Phosphates

Handling/Processing

Identification of Petitioned Substances

This report addresses the following phosphate salts allowed under the National Organic Program (NOP) regulations at 7 CFR 205.605(b): calcium phosphates (monobasic, dibasic and tribasic), potassium phosphate, sodium acid pyrophosphate, and sodium phosphates. Chemical identifications of these phosphates are included in Table 1.

Table 1: Chemical Identification of the Phosphates Listed at 7 CFR 205.605(b).

Chemical Names	Chemical Formula	CAS Nos.	E/INS No.
Calcium phosphate, monobasic Calcium dihydrogen phosphate Calcium biphosphate Calcium bis(dihydrogen phosphate) Monocalcium phosphate Primary calcium phosphate Acid calcium phosphate Calcium diorthophosphate	$Ca(H_2PO_4)_2$ (anhydrous)	7758-23-8	E 341(i)
	$Ca(H_2PO_4)_2 \cdot 1\ H_2O$	10031-30-8	
Calcium phosphate, dibasic Calcium hydrogen phosphate Monocalcium acid phosphate Dicalcium orthophosphate	$CaHPO_4$ (anhydrous)	7757-93-9	E 341(ii)
	$CaHPO_4 \cdot 2\ H_2O$	7789-77-7	
Calcium phosphate, tribasic Tricalcium diphosphate Tricalcium phosphate Tricalcium orthophosphate	$Ca_3(PO_4)_2$ (anhydrous)	7758-87-4	E 341(iii)
Dipotassium phosphate (anhydrous) Dipotassium hydrogen phosphate Potassium hydrogen phosphate Potassium dibasic phosphate Potassium phosphate dibasic	K_2HPO_4 (anhydrous)	7758-11-4	E 340(ii)
	$K_2HPO_4 \cdot 3\ H_2O$	16788-57-1	
Sodium acid pyrophosphate (SAPP) Disodium diphosphate Disodium dihydrogen pyrophosphate; Diphosphoric acid, disodium salt	$Na_2H_2P_2O_7$ (anhydrous)	7758-16-9	E 450(vi)
Monosodium phosphate Sodium acid phosphate Sodium dihydrogen phosphate Sodium phosphate, monobasic	NaH_2PO_4 (anhydrous)	7558-80-7 7632-05-5	E 339(i)
	$NaH_2PO_4 \cdot 1\ H_2O$	10049-21-5	
	$NaH_2PO_4 \cdot 2\ H_2O$	13472-35-0	
Disodium phosphate Disodium hydrogen orthophosphate Disodium hydrogen phosphate Sodium phosphate, dibasic	Na_2HPO_4 (anhydrous)	7558-79-4	E 339(ii)
	$Na_2HPO_4 \cdot 2\ H2O$	10028-24-7	
	$Na_2HPO_4 \cdot 7\ H_2O$	7782-85-6	
	$Na_2HPO_4 \cdot 12\ H_2O$	10039-32-4	
Trisodium phosphate	Na_3PO_4 (anhydrous)	7601-54-9	E 339(iii)

Sodium phosphate, tribasic Sodium phosphate Sodium orthophosphate	$Na_3PO_4 \cdot 12\ H_2O$	10101-89-0	

Summary of Petitioned Use

This report addresses the following phosphate salts allowed under the National Organic Program (NOP) regulations at 7 CFR 205.605(b): calcium phosphates (monobasic, dibasic and tribasic), potassium phosphate, sodium acid pyrophosphate, and sodium phosphates. These substances are allowed as ingredients in or on processed products labeled as "organic" or "made with organic (specified ingredients or food group(s))" unless otherwise specified by an annotation:

- Calcium phosphates (monobasic, dibasic, and tribasic) — no annotation
- Potassium phosphate—for use only in agricultural products labeled "made with organic (specific ingredients or food group(s))," prohibited in agricultural products labeled "organic"
- Sodium acid pyrophosphate (CAS # 7758-16-9)—for use only as a leavening agent
- Sodium phosphates—for use only in dairy foods

Several of these phosphate salts are available both as anhydrous substances (i.e., without water) and as hydrates. The hydrates have different physical properties from the anhydrous forms, which makes their use advantageous in certain applications.

These substances are also bioavailable sources of the nutrients calcium, phosphorus, potassium and sodium, and all but one are allowed by FDA as nutrient supplements in foods. However, their use as nutrient sources in foods labeled as organic is the subject of a separate Technical Report for Nutrient Vitamins and Minerals (OMRI 2015).

Characterization of Petitioned Substances

Composition of the Substance:

Chemical compositions of the phosphate salts address in this report are identified in Table 2.

Table 2: Chemical Composition of the Anhydrous Forms of the Phosphates Listed at 7 CFR 205.605(b).

Substance	Formula†	Phosphorus	Oxygen	Hydrogen	Metal
Calcium phosphate, monobasic	$CaHPO_4$	26.47%	54.69%	1.72%	17.12% calcium
Calcium phosphate, dibasic	$Ca(H_2PO_4)_2$	22.77%	47.04%	0.74%	29.46% calcium
Calcium phosphate, tribasic	$Ca3(PO_4)_2$	19.97%	41.27%	0%	38.76% calcium
Dipotassium phosphate	K_2HPO_4	17.78%	36.74%	0.58%	44.90% potassium
Sodium acid pyrophosphate	$Na_2H_2P_2O_7$	27.91%	50.49%	0.91%	20.72% sodium
Monosodium phosphate	NaH_2PO_4	25.82%	53.34%	1.68%	19.16% sodium
Disodium phosphate	Na_2HPO_4	21.82%	45.08%	0.71%	32.29% sodium
Trisodium phosphate	Na_3PO_4	18.89%	39.04%	0%	42.07% sodium

†anhydrous salt

Source or Origin of the Substances:

Sodium and potassium are isolated from brines or salt deposits. Calcium and phosphorus are sourced from limestone and phosphate rock, respectively. The food grade phosphates are formed by reacting purified phosphoric acid with sodium, potassium, or calcium hydroxides.

Phosphoric acid (H_3PO_4) is a triprotic acid, meaning that the phosphoric acid molecule has three protons (a proton is the positive hydrogen ion that characterizes an acid) that can dissociate from the molecule. Monobasic phosphates retain two hydrogen atoms; dibasic phosphates retain one hydrogen atom, and tribasic phosphates retain none.

Properties of the Substances:

Phosphates vary greatly in their solubility in water, ranging from the highly soluble sodium and potassium phosphates to practically insoluble bone ash (tricalcium phosphate). Phosphates also differ greatly in the pH values of their aqueous solutions. At high temperatures, many of the phosphates do not 'melt'; they decompose, forming pyrophosphates. Heating hydrated salts at relatively low temperatures (≤ 100°C) can drive off the water of hydration.

Table 3 below summarizes the major properties of phosphates allowed in organic handling. In the table, solubility is expressed in grams per 100 mL of water, generally at room temperature (20°-30°C) where such data are available. The pH is that of dilute aqueous solutions or slurries. Melting points ("MP") with the letter "d" indicate that the substance decomposes rather than melts. The data are drawn from the Merck Index (Budavari 1996), the Handbook of Chemistry and Physics, 40th Edition (Hodgman, Weast, and Selby 1959), U.S. government internet sources (e.g., PubChem Compound), and Material Safety Data Sheets (MSDS) of substance suppliers.

Table 3: Major Properties of the Phosphates Listed at 7 CFR 205.605(b).

Substance	Properties	Solubility	pH	MP °C
Calcium phosphate, monobasic	Crystalline; loses water of hydration at 100°C; decomposes at 200°C.	1.8	3.1 - 3.7	200 d*
Calcium phosphate, dibasic	White crystals; loses water of hydration at 109°C; upon ignition at 900°C forms calcium pyrophosphate.	0.02	7.0 – 8.0	900 d*
Calcium phosphate, tribasic	Amorphous, odorless, tasteless powder.	insoluble	insoluble	1670
Dipotassium phosphate	Anhydrous; white, somewhat hygroscopic granules; converted into potassium pyrophosphate by ignition.	167	8.5 - 9.6	d*
Sodium acid pyrophosphate	White, fused masses or crystalline powder. When heated to decomposition, it emits toxic fumes of phosphorus oxides and sodium oxide.	≥ 10	4.1 - 4.6	202 d*
Monosodium phosphate	Anhydrous salt is colorless; the monohydrate is white, odorless, slightly deliquescent crystals or granules; loses water of hydration at 100ºC.	~100	4.5	204 d*
Disodium phosphate	Heptahydrate - crystals or granular powder; stable in air; loses five water molecules at 48°C.	104	9.1	d*
Trisodium phosphate	Dodecahydrate - colorless or white crystals, melts at ~75°C if heated rapidly.	14.5	11.9	1583

*d = decomposes

Specific Uses of the Substance:

Calcium phosphate (mono-, di-, and tribasic): The 1995 Technical Advisory Panel (TAP) review indicates that calcium phosphates are used in conventional foods as leavening agents, dough strengtheners and conditioners, nutrients, malting or fermenting aids and yeast foods (all three forms); the monobasic form is used as a buffer, firming agent and sequestrant; tribasic is used as an anticaking agent or free-flow agent, buffer or pH control agent, thickener or stabilizer (Technical Advisory Panel 1995a). The NOP regulations at 7 CFR 205.605(b) do not impose additional restrictions on the use of calcium phosphates in processed organic foods. Tricalcium phosphate is commonly used in organic non-dairy beverages (soy 'milk', almond 'milk', orange juice, etc.) to provide the nutrients calcium and phosphorus. Dicalcium phosphate is the inert diluent and carrier for Vitamin B_{12} in fortified organic foods. Monocalcium phosphate is used as a component of chemical leavening agents ("baking powder").

Potassium phosphate: The 1995 TAP review indicates that potassium phosphate is used as a pH control agent in milk products, as a nutrient supplement, sequestrant and emulsifier, a malting or fermentation aid, and a stabilizer and thickener (Technical Advisory Panel 1995b). Dipotassium phosphate is the only form of potassium phosphate cited by FDA for use in pasteurized process cheese (21 CFR 133.169) and pasteurized process cheese food (21 CFR 133.173). The NOP regulations at 7 CFR 205.605(b) limit the use of potassium phosphate to only those foods labeled "made with organic (specific ingredients or food group(s))."

Sodium acid pyrophosphate: The 2010 Technical Report indicates that sodium acid pyrophosphate is used in conventional foods as a chemical leavening agent in baked goods; a sequestrant (chelating agent) to maintain the appearance of cooked and uncooked fruits and vegetables, particularly processed potatoes; an emulsifying agent and stabilizer in cheeses and related products; an inhibitor of struvite[1] formation in canned tuna; and a curing accelerator in processed meat and poultry products (Technical Services Branch 2010). The NOP regulations at 7 CFR 205.605(b) limit the use of sodium acid pyrophosphate in organic foods to use only as a leavening agent. Sodium acid pyrophosphate is used as a component of chemical leavening agents ("baking powder").

Sodium phosphate (mono-, di-, and tribasic): The 2001 Technical Report indicates that sodium phosphates are used in conventional foods as pH control agents and buffers, sequestrants, texturizers and nutrients (OMRI 2001). Monobasic sodium phosphate is used as an acidulant. The NOP regulations at 7 CFR 205.605(b) restrict the use of sodium phosphates to organic dairy products only. Some organic products containing cheddar cheese, such as cheese crackers or macaroni and cheese, may contain organic cheddar cheese with added sodium phosphate.

Approved Legal Uses of the Substance:
Each of the phosphate salts listed in the NOP regulations at 7 CFR 205.605(b) is identified by FDA in 21 CFR 182 as "Generally Recognized As Safe" (GRAS) for use in food for the various purposes shown below in Table 4. Note that the only potassium phosphate salt that is the subject of a GRAS citation as a food ingredient is dipotassium phosphate. Nevertheless, monopotassium phosphate is permitted in frozen eggs (21 CFR 160.110(b)), and all of the potassium phosphates (mono-, di- and tripotassium) are GRAS for incidental food use in adhesives in articles intended for use in packaging, transporting or holding food (21 CFR 175.105). The USDA Food Safety Inspection Service (FSIS) permits both monopotassium phosphate and dipotassium phosphate in certain meat- and poultry-containing products (9 CFR 318.7 and 9 CFR 424.21).

Table 4: FDA GRAS References, Allowed Uses, and NOP Restrictions of Phosphate Salts.

[1] Struvite is a crystal composed of magnesium, ammonium and phosphate, three mineral elements that naturally occur in fish. The three elements react during the canning (sterilization) process to form crystals. The crystals look like tiny, sharp pieces of glass stuck inside the layers of canned tuna, causing consumer alarm.

Substance	FDA GRAS Reference	FDA Allowed Uses	NOP Restriction (7 CFR 205.605(b))
Calcium phosphate, monobasic	21 CFR 182.1217 21 CFR 182.6215 21 CFR 182.8217	Multiple Purposes* Sequestrant Nutrient	No restriction
Calcium phosphate, dibasic	21CFR 182.1217 21 CFR 182.8217	Multiple Purposes* Nutrient	No restriction
Calcium phosphate, tribasic	21CFR 182.1217 21 CFR 182.8217	Multiple Purposes* Nutrient	No restriction
Dipotassium phosphate	21 CFR 182.6285	Sequestrant	For use only in agricultural products labeled "made with organic (specific ingredients or food group(s))," prohibited in agricultural products labeled "organic"
Sodium acid pyrophosphate	21 CFR 182.1087	Multiple Purposes*	For use only as a leavening agent
Monosodium phosphate	21 CFR 182.1778 21 CFR 182.6085 21 CFR 182.6778 21 CFR 182.8778	Multiple Purposes* Sequestrant Sequestrant Nutrient	For use only in dairy foods
Disodium phosphate	21 CFR 182.1778 21 CFR 182.6290 21 CFR 182.6778 21 CFR 182.8778	Multiple Purposes* Sequestrant Sequestrant Nutrient	For use only in dairy foods
Trisodium phosphate	21 CFR 182.1778 21 CFR 182.6778 21 CFR 182.8778	Multiple Purposes* Sequestrant Nutrient	For use only in dairy foods

* The prior TAP reviews and Technical Reports cited in the section *Specific Uses of the Substance* above enumerate the multiple purposes in conventional foods.

FDA permits addition of sodium phosphates by name as an optional ingredient in several classes of dairy foods: pasteurized process cheese (21 CFR 133.169); pasteurized process cheese food (21 CFR 133.173); pasteurized process cheese spread (21 CFR 133.179); ice cream and frozen custard (21 CFR 135.110); and frozen eggs (21 CFR 160.110). The generic optional ingredient designation "stabilizer," which frequently is sodium or potassium phosphate, is permitted in a variety of dairy foods, such as acidified milk (21 CFR 131.111), cultured milk (21 CFR 131.112), evaporated milk (21 CFR 131.130), heavy cream (21 CFR 131.150), light cream (21 CFR 131.155), light whipping cream (21 CFR 131.157), eggnog (21 CFR 131.170), yogurt (21 CFR 131.200), and cream cheese (21 CFR 133.133).

Because most dairy foods naturally contain substantial amounts of both sodium and phosphorus from the milk, the small incremental amount of sodium and phosphorus contributed by a sodium phosphate stabilizer may exempt sodium phosphate from the requirement to be declared as an ingredient on the label. This practice is allowed by FDA at 21 CFR 101.100(a)(3)(ii)(b). The only FDA-regulated foods where this exemption from labeling is not permissible are hypoallergenic foods (21 CFR 105.62) and infant foods (21 CFR 105.65). FSIS also requires labeling of all food additives for meat products. Thus, the absence of sodium phosphate from the ingredient declaration of an FDA-regulated food does not necessarily mean that this substance has not been added to the food.

FSIS regulates meat- and poultry-containing foods and is responsible for determining the suitability of FDA-approved substances in meat and poultry products. FSIS lists allowed food ingredients at 9 CFR 318.7 and 9 CFR 424.31. Phosphates, including sodium acid phosphates, trisodium phosphate, and mono- and dipotassium phosphates, are allowed at 9 CFR 319.180 in a variety of prepared meat-containing foods, particularly cooked sausage, which includes frankfurter, frank, hotdog, weiner, vienna sausage, bologna, knockwurst and similar products. The NOP regulations at 7 CFR 205.605(b) restrict the use of sodium phosphates to organic dairy products only, so added phosphates are not permitted in prepared organic meat products .

<u>Action of the Substances:</u>

Anticaking Agent and Free-Flow Agent: Anhydrous tricalcium phosphate is an effective carrier for vitamin and mineral premixes and other dry mixes because it is insoluble, non-hygroscopic, and chemically inert except in acidic environments. In an acidic environment, such as the normal stomach, tricalcium phosphate slowly dissolves, providing the nutrients calcium and phosphorus in nutritionally desirable proportions. Dicalcium phosphate (anhydrous dibasic calcium phosphate) is used for similar purposes.

pH Control, Buffering: Phosphate is a trivalent anion and the basis for many chemical buffers. A buffered solution can tolerate the addition of acid or alkali with minimal change in pH. Many liquid foods are very sensitive to pH. For example, adding acid and reducing the pH of milk can cause the protein casein to precipitate. (This is how cottage cheese is produced.) The pH is very important for ensuring food safety. Bacteria such as *Clostridium botulinum* will not grow or produce toxin in foods with a pH of 4.6 or lower. Decreasing and maintaining the pH to less than 4.6 can be achieved with a food-safe acidulant such as monobasic calcium phosphate or monosodium phosphate, which also can act as a buffer to prevent the food from becoming too acidic and changing the flavor profile. The two most commonly used food buffering systems are those based on phosphate and on citrate.

Non-Yeast Leavening: Monobasic calcium phosphate and sodium acid pyrophosphate are acidulants routinely combined with sodium bicarbonate (commonly called "baking soda") to create leavening mixtures (commonly called "baking powder"). The pH of a monobasic calcium phosphate solution is between 3.1 and 3.7, and the pH of a sodium acid pyrophosphate solution is between 4.1 and 4.6. Monobasic calcium phosphate and sodium acid pyrophosphate are stable powders at room temperature that can be mixed with baking soda and remain chemically stable in the dry state, even when mixed with dry baking ingredients such as flour. When fluid is added to make the dough, and the dough is put into a hot oven to bake, the leavening components dissolve and react chemically to liberate carbon dioxide gas. This gas leavens the dough and generates the desired 'airy' texture of the baked goods.

Monocalcium phosphate is used as the single acidulant in some aluminum-free baking powder products. Some baking powders, called "double-action baking powder," contain a second acidulant, either sodium acid pyrophosphate or sodium aluminum sulfate. Neither of these acidulants reacts with sodium bicarbonate until they are wet and hot. In practical terms, sodium acid pyrophosphate and sodium aluminum sulfate do not start reacting with the sodium bicarbonate until after the dough or batter is in the oven. This means that the batter rises for a longer period of time, making lots of bubbles and a fluffier cake, muffin, etc. (Shipman 2014). Note that aluminum sulfate is not allowed in organic processing.

Milk Protein Stabilization: The phosphates in sodium phosphate and potassium phosphate interact with milk proteins, such as casein, to function as emulsifiers that prevent the separation of fat and water in cheese (Gard 1996). These phosphates also stabilize milk and cheese by chelating ("sequestering") calcium (Scharpf 1971). The addition of sodium phosphate to evaporated milk prevents the separation of butterfat and aqueous phases and prevents gel formation (Molins 1991). Separated fat and protein can form an insoluble, non-dispersible layer (Webb, Deysher, and Potters 1951). Disodium phosphate also is used as a processing agent in heavy whipping cream, where it binds to milk minerals to prevent the milk from coating the equipment during processing. Sodium phosphates are used in some pasteurized organic milk products, such as half-and-half and whipping cream, to stabilize the milk protein and to ensure the products do not separate or lose protein prior to consumer use.

Combinations of the Substance:
Most aluminum-free baking powder used in the home is a mixture of monocalcium phosphate, corn starch carrier, and sodium bicarbonate (baking soda).

Status

Historic Use:
The most common historical use of sodium phosphates consistent with 7 CFR 205.605(b) is for stabilizing evaporated milk and similar fluid milk products, and stabilizing processed cheese. The use of phosphate emulsifiers in cheese apparently began about 1895 (Heidolph and Gard 2000; Corbridge 2013).

Organic Foods Production Act, USDA Final Rule:
The NOP regulations include the following listings of phosphate salts at 7 CFR 205.605(b):

- Calcium phosphates (monobasic, dibasic and tribasic)
- Potassium phosphate—for use only in agricultural products labeled “made with organic (specific ingredients or food group(s)),” prohibited in agricultural products labeled “organic”
- Sodium acid pyrophosphate (CAS # 7758-16-9)—for use only as a leavening agent
- Sodium phosphates—for use only in dairy foods

The NOP regulations also include a listing for “nutrient vitamins and minerals” at 7 CFR 205.605(b) which includes phosphates. The use of phosphates as a nutrient source in organic foods is the subject of a separate Technical Report (OMRI 2015).

International
The Canadian Organic Standards align with the NOP regulations with regard to the phosphate salts addressed in this report and the restrictions on their use. In contrast, the CODEX Guidelines, the European Regulation, the Japanese Agricultural Standard and the IFOAM norms only allow monocalcium phosphate and only for use as a leavening agent.

Canada
The Canadian General Standards Board Permitted Substances List (CAN/CGSB 32.311-2006) permits these phosphate salts with usage annotations identical to the NOP regulations.

CODEX Alimentarius Commission Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)
These guidelines only permit monocalcium phosphate (341(i)) and “only for raising flour” (as a leavening agent).

European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008
ANNEX VIII, Certain products and substances for use in production of processed organic food referred to in Article 27(1)(a), Section A – Food Additives, including Carriers, lists only monocalcium phosphate (341(i)) as a “Raising agent for self-raising flour” (as a leavening agent).

Japanese Agricultural Standard for Organic Processed Foods (Notification No. 1606 of the Ministry of Agriculture, Forestry and Fisheries of October 27, 2005)
Table 1, “Food Additives,” lists INS 341(i), Calcium dihydrogen phosphate (a.k.a. monocalcium phosphate), with the annotation “Limited to be used for powders as expanding agent” (as a leavening agent).

IFOAM – Organics International (IFOAM)
The IFOAM norms for Organic Production and Processing, Version 2014, list monocalcium phosphate, INS 341, as a food additive “Only for ‘raising flour’”(as a leavening agent).

Evaluation Questions for Substances to be used in Organic Handling

<u>Evaluation Question #1:</u> Describe the most prevalent processes used to manufacture or formulate the petitioned substances. Further, describe any chemical change that may occur during manufacture or formulation of the petitioned substances when this substance is extracted from naturally occurring plant, animal, or mineral sources (7 U.S.C. § 6502 (21)).

The phosphate salts addressed in this report are formed by combining aqueous solutions of phosphoric acid with either calcium hydroxide (or calcium carbonate), potassium hydroxide, or sodium hydroxide (or sodium carbonate). Manufacturing processes for phosphates and the raw materials are described in Table 5.

Table 5. Manufacturing Processes for Food Grade Phosphates and their Raw Materials.

Phosphoric acid	Phosphoric acid is produced by treating phosphate rock (tricalcium phosphate) with sulfuric acid, forming phosphoric acid and calcium sulfate (Budavari 1996).
Calcium hydroxide	Calcium hydroxide is produced by the hydration of lime (calcium oxide) (21 CFR 184.1205). Calcium oxide is produced from calcium carbonate, limestone or oyster shells by calcination at temperatures of 925° to 1350 °C (21 CFR 184.1210).
Calcium carbonate	Calcium carbonate is prepared by three common methods of manufacture: (1) as a byproduct in the "lime soda process" (adding lime (calcium oxide) and sodium carbonate to hard water precipitates calcium as the carbonate); (2) by precipitation of calcium carbonate from calcium hydroxide in the "carbonation process"; or (3) by precipitation of calcium carbonate from calcium chloride in the "calcium chloride process" (21 CFR 184.1191).
Calcium phosphate, monobasic	Monobasic calcium phosphate is produced by treating calcium hydroxide with phosphoric acid.
Calcium phosphate, dibasic	Dibasic calcium phosphate is produced by the reaction of phosphoric acid, calcium chloride, and sodium hydroxide. Calcium carbonate can be used in place of the calcium chloride and sodium hydroxide.
Calcium phosphate, tribasic	Tricalcium phosphate for food use is prepared from phosphoric acid and calcium hydroxide. Tricalcium phosphate is extremely insoluble in water, so in order to avoid settling in liquid nutritional formulations, calcium phosphate can be formed *in situ* as a colloidal, hydrated gel by adding concentrated phosphoric acid to a dilute solution of calcium hydroxide (Lin and Cho 1987).
Potassium hydroxide	Potassium hydroxide is obtained commercially by electrolysis of a potassium chloride solution in the presence of a porous diaphragm (21 CFR 184.1631).
Dipotassium phosphate	All orthophosphate derivatives of potassium can be generated by neutralization of phosphoric acid with potassium hydroxide (Budavari 1996).
Sodium hydroxide	Sodium hydroxide is prepared commercially by electrolyzing a sodium chloride solution or by reacting calcium hydroxide with sodium carbonate (21 CFR 184.1763).
Sodium carbonate	Sodium carbonate is produced (1) from purified trona ore that has been calcined to soda ash; (2) from trona ore calcined to impure soda ash and then purified; or (3) by synthesis from limestone in the Solvay process (21 CFR 184.1742).
Sodium acid pyrophosphate	Sodium carbonate is reacted with phosphoric acid to form monosodium phosphate, followed by heating the monosodium carbonate to 220ºC to form sodium acid pyrophosphate (U.S. National Library of Medicine 2002).
Monosodium phosphate	All of the orthophosphate derivatives of sodium can be generated by neutralizing phosphoric acid with sodium hydroxide (Budavari 1996).
Disodium phosphate	

Trisodium phosphate	

Evaluation Question #2: Discuss whether the petitioned substances are formulated or manufactured by a chemical process, or created by naturally occurring biological processes (7 U.S.C. § 6502 (21)). Discuss whether the petitioned substances are derived from an agricultural source.

The phosphate salts addressed in this report are made by the chemical processes described above, all of which involve the simple reaction of a mineral acid (phosphoric acid) with an alkaline substance such as calcium hydroxide or calcium carbonate, potassium hydroxide, or sodium hydroxide or sodium carbonate.

Evaluation Question #3: If the substances are synthetic substances, provide a list of nonsynthetic or natural source(s) of the petitioned substances (7 CFR § 205.600 (b) (1)).

Rock phosphate is a natural source of tricalcium phosphate. However, rock phosphate contains radionuclides in concentrations that are 10 to 100 times the radionuclide concentration found in most natural materials (Menzel 1968). Most of the radionuclides consist of uranium and its decay products. Some rock phosphate also contains elevated levels of thorium and its daughter products. The specific radionuclides of significance include uranium-238, uranium-234, thorium-230, radium-226, radon-222, lead-210, and polonium-210 (Menzel 1968). Another impurity of concern is fluorine, which can interfere with calcium and bone metabolism (Rama Rao and Reddy 2001). For food use, purified food grade materials must be used.

Evaluation Question #4: Specify whether the petitioned substances are categorized as generally recognized as safe (GRAS) when used according to FDA's good manufacturing practices (7 CFR § 205.600 (b)(5)).

All of the phosphate salts addressed in this report are GRAS. See Table 4 for regulatory references.

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

None of the phosphate salts addressed in this report are preservatives when used in accordance with 7 CFR 205.605(b). They have no killing effects on bacteria, fungi, mold or yeast. To the contrary, these sources of the nutritionally essential elements phosphorus, calcium, potassium and sodium are used as components of yeast food and bacterial culture media. In some meat- and poultry-containing processed foods, sodium acid pyrophosphate is used to accelerate color fixing or to preserve color during storage of cured pork and beef cuts, cured poultry, and cured comminuted poultry and meat food products. However, in organic foods, sodium acid pyrophosphate is permitted solely for leavening, so this color-fixing use is not permitted.

Evaluation Question #6: Describe whether the petitioned substances 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 substances recreate or improve any of these food/feed characteristics (7 CFR § 205.600 (b)(4)).

Sodium acid pyrophosphate is used as a leavening agent in baked goods, where it reacts with baking soda (sodium bicarbonate) to liberate carbon dioxide, 'leavening' the dough and creating the desired 'airy' texture that consumers expect of baked goods such as cakes and cookies. Monobasic calcium phosphate also is used as a leavening agent in household aluminum-free baking powder and in processed organic foods such as pancake and waffle mixes, cookies and crackers. Thus, the use of these phosphates as leavening agents improves the texture of these baked foods.

Potassium phosphate and sodium phosphates are used in evaporated milk and other milk products to prevent fat and protein separation and thus prevent the loss of the nutritional value of the fat and protein (and accompanying calcium and other minerals) that occur post-processing during product storage. Thus, this use of phosphates helps to retain nutritive value and pre-processing physical properties, rather than recreating or improving them.

Tricalcium phosphate is commonly used in non-dairy beverages as a source of calcium since these beverages displace cows' milk from the diet. Organic orange juice that is calcium-fortified contains tricalcium phosphate. Some organic yogurts and some non-dairy yogurt-like foods also contain tricalcium phosphate. Without this calcium fortification, these non-dairy beverages would be practically devoid of calcium.

<u>Evaluation Question #7</u>*:* Describe any effect or potential effect on the nutritional quality of the food or feed when the petitioned substances are used (7 CFR § 205.600 (b)(3)).

An important nutritional consideration of a diet is its calcium-to-phosphorus (Ca:P) ratio. The chemical information in Table 2 can be used to calculate this ratio for the phosphates allowed in 7 CFR 205.605(b). The Ca:P ratios in the three calcium phosphates vary from 0.65:1 for the monobasic salt to 1.3:1 for the dibasic salt to 1.9:1 for the tricalcium phosphate. The calcium-free sodium and potassium phosphates have a Ca:P ratio of zero. During periods of rapid skeletal growth, such as in infancy, the dietary calcium-to-phosphorus ratio should not fall below 1.0. The FDA infant formula regulation (21 CFR 107.100(e)) requires a Ca:P ratio not less than 1.0 and not more than 2.0. In later life, calcium metabolism is closely regulated by Vitamin D metabolites, particularly calcitriol. High levels of blood phosphorus suppress the formation of calcitriol (Institute of Medicine 1997). The dangers of too much dietary phosphate include excessive bone loss and other effects noted below.

The nutrient phosphorus is not subject to mandatory listing in the Nutrition Facts of a food label (21 CFR 101.9(c)(8)(ii)), and the ingredient declaration may not declare an added phosphate if exempted by 21 CFR 101.100(a)(3)(ii)(b). Consequently, 'silent' addition of phosphates as functional additives can alter the Ca:P ratio of food and thus the diet without the consumer being aware of the fact.

Sodium and potassium are two electrolyte minerals essential to life. Sodium and potassium interact nutritionally. Potassium salts are more expensive than their sodium counterparts, and potassium has a greater molecular weight than sodium, so a greater weight of potassium salts must be added. For these reasons, sodium phosphates are used far more frequently than are potassium phosphates in any application where the two are functionally interchangeable. However, since our diets in general provide much less potassium than is advised and much more sodium than is advised, using the potassium salt would be nutritionally advantageous. Note that sodium chloride (table salt) is the primary source of sodium in the diet and a much greater contributor of sodium to the American diet than the sodium phosphates (Institute of Medicine 2005).

Some highly processed conventional dairy foods, such as pasteurized process cheese food (21 CFR 133.173), a product with a moisture content of not more than 44% (i.e., not less than 56% solids), may contain up to 3% of the wet weight of the cheese food as sodium phosphate (anhydrous basis). Consequently, the additive sodium phosphate may represent more than 5% of the total solids in this food. Nevertheless, the phosphorus content of the process cheese food may be very similar to that of a natural cheese. Below in Table 7 is a partial nutritional comparison of two slices of pasteurized process American cheese food and the same weight of a natural cheese such as Monterey cheese, using standard values of the USDA National Nutrient Database for Standard Reference. In contrast to the minor difference in total phosphorus content, the sodium content of the process cheese food is over twice that of the natural cheese. Note that the process cheese food provides three times as much potassium as the natural cheese does, since process cheese food normally includes whey and milk solids among its ingredients.

Table 7: Comparison of the Nutrient Content of Pasteurized Process Cheese Food and Monterey Cheese.

Product	Total Weight	Water	Protein	Fat	Calcium	Phosphorus	Potassium	Sodium
Process American cheese food, two ¾-oz. slices	42 g	18.5 g	7.08 g	10.76 g	286 mg	184 mg	107 mg	539 mg
Monterey cheese, 42 grams	42 g	17.2 g	10.28 g	12.72 g	313 mg	186 mg	34 mg	252 mg

A more direct comparison of the nutritional effects of added sodium phosphate can be gleaned from a compositional comparison of stabilized evaporated milk and the calorically equivalent amount of fresh milk as shown in Table 8.

Table 8: Comparison of the Nutrient Content of Evaporated Milk and Whole Milk.

Product	kcal	Protein	Fat	Calcium	Phosphorus	Ca:P ratio	Potassium	Sodium
Evaporated milk, 16 fl. oz. (504 g)	675	34.32 g	38.10 g	1315 mg	1023 mg	1.285	1527 mg	534 mg
Whole milk	675	34.84 g	35.94 g	1250 mg	929 mg	1.346	1460 mg	476 mg

The Ca:P ratio of whole milk is about 5% greater than that of evaporated milk. Assuming that the same supply of whole milk was the raw material for both products, the milk contribution of phosphorus to the evaporated milk would be 977 mg, compared to the database value of 1023 mg, suggesting that about 46 mg of phosphorus has been contributed by sodium phosphate stabilizer. Early work on the stabilization of evaporated milk indicated that an addition of 4 to 10 oz (113 to 284 g) of crystalline disodium phosphate (heptahydrate = 11.56% P) per 1000 lb (454 kg) of evaporated milk was effective in most situations, but as much as 16 oz. of disodium phosphate were required in unusual circumstances (Sommer and Hart 1926). These amounts of disodium phosphate would contribute 14 to 36 to 58 mg of phosphorus per 16 fl oz of evaporated milk, amounts which bracket the estimate of 46 mg of phosphorus calculated from the compositional comparison. Thus, the assumption that phosphate addition reduces the Ca:P ratio of evaporated milk by about 5% is reasonable. The sodium phosphate addition level estimated from the phosphorus differential is equivalent to about 12 oz per 1000 lb. The estimate for the addition level based on the sodium differential is about 11 oz per 1000 lb of evaporated milk. Thus, the amount of sodium phosphate used to stabilize evaporated milk has changed little in 90 years.

Evaluation Question #8: List any reported residues of heavy metals or other contaminants in excess of FDA tolerances that are present or have been reported in the petitioned substances (7 CFR § 205.600 (b)(5)).

The Food Chemicals Codex, originally created by the Food Protection Committee, National Academy of Sciences - National Research Council and now published by the United States Pharmacopeial Convention, provides FDA-recognized standards for these purified and chemically defined food additives. The 1996 Food Chemicals Codex specifications for these phosphates included limits for arsenic of not more than 3 mg/kg, for fluoride of not more than 0.005%, and for heavy metals, expressed as lead, of not more than 10 mg/kg. The 2010 Food Chemicals Codex (U. S. Pharmacopeia 2010) standards are listed in Table 9.

Table 9: Heavy Metals and Impurities in Food Grade Phosphates.

Substance	Fluoride	Arsenic	Lead
	Not more than		

Calcium phosphate, monobasic	0.005%	3 mg/kg	2 mg/kg
Calcium phosphate, dibasic	0.005%	3 mg/kg	2 mg/kg
Calcium phosphate, tribasic	0.0075%	3 mg/kg	2 mg/kg
Dipotassium phosphate	10 mg/kg	3 mg/kg	2 mg/kg
Sodium acid pyrophosphate	0.005%	3 mg/kg	2 mg/kg
Monosodium phosphate	0.005%	3 mg/kg	2 mg/kg
Disodium phosphate	0.005%	3 mg/kg	2 mg/kg
Trisodium phosphate	0.005%	3 mg/kg	2 mg/kg

<u>Evaluation Question #9:</u> 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)).

Over 20 years ago, trisodium phosphate was used as a major component of detergents and alone as a robust cleaning agent. The result was that sodium and phosphate entered the waste water stream and eventually ended up in lakes, rivers and streams. The phosphate contributed by detergents caused algal blooms and eutrophication of the Great Lakes. This environmental disaster was remedied by the development of low-phosphate detergents, and by bans on high-phosphate detergents in the states where waterways drain into the Great Lakes (US Environmental Protection Agency 1997). Today most detergents are low in phosphate. This environmental damage was primarily related to sodium phosphate used as a detergent or cleaner, and has little bearing on the use of sodium phosphates as food additives, beyond confirming that sodium phosphates are bioavailable nutrient sources for growing microorganisms such as yeast and bacteria.

<u>Evaluation Question #10:</u> 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)).

Sodium and potassium phosphates are used widely in processed foods, and this evaluation question further explains how they can contribute a substantial amount of phosphorus to the American diet. Calcium phosphates contribute calcium, with Ca:P ratios of 0.65:1 for the monobasic salt, 1.3:1 for the dibasic salt, and 1.9:1 for tricalcium phosphate.

Nutritional status of the adult American population with respect to the major mineral nutrients

Phosphorus interacts with other mineral elements, particularly calcium, magnesium and potassium, in bone formation, kidney function, and other physiological processes. Understanding this interaction is important for understanding the effects of phosphates on human health and nutrition. As mentioned earlier, the Ca:P ratio of a diet is important. The relation of these two well-known minerals to the lesser studied mineral magnesium is also important. Sodium also interacts with these mineral nutrients, particularly potassium.

The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to continuously assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations. The resulting database has been mined extensively by researchers to establish the correlation of nutrient intakes with health as well as socioeconomic status. The NHANES data on phosphorus, sodium, calcium and magnesium, and potassium intakes for adult American (~20 to ~50 years of age), compared to the dietary reference intakes for these nutrients, indicate the following:

<u>Phosphorus:</u> The Estimated Average Requirement (EAR) for adult men and women is 580 mg per day. The Recommended Dietary Allowance (RDA) is 700 mg per day and the Tolerable Upper Intake Level (UL) is

4000 mg per day (Institute of Medicine 1997). Mean daily intakes were reported as 1701 mg for men (243% of the RDA) and 1179 mg for women (168% of the RDA). The average intake of women in the lowest quartile of phosphorus intakes was reported as 671 mg per day, 15% greater than the EAR (Lee and Cho 2015).

It is critical to point out that the phosphorus intake figures in NHANES reports are estimated from nutrient databases**.** Comparison of these nutrient database estimates with direct chemical analyses show significant underestimation of phosphorus intake from processed food containing phosphates, with the analytical results for specific foods being 25% to 70% higher than the estimates (Calvo, Moshfegh, and Tucker 2014; Oenning, Vogel, and Calvo 1988; Sullivan, Leon, and Sehgal 2007; Sherman and Mehta 2009; Benini et al. 2011). The actual total phosphorus intake may be as a much as 1000 mg/day greater than the estimate derived from the nutrient database when foods containing phosphate additives comprise a significant portion of the diet (Uribarri and Calvo 2003).

An analysis of NHANES data found that, after adjusting for demographics, cardiovascular risk factors, kidney function, and energy intake, a higher phosphorus intake was associated with higher all-cause mortality in individuals who consumed more than 1400 mg/day, but at intake levels less than 1400 mg/day, there was no association (Chang et al. 2014). Analysis of the NHANES data for individuals with moderate chronic kidney disease ("CKD") found that high dietary phosphorus intakes were not associated with increased mortality in moderate CKD (Murtaugh et al. 2012).

A higher phosphorus intake was associated with higher calcium intake and was positively associated with bone mineral content in female teenagers, and it was also positively associated with bone mineral content and bone mineral density, as well as reduced risk of osteoporosis, in adults over 20 years of age (Lee and Cho 2015).

<u>Sodium:</u> The Adequate Intake (AI) of sodium for adult (19- 50 year old) men and women is 1.5 g day, and the UL is 2.3 g/day. The mean daily intakes are over 4 g for men and over 3 g for women (Institute of Medicine 2005).

<u>Calcium:</u> The EAR for adult men and women is 800 mg per day. The RDA is 1000 mg/day and the UL is 2500 mg/day (Institute of Medicine 2011). The mean daily intake of calcium was 1157 mg for men and 880 mg for women, 12% less than the RDA but 10% more than the EAR. Mean daily calcium intakes of men and women in the lowest quartiles of calcium intakes were 477 mg and 503 mg, respectively, or 35% lower than the EAR (Lee and Cho 2015).

<u>Magnesium:</u> The EAR for men 19- 30 years old is 330 mg/day, and for men 31-50 years old it is 350 mg/day. The EARs for women these ages are 310 mg/day and 265 mg/day, respectively. The RDA is 400 mg and 420 mg for men and 310 mg and 320 mg for women for the two age brackets. Magnesium ingested as a naturally occurring substance in food has not been demonstrated to exert any ill effects. Thus, the UL for magnesium is established for magnesium supplements, which can cause diarrhea and other gastrointestinal effects at high doses. The UL for adolescents and adults is 350 mg of supplementary magnesium (Institute of Medicine 1997).

Magnesium is the nutrient with the greatest prevalence of usual intakes below the weighted EAR for essential minerals among the U.S. population, ages 4 years and older, considering both the magnesium intake from food (56% below the EAR) and the intake from food plus dietary supplements (53% below the EAR) (FDA 2014).

Magnesium interacts with calcium. Foods and supplements are frequently enriched with calcium. Magnesium inhibits the release of calcium ions from the sarcoplasmic reticulum, blocks the influx of calcium ions into the cell by inactivating the calcium channels in the cell membrane, and competes with calcium ions at binding sites on troponin C and myosin, thereby inhibiting the ability of calcium ions to stimulate myocardial tension (Iseri, Chung, and Tobis 1983; Iseri, Freed, and Bures 1975; Iseri and French 1984). Magnesium, a calcium antagonist, may substitute itself for the calcium ions on hydroxyapatite, producing more soluble phosphate salts and thus inhibiting bone formation and perhaps aortic valve stenosis (Dritsa et al. 2014). Magnesium deficiency in the face of a normal calcium intake has been documented to lead to soft tissue calcification in animals (Chiemchaisri and Phillips 1963, 1965). The most prominent feature of magnesium deficiency is calcification, predominantly of arteries (Kruse, Orent, and McCollum 1933; Tufts and Greenberg 1938; Seelig 1964). Low serum magnesium and high serum phosphorus and calcium are independently associated with greater risk of incident heart failure (Lutsey, Alonso, Michos, et al. 2014).

Magnesium interacts with potassium. Magnesium is necessary for an enzyme responsible for active transport of potassium (Dorup and Clausen 1993). Magnesium regulates the outward movement of potassium in myocardial cells (Matsuda 1991). Magnesium deficiency causes arrhythmia, which may be related to magnesium's role in maintaining intracellular potassium levels (Institute of Medicine 1997).

<u>Potassium:</u> An AI level has been set for potassium because there are insufficient data to estimate an EAR and RDA. The AI for potassium is 4700 mg/day for all adults. "This level of dietary intake should maintain lower blood pressure levels, reduce the adverse effects of sodium chloride intake on blood pressure, reduce the risk of recurrent kidney stones, and possibly decrease bone loss"((Institute of Medicine 2005). The percentages of American men and women who consume amounts of potassium equal to or greater than the AI were estimated to be less than 10% and 1%, respectively (Institute of Medicine 2005). The mean total daily potassium intake of American adults in NHANES 2003-2006 was 2740 mg, only 58% of the AI (Fulgoni et al. 2011). Furthermore, 0% of the population had a potassium intake as high as the AI (Wallace, McBurney, and Fulgoni 2014). Potassium was identified by the 2010 Dietary Guidelines Advisory Committee as being a nutrient of public health concern (Dietary Guidelines Advisory Committee 2010).

<u>Other considerations:</u> Total dietary intakes reflect the sum of the contributions from food and from dietary supplements. NHANES data indicate that in 2003-2006, 51% of Americans consumed multivitamin and mineral supplements containing nine or more micronutrients (Wallace, McBurney, and Fulgoni 2014). Supplement use is growing. For example, use of supplemental calcium increased from 28% among women aged 60 and over during 1988-1994 to 61% during 2003-2006 (Gahche et al. 2011). Dietary intakes of minerals from food sources were higher for magnesium and potassium in male supplement users than in nonusers. For women, dietary intakes of minerals from food sources were higher for users than for nonusers for each mineral examined except for selenium. Supplements reduce the risk of nutrient intakes below the EAR. Women who used calcium-containing dietary supplements were much more likely to meet the EAR than were nonusers. However, even after considering supplement use, more than 14% of adults had inadequate intakes for calcium and magnesium on the basis of the percentage of adults with usual intakes below the EAR (Bailey et al. 2011).

Analysis of the first NHANES in 1984 revealed that a dietary pattern with low mineral intake, specifically calcium, potassium, and magnesium, was associated with hypertension in American adults. Using more recent survey data from NHANES III and NHANES IV, the validity of this relationship was re-examined. Blood pressure (BP) and nutrient intake data from 10,033 adult participants in NHANES III and 2,311 adults in NHANES IV revealed findings similar to those of the earlier analysis, demonstrating that the association between inadequate mineral consumption and higher BP is valid and has persisted over two decades. Exploring this relationship further by separating untreated hypertensive persons by hypertension type (systolic, diastolic or both), the BP effect of low mineral intake was found to be most pronounced in those with only systolic hypertension. Sodium intake was found to be significantly lower in the systolic hypertension group and significantly higher in the diastolic hypertension group compared with the other groups (Townsend et al. 2005).

<u>Summary:</u> The American diet provides very large amounts of phosphorus and sodium. The published phosphorus content is not based on analysis, so the amount of phosphorus consumed is understated. Half of the adult American population consumes less than the EAR of magnesium and essentially no one nowadays consumes the AI of potassium. A substantial proportion of Americans, almost 40%, consume less than the EAR of calcium (Fulgoni et al. 2011). Thus, the major mineral content of the adult American diet is severely imbalanced.

Health effects of phosphorus provided by phosphate additives versus natural phosphorus in foods

Elevated serum phosphate is a risk factor for certain diseases and disease outcomes. In healthy individuals, higher serum phosphate levels have been associated with greater risk for end-stage renal disease and mortality (Sim et al. 2013; Dominguez et al. 2013), abnormally low blood circulation (Meng et al. 2010), abnormally high arterial stiffness (Ix et al. 2009; Kendrick et al. 2010), increased risk of cardiovascular disease (Dhingra et al. 2007) and twice the risk of developing heart failure (Dhingra et al. 2010). Higher levels of serum phosphorus have also been shown to predict coronary artery disease development and progression (Tuttle and Short 2009).

Sodium and potassium phosphates and sodium acid pyrophosphate are very soluble in water, as shown in Table 3. Consequently, the phosphorus in these additives, commonly referred to as "additive phosphorus," is immediately and completely bioavailable upon consumption. In contrast, the phosphorus naturally present in most foods ("food phosphorous") is much less available, in part due to the physical structure of the food and also because digestion of phosphate complexes may be required before the phosphorus can be absorbed.

The digestibility of phosphorus in various foods has been estimated by *in vitro* studies (Karp, Ekholm, Kemi, Hirvonen, et al. 2012; Karp, Ekholm, Kemi, Itkonen, et al. 2012). Only 6% of the phosphorus in sesame seeds with intact hulls was found to be digestible. In legumes, where much of the phosphorus is present as phytate, the average *in vitro* phosphorus digestibility was 38%. In contrast, the "additive phosphorus" in cola drinks and beer was 87-100% digestible. In cereal products the highest total phosphorus content and digestibility were found in industrial muffins containing "additive phosphorus" in the form of sodium pyrophosphate as a leavening agent.

The effect of phosphate on metabolism has been studied in humans using several biomarkers: the blood level free phosphorus ("serum phosphate"), the amount of phosphorus excreted in the urine, the blood level of parathyroid hormone (PTH), the blood level of serum fibroblast growth factor 23 (FGF-23)[2], and the mathematical product of the blood calcium level and the blood phosphorus level score (Takeda et al. 2014; Kwak et al. 2014; Park et al. 2011).

A study by Gutierrez et al. (2015) showed that phosphate additives are more likely to increase serum phosphate levels than natural phosphate from food. Ten healthy individuals were fed a diet providing approximately 1000 mg/day of phosphorus using foods known to be free of phosphorus additives for one week (low-additive diet), immediately followed by a diet comprising identical food items that contained phosphorus additives (additive-enhanced diet). Feeding the additive-enhanced diet for one week significantly increased serum phosphorus as reflected by an increase in circulating FGF-23 levels (Gutierrez et al. 2015).

Another study showed that high total habitual dietary phosphorus intake adversely affected PTH (Kemi et al. 2009). Healthy premenopausal women aged 31-43 years old kept a 4-day food record for calculation of the natural phosphorus (milk and cheese) intake and the additive phosphorus (processed cheese) intake. Comparing the highest total dietary phosphorus quartile to the lowest, mean serum PTH was higher and mean serum ionized calcium was lower where phosphorus intake was higher. Mean PTH was higher among participants who consumed processed cheese and those who consumed less milk and cheese other than processed cheese. Phosphate additives were more harmful to bone than other phosphorus sources, as indicated by higher PTH concentrations (Kemi et al. 2009).

However, a high dietary intake of phosphorus does not always lead to a high serum phosphate level or the associated negative health effects. According to deBoer, Rue and Kestenbaum (2009), dietary intake of phosphorus additives and phosphorus-rich foods are only weakly associated, if at all, with circulating serum phosphorus concentrations, and higher serum phosphorus levels are associated with lower coronary

[2] FGF-23 is a newly discovered growth factor that acts on the parathyroid gland to decrease PTH (parathyroid hormone) mRNA (messenger RNA) and thus reduces PTH secretion in animals with normal kidney function.

heart disease risk scores. In healthy Korean men, neither dietary calcium nor phosphorus intake was consistently associated with coronary artery calcification (CAC) scores. On the other hand, the CAC scores were significantly associated with the blood calcium levels, blood phosphorus levels, and the mathematical product of the blood calcium and phosphorus levels (Kwak et al. 2014; Park et al. 2011). A similar correlation of the serum calcium-phosphorus product with CAC score was reported in individuals with metabolic syndrome (Kim, Lee, and Youn 2013).

One study associated higher FGF-23 levels with higher risks of incident coronary heart disease, heart failure, and cardiovascular mortality (Lutsey, Alonso, Selvin, et al. 2014). The study evaluated the independent association of baseline serum active FGF-23 with incident outcomes involving 11,638 study participants over time. This association was independent of traditional cardiovascular risk factors and kidney function (Lutsey, Alonso, Selvin, et al. 2014).

Serum calcium and phosphorus interact with PTH and FGF-23 to maintain a balance under normal conditions. However, when healthy individuals habitually consume a high phosphorus diet containing insufficient calcium intake, the body compensates to maintain a normal blood calcium level, and bone health is adversely affected (Takeda et al. 2014; Brown and Razzaque 2015). An adequate dietary intake of calcium is needed to overcome the adverse effects of a high phosphorus intake on PTH and FGF-23 secretion. Calcium supplements, providing as little as 100 mg, can reduce serum PTH concentrations and bone resorption (Karp, Ketola, and Lamberg-Allardt 2009).

Increasing dietary calcium to offset high intakes of phosphate impacts the need for other nutrients, particularly magnesium. The magnesium requirements of experimental animals can be doubled by increasing the dietary levels of calcium and phosphorus (Morris and O'Dell 1963). Magnesium deficiency in the face of normal calcium intake has been documented to lead to soft tissue calcification in animals (Chiemchaisri and Phillips 1963, 1965), and a prominent feature of magnesium deficiency is arterial calcification (Kruse, Orent, and McCollum 1933; Tufts and Greenberg 1938; Seelig 1964). Low magnesium status increases serum PTH levels (Paunier 1992). Only about half of American adults consume an adequate amount of magnesium (Rosanoff, Dai, and Shapses 2016).

<u>Summary:</u> The phosphate in phosphate additives is highly bioavailable and more potent for increasing blood phosphate levels than natural phosphate from food. High blood phosphate levels are associated with kidney and vascular disease. A sufficiently high intake of calcium appears to counteract some of the ill effects of excess dietary phosphorus but leads to an increased requirement for magnesium.

Phosphate in organic foods

Due to the restrictions on phosphate use in organic foods, it would be expected that basing a diet on organic foods would reduce the phosphorus intake. De Lorenzo et al. (2010) compared those who ate an "Italian Mediterranean Organic Diet" to participants who followed a similar diet with phosphate additives and found reduced serum homocysteine and phosphorus levels, reduced microalbuminuria, and reduced cardiovascular disease risk in healthy individuals and in those with CKD. The results of this European trial cannot be extrapolated to the U.S. without some reservations. The EU organic regulations allow addition of only one phosphate, monocalcium phosphate, which can only be used as a leavening agent, whereas USDA organic regulations allow sodium pyrophosphate for this purpose and several other phosphates for other uses. These differences could be important, since Karp et al. (Karp, Ekholm, Kemi, Itkonen, et al. 2012) found that the conventional cereal product with the highest total phosphate content (216 mg/100 g), all of which was digestible, was industrial muffins that contained sodium acid pyrophosphate as the leavening agent.

A survey and sampling of grocery stores in the Cleveland, Ohio, area found that 44% of the best-selling grocery items contained phosphorus additives. The additives were particularly common in prepared frozen foods (72%), dry food mixes (70%), packaged meat (65%), bread and baked goods (57%), soup (54%), and yogurt (51%) categories. Some of the comparative non-additive products were "organic," e.g., Kraft Macaroni & Cheese Dinner™ with added phosphate versus Kraft Organic Cheddar Macaroni & Cheese

Dinner™ without added phosphate. Phosphorus additive-containing foods averaged 67 mg phosphorus per 100 g more than matched non-additive containing foods. Sample meals comprised mostly of phosphorus additive-containing foods had 736 mg more phosphorus per day compared to meals consisting only of additive-free foods. Phosphorus additive-free meals cost an average of $2.00 more per day (Leon, Sullivan, and Sehgal 2013).

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

Anticaking Agent and Free-Flow Agent: Dicalcium phosphate is used as the diluent of many Vitamin B12 preparations. Other diluents are inert sugar alcohols such as mannitol, or combinations of dicalcium phosphate with microcrystalline cellulose.

pH Control, Buffering: Citrate salts and phosphate salts are effective buffering agents and metal chelators in food systems. They can replace each other in some applications.

Non-Yeast Leavening: Yeast has been used to leaven baked goods since time immemorial. However, yeast-leavened baked goods have a different physical texture and require more time than chemically-leavened foods. Chemical leavening is used instead of yeast for products where fermentation flavors would be undesirable (Matz 1992), or where the batter lacks the elastic structure to hold gas bubbles for more than a few minutes (McGee 2004), or for convenience. For these reasons, muffins, tea breads, scones, pancakes, cakes and cookies could not practically be made without chemical leavening.

Milk Protein Stabilization: Potassium and sodium citrates can replace sodium phosphates and dipotassium phosphate as stabilizers in several dairy food applications. Section 21 CFR 133.173, "pasteurized process cheese food," includes these three citrates along with sodium phosphates and dipotassium phosphate as acceptable emulsifying agents. Sodium citrate is an alternative to sodium phosphate in condensed, evaporated, and non-fat milk processing (Ellinger 1972), and in processed dairy cheese manufacture (Rippen 1986). Potassium citrate and sodium citrate are listed at 7 CFR 205.605(b) as allowed for use in organic food with no annotations. Potassium citrate has positive effects on bone, decreasing bone resorption markers and increasing calcium retention (Karp, Ketola, and Lamberg-Allardt 2009), whereas phosphate food additives have adverse effects on bone biomarkers (Kemi et al. 2009; Karp et al. 2007).

Source of Calcium: Given the importance of the calcium-phosphorus ratio in human nutrition, the only food grade additives currently permitted in foods labeled as "organic" that are capable of supplying substantial amounts of both calcium and phosphorus are the calcium phosphates.

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)).

Anticaking Agent and Free-Flow Agent: Rice hull powder, a natural food form of silica, may be a suitable substitute for tricalcium phosphate and dicalcium phosphate as an anti-caking agent, flavor carrier and flow aid, since it can replace silicon dioxide for such uses (Pierce 2010).

pH Control, Buffering: Cream of tartar is a natural material purified from argol, the crude tartar deposited in wine casks during aging, which has been used in food preparation for centuries (Farmer 1896). Cream of tartar is identified chemically as potassium bitartrate, potassium acid tartrate, or potassium hydrogen tartrate, and is the standard used to standardize buffer solutions (Lingane 1947). However, this substance is classified as synthetic at 7 CFR 205.605(b).

Non-Yeast Leavening: Historically, baking powder used for chemical leavening was a combination of three nonsynthetic substances: baking soda (sodium bicarbonate), cream of tartar (potassium acid tartrate), and cornstarch (Farmer 1896). It is unknown whether this preparation would be suitable in modern baking systems. Baking soda (sodium bicarbonate) can function as the only chemical leavening agent in some cookie recipes.

Milk Protein Stabilization: The mechanism for milk protein stabilization is primarily chelation of free calcium to prevent curdling. The two major edible calcium-chelating anions are phosphate and citrate. Nonsynthetic citric acid is a source of citrate, but adding acid to milk curdles the milk protein, similar to making cottage cheese.

Source of Calcium: Bone meal, oyster shell, and dolomite are natural materials that have been used as human dietary calcium supplements. Bone meal and oyster shell preparations were found to be contaminated with lead and other toxic metals (Whiting 1994), and bone meal is no longer recommended as a calcium source in the human diet. Dolomite also can have high lead levels (Boulos and von Smolinski 1988). Rock phosphate is a natural form of calcium phosphate but it is naturally contaminated with fluoride (Rama Rao and Reddy 2001) and radionuclides (Menzel 1968).

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

The phosphates addressed in this report are purified inorganic chemicals; they are not agricultural products, and they are not foods *per se,* so they cannot be made available as organic agricultural products.

Organic yeast is available for use as a leavening agent for traditionally yeast-leavened baked good, but yeast would not satisfy the leavening need for baked goods requiring chemical leavening.

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