enzymes—(Rennet—animals derived; Catalase—bovine liver; Animal lipase; Pancreatin; Pepsin; and Trypsin),
- Enzymes—must be derived from edible, nontoxic plants, nonpathogenic fungi, or nonpathogenic bacteria
- Egg white lysozyme (CAS #9001-63-2).

A full Technical Report on Enzymes is available from 2011 (NOP 2011). However, a new, limited scope Technical Report was requested to specifically address ancillary substances in enzymes per the 2014 National Organic Program (NOP) Memo on Ancillary Substance Review (NOP 2014).

Characterization of Petitioned Substance

Combinations of the Substance:
Enzyme products used in food processing may be single ingredient, stand-alone preparations of the enzyme, or formulated with other ingredients (OMRI 2015). In many cases the enzyme product which results from a fermentation process is not effective in food applications without further formulation (Whitehurst and Van Oort 2009). Enzyme preparations therefore commonly contain other substances, not only as incidental secondary metabolites and residual growth media from the enzyme production, but also intentionally added ingredients which function as diluents, preservatives, stabilizers, antioxidants, etc. (FDA 2010). These additives must be generally recognized as safe (GRAS), or be FDA approved food additives for this use (FDA 2014). Additives can make up the majority of an enzyme formulation's weight, with the active enzyme itself comprising only a small fraction (Wieland 1972).

[1] The NOP issued a memorandum to the National Organic Standards Board on February 3, 2014 which describes ancillary substances as those that are intentionally added to a formulated product (specifically, to a substance on the National List at 205.605) but not considered part of the manufacturing process that is already reviewed by the NOSB. These substances are not removed and are not considered ingredients. Such substances fall into categories including, but not limited to, carriers, stabilizers and preservatives.

Following in Table 1 is a list of known ancillary substances in enzyme products gathered from various sources, including technical data sheets of commercial enzyme preparations (Aehle 2006; Cargill 2006; Danisco 2011; Ensymm 2015; FDA 2013; Lenoir 2001; Novozymes 2010; OMRI 2015; VGP Pharmachem 2015; Whitehurst and Law 2001; Wieland 1972).

Table 1. Ancillary substances in enzyme formulations (*appears on the National List at 205.605 or 205.606)

Carriers, diluents, fillers	Starch (native corn starch*) and starch derivatives such as maltodextrin; glucose; lactose; whey (whey protein concentrate*); flour fractions; diatomaceous silica
Stabilizers	Carbohydrates such as sucrose, dextrose, trehalose; polyols and sugar alcohols such as sorbitol; sodium borate; boric and boronic acids; propylene glycol; small organic acids; ammonium sulfate; glutaraldehyde; sodium acetate; glycerin*; sodium chloride; calcium chloride*; potassium sulfate; bovine serum albumin
Preservatives	Sodium borate; potassium sorbate; sodium chloride; sorbic acid; potassium borate; sodium sorbate; sodium benzoate; methyl and propyl parabens
Buffers	Dibasic and monobasic phosphate salts; sodium acetate
Enzyme inhibitors	Boric acid, boronic acids, sodium borate, and amino acid salts
Coatings	Carbohydrates such as sucrose, lactose and maltose; methyl cellulose

Diluents or carriers are often used with dry enzyme products. Common carriers are starch derivatives such as maltodextrin. Glucose is another substance used as a carrier in dry enzyme preparations (Danisco 2011).

Stabilizers are added to enzyme formulations to prevent loss of enzyme activity and are particularly important in liquid enzyme preparations due to the destabilizing effect of water. Common stabilizers for this application include carbohydrates such as sucrose and dextrose, trehalose, sugar alcohols and polyols (Whitehurst and Van Oort 2009). Stabilizers such as boric acid, glycols, small organic acids and calcium chloride help to rigidify enzyme structures against degradation (Lenoir 2011). Degradation may also occur from protease enzymes attacking themselves (autolysis) or other enzymes (proteolysis), leading formulators to add materials such as boric acid, boronic acids, proteinaceous materials and sodium borate to inhibit protease activity (Lenoir 2011). Enzymes may be stabilized in lyophilized form for long periods of time when formulated with salts, carbohydrates, or inert proteins such as bovine serum albumin (Aehle 2006). Liquid rennet has been reported to be stabilized with sodium chloride, sodium acetate, sorbitol, propylene glycol and/or glycerol (Whitehurst and Van Oort 2009) (Cargill 2006).

The most common preservatives for controlling microbial contamination in enzyme preparations are sodium benzoate and potassium sorbate (Whitehurst and Van Oort 2009). The Select Committee on GRAS Substances (SCOGS) reported in 1977 the use of sodium benzoate or methyl and propyl parabens in rennet (FDA 2013). The use of parabens as preservatives in rennet preparations does not appear in more recent literature reviewed for this report. Sodium benzoate may be included in enzyme preparations at rates of around 0.5% - 1% (Ensymm 2015; VGP Pharmachem 2015). Sorbate preservatives are added at reported rates of 0.025 to 0.10% by weight in enzyme formulations (Wieland 1972). The development of natural alternatives as preservatives, such as plant extracts and peptides, is increasing (Whitehurst and Van Oort 2009). In food applications, Wilson et al. (1997) reported high anti-fungal activity against *Botrytis cinerea* in 13 different plant extracts primarily in species of *Allium* and *Capsicum* and in various constituents of essential oils. Brul and Coote (1999) reported on the presence of non-proteinaceous antimicrobial compounds in numerous herbs and spices, as well as peptides, proteins and lytic enzymes that can attack cell walls and membranes of spoilage-causing organisms. They also discuss microbial resistance challenges

in the use of such preservatives and cited the need for continued research to understand microbial growth and responses to various food preservation compounds and methods (Brul and Coote 1999). It is unknown whether natural preservatives have been or are currently used in any enzyme formulations.

In meat tenderizing applications, several older patents report that the use of monosodium glutamate (MSG) in proteolytic enzyme preparations inhibits proteolysis beyond the desired stage of tenderness (Baxter Laboratories Inc. 1966). However, more current literature could not be found to support this use of MSG.

Enzyme formulations may also contain colors and flavorings (Cargill 2006).

Incidental additives to enzyme preparations may occur to a limited extent when an immobilized enzyme is used to catalyze a reaction in food processing. Enzyme immobilization is a method for stabilizing enzyme preparations by confining them to a matrix or support that is different from that of the substrates catalyzed. Inorganic materials, along with some inert polymers, are generally used for this purpose (Datta, Christena and Rajaram 2013). Typically, the food comes into contact with the immobilized enzymes in a column such that the reaction is catalyzed, but the enzyme isn't actually added to the food. The FAO sets specific limits on the leakage of carriers, immobilizing agents and active enzymes into the product catalyzed (JECFA 1990).

It is noted that the ancillary ingredients used in combination with enzymes may contain ancillary substances themselves, such as flowing aids, anticaking agents, etc. Salt, for example, sometimes contains anticaking agents such as yellow prussiate of soda or tricalcium phosphate (OMRI 2015).

Evaluation Questions for Substances to be used in Organic Handling

Evaluation Question #4: Specify whether the petitioned substance is categorized as generally recognized as safe (GRAS) when used according to FDA's good manufacturing practices (7 CFR § 205.600 (b)(5)). If not categorized as GRAS, describe the regulatory status.

At least 19 enzyme preparations are listed in 21 CFR 184 as direct food substances affirmed as generally recognized as safe. The GRAS listings for these materials do not address ancillary ingredients. The good manufacturing practices (GMPs) described at 21 CFR 184.1(b) do not address ancillary substances either.

In addition to enzyme preparations listed as GRAS, at least 7 enzyme preparations are approved as food additives in 21 CFR 173, and some of these listings do reference ancillary ingredients. Diatomaceous silica is noted as a carrier for amyloglucosidase derived from *Rhizopus niveus* at 21 CFR 173.110. Glutaraldehyde is stated to be a stabilizer for the alpha-acetolactate decarboxylase described at 21 CFR 173.115. The listing for esterase at 173.140 references maltodextrin and sweet whey as carriers.

The Food Chemicals Codex describes enzyme preparations and states that carriers, diluents and processing aids used to produce enzyme preparations must be acceptable for general use in foods, including water and substances that are insoluble in foods but removed from the food after processing (Committee on Food Chemicals Codex 2003).

Evaluation Question #5: Describe whether the primary technical function or purpose of the petitioned substance is a preservative. If so, provide a detailed description of its mechanism as a preservative (7 CFR § 205.600 (b)(4)).

As discussed under 'Combinations of the Substance,' various preservatives are included in enzyme formulations to extend the life of enzyme activity so that the enzymes can be utilized in food applications. Typically, chemical preservatives are applied to food as direct additives or develop in situ via processes such as fermentation (FAO 1995), and the FDA limits the amount which may be added. The Federal Code of Regulation Title 21 Part 184.1733 limits sodium benzoate to 0.1% of a product by weight. The rates at which preservatives are added to enzyme formulations are typically less than 1%. Enzymes in turn are

added to foods in relatively small quantities and specifically, between 0.1-5% in organic foods. Thus, the potential for preservatives in enzymes to function as preservatives in the final food product to which the enzymes are added is negligible. The literature reviewed for this report does not suggest that ancillary preservative ingredients in enzyme products exert any technical or functional effect in the final food product to which the enzyme preparation is added.

Evaluation Question #6: Describe whether the petitioned substance will be used primarily to recreate or improve flavors, colors, textures, or nutritive values lost in processing (except when required by law) and how the substance recreates or improves any of these food/feed characteristics (7 CFR § 205.600 (b)(4)).

Many substances commonly used as ancillary ingredients in enzyme preparations themselves have flavoring and or nutritive properties including maltodextrin, trehalose, flour, whey, sorbitol, glucose, sucrose, maltose and lactose. However, the main contribution of ancillary ingredients in enzyme preparations is to ensure the enzymes' optimal activity in food processing. As mentioned, enzyme preparations are used in food processing at relatively low rates. Thus, the extent to which their ancillary ingredients may indirectly affect color, flavor, texture or nutrient values is expected to be negligible. They are not added for the purpose of recreating these properties in food. The active enzyme portion, on the other hand, may be added primarily to affect properties such as flavors, colors, textures or nutritive values. However, the literature does not suggest that they *recreate* these properties that have been lost in processing. Some enzyme preparations function to increase volume and improve softness or crumb structure of baked goods, to produce lactose-free dairy products, to create higher viscosity egg products, to clarify and intensify juice colors, or to help retain the flavor and nutritional value of fruit during processing, among many other functions (DSM 2015).

Evaluation Question #7: Describe any effect or potential effect on the nutritional quality of the food or feed when the petitioned substance is used (7 CFR § 205.600 (b)(3)).

The literature does not suggest that carriers, diluents, stabilizers, preservatives or other ancillary ingredients in enzyme formulations are added primarily to affect the nutritional quality of the final food product. The function of such ancillary ingredients is to ensure proper functioning of the enzyme, with *its* associated effects on the nutritional quality of the food being processed. Enzymes are added to food to help catalyze biological reactions, from meat tenderization to fruit preservation and dough conditioning. Enzymes are commonly used to break down proteins, lipids and other components of food, thereby affecting digestibility and nutrient availability. By aiding in the maintenance of enzymes' efficacy, ancillary substances used in enzyme formulations indirectly affect the nutritional quality of the food.

Ancillary ingredients are added to enzyme formulations to ensure efficacy of the enzyme's activity. The enzyme concentrate that results from a fermentation process is typically not capable of being utilized in food applications (Whitehurst and Van Oort 2009). Diluents are added so as to make the enzyme available at the appropriate rate. As noted earlier, stabilizers are added to enzyme formulations to prevent loss of enzyme activity. Preservatives further extend the shelf life of enzyme formulations to ensure their efficacy once added to food. Coatings also help stabilize and preserve enzyme activity and facilitate slow release in certain applications. Buffers help maintain pH, which also affects enzyme activity (Wieland 1972).

Evaluation Question #9: Discuss and summarize findings on whether the manufacture and use of the petitioned substance may be harmful to the environment or biodiversity (7 U.S.C. § 6517 (c) (1) (A) (i) and 7 U.S.C. § 6517 (c) (2) (A) (i)).

There is no literature to suggest that the manufacture or use of enzyme preparations with ancillary substances is harmful to the environment or biodiversity. However, the production of individual components in enzyme formulations may have certain adverse environmental impacts. Starch and starch derivatives, for example, are made from agricultural commodities such as corn and potatoes. Intensive corn production causes pollution from fertilizer runoff, requires intensive irrigation, and produces greenhouse gasses from land conversion. It has even been reported to have a greater overall environmental

impact than gasoline production (Yang, et al. 2012). In addition, most industrially produced corn is genetically modified for herbicide resistance. This practice is thought to lead to increased use of pesticides such as glyphosate as resistant weeds develop (Benbrook 2009). Sucrose and glucose are made from sugar beets or sugarcane, the production of which also has notable environmental impacts. According to the World Wildlife Fund (2015), some of the most biodiverse regions on earth have been cleared for sugarcane production. Sugar plantations and mills create pollution from eroded soils and synthetic fertilizers, wastewater, emissions from flue gases, soot and ash. Sugar beets may also be genetically modified for herbicide resistance.

Evaluation Question #10: Describe and summarize any reported effects upon human health from use of the petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (i), 7 U.S.C. § 6517 (c) (2) (A) (i)) and 7 U.S.C. § 6518 (m) (4)).

The use of enzymes in food has potential effects on human health, particularly in regard to the toxicity potential of specific enzymes. The literature on enzyme safety concerning human health focuses on the safety of the organisms which produce the enzymes (Hammond 2007). In fact, the FDA does not consider ancillary ingredients in safety evaluations of enzymes (West-Barnette and Srinivasan 2013). Additionally, there is no literature to suggest that the use of ancillary ingredients in enzymes poses a threat to human health.

Many of the ancillary substances used in enzyme formulations are agricultural or specifically approved for use in organic food processing at §205.605. This response will therefore focus on the substances in Table 1 that do not fall under either of those categories.

The Select Committee on GRAS Substances (SCOGS) concluded in 1977 that there is no evidence to show that sodium benzoate as a food ingredient constitutes a hazard to the general public when used at levels prescribed in 22 CFR 184.1733. When used in rennet, only small amounts of sodium benzoate or methyl and propyl parabens (0.1 mg or less per person per day) would be expected to be consumed in the diet, and the committee found no evidence of hazard at those levels in prior evaluations. They concluded that there was no evidence to suggest that use of rennet with said preservatives posed a hazard to the public when used at the reported levels or at levels that might reasonably be expected in the future (FDA 2013). Methyl paraben is listed as GRAS for use as a food preservative at 21 CFR 184.1490.

As part of its national biomonitoring program, the Centers for Disease Control and Prevention (2013) summarized numerous studies on the safety of parabens. While not found to be acutely toxic at levels administered in animal tests, there have been some reported cases of skin reaction in humans when exposed topically. Ingested parabens are said to be generally absorbed into the gastrointestinal tract and ultimately eliminated in the urine within a short period of time. Parabens have not been found to be carcinogenic in animals, and while they do have weak estrogenic activity, numerous studies suggest that estrogenic effects in humans are unlikely (CDC 2013). None of the literature reviewed for this report indicated that parabens are currently used in enzyme formulations applied to the processing of organic foods.

SCOGS concluded for sorbic acid and its sodium, potassium and calcium salts, as well as propylene glycol, sorbitol, and sodium acetate that there is no evidence to suggest a hazard to the public when the substances are used at current levels or levels reasonably expected in the future. The committee made the same conclusion for methyl cellulose, with the exception that they could not determine, without additional data, whether a significant increase in consumption would constitute a dietary hazard (FDA 2014).

Glutaraldehyde is listed at 21 CFR 173.357 for use as a fixing agent in the immobilization of enzyme preparations, with the stipulation that the fixed enzyme preparation be washed to remove residues of the fixing material. Glutaraldehyde when inhaled has been linked with adverse health effects such as asthma, breathing difficulties, respiratory irritation and skin rashes, ranging from mild to severe (OSHA 2006). Most of the literature related to the health effects of glutaraldehyde focuses on occupational exposure to its vapor, and there is none to suggest that its use in enzymes has any impact on human health

Phosphates are an essential component in the human diet, consumed primarily in the form of free orthophosphates (JECFA 1974). Excretion of excess phosphate is mainly in the form of calcium phosphate, which can cause calcium deficiency. However, humans can tolerate a wide range of phosphate intake without upsetting the balance of minerals (JECFA 1974). Phosphate salts have various medicinal uses including treatment of blood phosphate imbalance, rickets in children, prevention of kidney stones, as an antacid or laxative, and in reduction of dental sensitivity (WebMD 2015). However, phosphate salts must be used with caution since regular, long-term use can cause abdominal pain, muscle weakness, and other problems. It is recommended that phosphate intake be limited to 3-4 g/day (WebMD 2015). It is not expected that the intake of phosphates used to buffer enzyme formulations would exceed this amount.

Diatomaceous earth (DE) dust in its amorphous form can cause temporary irritation to the eyes and respiratory system when inhaled. Long-term exposure to dust of the less common crystalline form can cause chronic respiratory problems and be carcinogenic. However when eaten very little DE is absorbed into the body. Rats fed high doses of silica for two years showed no increase in cancer development. (National Pesticide Information Center 2013).

Boron occurs naturally in the environment and normal human intake occurs from the diet, drinking water and environmental exposure. Exposure from commercial products is estimated to be 0.1mg/day (WHO 1998). For boron, the EPA has established an oral reference dose (RfD) of 0.2 mg/kg/day. Boron has been shown to be absorbed from the gastrointestinal and respiratory tracts and eliminated in urine. It has not been shown to be carcinogenic. Boron toxicity to male reproductive system in animals has been reported from chronic oral doses of 29 mg boron/kg body weight per day over two years (WHO 1998). However, the level of exposure from ancillary substances in enzyme formulations is expected to be within established legal and safe limits.

Ammonium sulfate in aqueous media dissolves into its ion components of ammonium and sulfate, the former being metabolized to urea by the liver and excreted via the kidneys, the latter being excreted unchanged in the urine (IPCS 2006). It has relatively low acute toxicity (LD_{50} value (or lethal dose to 50% of test animals), orally in rats of 2000 - 4250 mg/kg of body weight). Clinical signs after oral exposure included staggering, prostration, apathy, and labored and irregular breathing. However, ammonium intake via food is estimated to be 18 mg/day. Sulfate intake from food in the US is estimated to be 453 mg/day (IPCS 2006). Intake from food processed by enzyme formulations containing ammonium sulfate as a stabilizer is not expected to pose a health risk.

Evaluation Question #11: Describe any alternative practices that would make the use of the petitioned substance unnecessary (7 U.S.C. § 6518 (m) (6)).

The uses of enzymes in food cover a broad range of applications, each with its specific substrates and requirements for enzyme activity. Therefore, alternative practices that would make the use of ancillary ingredients unnecessary in an enzyme preparation would be highly dependent on the application in question. Therefore, no generalizations about alternative practices can be made.

Evaluation Question #12: Describe all natural (non-synthetic) substances or products which may be used in place of a petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (ii)). Provide a list of allowed substances that may be used in place of the petitioned substance (7 U.S.C. § 6518 (m) (6)).

Some ancillary substances in enzyme formulations are nonsynthetic, such as starch and sodium chloride; some are synthetic, such as sodium benzoate and potassium sorbate; and some can be obtained commercially in either synthetic or nonsynthetic form, such as dextrose. Dextrose is typically formed via chemical, heat, pressure, or enzyme hydrolysis (OMRI 2015). When formed via heat, pressure, or enzyme hydrolysis, it is considered nonsynthetic. When made by chemical hydrolysis, it is considered synthetic. It should be noted that for substances available in both synthetic and nonsynthetic forms, documentation regarding their manufacturing processes needs to be evaluated to determine the synthetic/nonsynthetic status.

Evaluation Information #13: Provide a list of organic agricultural products that could be alternatives for the petitioned substance (7 CFR § 205.600 (b) (1)).

A number of common ancillary ingredients in enzyme preparations are agricultural products which are available in organic form, such as maltodextrin and sucrose. Table 2 lists the number of organic sources at the time of this report for various ancillary substances commonly found in enzyme preparations.

Table 2. Number of organic sources for agricultural substances commonly used as ancillary ingredients in enzyme preparations. Adapted from the National Organic Program's List of Certified Operations (NOP 2013).

Ancillary substance	Number of organic sources available
Dextrose	8
Glucose	13
Lactose	11
Maltodextrin	16
Maltose	5
Starch	53
Sucrose	7
Whey	41

References

Aehle, Wolfgang. *Enzymes in Industry: Products and Applications.* John Wiley & Sons, 2006.

Baxter Laboratories Inc. Method of tenderizing meat. USA Patent US 3276879 A. Oct 4, 1966.

Benbrook, C. *Impacts of genetically engineered crops on pesticide use in the United States: The first thirteen years.* Critical Issue Report, The Organic Center, 2009.

Brul, S., and P. Coote. "Preservative agents in foods: Mode of action and microbial resistance mechanisms." *International Journal of Food Microbiology Vol. 50* , 1999: 1-17.

Cargill. "American SF-100 Veal Rennet." *Product Data Sheet.* Waukesha: Cargill Texturizing Solutions, 09 15, 2006.

CDC. "National Biomonitoring Program, Biomonitoring Summary: Parabens." *Centers for Disease Control and Prevention.* 2013. http://www.cdc.gov/biomonitoring/Parabens_BiomonitoringSummary.html (accessed April 30, 2015).

Committee on Food Chemicals Codex. *Food Chemicals Codex, Fifth Edition.* The National Academic Press., 2003.

Danisco. "Product Description - PD 214721-5.5EN." March 31, 2011. http://mags.datagraf.dk/epub/files/brewing%20e-guide/amylex_3t.pdf (accessed January 29, 2015).

Datta, Sumitra, L. Rene Christena, and Yamuna Rani Sriamulu Rajaram. "Enzyme immobilization: an overview on techniques and support materials." *3 Biotech Vol. 3 No. 1*, 2013: 1-9.

DSM. *Enzymes for food processing: nature's great ingredients.* 2015. http://www.dsm.com/markets/foodandbeverages/en_US/products/enzymes.html (accessed February 25, 2015).

Ensymm. "Catalogue for Microbial Rennet." *Ensymm.com.* 2015. http://ensymm.com/pdf/food_supplement/ensymm_microbial_rennet_catalogue.pdf (accessed February 9, 2015).

FAO. "5.3 Chemical Preservation." *FAO Corporate Document Repository, Fruit and Vegetable Processing.* 1995. http://www.fao.org/docrep/V5030E/V5030E0d.htm (accessed February 9, 2015).

FDA. "Code of Federal Regulations Title 21 Sec. 184.1685." *U.S. Food and Drug Administration.* April 4, 2014. http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=184.1685 (accessed February 24, 2015).

—. *GRAS Substances (SCOGS) Database.* August 19, 2014. http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm2006852.htm (accessed February 12, 2015).

—. "Guidance for Industry: Enzyme Preparations: Recommendations for Submission of Chemical and Technological Data for Food Additive Petitions and GRAS Notices." *U.S. Food and Drug Administration.* July 2010. http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm217685.htm (accessed January 15, 2015).

—. "Select Committee on GRAS Substances (SCOGS) Opinion: Rennet." *U.S. Food and Drug Administration.* April 18, 2013. http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm261090.htm (accessed February 23, 2015).

Hammond, Bruce C. *Food Safety of Proteins in Agricultural Biotechnology.* CRC Press, 2007.

IPCS. "Ammonium Sulfate." *Interational Programme on Chemical Safety: Screening Information Data Set.* 2006. http://www.inchem.org/documents/sids/sids/7783202.pdf (accessed May 4, 2015).

JECFA. "Phosphoric Acid and Phosphate Salts." *IPCS Inchem Home.* 1974. http://www.inchem.org/documents/jecfa/jecmono/v17je22.htm (accessed May 4, 2015).

JECFA. *Specifications for identity and purity of certain food additives.* Food and Nutrition Paper 49, Rome: FAO, 1990.

Lenoir, Pierre Marie. Enzyme Stabilization. USA Patent US7928052 B2. April 19, 2011.

National Pesticide Information Center. "Diatomaceous Earth General Fact Sheet." *National Pesticide Information Center (NPIC).* January 2013. http://npic.orst.edu/factsheets/degen.html (accessed April 28, 2015).

NOP. *2013 List of certified USDA organic operations.* 2013. http://apps.ams.usda.gov/nop/ (accessed February 12, 2015).

—. "Enzymes Technical Evaluation Report." *National Organic Program Petitioned Substances Database.* 2011. http://www.ams.usda.gov/AMSv1.0/getfile?dDocName=STELPRDC5094942 (accessed February 5, 2015).

—. "Memorandum to the National Organic Standards Board." *National Organic Program.* February 3, 2014. http://www.ams.usda.gov/AMSv1.0/getfile?dDocName=STELPRDC5106319 (accessed February 3, 2015).

Novozymes. "Novamyl 1500 MG Product Data Sheet." *Novozymes.* March 3, 2010. http://www.novozymes.com/en/about-us/quality-and-supplier-management/quality-management/Documents/PDS_Novamyl%201500MG_EN.pdf (accessed February 10, 2015).

OMRI. "OMRI Products Database." Eugene, OR: Organic Materials Review Institute, February 9, 2015.

OSHA. "Best Practices for the Safe Use of Glutaraldehyde in Health Care." *Occupational Safety and Health Administration.* 2006. https://www.osha.gov/Publications/glutaraldehyde.pdf (accessed May 4, 2015).

Pariza, M. W., and E. A. Johnson. "Evaluating the Safety of Microbial Enzyme Preparations Used in Food Processing: Update for a New Century." *Regulatory Toxicology and Pharmacology 33*, 2001: 173-186.

VGP Pharmachem. "Microbial Rennet N150G Data Sheet." *Marvel Import Export.* 2015. http://i-mimex.com/MyFiles/5-3MICROBIAL%20RENNET%201-150000,%20Data%20Sheet.pdf (accessed February 9, 2015).

WebMD. "Phosphate Salts." *WebMD.* 2015. http://www.webmd.com/vitamins-supplements/ingredientmono-735-phosphate%20salts.aspx?activeingredientid=735&activeingredientname=phosphate%20salts (accessed April 28, 2015).

West-Barnette, Shayla, and Jannavi R. Srinivasan. "Regulatory Aspcts of Food Ingredients in the United States: Focus on the Safety of Enzyme Preparations Used in Food." In *Advances in Food Science and Technology*, by P. M. Visakh, Sabu Thomas, Laura B. Iturriaga and Pablo Daniel Ribotta, 201-225. Scrivener Publishing, 2013.

Whitehurst, Robert J., and Barry A. Law. *Enzymes in Food Technology.* Boca Raton, FL: Sheffield Academic Press Ltd., 2002.

Whitehurst, Robert J., and Maarten Van Oort . *Enzymes in Food Technology.* Wiley & Sons, 2009.

WHO. "Boron." *Inertnational Programme on Chemical Safety.* 1998. http://www.inchem.org/documents/ehc/ehc/ehc204.htm#PartNumber:1 (accessed May 4, 2015).

Wieland, Henry. *Enzymes in food processing and products.* Park Ridge, N.J.: Noyes Data Corp., 1972.

Wilson, C. L., J. M. Solar, A. El Ghaouth, and M. E. Wisniewski. "Rapid Evaluation of Plant Extracts and Essential Oils for Antifungal Activity Against Botrytis cinerea." *Plant Disease Vol. 81, No. 2*, 1997: 204-210.

World Wildlife Fund. *Sustainable Agriculture: Sugarcane.* 2015. http://www.worldwildlife.org/industries/sugarcane (accessed February 27, 2015).

Yang, Yi, Junghan Bae, Junbeum Kim, and Sangwon Suh. "Replacing Gasoline with Corn Ethanol Results in Significant Environmental Problem-Shifting." *Environmental Science and Technology Vol. 46 No. 7*, 2012: 3671-3678.