ORIGINAL SUBMISSION

KELLER AND HECKMAN LLP
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#663

GRN 000663

Writer's Direct Access
Melvin S. Drozen
(202) 434-4222
drozen@khlaw.com

August 10, 2016

Via FedEx

Antonia Mattia, Ph.D., Director
Division of Biotechnology and GRAS Notice Review (HFS-225)
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5001 Campus Drive
College Park, MD 20740

Re: GRAS Notification for Distarch Phosphate Modified Food Starch

Dear Dr. Mattia:

We respectfully submit the attached GRAS Notification on behalf of our client, Ingredion Incorporated (Ingredion), for distarch phosphate (DSP) modified food starch. DSP will be used as a source of dietary fiber and for functional uses such as a thickener or texturizing agent at levels consistent with good manufacturing practices in food generally, such as bread, ready-to-eat cereals, cereal bars, and other foods. The attached GRAS Notification provides a review of the information related to the intended uses and manufacturing and safety of the ingredient. We have included three (3) hard copies of the complete GRAS Notification for your review.

Ingredion has determined that its DSP modified food starch is generally recognized as safe (GRAS) based on scientific procedures in accordance with 21 C.F.R. § 170.30(b) and in conformance with the guidance issued by the Food and Drug Administration (FDA) under *proposed* 21 C.F.R. § 170.36, 62 Fed. Reg. 18938 (Apr. 17, 1997). Therefore, the use of the DSP modified food starch as described in this GRAS Notification is exempt from the requirement of premarket approval as set forth in the Federal Food, Drug, and Cosmetic Act.

The analytical data, published studies, and information that are the basis for this GRAS determination are available for FDA review and copying at reasonable times at Keller and Heckman LLP, 1001 G Street, NW, Suite 500W, Washington, DC 20001, or will be sent to FDA upon request.

We look forward to the Agency's review of this submission and would be happy to provide Agency officials with any information they may need to complete their assessment. Thank you for your attention to this matter.

Sincerely,

(b) (6)

Melvin S. Drozen

Enclosures

GR

RECEIVED
AUG 11 2016
OFFICE OF FOOD ADDITIVE SAFETY

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

GENERALLY RECOGNIZED AS SAFE (GRAS) NOTICE

Form Approved: OMB No. 0910-0342; Expiration Date: 03/31/2019
(See last page for OMB Statement)

FDA USE ONLY

GRN NUMBER	DATE OF RECEIPT
GRN 000663	
ESTIMATED DAILY INTAKE	INTENDED USE FOR INTERNET
NAME FOR INTERNET	
KEYWORDS	

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: Office of Food Additive Safety *(HFS-200)*, Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740-3835.

PART I – INTRODUCTORY INFORMATION ABOUT THE SUBMISSION

1. Type of Submission *(Check one)*
   [x] New [ ] Amendment to GRN No. _____ [ ] Supplement to GRN No. _____

2. [ ] All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3a For New Submissions Only: Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd)*: 2016/03/22

3b. For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* [ ] Yes [ ] No If yes, enter the date of communication *(yyyy/mm/dd)*: _____

PART II – INFORMATION ABOUT THE NOTIFIER

1a. Notifier

Name of Contact Person	Position
Debbie Levine	Director, Product Assurance & Regulatory Affairs

Company *(if applicable)*: Ingredion Inc.

Mailing Address *(number and street)*: 10 Finderne Ave.

City	State or Province	Zip Code/Postal Code	Country
Bridgewater	NJ	08807	USA

Telephone Number	Fax Number	E-Mail Address
908-575-6203	908-707-3688	debra.levine@ingredion.com

1b. Agent or Attorney *(if applicable)*

Name of Contact Person	Position
Melvin S. Drozen	Partner

Company *(if applicable)*: Keller and Heckman LLP

Mailing Address *(number and street)*: 1001 G Street, NW Suite 500W

City	State or Province	Zip Code/Postal Code	Country
Washington	DC	20001	USA

Telephone Number	Fax Number	E-Mail Address
202-434-4222	202-434-4646	drozen@khlaw.com

PART III – GENERAL ADMINISTRATIVE INFORMATION

1. Name of Substance

Distarch Phosphate Modified Food Starch

2. Submission Format: *(Check appropriate box(es))*

☐ Electronic Submission Gateway
☐ Electronic files on physical media with paper signature page
☒ Paper

If applicable give number and type of physical media

3. For paper submissions only

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in FDA's files by reference? *(Check one)*

☐ Yes *(Proceed to Item 5)* ☒ No *(Proceed to Item 6)*

5. The submission incorporates by reference information from a previous submission to FDA as indicated below *(Check all that apply)*

☐ a) GRAS Notice No. GRN _____
☐ b) GRAS Affirmation Petition No. GRP _____
☐ c) Food Additive Petition No. FAP _____
☐ d) Food Master File No. FMF _____
☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for determination of GRAS status *(Check one)*

☒ Scientific Procedures *(21 CFR 170.30(b))* ☐ Experience based on common use in food *(21 CFR 170.30(c))*

7. Does the submission (including information that you are incorporating by reference) contain information that you view as trade secret or as confidential commercial or financial information?

☐ Yes *(Proceed to Item 8)*
☒ No *(Proceed to Part IV)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, see attached Designation of Confidential Information
☐ Yes, information is designated at the place where it occurs in the submission
☐ No

9 Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission
☐ Yes, a redacted copy of part(s) of the submission
☐ No

PART IV – INTENDED USE

1. Describe the intended use of the notified substance including the foods in which the substance will be used, the levels of use in such foods, the purpose for which the substance will be used, and any special population that will consume the substance *(e.g., when a substance would be an ingredient in infant formula, identify infants as a special population).*

Distarch phosphate modified food starch is intended for use in food as a source of dietary fiber and for other functional uses such as a thickener or texturizing agent. The level of use is limited by the amount that can technically be added to a given food without jeopardizing its quality and consumer acceptability. Further, manufacturers will generally only use the amount necessary for it to contribute a meaningful amount of fiber per serving; use as a thickener or texturizing agent may similar to or lower than the fiber uses. We estimate use in various food categories at 3.5-7.0 grams per serving. Food categories considered include: bread, biscuits, cookies, pancakes/waffles, pizza crust, nutrition bars, hot cereal, RTE cereal, cakes (light weight), muffins, tortillas, pretzels, pasta, and meal replacements. This product is not intended for use as an ingredient in infant formula.

2. Does the intended use of the notified substance include any use in meat, meat food product, poultry product, or egg product? *(Check one)*

☐ Yes ☒ No

PART V – IDENTITY

1. Information about the Identity of the Substance

	Name of Substance[1]	Registry Used (CAS, EC)	Registry No.[2]	Biological Source (if applicable)	Substance Category (FOR FDA USE ONLY)
1	Distarch Phosphate Modified Food Starch	CAS	55963-33-2		
2					
3					

[1] Include chemical name or common name. Put synonyms *(whether chemical name, other scientific name, or common name)* for each respective item (1 - 3) in Item 3 of Part V *(synonyms)*

[2] Registry used e.g., CAS *(Chemical Abstracts Service)* and EC *(Refers to Enzyme Commission of the International Union of Biochemistry (IUB), now carried out by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (IUBMB))*

2. Description

Provide additional information to identify the notified substance*(s)*, which may include chemical formula*(s)*, empirical formula*(s)*, structural formula*(s)*, quantitative composition, characteristic properties *(such as molecular weight(s))*, and general composition of the substance. For substances from biological sources, you should include scientific information sufficient to identify the source *(e.g., genus, species, variety, strain, part of a plant source (such as roots or leaves), and organ or tissue of an animal source), and include any known toxicants that* could be in the source.

Distarch phosphate (DSP) modified food starch is a type of resistant starch (type 4) that is identified by CAS No. 55963-33-2. DSP has been modified using phosphorus oxychloride and is resistant to digestion and is by chemical structure one of a class of phosphated starch products referred to as distarch phosphate.

3. Synonyms

Provide as available or relevant:

1	Modified food starch, food starch-modified
2	Resistant starch, resistant modified food starch, resistant food starch-modified
3	Distarch phosphate

PART VI – OTHER ELEMENTS IN YOUR GRAS NOTICE

(check list to help ensure your submission is complete – check all that apply)

- [x] Any additional information about identity not covered in Part V of this form
- [x] Method of Manufacture
- [x] Specifications for food-grade material
- [x] Information about dietary exposure
- [x] Information about any self-limiting levels of use *(which may include a statement that the intended use of the notified substance is not-self-limiting)*
- [ ] Use in food before 1958 *(which may include a statement that there is no information about use of the notified substance in food prior to 1958)*
- [x] Comprehensive discussion of the basis for the determination of GRAS status
- [x] Bibliography

Other Information

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

[ ] Yes [x] No

Did you include this other information in the list of attachments?

[ ] Yes [ ] No

PART VII – SIGNATURE

1. The undersigned is informing FDA that Ingredion Inc.
(name of notifier)

has concluded that the intended use(s) of Distarch Phosphate Modified Food Starch
(name of notified substance)

described on this form, as discussed in the attached notice, is (are) exempt from the premarket approval requirements of section 409 of the Federal Food, Drug, and Cosmetic Act because the intended use(s) is (are) generally recognized as safe.

2. [x] Ingredion Inc. *(name of notifier)* agrees to make the data and information that are the basis for the determination of GRAS status available to FDA if FDA asks to see them.

Ingredion Inc. *(name of notifier)* agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so.

Keller and Heckman LLP, 1001 G Street, NW Suite 500W, Washington, DC 20001
(address of notifier or other location)

Ingredion Inc. *(name of notifier)* agrees to send these data and information to FDA if FDA asks to do so.

OR

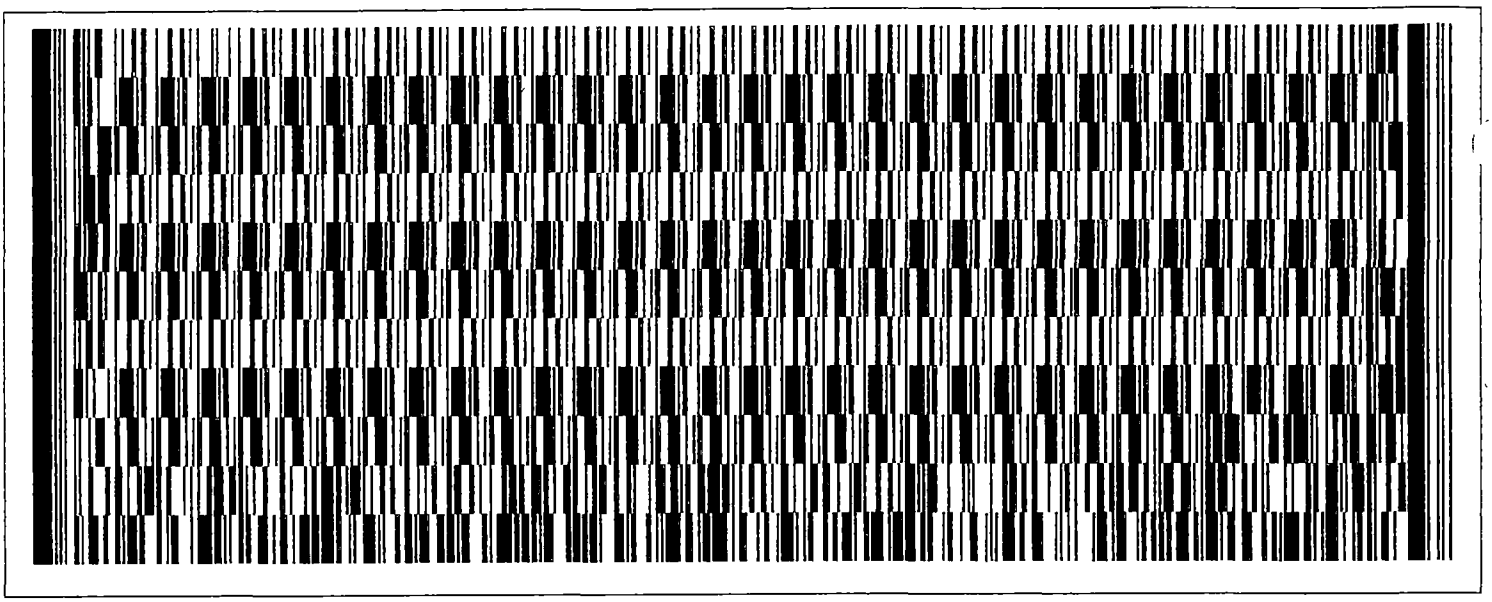
[ ] The complete record that supports the determination of GRAS status is available to FDA in the submitted notice and in GRP No. ____
(GRAS Affirmation Petition No.)

3. Signature of Responsible Official, Agent, or Attorney	Printed Name and Title	Date (mm/dd/yyyy)
(b) (6)	Melvin S. Drozen	08/10/2016

PART VIII – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

Attachment Number	Attachment Name	Folder Location (select from menu) (Page Number(s) for paper Copy Only)
	Cover Letter to Dr. Antonia Mattia	N/A
	GRAS Notification for Distarch Phosphate Modified Food Starch (Complete)	N/A



GRAS Notification for Distarch Phosphate

Modified Food Starch

Prepared for:

U.S. Food and Drug Administration
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
5100 Paint Branch Parkway
College Park, MD 20740-3835

Prepared by:

Keller and Heckman LLP
1001 G Street, NW
Suite 500W
Washington, DC 20001

Date:

August 10, 2016

Table of Contents

A. Introduction

Keller and Heckman LLP submits the enclosed information on behalf of our client Ingredion Incorporated (Ingredion) in support of this notification that Distarch Phosphate (DSP) modified food starch is Generally Recognized as Safe (GRAS) for use as a source of dietary fiber[1] and for functional uses such as a thickener or texturizing agent at levels consistent with good manufacturing practices in food generally, such as bread, ready-to-eat cereals, cereal bars, and other foods. The modified food starch is produced from food grade starches such as potato, corn, tapioca, wheat or any other food grade starch source. We will refer to Distarch Phosphate modified food starch as DSP throughout the document.

Ingredion has determined that DSP is GRAS based on scientific procedures in accordance with 21 C.F.R. § 170.30(b) and conforms to the guidance issued by the Food and Drug Administration (FDA) under *proposed* 21 C.F.R. §170.36, 62 Fed. Reg. 18938 (Apr. 17, 1997). The GRAS determination has also been evaluated by experts qualified by scientific training and experience to assess the safety of DSP under the conditions of its intended use in food. The analytical data, published studies, and information that are the basis for this GRAS determination are available for Food and Drug Administration (FDA) review and copying at reasonable times at Keller and Heckman LLP, 1001 G Street, NW, Suite 500W, Washington, DC 20001 or will be sent to FDA upon request.

We submit information in the following areas:

- Identity and characteristics of DSP.
- The manufacturing process of DSP.
- Digestibility of DSP.
- Intended general uses and an estimation of consumption of DSP.
- Relevant animal and human safety data on DSP.
- External panel reviewers' evaluation and conclusion that DSP is GRAS for its intended uses.

It is our expectation that FDA will concur that the information presented fully supports the determination that DSP as produced by Ingredion is GRAS for use as a source of dietary fiber ingredient and for other uses such as a thickener or texturizing agent in food excluding meat products, poultry products, and infant formula.

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[1] We understand that as an isolate or synthetic non-digestible carbohydrate Ingredion will now have to submit a citizen petition to FDA demonstrating that the substance has a beneficial physiological effect and request that FDA consider it a dietary fiber under 21 CFR 101.9(c)(6)(i). See 81 Fed. Reg. 33741 (May 27, 2016).

B. Administrative Information

1. Claim Regarding GRAS Status

Keller and Heckman LLP on behalf of Ingredion, hereby notifies the agency of its determination that DSP is GRAS based on scientific procedures for use in food as a source of dietary fiber and for other uses such as a thickener or texturizing agent.

2. Name and Address of the Notifier

Ingredion Incorporated
5 Westbrook Corporate Center
Westchester, IL 60154
USA

All communications on this matter are to be sent to Counsel for the Notifier

Melvin S. Drozen
1001 G Street, NW
Suite 500W
Washington, DC 20001
Telephone: (202) 434-4222
Facsimile: (202) 434-4646
Email: drozen@khlaw.com

3. Common or Usual Name of the Subject Substance

Food starch-modified, modified food starch, resistant starch, resistant food starch-modified, resistant modified food starch, distarch phosphate.

4. Intended Use and Self-Limiting Levels of Use

DSP is proposed for use in food as a source of dietary fiber and for other functional uses such as a thickener or texturizing agent. The use of DSP as a food ingredient is limited by the level that can technically be added to a given food without jeopardizing its quality and consumer acceptability. Further, use is limited by the cost of DSP; food manufacturers will generally only use the amount of DSP necessary for it to contribute a meaningful amount of fiber per serving of the finished food product. Use levels as a thickener or texturing agent may be similar to or lower than the fiber uses.

Our estimate of an estimated daily intake (EDI) for DSP based on its use in seventeen food categories is 3.5 - 7.0 grams per serving or an average of 5 grams per serving. The fifteen food categories were selected as the most common use applications for this ingredient. The U.S. Per Capita mean intake from these selected food categories is 16.8 - 34.5 g/day and the corresponding 90^{th} percentile intake is 33.6 - 69.0 g/day. See further discussion in Section E. These estimates provide the absolute maximum intake of the ingredient that would occur only if all food consumed contained the added fiber ingredient.

C. Criteria for GRAS Status

Ingredion has concluded that Distarch Phosphate is GRAS, and has obtained confirmation of the GRAS status of DSP from a panel of experts that are qualified by scientific training and expertise to evaluate the safety of food ingredients. It is respectfully submitted that this Notification establishes GRAS status for DSP for use in food based on the published safety data on DSP and other Type IV resistant starches.

Food starch modified with the use of phosphorus oxychloride ($POCl_3$) is recognized as an approved food additive at 21 C.F.R. § 172.892. Section 172.892 sets forth the various treatments that can be used to modify starch including the esterification of starch by $POCl_3$ at up to 0.1%. There is also a Food Chemicals Codex (FCC) monograph for Food Starch-Modified that recognizes the use of 0.1% $POCl_3$ to produce distarch phosphate modified food starch. Ingredion would like to manufacture DSP with higher levels of $POCl_3$. Thus, we have reviewed Ingredion's DSP to confirm that it is generally recognized as safe (GRAS) when produced with this higher level of $POCl_3$. Modified food starch produced with 0.1% $POCl_3$ and 4.5% $POCl_3$ results in an end product that has levels of residual phosphorus below 0.4% and 0.5% for potato and wheat starches.[2] The level of residual phosphorus and not the treatment level of $POCl_3$ is the focus of modified food starch regulations in the EU, Codex/JECFA, China and Japan.

Ingredion's DSP is produced from potato starch, wheat starch or any other food grade starch source. Section 172.892 does not reference or limit the starch source and the FCC monograph recognizes the production of modified food starch by treatment of "any of several grain- or root-based native starches (for example, corn, sorghum, wheat, potato, tapioca, and sago)".

As discussed further below, numerous expert committees including the European Food Safety Authority (EFSA), the Joint FAO/WHO Expert Committee on Food Additives (JECFA), and the Scientific Committee for Food (SCF) have evaluated the safety of phosphated starches and concluded that they are safe without any limitation on use. In 1979, the Select Committee on GRAS Substances (SCOGS) concluded that phosphated starches are safe but that unlimited use was not justified based on one report of adverse effects in the kidneys of rats; however, subsequent studies have concluded that these adverse effects are artifacts, and that the rats had similar issues when fed lactose (milk sugar) at high levels in the diet. Further, there are numerous toxicology studies available in the public scientific literature that are based on published and unpublished toxicological studies of animals and humans to support the safety of phosphated starches, including the safety of type 4 resistant starches like DSP.

We have also considered the residual phosphorus that is present in the DSP and conclude that the amount of available phosphorus in the DSP is very low. In addition, a large fraction of the phosphorus is covalently bound and therefore biologically unavailable. Even if all of the phosphorus in the resistant starch were available, the total amount would result in a small fraction of the level of phosphorus tolerable in the human diet.

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[2] Modified food starch produced with 0.1% POCl3 results in $\leq$ 0.1% residual phosphorus and modified food starch produced with 4.5% POCl3 results in residual phosphorus of $\leq$ 0.5%, 0.4% from the production process and 0.1% from naturally occurring phosphorus in the potato or wheat.

Thus, for all of the reasons set forth in this GRAS Notice, we conclude that the intended uses of DSP are GRAS.

D. Detailed Information about the Identity of the Notified Substance

1. Name and Other Identities

Chemical Name:	Distarch Phosphate
CAS No.	55963-33-2
Synonyms:	Resistant Starch Type 4; RS4

DSP is a food-grade modified resistant starch that can be used to increase the total dietary fiber of food. DSP contains at least 85% insoluble total dietary fiber on the starch dry solids basis (dsb). It contributes minimal viscosity to food systems. DSP is sold under the brand name PenFibe® RS and/or Versafibe®.

2. Chemical and Physical Properties

DSP is food starch that has been modified using phosphorus oxychloride ($POCl_3$). DSP is resistant to digestion and is by chemical structure one of a class of phosphated starch products referred to as distarch phosphate a form of starch that contains esterified phosphate crosslinks. Potato starch has the approximate composition: amylopectin 75-80%; amylose 20-25%; ash 0.35%; nitrogen, trace; and fat, practically none. Potato and wheat starch are unusual, relative to starch from other foods, in that they contain 0.06-0.10% phosphorus. Phosphorus is present as dihydrogen orthophosphate groups esterified to the amylopectin fraction.[3] DSP contains up to 0.5% total phosphorus resulting from the combination of additional phosphorylation with $POCl_3$, which is approximately 0.4%, plus the phosphorus naturally occurring in potato and wheat starch, which is approximately 0.1%.

DSP can be used to increase total dietary fiber of food products. It is bland in flavor and cannot be detected organoleptically in most applications. DSP contains at least 85% insoluble total dietary fiber analyzed on the dry solids basis. It contributes minimal viscosity to processed foods. Modification of the food starch results in crosslinking of starch polymers with phosphate groups and the presence of starch phosphate esters on the external surface of the starch granules. The structure of starch is provided in the Figure below.

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[3] Treadway, R. H. (1967). Manufacture of potato starch. R. L. Whistler and E. F. Paschall, eds. Starch: Chemistry and Technology, Vol. II, Academic Press, New York, at 87-101.

Figure 1. Structural Formula for Starch

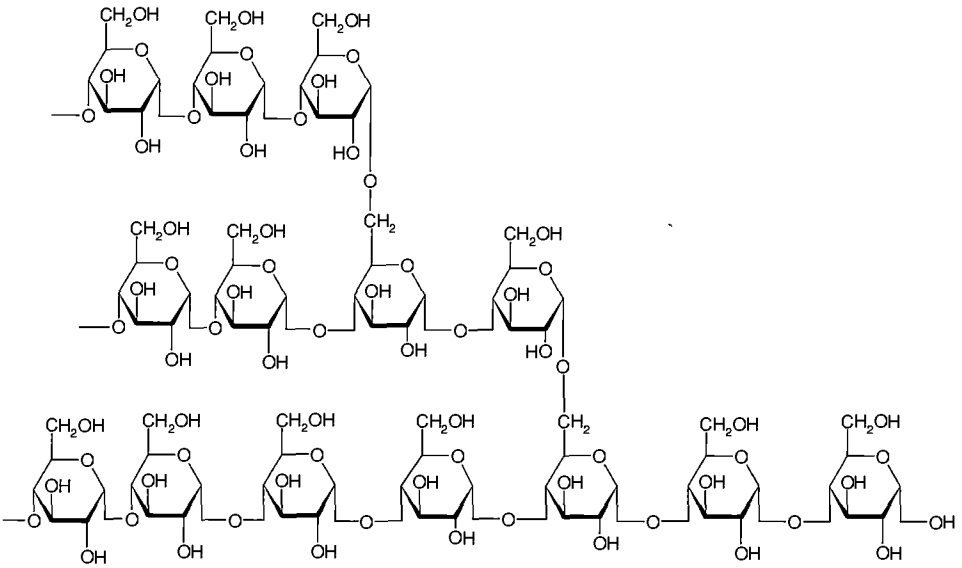
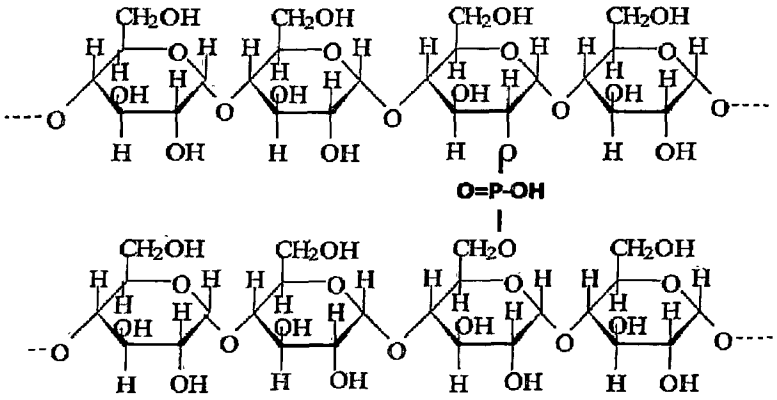


Figure 2. Structural Formula for Distarch Phosphate



Previous safety evaluations of DP products and phosphated DP, where additional monophosphate esters are added to the surface of the starch, have inferred the presence of phosphodiester crosslinks based on indirect evidence.[4] For example, crosslinking has a dramatic effect on the viscosity profile of starch. Starch that is susceptible to changes in viscosity after prolonged heating, high shear, or acidic conditions shows a stable viscosity profile over time once it is crosslinked. Crosslinked starch is sometimes referred to as "inhibited" starch because crosslinking inhibits swelling during cooking. Starch that is lightly crosslinked tends to show a peak viscosity that is actually higher than that of its native unmodified starch. The key benefits

[4] SCOGS (1979). Evaluation of the Health Aspects of Starch and Modified Starches as Food Ingredients. Contract No. FDA 223-75-2004. Life Sciences Research Office, Federation of American Societies for Experimental Biology.

of crosslinking are stability and improved paste texture; the normally cohesive, gummy consistency associated with native waxy corn starch is eliminated, and a smooth, salve-like texture is produced. In general, as the level of crosslinking increases, the starch becomes more resistant to the changes generally associated with cooking and pasting.

More recently, Kasemsuwan and Jane reported direct evidence for phosphodiester bonds that crosslink starch after treatment with $POCl_3$ or sodium trimetaphosphate has been obtained using nuclear magnetic resonance.[5] The authors found that starch crosslinked with $POCl_3$ contained almost no detectable monophosphate esters, thus demonstrating the high selectivity of this reagent for producing only distarch phosphate.

3. Manufacture

a. Production of Distarch Phosphate Modified Food Starch

DSP is made from raw food starch that is blended into a slurry and maintained at a temperature of 59-75°F. Sodium chloride or sodium sulfate is added to the slurry followed by the addition of sodium hydroxide until the pH of the slurry is 11.4-11.6. Treatment with up to 4.5% phosphorus oxychloride is added to the slurry while maintaining a pH of 11.4-11.6 by the addition of a sodium hydroxide solution. After the phosphorylation step is complete, the pH is lowered to 5.5 with hydrochloric acid. The starch is washed on a filter drum and flash dried to a moisture content of 10-13 percent. A typical flow chart for the manufacture of DSP is shown below.

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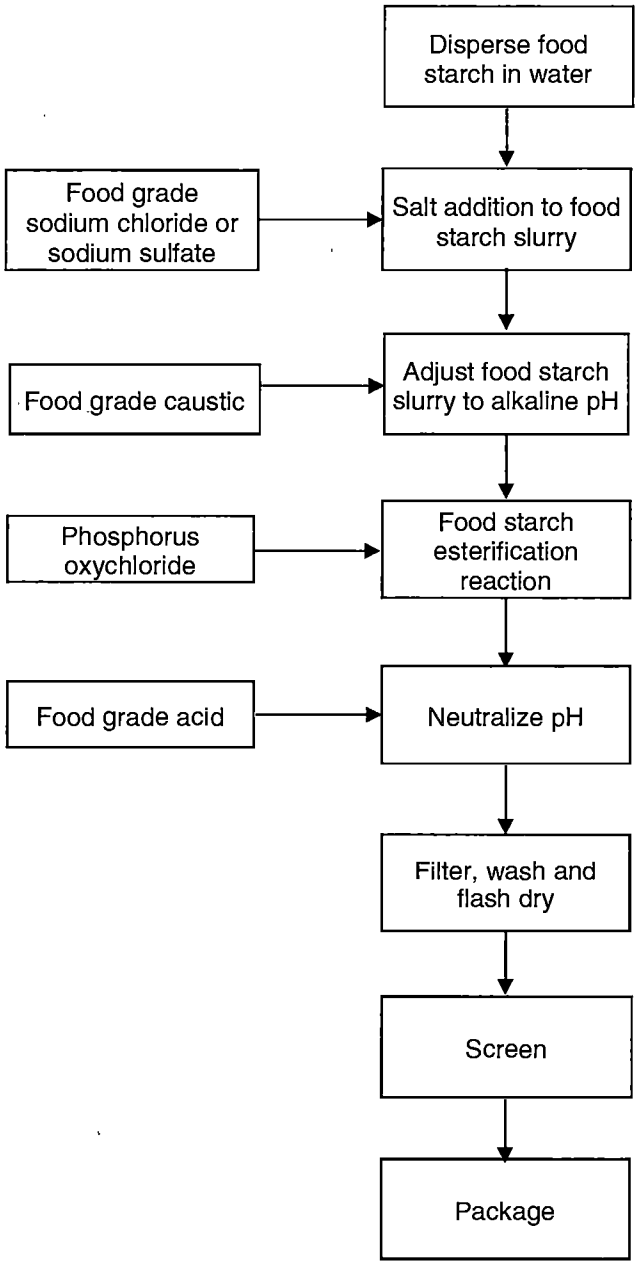
[5] Kasemsuwan, T. and Jane, J. J. (1994). Location of Amylose in Normal Starch Granules II and Locations of Phosphodiester Cross-Linking Revealed by Phosphorus-31 Nuclear Magnetic Resonance, Cereal Chemistry, 71 at 282-287.

Figure 3. Distarch Phosphate Process Flow Diagram



b. Specifications and Data on Representative Lots

The typical characteristics of DSP are provided in Table 1 below. Six lots of DSP were analyzed to confirm that the product is consistently produced; these results are reported in Table 2 below. DSP conforms to the finished ingredient specifications set forth in the Food Chemicals Codex (FCC) monograph for Food Starch, Modified.

Table 1. Typical Characteristics of DSP Modified Food Starch

	Method	Typical Analysis
Color	internal method	White to Off White
Form	internal method	Fine powder
pH	internal method	5.5-7.5
Moisture	internal method	16% max
Total Dietary Fiber	(AOAC 991.43)	85% min (dry solids basis)
Granulation	internal method	Through U.S. 200 Mesh: 95.0%
Fat	AOAC 006.06	<0.1g/100g
Protein	internal method	0.1g/100g
Ash	internal method	1.6g/100g
Phosphorus[6]	AOAC 2011.14	0.4g/100g
Total plate count	USP Chapter 61	10,000 max/g
Yeast	USP Chapter 61	200 max/g
Mold	USP Chapter 61	200 max/g
Coliforms	APHA Chapter 8	100 max/g
E. coli	UPS Chapter 62	Negative
Salmonella	UPS Chapter 62	Negative in 25 g

[6] Not more than 0.40% phosphorus in the finished modified food starch as a result of the manufacturing process; there is an additional 0.10% naturally occurring phosphorus from the potato and wheat starch for a total maximum of 0.50% phosphorus.

Table 2. Analysis of Six Lots of DSP Modified Food Starch

	Typical Analysis	Lot No. A	Lot No. B	Lot No. C	Lot No. D	Lot No. E	Lot No. F
Total Carbohydrate[7] (dry basis)	By difference	84	84	84	84	85	85
Total Dietary Fiber[8] (dry solids basis)	85% min	98.89	100	100	100	96.15	100
Phosphorus[5] (%)	0.409	0.50	0.50	0.50	0.50	0.44	0.47
Moisture[6] (%)	16% max	13.65	13.65	13.01	13.64	13.06	12.89
pH	5.5-7.5	7.17	6.97	7.11	6.93	7.01	6.92
Ash[6] (%)	1.6	1.64	1.72	1.70	1.96	1.58	1.80
Fat[6] (%)	<0.10	0.01	0.01	0.02	0.01	0.02	0.01
Protein[6] (%)	0.10	0.075	0.072	0.077	0.071	0.072	0.073
Lead (mg/kg)	<1.0	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10

c. Contaminants

Microbiological controls are incorporated in the DSP manufacturing process to ensure that the substance is free of pathogenic or other objectionable organisms or unwanted microbial metabolites, and that DSP is otherwise suitable for its intended use. The production methods are consistent with current U.S. good manufacturing practices (cGMP) at 21 C.F.R. Part 110. The ingredient also does not contain more than 1 mg/kg lead and less than 10 ppm sulfur dioxide consistent with the Food Chemicals Codex (FCC) monograph for Food Starch, Modified.

d. Technological Properties: Digestion Studies of Distarch Phosphate

Ingredion has confirmed that DSP produced using up to 4.5% $POCl_3$ is highly resistant to digestion, based on the *in vitro* Englyst procedure. Further, the additional crosslinking of DSP created by using a higher level of $POCl_3$ treatment results in a significant decrease in the portion of the product that is digestible. Compared to product produced with 0.1% $POCl_3$ the quantity of starch in DSP that is not digestible is increased from 88% to 97%.

Ingredion evaluated the relative digestibility of uncooked, granular native, potato starch (PenPure® 10), modified potato starch (PenBind® 1381 and PenBind® 196),[10] and resistant

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[7] Total composition of Distarch Phosphate accounted for by addition of percent moisture, ash (includes phosphorus & lead), fat and protein and carbohydrate (determined by percent difference from 100%).

[8] Total dietary fiber expressed as percent of total carbohydrate.

potato starch (PenFibe® RS). As summarized in the table below, PenPure® 10, PenBind® 1381 and PenBind® 196 showed similar *in vitro* digestion profiles. All three lots of PenFibe® RS showed similar *in vitro* digestion profiles to one another. *In vitro* glycemic response at 20 minutes was similar for the native and modified potato starches. *In vitro* glycemic response at 120 minutes was higher for the PenPure® 10 native potato starch, PenBind® 1381 and PenBind® 196 modified potato starches versus the PenFibe® RS.

Table 3. *In vitro* Digestion as Glucose Release for Penford Potato Starches by the Modified Englyst Method†

Ingredient	Moisture (%)	*In vitro* glycemic response (%)			Rapidly digested starch (% db)	Slowly digested starch (% db)	Resistant starch (% db)
		20 min.	120 min.	240 min.			
PenPure® 10	12.4	3.1	12.0	26.0	3.1	8.8	88.1
PenBind® 1381	16.5	3.1	12.4	23.3	3.1	9.8	87.6
PenBind® 196	11.4	3.3	11.8	20.3	3.3	8.5	88.2
PenFibe® RS	12.6	1.2	3.1	3.7	1.2	1.9	96.9
PenFibe® RS	9.9	0.6	3.2	6.6	0.6	2.6	96.8
PenFibe® RS	13.5	0.8	4.0	6.5	0.8	3.2	96.0

† Internal test measurement error for the Modified Englyst method is ±2 at T=20 and ±4 at T=120 and T=240 established for dent (native) corn starch (Melojel®). Percent dried basis is abbreviated % db.

The *in vitro* digestion study was performed on un-swollen, granular starches. Granular starch is the native form of starch as it is extracted from the source such as corn, or potato in this instance. The granular starch undergoes $POCl_3$ chemical treatment to produce a modified food starch. The unmodified, or native granular potato starch (PenPure® 10), lightly $POCl_3$ crosslinked modified potato starches (PenBind® 1381 and PenBind® 196), and PenFibe® RS samples were all exposed to enzyme digestion by the modified Englyst method. The digestion results show that all the granular starches tested have some degree of inherent resistance to digestion with the PenFibe® RS samples exhibiting the highest resistance. Food applications that utilize unmodified and modified food starches invariably undergo a heat processing as either a kill step or part of the preparation process, such as baking. Heat treatment intentionally causes granular unmodified and modified food starches to swell due to absorption of water from the food matrix resulting in a desired textural outcome. The PenPure® and PenBind® products would swell under typical food heating conditions to contribute viscosity or texture to the final food. PenFibe® RS would not swell to any appreciable extent under normal food processing conditions due to the extensive crosslinking. Thus PenFibe® RS is typically used for its fiber contribution. The heated, and swollen unmodified and modified potato starch granules are very susceptible to enzyme digestion. Thus if the PenPure® and PenBind® starches were heated and cooled and then exposed to the modified Englyst method, they would be almost completely

[10] PenBind® 196 and PenBind® 1381 are potato starch treated with phosphorus oxychloride within the treatment limitation of not more than 0.1% listed under 21 CFR 172.892, food starch-modified.

digested with little resistant starch remaining. The PenFibe® RS would continue to resist enzyme digestion thereby retaining its fiber contribution to the finished food.

In summary, the data displayed in the above table confirm that PenFibe® RS produced using up to 4.5% $POCl_3$ is highly resistant to digestion, based on the *in vitro* Englyst procedure. The additional crosslinking of DSP created by using a higher level of $POCl_3$ treatment results in a significant decrease in the portion of the product that is digestible. Compared to product produced with 0.1% $POCl_3$ the quantity of starch in DSP that is not digestible is increased from 88% to 97%.

E. Estimated Consumption of Distarch Phosphate from Proposed Food Uses

The typical maximum level of use for DSP will be at a level that will support a nutrient content claim of "high" or "good source" of fiber on the label of the processed food product.[11] As displayed in the following table, the use levels indicated (3.5 g – 7.0 g per serving) will provide a daily intake of at least 2.8 grams or 5.6 grams per serving. These levels enable the finished product to qualify for a "high" or "good source" of fiber nutrient content claim. A "high," "excellent source of" or "rich in" fiber claim is permitted when the product contains 20 percent or more of the daily reference value (DRV) for fiber. The new DRV for fiber is 28 grams per day[12] so that product must contain at least 5.6 grams of fiber per reference amount customarily consumed (RACC) to make a "high fiber" claim. A "good source of," "contains" or "provides" fiber claim is permitted when the product contains 10 percent or more of the DRV for fiber. The DRV for fiber is 28 grams per day so that product must contain at least 2.8 grams of fiber per RACC to make a "good source of fiber" claim. We have assumed that 3.5 grams of DSP, which is 2.975 grams of dietary fiber, meets the requirements for a "good source" claim at 2.8 grams and that 7.0 grams of DSP, which is 5.95 grams dietary fiber, meets the requirements for a "high in fiber" claim at 5.6 grams dietary fiber.

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[11] 21 C.F.R. §101.54(b) and (c).

[12] 21 C.F.R. §101.9(c)(9). Please note that the old regulation cites the DRV for dietary fiber as 25 grams but the new regulation cites the DRV for dietary fiber as 28 grams. See 81 Fed. Reg. 33741 (May 27, 2016).

Table 4. Use Levels and Estimated Intake of Distarch Phosphate

Food	Serving Amount[13]	Good Source Amount	High Fiber Amount	NHANES Intake[14]	USDA Intake[15]	Distarch Phosphate Intake based on USDA or NHANES Data	
	g	%	%	grams/ day	grams/ day	"Good source" grams/ day	"High" grams/ day
Bread	50	7.0	14.0	-	63	4.4[16]	8.8[17]
Biscuits	55	6.4	12.8	-	4	0.2	0.5
Cookies	30	11.7	23.4	-	8	0.9	1.8
Pancakes/Waffles	110	3.2	6.4	-	5	0.2	0.3
Pizza Crust	55	6.4	12.8	-	19	1.2	2.4
Nutrition Bars*	40	8.8	17.5	4.52[18]	-	0.4	0.8
Hot Cereal	55	6.4	12.8	-	16	1.0	2.0
RTE Cereal	15	23.3	46.7	-	16	3.7	7.5
Cakes (light weight)	55	6.4	12.8	-	9	0.6	1.2
Muffins	110	6.4	12.8	-	6	0.4	0.8
Tortillas	55	6.40	12.8	-	7	0.4	0.9
Pretzels	30	11.7	23.3	-	4	0.5	0.9
Pasta, plain	55	6.40	12.8	-	35	2.2	4.5
Meal Replacement*	240	1.5	2.9	25.2[19]	-	0.4	0.7
Average						16.8 g/day	34.5 g/day
Overall Average						26 g/day	

[13] Serving amount based on reference amounts customarily consumed (RACCs) set forth at 21 C.F.R. §101.12(b). The RACCs used are consistent with the revisions set forth in 81 Fed. Reg. 3400 (May 27, 2016).

[14] Estimates of intakes for meal replacements and nutrition bars were made using NHANES 2003-2004 frequency consumption data (eating occasions per day). Average frequency of consumption of each food in units of intake per day from NHANES food frequency files were averaged over all eaters (only) of each food for the two days of the survey. Meal replacements were consumed at rate of 0.105 per day and nutrition bars (as granola bars) were consumed at rate of 0.113 per day. Multiplication of the intake frequency (eating occasions per day) by the amount consumed per day (grams per day, as the serving size from FDA's RACCs (reference amount customarily consumed) yielded the average intake per day.

[15] USDA intakes are based on surveys performed in the 1990s, i.e., Continuing Survey of Food Intakes by Individuals (CSFII 1994-96). See: USDA (2002). Foods Commonly Eaten in the United States. Quantities Consumed Per Eating Occasion and in a Day, 1994-96. Helen Smiciklas-Wright, Diane C. Mitchell, Sharon J. Mickle, Annetta J. Cook, Joseph D. Goldman.

[16] Intake of DSP based on USDA and NHANES intake data and level that would enable the finished food to make a "Good Source of Fiber" claim: 63 g bread/day x 7.0% DSP = 4.4 g DSP/day.

[17] Intake of DSP based on USDA and NHANES intake data and level that would enable the finished food to make a "High in Fiber" claim: 63 g bread/day x 14% DSP = 8.8 g DSP/day.

[18] 0.113 eating occasions/day x 40 g/eating occasion = 4.52 g/day.

[19] 0.105 eating occasions/day x 240 g/eating occasion = 25.2 g/day.

*Note: We have used NHANES data for the meal replacement and nutrition bar categories and USDA intake data for the other food categories.

The average amount of DSP that would be added to result in a "good source" of fiber claim is 3.5 grams per serving and 7 grams per serving would result in a "high" fiber claim for an average of 5 grams DSP per serving of food. The estimate of intake for DSP from the above table suggests that the average estimated daily intake (EDI) could be as high as 34.5 g/day and that the 90th percentile intake could be as high as 69 g/day, based on the conventional estimate of the 90th percentile intake as approximately twice the average.[20] Needless to say this EDI is grossly exaggerated. It assumes that all foods would contain DSP as a source of fiber which certainly will never be the case. In addition, FDA's new daily reference value for fiber is 28 g per day.[21] It is extremely unlikely that an individual would obtain their entire daily fiber intake from foods containing DSP. The use of DSP as a food ingredient is also limited by the level that can technically be added to a given food without jeopardizing its quality and consumer acceptability. Further, use is limited by the cost of DSP; food manufacturers will generally only use the amount of DSP necessary for it to contribute a meaningful amount of fiber per serving of the finished food product. Thus, the notifier would expect that even if several foods containing DSP were consumed a day, the actual average daily intake of DSP would be reasonably below 28 g per day.

We estimated usual intakes of food products and DSP using the USDA CSFII 1994-96 survey (see footnote 12) except when a specific product did not occur in the survey. In that case we used NHANES data from 2003-2004, the most recent NHANES database for which frequency of use data are available. Our evaluation of the USDA survey data for the products of interest in this notification indicate insignificant differences of intakes between CSFII 1994-96 and NHANES 2003-2004. In our view, the data from each survey may be used interchangeably to estimate food product intakes for those years. USDA data are more accessible in the form of secondary publications (such as the reference noted in footnote 12) that provide average food product intakes directly, whereas NHANES data require specialized software and analysis to provide the same information. We also reference GRAS Notice 436, which was for a resistant dextrin (enzyme-modified dextrin).[22] The resistant dextrin was used in similar food categories and at similar use levels (3-9 grams per serving). The estimated daily intake (EDI) calculated in that GRAS Notice was based on the National Health and Nutrition Examination Surveys (NHANES) from 2003-2004 and 2005-2006, and the U.S. Per Capita mean intake was 17.1 g/day, and the corresponding 90th percentile intake was 32.5 g/day. This further supports the proposition that the above calculated EDI is grossly over exaggerated.

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[20] DiNovi, M.J. and Kuznesof, P.M. (1995) FDA, Estimating Exposure To Direct Food Additives and Chemical Contaminants in the Diet. U.S. Food & Drug Administration Center for Food Safety & Applied Nutrition Office of Premarket Approval September 1995.

[21] 21 C.F.R. § 101(c)(9).

[22] GRAS Notice 436, available at, http://www.fda.gov/downloads/Food/IngredientsPackaging Labeling/GRAS/NoticeInventory/ucm316569.pdf.

F. Safety Assessment

This section provides documentation that DSP is safe and GRAS, based on published and unpublished studies and reviews by expert committees. Starches modified for use as food ingredients have been produced for use in food products since the 1950s and have been studied and evaluated several times since then. Modified food starch products have been used in infant foods since the early 1950s to provide uniform consistency.[23] The following brief narrative summarizes the current effects induced by modified starches and other poorly digested substances. References are provided more extensively in the following sections.

Early reviews by expert panels evaluated the safety of modified starches as a class.[24] The conclusions of safety for the use of modified starches in food based on early reviews have been confirmed by more recent reviews.[25] By the mid-1980s, a definitive model explaining the physiological effects (described as adaptive) reported for the class of cross-linked modified food starches had been developed and has not been challenged. Early studies performed at TNO laboratories in the Netherlands[26] supported by studies by Buttolph, Newberne, and colleagues[27] supported a model for induced physiological effects based on the osmotic effect of poorly digested starches fermented in the cecum, the initial portion of the large intestine. Other than the adaptive physiological effects engendered by osmotic changes in the cecum and colon, no adverse effects based on target organ toxicity have been reported for the class of cross-linked modified starches to which DSP belongs. The absence of challenges to this model in the current literature indicates that it is generally recognized as valid. It has been used to explain the physiological aspects of exposures to a variety of osmotically active substances, such as

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[23] Filer, L.J. Jr. et al. (1971). Modified Food Starches for Use in Infant Foods. Nutr. Rev., 29(3): 55-59.

[24] Second Report of the Scientific Committee for Food on Modified Food Starches, 13th Series; JECFA (1974). WHO Technical Report Series No. 539. JECFA (1982). Phosphated distarch phosphate: In Toxicological Evaluation of Certain Food Additives. 26th JECFA Session, Apr. 19-28, 1982, Rome. WHO Food Additives Series, No. 17. SCF (Scientific Committee for Food), 1982. Second report on modified starches. In: Food Science and Techniques. Commission of the European Communities (EEC), Scientific Committee for Food (SCF); Reports of the Scientific Committee for Food (13th Series), Brussels, Belgium, 7-9.

[25] 21 CFR §172.892; EFSA (2010). Scientific Opinion on the safety of 'phosphated distarch phosphate' as a Novel Food ingredient. EFSA Journal 8(9) 1772. SCF (1982).

[26] de Groot, A.P., Til, H.P., Feron, V.J., Van der Meulle, H.C.D., Willems, M.I., (1974). Two-year feeding and multigeneration studies in rats on five chemically modified starches. Food and Cosmetics Toxicology, 12, 651-664. Leegwater, D.C., et al. (1974). The aetiology of caecal enlargement in the rat. Food Cosmet Toxicol., 12(5-6): 687-697.

[27] Newberne, P.M., Conner, M.W., Estes P. (1988). The influence of food additives and related materials on lower bowel structure and function. Toxicol Pathol.,16(2):184-197. Buttolph, M.L., Newberne P.M. (1980). Food Cosmet Toxicol., 18(4):357-62. Subchronic studies in rats fed octenyl succinate-modified food starch. Buttolph, M.L., Misa, T., and Newberne, P.M. (1981). Effects of caramel diets and other dietary manipulations on cecal enlargement, kidney pathology and hematology. Nutrition Reports International 23: 1043-1054.

maltodextrins[28] and smaller molecular weight indigestible substances, such as sugar alcohols and synthetic sweeteners consumed in the diet.[29]

In brief, the model supported by published and unpublished reports, summarized below, indicates that modified starches, including distarch phosphates such as DSP and others in the class, contain some components that are digestible and some that are indigestible. The components that are digested and absorbed are the components of natural starch (glucose and a small amount of phosphate) and are absorbed without consequence. The undigested components pass through the small intestines into the cecum where colonic bacteria begin to degrade the resistant starches. The starches are broken down into osmotically active particles that cause retention of water in the colon accompanied by soft stools, diarrhea, enlargement of the cecum, and enhanced absorption of calcium. The effects are dose dependent.

Early reports of test animal studies of various modified starches indicated that in some cases calcium deposits were formed in the kidney (nephrocalcinosis) and higher than usual amounts of calcium appeared in the urine. Further investigations of these effects determined that enlargement of the cecum and increased permeability to calcium in the colon was a physiological adaptation that did not occur in the absence of excessive intakes. In fact, many substances common in the human diet, such as lactose, sugar alcohols, and synthetic sweeteners that are not easily broken down in the small intestine cause similar effects (see Newberne et al. 1990, in footnote 24). Recent studies with humans that ingested starches resistant to digestion have confirmed that intakes of up to 60 grams per day, as dietary fiber, were not accompanied by gastrointestinal effects resulting from osmotic activity of partially digested starch. Thus, according to the current model, there is reasonable expectation of no harm from the ingestion of modified starches, and no accompanying GI effects, at relatively high levels in the diet.

Because DSP is greater than 85% indigestible (See Table 1, page 8), it passes through the gastrointestinal (GI) tract essentially intact and is unmodified until it reaches the colon where colonic bacteria ferment the starch into small osmotically active particles and then into small molecular weight organic acids. Because DSP is an insoluble fiber, the amount of fermentation in the colon is expected to be minimal and therefore osmotic effects due to partially digested fiber are expected to be minimal.[30] The 15% or smaller portion of DSP that is digested is potato starch and is absorbed and metabolized without consequence. Only the colonic fermentation products of the indigestible portion of DSP are potentially bioavailable. The products of

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[28] Yoshikawa, Y. (2013). Assessment of the safety of hydrogenated resistant maltodextrin: reverse mutation assay, acute and 90-day subchronic repeated oral toxicity in rats, and acute no-effect level for diarrhea in humans. J. Toxicol. Sci. 38(3): 459-470.

[29] Elia, M. and Cummings, J.H. (2007). Physiological aspects of energy metabolism and gastrointestinal effects of carbohydrates. European Journal of Clinical Nutrition, 61, S40-74. Grabitske, H.A. and Slavin, J.L. (2009). Gastrointestinal effects of low-digestible carbohydrates. Critical reviews in food science and nutrition, 49, 327-360. Lord, G.H., Newberne, P.M. (1990). Renal mineralization--a ubiquitous lesion in chronic rat studies. Food Chem. Toxicol. 28(6):449-455.

[30] Dahl, W. J. et al. (2016). Resistant potato starch (RS4) influences laxation with phylum level changes in microbiota: a randomised trial in young adults. J. Funct. Foods. 23:1–11. Jha, R. and Berrocoso, J.D. (2015). Review: Dietary fiber utilization and its effects on physiological functions and gut health of swine. Animal, 9(9):1441-1452.

fermentation of all resistant starches are small molecular weight acids, such as acetic, propionic, and butyric acids that are used as sources of metabolic energy and do not present a risk of harm to consumers. Many positive effects of resistant starches have been confirmed in the scientific literature.[31] Only one potentially adverse consequence of resistant starch fermentation has been documented: osmotic diarrhea and its accompanying secondary effects, including GI discomfort, soft stools, and potentially increased absorption of calcium at high levels of ingestion.

Reviews by expert committees have treated distarch phosphates as toxicologically equivalent to other cross-linked modified starches.[32] Consequently, toxicological studies performed with one type of phosphated starch may be used to infer conclusions with regard to other forms and the class as a whole. This view is supported by the published observations and reviews by experts who have concluded that similar effects due to the osmotic activity of partially digested modified starches are observed for different types of modifications, including crosslinking and surface modifications. The modified starches cleared at 21 CFR §172.892 for use as food additives and originally reviewed by SCOGS induced osmotic effects even though the degree of modification was smaller than resistant starches now used as dietary fiber. They also were reported in some cases to have similar amounts of total phosphorus. A higher degree of crosslinking simply results in a greater proportion of material that is transported to the cecum and colon. The published and unpublished literature clearly supports a physiological model that indicates that no adverse effects of resistant starches are expected as long as intakes are limited to amounts that preclude osmotic effects.

As explained more fully in the following sections on test animal and human exposures to modified starches, the safety evaluation and GRAS status of DSP in this notification rests on the publicly available data and information found in published peer reviewed studies of modified starches of limited digestibility, of all types, in conjunction with, and supported by, similar information on the safety of modified starches in unpublished reports, and as reviewed in the secondary literature by panels of experts qualified by training and experience to evaluate the safety of food ingredients. The weight of the available information in published and unpublished reports, including reviews of all available information on exposures to modified starches by expert panels indicates that no modified partially digestible starch product has induced an adverse effect directly in an organ or tissue when exposures occurred in test animals at levels as high as 60 mg/kg bw/day. In the studies reviewed below, we summarize data primarily for exposures to phosphate cross-linked starches with structures similar to that of DSP as the most relevant to the GRAS status of the product.

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[31] Keenan, M.J. et al. (2015). Role of Resistant Starch in Improving Gut Health, Adiposity, and Insulin Resistance. Adv. Nutr., 6:198-205.

[32] Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives. Modified Food Starch, available at, http://www.inchem.org/documents/jecfa/jeceval/jec_1663.htm

1. Animal Studies[33]

In this section we review the studies of modified starches crosslinked with phosphate. We focus primarily on published articles because they comprise the basis of the common knowledge element of our GRAS determination. In addition, the same unpublished studies were reviewed in virtually all expert panel evaluations of modified starches and most of the studies that were unpublished at the time of those reviews were subsequently published in the peer reviewed literature, often as compilations of separate studies on different types of modified starches. The animal studies reviewed here that form the basis of our GRAS determination are summarized in tabular form in Appendix I.

a. Acute Studies

The SCOGS report cited two acute studies with distarch phosphate, a modified starch prepared through cross-linking with sodium trimetaphosphate or phosphorus oxychloride, using mice, rats, guinea pigs, rabbits and cats. These tests gave high LD50 values of between 7 and 35 g/kg bw. These studies were unpublished and are not relevant to long-term exposures by humans.[34]

In another study, groups of eight Pitman-Moore miniature pigs three days of age were fed synthetic diets containing acid-modified waxy starch or distarch phosphate prepared by treatment of the acid-modified starch with 0.08 percent (dry weight basis) phosphorus oxychloride.[35] Starch provided 24 percent of the calories in the diet and each diet was fed for 25 days. Body weight gains were similar for test and control animals. The distarch phosphate diet had no statistically significant effects on organ weights expressed as a percentage of body weight. Serum cholesterol, triglyceride, calcium, phosphorus, alkaline phosphatase, urea nitrogen, total protein, albumin and globulin levels were similar for the exposed and control animals.

b. Long-term and Multigeneration Studies

Five chemically modified starches, acetylated distarch phosphate, acetylated diamylopectin phosphate, starch acetate, hydroxypropyl distarch glycerol and phosphated distarch phosphate, were fed to groups of 10 male and 20 female weanling CIVO (Wistar derived) rats at dietary levels of 0 (control), 5, 10 and 30% for 2 years and at one level, 10%, over three generations.[36] The dietary exposures resulted in approximate intakes of 2.5, 5.0, or 15.0 mg/kg bw/day for both males and females. No adverse effects were observed on mortality,

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[33] See Appendix II for citations and a tabulated summary of all except acute studies.

[34] SCOGS (1979). Evaluation of the Health Aspects of Starch and Modified Starches as Food Ingredients. Contract No. FDA 223-75-2004. Life Sciences Research Office, Federation of American Societies for Experimental Biology, page 33.

[35] Anderson, T.A., Filer, Jr., L.J., Fomon, S.J., Andersen, D.W., Jensen, R. L., and Rogers, R.R. (1973). Effect of waxy corn starch modification on growth, serum biochemical values and body composition of Pitman-Moore miniature pigs. Food Cosmet. Toxicol. 11: 747-754.

[36] de Groot, A.O., et al. (1974). Two-year feeding and multigeneration studies in rats on five chemically modified starches. Food Cosmet. Toxicol. 12:651- 663.

food intake, hematology, blood biochemistry or urine composition. Each of the modified starches examined, except the phosphated distarch phosphate, slightly reduced body weights at the 30% level and caused distinct cecum enlargement at 10 and 30%. The microscopic structure of the cecum wall was normal. In comparison with the controls, the males fed the 30% level of any of the modified starches showed a slightly increased degree and incidence of focal hyperplasia of the renal papillary and pelvic epithelium, accompanied by calcified patches in the underlying tissue. The studies did not provide any indication of carcinogenicity. The authors concluded that the feeding of each of the modified starches at dietary levels up to 30% for 2 years and at a level of 10% over three generations did not result in any distinct effect of toxicological significance.

The same authors fed groups of 10 male and 20 female weanling Wistar derived rats a diet containing 10 percent (about 5 g/kg bw/day) hydroxypropyl distarch glycerol and 20 percent precooked potato starch for three generations. The test starch was potato starch which had been cross-linked with 0.1 percent epichlorohydrin and etherified with 5 percent propylene oxide. Rats were mated at weeks 12 and 20 after weaning. The second litter of each generation was used to produce the next generation. The F3b generation was kept for 3 weeks after weaning and then sacrificed for histopathological study. Implantation sites were counted in the parental, Flb, and F2b parents. Body weights did not differ among groups in successive generations and no treatment-related differences were observed in the test groups. No adverse effects were reported regarding resorption quotient, litter size, weight of pups, pre-weaning mortality or growth rate of pups. No gross or histological changes attributable to feeding the modified starch were reported.

The two year exposure summarized above identified the only potentially adverse effect after feeding any modified starch product, deposition of calcium in the kidney and focal hyperplasia associated with the same sites. The table below displays the incidence of the nephrocalcemic effect. Only rats fed the highest level of modified starch showed significant increases in the kidney lesion relative to controls.

Table 5. Incidence Kidney Lesions (as nephrocalcinosis) in Rats

Modified Starch Product	Control	2.5	5	15
		mg/kg bw/day		
acetylated distarch phosphate	1/59	6/57	5/56	10/58
acetylated diamylopectin phosphate		6/55	5/56	4/56
hydroxypropyl distarch glycerol		2/58	0/59	7/56
phosphated distarch phosphate	1/57	4/57	0/58	10/57
starch acetate	3/58	1/57	3/57	4/57
Totals	5/174	19/284	13/586	35/284

The identification of the kidney lesion (deemed non-pathological in subsequent studies), in the studies performed at TNO Laboratories in the Netherlands, was found to be associated with calcium deposition (nephrocalcinosis) and increased levels of calcium in the urine initiated several investigations into the physiology of the effect. The explanation for the lesion as a physiological adaptation resulting from increased osmotic pressure in the cecum due to partially fermented starch was derived from previous observations on other types of dietary

carbohydrates[37] and developed from the time of the first published study in 1974 until a final review in 1990. For example, Leegwater et al. (1974) evaluated the relation of cecum size and osmotic effects by hydroxypropyl starch (degree of substitution 2.5%-10.6%), lactose, raw potato starch, polyethylene glycol 1000, or magnesium sulfate in male rats of ages varying from 4 weeks to 3 months in experiments lasting from 10 days to 3 months.[38] All of the test compounds induced cecum enlargement under the experimental conditions. Cecum enlarged by hydroxypropyl starch (degree of substitution 4.7%), lactose, or raw potato starch, returned to normal sizes within 4 weeks after the animals reverted to a control diet. The analytical data did not show a consistent relationship between cecum size and the percentages of dry matter, sodium, potassium, chloride or volatile fatty acids in the cecum contents. The osmotic values of the cecum contents of control and experimental groups were of the same order of magnitude. The authors postulated that the size of the rat caecum is controlled by the osmotic pressure of the cecum contents, irrespective of the nature or origin of the compounds contributing to this value, and the conclusion is drawn that cecum enlargement is a process of physiological adaptation.

In a second study of the physiological effects of modified starches, Fisher 344 rats were fed poorly digested octenyl succinate-modified food starch in a semi-purified diet from conception until they were killed 30 or 90 days after weaning.[39] Complete autopsies and histopathological evaluations showed that growth and hematology were unaffected, but that liver, kidney and cecum weights tended to increase with increasing concentrations of the modified starch. There were no consistent changes in serum chemistry values that could be attributed to starch intake. Female rats had higher concentrations of urinary magnesium and calcium than did male rats and these higher mineral concentrations correlated with an increased incidence of renal calcium at the corticomedullary mineralization. The increase in mineralization occurred in both control and in octenyl succinate starch-treated female rats. Nephrocalcinosis specific to the pelvic region of the kidney was not observed in any of the rats. The authors concluded that no adverse effects were found that could be reported to feeding octenyl succinate starch to rats under the conditions of this study.

The above study was followed by an evaluation of kidney lesions induced by two modified starches crosslinked with phosphate or adipic acid added to the diets of Syrian Golden hamsters.[40] The incidence and severity of the lesion were dependent on the type and degree of modification of the starch and the magnesium content of the diet; increased dietary magnesium inhibited or prevented the morphologic expression of the lesion. This observation led to a series in the same publication of similar studies in rats where both the carbohydrate and dietary mineral content of the diets were varied. The renal lesion observed in these rats consisted of tubular mineralization at the corticomedullary junction and differed from the hamster lesion induced by

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37 See references in de Groot et al. (1974), page 657.

38 Leegwater, D.C. et al. (1974). The aetiology of caecal enlargement in the rat. Food Cosmet. Toxicol., 12(5-6):687-97.

39 Buttolph, M.L. and Newberne, P.M. (1980). Subchronic studies in rats fed octenyl succinate-modified food starch. Food Cosmet. Toxicol. 18(4):357-362.

40 Buttolph, M.L. and Newberne, P.M. (1980). Modified food starch: effects on mineral availability in rats and hamsters. In Trace Substances in Environmental Health - XIV. Proc. Univ. Missouri's 14th Ann.l Conf. Trace Subst. Environ. Health. Univ. Missouri.

similar starch products and was more dependent on the calcium/phosphorus ratio and levels than the magnesium content or the type of modified food starch in the diet. The authors concluded that modified food starch ingestion increases the magnesium requirement of hamsters, but a more complex mineral-carbohydrate interaction is apparent in rats fed modified food starch.

In a review of the literature on the osmotic effects induced by modified food starches Newberne and colleagues discussed the evidence that food additives, drugs, and other chemicals are known to influence the lower gastrointestinal tract resulting in morphological alterations in the mucosa and other tissues, changes in absorption and excretion of nutrients, and, in some cases, injury to other organs and tissues as a secondary phenomenon.[41] In rats, hamsters, and dogs, there is increased absorption and urinary excretion of calcium, soft stools or diarrhea, and enlargement of the cecum. In the rat, hamster, and dog, renal lesions accompany the hypercalcemia and elevated excretion of calcium. These signs, symptoms, and lesions are typical of exposure to sugar alcohols (sorbitol, mannitol, xylitol, lactitol), lactose, caramel, some of the chemically modified food starches, and synthetic polydextrose. Soft stools and diarrhea, as well as cecum enlargement and variable hyperplasia of the colon mucosa, occur frequently when substances are absorbed incompletely in the small intestine and subjected to microbial metabolism in the cecum and colon. The remarkable cecum enlargement, mucosal hyperplasia, and when present, colonic mucosal hyperplasia, are reversible even when long-standing. Renal lesions are reversible only if exposure is of short duration, before significant mineralization and scarring has occurred.

Lord and Newberne (1990) further indicated that renal mineralization is a commonly encountered lesion in aged rats and its presence at times complicates the interpretation of data derived from chronic rat studies.[42] For example, the feeding of sucralose resulted in cecum enlargement and an increase in the incidence of renal mineralization and pelvic epithelial hyperplasia. Data on sucralose and other small molecular weight poorly digested substances and the data on modified food starches, such as that discussed above, supports the view that cecum and renal changes occur frequently in response to feeding poorly absorbed osmotically active substances to rats. While increased calcium absorption and excretion appear to be important predisposing factors in the development of renal mineralization, the alterations in calcium metabolism are not in themselves pathognomonic (a sign or symptom specifically characteristic of a particular disease), as exemplified by the observation of MacKenzie *et al.* (1986) with sorbitol, that elevated serum calcium did not result in an increase in the incidence of renal mineralization.[43] The weight of the evidence in the public literature indicates that the feeding of substances that are poorly absorbed and osmotically active to rodents, especially rats, initiates a series of events leading in some cases to an alteration in mineral disposition and to an increase in cecum intraluminal pressure. Increased cecum intraluminal pressure results from retention of

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41 Newberne, P.M. et al. (1988). The influence of food additives and related materials on lower bowel structure and function. Toxicol. Path., 16(2): 184-197.

42 Lord, G.H. and Newberne P.M. (1990). Renal mineralization: A ubiquitous lesion in chronic rat studies. Food Chem. Toxicol., 28(6): 449-455.

43 MacKenzie, K.M. et al. (1986). Three-generation reproduction study of rats ingesting up to 10% sorbitol in the diet--and a brief review of the toxicological status of sorbitol. Food Chem. Toxicol., 24(3):191-200.

water resulting in a compensatory distention of the organ and, in some cases, hyperplasia that is reversible. One manifestation of altered renal mineral disposition is an increase in urinary calcium excretion and the development of renal mineralization.

c. Conclusion with Regard to the Renal Lesions Reported

It is evident from the several publications in the peer reviewed scientific literature that the feeding of modified starches that are poorly absorbed and ultimately fermented in the proximal colon results in osmotic changes that result in increased water retention, softening of stools, diarrhea, and ultimately increased absorption of calcium. Increased absorption of calcium can result in accumulation in the kidney and increased calcium excretion in the urine. These adaptive effects are observed after the ingestion of many poorly digested and osmotically active substances. In addition, the kidney effects reported are not specifically pathologic or hazardous because of their location in the kidney, and are reversible. Consequently, the several studies reviewed that address specific effects associated with modified starch ingestion indicates that such products are not reasonably considered hazardous nor do they pose a risk of harm to consumers ingesting either chemically modified starches or resistant starches added as dietary fiber to food products because GI effects do not occur at reasonable levels of intake.

d. Unpublished Short-term Studies.

The studies below further support the safety and GRAS status of modified food starches including DSP. In a 90-day unpublished study groups of 25 male and 25 female Sprague-Dawley weanling rats were fed diets containing 0, 0.2%, 1.0%, or 5.0% (about 0, 0.2 0.8, or 4.0 g/kg bw/day) of distarch phosphate prepared by treating white milo starch with sodium trimetaphosphate.[44] Blood and urine analyses were performed at 45 and 90 days of exposure. Blood analyses were done individually on five males and five females of the highest dietary group. No abnormalities were reported in hematological parameters or urinalyses of the exposed animals. Body weight gains and organ-body weight ratios showed only a few, randomly distributed, intergroup differences, none of which were attributed to modified starch ingestion. Gross pathologic findings among test animals were comparable to those reported among control animals and no adverse histopathologic changes attributed to the test starches were reported.[45]

In a 90-day unpublished study, groups of 10 male and 10 female rats received 0, 5%, 15%, or 45% (about 4, 12, or 36 g/ kg bw/day) of two types of distarch phosphate (0.085% or 0.128% esterified phosphate) in their diet. No abnormalities compared to controls were reported in regard to general appearance, behavior, mortality, food consumption, hematology, serum chemistry and urinalysis that could be attributed to the test starches. No diarrhea or increased cecum weights were reported. Gross and histopathologic examination revealed no abnormalities

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[44] As discussed in SCOGS (1979). Evaluation of the Health Aspects of Starch and Modified Starches as Food Ingredients. Contract No. FDA 223-75-2004. Life Sciences Research Office, Federation of American Societies for Experimental Biology. Pages 33-34.

[45] Kohn, F.E. et al. (1964). Subacute oral toxicity of phosphate starch code number 4822. Report of Industrial Bio-Test Laboratories, Inc., Northbrook, Ill. Reviewed by SCOGS (1979).

attributable to the distarch phosphate exposures.[46] In an unpublished 90-day study groups of three male and three female adult beagles were fed for a standard dog chow supplemented daily with 0.05, 0.25, or 1. 25 g/kg bw/day of distarch phosphate (trimetaphosphate-treated white milo starch) administered in gelatin capsules. Hematological studies and urinalyses were performed at the inception and conclusion of the feeding period and also after 45 days for the dogs fed the highest level of distarch phosphate. No significant abnormalities were reported. Mean body weight gains and organ-body weight ratios of the test animals did not differ significantly from the controls. Gross and histopathologic examination revealed no abnormalities attributable to the test substance.[47]

2. Human Studies

Dietary fiber comprises a macronutrient in the human diet. Consequently, consistent with Redbook requirements,[48] human studies cannot explicitly provide a basis for a safety evaluation of this ingredient. Human studies of any macronutient can provide supportive evidence of safety, provided that observations on the effects of the dietary component support the model of safety developed in test animals. Two human studies of DSP have been performed and published in the peer reviewed scientific literature. No adverse effects of any kind were reported in those studies after the ingestion of up to 60 grams of DSP for up to 12 weeks or 30 grams for two weeks. Distarch Phosphate is classified as a resistant starch type 4; i.e., a starch that has been rendered partially indigestible by chemical modification with $POCl_3$. This characteristic places Distarch Phosphate in the general classification of type 4 resistant starches, which have been extensively studied in animals and humans.

A search of the literature for clinical trials using type 4 resistant starches revealed at least 13 studies in which healthy subjects and individuals with diabetes mellitus consumed up to 60 grams of resistant starch for various periods of time up to 12 weeks. These studies are cited in Appendix II. None of these studies reported any adverse effects. Usually, the specific form of the resistant starch is not characterized in the clinical trials due to proprietary considerations. These clinical trials indicate that the non-digestibility of the starches, as expected, is not expected to have any adverse effect, as the products pass directly through the gastrointestinal (GI) tract without substantive change, until partial digestion by bacteria in the colon occurs. The safety of these resistant starches is clearly evident from these studies, and is widely recognized by the absence of virtually any contraindications for intake for individuals regardless of their health status.

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[46] Til, H. P., van der Meulen, H. C. and de Groot, A. P. (1970). Report No. R 3303 of the Centraal Instituut voor Voedingsonderzoek, Zeist, Holland. As reported in WHO Food Addit. Ser. No. 5:345-349, 1974. Reviewed by SCOGS.

[47] Cervenka, H. and Kay, J.H. (1963). Subacute oral toxicity of phosphate starch code number 4822: beagle dogs. Report of Industrial Bio-Test Laboratories, Inc., Northbrook, Ill. Reviewed by SCOGS (1979).

[48] Redbook 2000. Guidance for Industry and Other Stakeholders Toxicological Principles for the Safety Assessment of Food Ingredients. Revised July 2007. Pages 195 and 208.

Distarch Phosphate was studied in a clinical trial in conjunction with five other type 4 resistant starches. Ten adult subjects consumed 30 grams of resistant starch at a single sitting.[49] All resistant starches were well tolerated with no adverse effects reported. This study was designed to determine the efficacy of two novel type-four resistant starches (RS4) on postprandial glycemia and ratings of fullness. Ten healthy young adult volunteers completed five interventions designed to determine the glycemic and satiety (fullness) effects of the starches consuming 38 g alone and when added to available carbohydrate. The dose of each resistant starch provided 30 g per treatment. The treatments were commercial resistant starch added to water, noncommercial resistant starch added to water, dextrose solution, dextrose mixed with Distarch Phosphate starch, and dextrose added to noncommercial starch. Blood glucose was measured in the fasted state and following the randomly assigned treatments at 30, 45, 60, 90, and 120 minutes post-consumption. A visual analog scale was used to determine fullness at each time point. There were no differences in the glucose incremental areas under the curve for treatments that included dextrose. The Distarch Phosphate treatments had decreased areas for glucose. There were no treatment differences for satiety. No indications of adverse effects were reported.

A 6-week randomised, double-blinded crossover intervention study was conducted during the spring of 2014.[50] The objective was to study the effects of resistant potato starches on gastrointestinal (GI) function and microbiota in healthy individuals. In a 6-week, double-blind, cross-over study, participants (N = 57, 21 male, 36 female healthy adults were randomised to consume 30 g fibre per day from one of three chemically modified resistant potato starches: RS4-A, soluble and viscous, RS4-B, soluble non-viscous; Distarch Phosphate (Penfibe® RS) RS4-C, insoluble, non-viscous, or a control starch in fruit-flavoured beverages (Kool-Aid®, Kraft Foods Inc.). Two beverages a day, each containing 15 g/serving of fibre were provided for two-week periods separated by a one-week washout. The Kool-Aid® vehicles provided 168 kcal/day. Beverages were consumed for 2 weeks with a 1-week washout between crossovers. Stools were analysed by qPCR and 16S rRNA sequencing. Stool frequency and the self-reported Bristol Stool Form Scale (BSFS) increased only with RS4-B, the soluble non-viscous starch. GI symptoms were minimal with slight increases in flatulence with all interventions. There were no changes in *Lactobacillus* or *Bifidobacteria* spp. However, RS4-B decreased Firmicutes species and the Firmicutes to Bacteriodetes ratio. Resistant potato starches vary in their effects on GI function which may be related to shifts in intestinal microbiota.

3. Reviews and Secondary Literature

Cross-linked starch phosphate products, such as Distarch Phosphate, have been extensively reviewed for safe use in food products. Expert committees for the specific review of phosphated starches were convened by EFSA (2010),[51] JECFA (1969, 1973, 1982),[52] SCF (the

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[49] Haub, M.D. et al. (2012). Novel resistant potato starches on glycemia and satiety in humans. J. Nutr. Metab., Vol. 2012, pages 1-4.

[50] Dahl, W. J. et al. (2016). Resistant potato starch (RS4) influences laxation with phylum level changes in microbiota: a randomised trial in young adults. J. Funct. Foods. 2:1–11.

[51] EFSA Journal 2010; 8(9):1772 Scientific Opinion on the safety of 'phosphated distarch phosphate' as a Novel Food ingredient. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA).

Scientific Committee for Food, 1976, 1982),[53] and SCOGS (1979).[54] When sufficient data and reports were available to these expert committees, they concluded without exception that the available information justified the safe use of phosphated starches without limitation, except for the review by SCOGS. SCOGS concluded that unlimited use of phosphated starches was not justified, based on a single report that adverse effects in the kidney were found after the feeding of rats with phosphated distarch phosphate (PDP) for two years at a dietary level of 30%.[55] Subsequent studies of the same class of phosphated starches concluded that the kidney effects were artifacts.[56] Similar effects were reported when rats were fed lactose (milk sugar) at high levels in the diet. Reviews of phosphated starches subsequent to the findings of Hodgkinson et al. (1982) by EFSA (2010), JECFA (1982), and SCF (1982) concluded that the rat was a particularly sensitive species. Slow degradation of carbohydrates in the upper intestine led to the formation of absorbable breakdown products in the lower intestine, which was associated with enhanced calcium absorption leading to the kidney observations. The expert committees agreed

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[52] JECFA (1982). Phosphated distarch phosphate: In Toxicological Evaluation of Certain Food Additives. 26th JECFA Session, Apr. 19-28, 1982, Rome. WHO Food Additives Series, No. 17. See summary evaluations of distarch phosphates at http://www.inchem.org/documents/jecfa/jeceval/jec_674.htm; JECFA (1974). Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, WHO Tech. Rep. Ser., 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53; JECFA (1969). Phosphated distarch phosphate: In Thirteenth report of the Joint FAO/WHO Expert Committee on Food Additives, FAO Nutrition Meetings Report Series. The earlier reviews by JECFA (1969) concluded that insufficient data were available for a complete review.

[53] SCF (Scientific Committee for Food), 1982. Second report on modified starches (Opinion expressed 12 June 1981). In: Food Science and Techniques. Commission of the European Communities (EEC), Scientific Committee for Food (SCF); Reports of the Scientific Committee for Food (13th Series), Brussels, Belgium, 7-9. The earlier reviews by SCF (1976) concluded that insufficient data were available for a complete review.

[54] SCOGS (1979). Evaluation of the Health Aspects of Starch and Modified Starches as Food Ingredients. Contract No. FDA 223-75-2004. Life Sciences Research Office, Federation of American Societies for Experimental Biology.

[55] Unpublished studies cited by SCOGS as: (1) de Knecht-van Eekelen, A., Til, H.P., Willems, M. I., de Groot, A.P. 1971. Chronic (2-Year) feeding study in albino rats with phosphated distarch phosphate (a chemically modified starch). Report No. R 3392. Centraal Instituut voor Voedingsonderzoek; Zeist, Holland. Cited In: JECFA, 1982. (2) Feuillet, X. 1975. Urolithiase chez les rats OFA traites par les amidons modifies de Roquette. Report No. 750802. Centre de Recherche et d'Elevage des Oncins. Submitted to Federation of American Societies for Experimental Biology, Bethesda, Md., by National Starch and Chemical Corporation, Bridgewater, N. J.

[56] Hodgkinson, A., Davis, D., Fourman, J., Robertson, W.G., Roe, F.J.A. (1982). Comparison of the effects of lactose and of two chemically modified waxy maize starches on mineral metabolism in the rat. Food Chem. Toxicol., Vol. 20(4):371-382.

that the findings were peculiar for the rat, and had little relevance for the safety assessment of modified starches for humans.[57]

The conclusions of the expert committees noted above, after resolution of the kidney findings, were based on the identical studies reviewed by SCOGS and other newer evaluations. In total, the conclusions that phosphated starches are safe for use in foods without limitation were based on studies using repeated dose designs and that used dietary exposures as high as 30% in the diet. Many of the studies were not initially published and were performed by TNO Laboratories in Holland, a widely known and respected laboratory. Subsequently, the five pivotal studies done at TNO and reviewed by virtually all expert committees were published in a single report.[58] A comprehensive list of all studies on phosphated starches that were reviewed by the expert committees is provided in Appendix IV.

4. Residual Phosphorus

We have also evaluated the residual level of phosphorus in the ingredient and confirmed that it does not contribute meaningful amounts of phosphorus in the human diet. The Food and Nutrition Board of the Institute of Medicine has set an upper level for phosphorus of 4.0 g/day for adults (IoM, 1997).[59] A panel of experts in the UK on Vitamins and Minerals established a guidance level for the supplemental intake of phosphorus of 250 mg/day, equivalent to 4.2 mg/kg bw in a 60 kg adult, which was expected not to produce adverse effects.[60] An EFSA report estimated the dietary intakes of phosphorus in European countries to be on average 1000 to 1500 milligrams per person per day, ranging up to about 2600 mg/day.[61] EFSA concluded that the available data indicated that healthy individuals can tolerate phosphorus (as phosphate) intakes up to at least 3000 mg/person per day without adverse systemic effects. Obviously, very high levels of phosphorus in the diet are required for adequate human nutrition and very high levels are well tolerated without adverse effects. The amount of available phosphorus in PenFibe® RS is very low, as a large fraction of the phosphorus is unavailable in the stable crosslinks that make the starch resistant to digestion. Even if all of the phosphorus in the resistant starch were

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57 See the discussion in EFSA Journal 2010; 8(9):1772. Scientific Opinion on the safety of 'phosphated distarch phosphate' as a Novel Food ingredient; pages 12-13.

58 de Groot, A.O., et al. (1974). Two-year feeding and multigeneration studies in rats on five chemically modified starches. Food Cosmet. Toxicol. 12:651- 663.

59 IOM (Institute of Medicine), 1997. Phosphorus. In: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy of Sciences, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine (IOM). National Academy Press (NAP); Washington, DC.

60 EVM (Expert Group on Vitamins and Minerals), 2003. Safe Upper Levels for Vitamins and Minerals: Report of the Expert Group on Vitamins and Minerals. Food Standards Agency (FSA), Expert Group on Vitamins and Minerals (EVM), London, UK.

61 EFSA (European Food Safety Authority), 2005. Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of Phosphorus. The EFSA Journal, 233, 1-19.

available, the total amount would result in an intake of 0.2 g/day, a small fraction of the level of starch tolerable in the human diet.[62]

G. Conclusion

Based on the foregoing discussion, we conclude that the proposed use of Distarch Phosphate as a source of dietary fiber and as a functional ingredient such as a thickener or texturizing agent in processed foods is GRAS. Information and data on the toxicology and other relevant properties of modified starch products in the same class of resistant starch as Distarch Phosphate are available in the public scientific literature and are based on published and unpublished toxicological studies of animals and humans. This class of modified starch products has been reviewed extensively by expert committees qualified by education and training to evaluate the safety of such products that have independently concluded that products such as Distarch Phospahte require no limit when used as direct ingredients in food products.

H. Appendices

Appendix I Table of Published Animal Studies of Modified Starches

Appendix II Table of Human Studies of Resistant Starches

Appendix III GRAS Expert Panel Opinion

Appendix IV References

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[62] 5 g PS/day x 0.04 g P/g PS = 0.2 g P/day.

APPENDIX I:
TABLE OF PUBLISHED ANIMAL STUDIES OF MODIFIED STARCHES

Pub. Year	Authors/Journal	Title	Type of Starch/Focus
1973	**Anderson**, T.A., L.J. Filer, Jr., S.J. Fomon, D.W. Andersen, R. L. Jensen, and R.R. Rogers. Food Cosmet. Toxicol. 11: 747-754.	Effect of waxy corn starch modification on growth, serum biochemical values and body composition of Pitman-Moore miniature pigs	Four groups eight miniature pigs were weaned at 3 days of age and then fed for 25 days on formula diets identical except for the type of carbohydrate. The diets contained thin-boiling waxy corn starch or one of three chemical modifications of this starch (distarch phosphate, distarch phosphate and hydroxypropylated distarch glycerol).
Summary Results	No statistically significant treatment-related effects were observed on growth, biochemical values of blood or serum, or carcass or liver composition.		
Pub. Year	**Authors/Journal**	**Title**	**Type of Starch/Focus**
1974	**de Groot**, A.P., Til, H.P., Feron, V.J., Van der Meulle, H.C.D., Willems, M.I. Food and Cosmet. Toxicol. 12: 651-664.	Two-year feeding and multigeneration studies in rats on five chemically modified starches.	Five chemically modified starches, acetylated distarch phosphate; acetylated diamylopectin phosphate; starch acetate, hydroxypropyl distarch glycerol; 33ccompany distarch phosphate were fed to rats at dietary levels of 0, 5, 10 and 30% for 2 yr and at one level, 10%, over three generations.
Summary Results	2-yr study: no adverse effects were observed on mortality, food intake, haematology, blood biochemistry or urine composition. Each of the modified starches examined, except the 33ccompany distarch phosphate, slightly reduced body weights at the 30% level and caused distinct caecal enlargement at 10 and 30%; the microscopic structure of the cecal wall was normal. Males fed the 30% of any modified starch had a slightly increased degree and incidence of focal hyperplasia of the renal papillary and pelvic epithelium, with calcified patches in the underlying tissue. There was no indication of carcinogenicity. Multigeneration study: no effect on fertility, on lactation performance or on embryonic or pre-weaning mortality. Extensive microscopic examination of the F3b-generation rats failed to reveal any changes attributable to treatment. Conclusion: modified starches at dietary levels up to 30% for 2 yr and at a level of 10% over three generations did not result in any distinct effect of toxicological significance.		
Pub. Year	**Authors/Journal**	**Title**	**Type of Starch/Focus**
1974	**Leegwater D.C.**, de Groot, A.P., van Kalmthout-Kuyper M.	The aetiology of caecal enlargement in the rat.	The effect of hydroxypropyl starches (2.5%-10.6%) lactose, raw potato starch, polyethylene glycol 1000 or magnesium sulfate on

	Food Cosmet Toxicol. 1974 Oct;12(5-6):687-97.		cecum size was studied in male rats of ages varying from 4 wk to 3 months for 10 days to 3 months.
Summary Results	All the test compounds induced caecal enlargement under the experimental conditions and returned to normal sizes within 4 wk after the animals reverted to a control diet. The analytical data did not show a consistent relationship between cecum size and the percentages of dry matter, sodium, potassium, chloride or volatile fatty acids in the cecum contents. The osmotic values of the cecum contents of control and experimental groups were of the same order of magnitude. The authors postulated that the size of the rat caecum is controlled by the osmotic value of the cecum contents, irrespective of the nature or origin of the ingested compounds and is a process of physiological adaptation.		
Pub. Year	**Authors/Journal**	**Title**	**Type of Starch/Focus**
1982	**Hodgkinson**, A., Davis, D., Fourman, J., Robertson, W.G., Roe, F.J.A. Food Chem. Toxicol. 20(4): 371-382.	Comparison of the effects of lactose and of two chemically modified waxy maize starches on mineral metabolism in the rat.	Diets containing 30% waxy maize starch, lactose monohydrate, acetylated distarch phosphate, or acetylated distarch adipate were fed to weanling female Specified Pathogen-Free Sprague–Dawley rats for 1 yr and to similar 9-month-old rats for 34 wk.
Summary Results	Behavior and general health were unaffected by the different diets and there were no diet-related differences in food consumption. The body weight of 9-month-old rats receiving lactose was lower than that of the controls receiving starch. The animals receiving the modified starches were slightly but not significantly heavier than the controls at the end of both experiments. The main treatment-related changes in rats on the three test diets were (1) caecal enlargement, (2) increased urinary excretion of calcium, (3) increased renal calcification as measured by chemical analysis of renal tissue obtained at autopsy and (4) increased medullary and pelvic nephrocalcinosis as assessed histopathologically. Acetylated distarch adipate had a slightly greater effect on the above parameters than acetylated distarch phosphate but both modified starches had less effect than lactose. The calcium content of the kidneys increased with age, even in the animals receiving the control diet		
Pub. Year	**Authors/Journal**	**Title**	**Type of Starch/Focus**
1980	**Buttolph**, M.L. and Newberne, P.M. Food Cosmet. Toxicol. 18: 357-362	Subchronic Studies in Rats Fed Octenyl Succinate-Modified Food Starch.	Fischer 344 rats were fed octenyl succinate-modified food starch in a semi-purified diet from conception until they were killed 30 or 90 days after weaning.
Summary Results	First study to relate modified starch intake with cecal enlargement and calcium and magnesium imbalances. No adverse effects associated with feeding octenyl succinate starch occurred in rats under the conditions of this study. Complete autopsies and histopathological evaluations showed that growth and hematology were unaffected. Liver, kidney and cecal weights tended to increase with increasing concentrations of dietary octenyl succinate starch. There were no consistent changes in serum chemistry values that could be associated with octenyl succinate starch intake. Female rats had higher concentrations of urinary magnesium and calcium than did male rats, and these higher mineral concentrations correlated with an increased incidence of renal cortico-medullary mineralization. The increase in mineralization of the cortico-medullary junction occurred in both control and in octenyl succinate starch-treated female rats. Pelvic nephrocalcinosis was not		

	observed in any of the rats.		
Pub. Year	**Authors/Journal**	**Title**	**Type of Starch/Focus**
1980	**Maria Lynn Buttolph** and Paul M. Newberne Trace Substances in Environmental Health – XIV. Proc. Univ. Missouri's 14th Ann.l Conf. Trace Subst. Environ. Health. Univ. Missouri.	Modified Food Starch: Effects on Mineral Availability in Rats and Hamsters	This study examined the impact of modified food starches on mineral status. A series of metabolic and histologic studies were performed. In the first experiment, hamsters were fed diets with different magnesium levels and types of modified food starches: one level of acetylated distarch phosphate and two levels of hydroxypropyl distarch phosphate. The second experiment, with rats, manipulated the calcium/phosphorus ratios and levels in diets containing different types and levels of the same modified food starch in the first experiment.
Summary Results	Modified food starch ingestion increases the Mg requirement of hamsters, but a more complex mineral-carbohydrate interaction is apparent in rats fed modified food starch. Selected modified food starches added to the diets of Syrian Golden hamsters were associated with a renal lesion consisting of tubular dilation and cortical scarring. The incidence and severity of the lesion were dependent on the type and degree of modification of the starch and the magnesium content of the diet; increased dietary Mg inhibited or prevented the morphologic expression of the lesion. This observation led to a series of similar studies in rats where both the carbohydrate and dietary mineral content of the diets were varied. The renal lesion observed in these rats was tubular mineralization. This lesion differed from the hamster lesion and was more dependent on the calcium phosphorus ratio and levels than Mg content or the type of modified food starch in the diet.		
Pub. Year	**Authors/Journal**	**Title**	**Type of Starch/Focus**
1988	**Newberne**, P.M., Conner, M.W., Estes, P. Toxicologic Pathology. 16(2): 184-197	The Influence of Food Additives and Related Materials on Lower Bowel Structure and Function	This paper reviews the safety of lactose, modified food starches, sugar alcohols, and polydextrose when used as dietary ingredients. These substances cause changes in the lower gastrointestinal tract, specifically the part of the colon called the cecum. Some of the GI effects are induced secondary effects expressed as mineral imbalances that can under certain circumstances cause changes in the kidneys and adrenal glands. The paper provides a rationale for the secondary effects in the kidney and adrenals by osmotically active substances generated by the above ingredients based on the totality of evidence in the scientific literature.
Summary Results	Morphological and functional anomalies of the kidney and adrenal glands are associated with cecal enlargement, osmotic diarrhea, and occur secondary to these physical effects induced by high exposures. Food additives, drugs, and other chemicals are known to influence the lower gastrointestinal tract under certain conditions resulting in morphological changes in the mucosa and other tissues, altered absorption and excretion of nutrients, and, in some cases, injury to other organs and tissues as a secondary phenomenon. In rats, hamsters, and dogs, there is cecal enlargement, increased absorption and urinary excretion of calcium, soft stools, and diarrhea. In the rat, hamster, and dog renal lesions were found in addition to hypercalcemia and elevated excretion of calcium. These effects are typical of exposure to sugar alcohols (sorbitol,		

	mannitol, xylitol, lactitol), lactose, caramel, some of the chemically modified food starches, and polydextrose. Soft stools and diarrhea, as well as cecal enlargement and variable hyperplasia of the colon mucosa, occur frequently when substances are absorbed incompletely in the small intestine and subjected to microbial metabolism in the cecum and colon. The remarkable cecal enlargement, mucosal hyperplasia and, when present, colonic mucosal hyperplasia are reversible, even when long-standing. Renal lesions are reversible if exposure is of short duration, before significant mineralization and scarring has occurred.

APPENDIX II:
TABLE OF HUMAN STUDIES OF RESISTANT STARCHES

Year	Authors/Journal	Title	Type of Starch/Focus	Summary Results
	STUDIES USING DISTARCH PHOSPHATE TYPE 4 RESISTANT STARCHES			
2016	Dahl, W.J. et al. (2016). J.Funct. Foods. Vol. 23: 1–11.	Resistant potato starch (RS4) influences laxation with phylum level changes in microbiota: a randomised trial in young adults.	Intervention: 30 g of fiber per day. RS4-A, PenFibe® RS, hydroxypropyl starch, soluble with high viscosity; RS4-B, PenFibe® RO – 177; hydroxypropyl starch, enzyme hydrolysed, soluble with low viscosity; RS4-C (**PenFibe® RS**; insoluble with low viscosity.	Stools were analysed by qPCR and 16S rRNA sequencing. Stool frequency and form increased only with RS4-B. GI symptoms were minimal with slight increases in flatulence with all interventions. There were no changes in *Lactobacillus* or *Bifidobacteria* spp. RS4-B decreased Firmicutes and the Firmicutes-Bacteriodetes ratio. RS4 resistant potato starches vary in their effects on GI function and may be related to shifts in intestinal microbiota.
2012	Haub, M.D. et al. Novel Resistant Potato Starches on Glycemia and Satiety in Humans. J. Nutr. Metab., Vol. 2012: 1-4.	Novel Resistant Potato Starches on Glycemia and Satiety in Humans	**Penfibe Resistant Starch**, Cross-linked potato starch treated with 4.5% $POCL_3$. Interventions with 30 g of dietary fiber per day in 38 g of starch with or without glucose measured blood glucose for 2 hours. PF = Penfibe RS, PR = noncommercial RS, + indicates RS+dextrose (DEX), – indicates RS + water.	There were no differences in the glucose incremental areas under the curve (iAUC) for PF+ and PR+ compared with DEX. The PF–and PR– treatments had decreased iAUCs for glucose compared with DEX, PF+, and PR+. There were no treatment differences for satiety. The dose (38 g) of starches did not to alter glucose responses when added to 50 g of dextrose and caused no effects on blood glucose levels.

	STUDIES USING OTHER TYPE-4 RESISTANT STARCHES			
2014	Nichenametla, S.N., Weidauer, L.A., et al. Mol. Nutr. Food Res. 58(6) 1365-1369.	Resistant starch type 4-enriched diet lowered blood cholesterols and improved body composition in a double blind controlled cross-over intervention.	Blinded exchange of RS4-enriched flour (30%) with regular/control flour on multiple metabol. syndrome comorbidities. RS4 starch identified as Fibersym, phosphated distarch phosphate.	A small but significant 1% increase in fat-free mass was observed in all participants combined. No significant effect of RS4 was observed for glycemic variables and blood pressures. RS4 intake improved dyslipidemia.
	STUDIES USING RESISTANT STARCHES OTHER THAN TYPE 4			
2013	Wutzke, K.D., and Scholübbers, D. Isotopes Environ Health Stud. 49(4):464-470.	The metabolic effect of resistant starch and yoghurt on the renal and faecal nitrogen and ammonia excretion in humans as measured by lactose-^{15}N-ureide (LU).	Intervention: 2 g RS1 potato starch and 10.5 g RS2 pea starch for 20 days in 190 g of *Lactobacillus acidophilus* yoghurt.	The intervention significantly lowered the colonic amount and renal excretion of toxic ^{15}NH3 and shifted ammonia excretion from urinary to faecal when using ^{15}N-LU as a xenobiotic marker.
2012	Kwak, J.H., et al. Atherosclerosis. 224(2):457-464.	Dietary treatment with rice containing resistant starch improves markers of endothelial function with reduction of postprandial blood glucose and oxidative stress in patients with prediabetes or newly 2012 diagnosed type 2 diabetes.	Patients with impaired fasting glucose or impaired glucose tolerance consumed either rice containing 6.5 g resistant starch (type not defined) for 4 weeks or rice with no added resistant starch.	Consumption of rice with resistant starch was linked with improved endothelial function and reduction of blood glucose, postprandial, and multiple measures of oxidative stress.
2012	Maki, K.C., et al. J. Nutr. 142(4):717-723.	Resistant starch from high-amylose maize increases insulin sensitivity in overweight and obese men.	High amylose starch, type RS2, was consumed in obese patients at 15 g/d or 30 g/d for 4 weeks in a double blind crossover trial.	Insulin resistance was improved in males but not in females. Reported adverse events were not different in treated and controls. Most adverse events were mild and not related to consumption of the study product (RS2 starch)
2010	Johnston, K.L., et al. Diabet Med. 27(4):391-397.	Resistant starch improves insulin sensitivity in metabolic syndrome.	High amylose starch, type RS2, was consumed healthy subjects at 30 g/d for 12 weeks in a single blind placebo controlled trial.	Resistant starch consumption did not significantly affect body weight, fat storage in muscle, liver or visceral depots. There was no change with RS feeding on vascular function or markers

				of inflammation. Insulin sensitivity improved relative to placebo group.
2010	Penn-Marshall, M., et al. J Med Food. 2010 Aug;13(4):999-1004. Erratum in: J Med Food. 13(5):1286.	African Americans may have to consume more than 12 grams a day of resistant starch to lower their risk for type 2 diabetes.	A 14-week, double-blind, crossover design study was conducted with African American male and female subjects at risk for type 2 DM. All subjects consumed bread containing 12 g of added high amylose maize RS2 or control bread for 6 weeks, separated by a 2-week washout period.	Mean homeostasis model assessment of insulin resistance decreased to normal values (>2.5) at the end of the 14-week study, although there were no significant treatment effects positive or negative.
2010	Li, M., et al. Br J Nutr. 103(7):1029-34.	Postprandial glycaemic and insulinaemic responses to GM-resistant starch-enriched rice and the production of fermentation-related H2 in healthy Chinese adults.	Glycemic and insulin responses to intake of rice with or without high amylose maize RS2 starch in young and healthy Chinese adults. A total of sixteen young adults were divided into three groups. Postprandial glycemic and insulin responses to 40 g glucose, RS2 or rice were tested by a crossover model with a washout period of 7 d. Concentrations of blood glucose and insulin as well as breath H2 were measured before and after food intake.	Consumption of the RS2 enriched rice meal decreased postprandial glycemic and insulin responses and promoted RS fermentation-related production of H2 in the large bowel of young and healthy Chinese adults. Clinically adverse effects were monitored but were not found.
2009	Maki, K.C., et al. Int J Food Sci Nutr. 2009;60 Suppl 4:296-305.	Beneficial effects of resistant starch on laxation in healthy adults.	25 g RS3 or wheat bran were consumed for 14 days, then crossed over to the opposite treatment after a 7-day washout. A double-blind crossover design	Daily faecal output increased with RS3 intake and with WB. No differences in bowel habits were observed. Fecal consistency ratings were increased with WB but unchanged with RS. Safety

			evaluated the effects of a type 3 resistant starch (RS3) versus wheat bran on fecal weight, freq., and consistency in healthy adults following a 14-day baseline period when 14 subjects consumed low fiber test products.	evaluations were monitored in all subjects who provided informed consent and received at least one dose of product during the baseline period. No indication of intolerance for either RS3 or WB were found.
2007	Storey, D., et al. Eur J Clin Nutr. 61(11):1262-70.	Gastrointestinal responses following acute and medium term intake of retrograded resistant maltodextrins, classified as type 3 resistant starch.	GI responses of young adults following consumption of 0–60 g resistant maltodextrin (RS3) to define the no adverse effect level (NOAEL). Part 2 determined whether a gradual increase in the daily dose of retrograded resistant RS3 was tolerated. Part 1 was a randomized double-blind placebo-controlled crossover study. Part 2 was longitudinal. Forty-one healthy adult volunteers aged 18–24 years participated.	Consumption of up to 60 g RS3 was tolerated by most individuals with no evidence of any significant dose dependent increase in symptoms or the occurrence of multiple GI symptoms. A mild laxative effect when consuming >60 g R3 is suggested. There was no change in GI responses following consumption of increasing doses of R3 over 21 days.
1995	de Roos, N., et al. Eur J Clin Nutr. 49(7):532-41.	Resistant starch has little effect on appetite, food intake and insulin secretion of healthy young men.	For 4 weeks 24 healthy males consumed either glucose, high-amylase corn starch (RS2), or extruded and retrograded high-amylase corn starch (RS3) in a cross-over, single-blind, randomized and balanced design. Each type of supplement was consumed for a week. In the first week each subject consumed the glucose supplement. The RS2 and RS3 supplements provided 30 g RS/day. At the end of weeks 2, 3 and 4, subjects rated their appetite each whole hour on a visual analogue scale. Food	Consumption of 30 g/day RS2 and RS3 had little influence on appetite and food intake, but RS3 reduced the insulin secretion. No adverse effects were reported.

			intake was assessed and C-peptide excretion in urine as a measure for 24-h insulin secretion.	

APPENDIX III

EXPERT PANEL REPORT

The Generally Recognized as Safe (GRAS) Status of the Proposed Uses of Distarch Phosphate Modified Food Starch

05 August 2016

We, an independent panel of experts, qualified by scientific training and national and international experience to evaluate the safety of food and food ingredients (the "Expert Panel"), were specially convened by Keller and Heckman LLP, on behalf of their client, Ingredion, to evaluate the safety and "Generally Recognized As Safe" ("GRAS") status of the proposed uses of Distarch Phosphate (DSP) modified food starch made using phosphorus oxychloride (POCl3) at concentrations exceeding the 0.1% limit established in the food starch-modified regulation (21 C.F.R. §172.892). The Expert Panel critically evaluated relevant data on Ingredion's DSP. Following its critical evaluation of all the information submitted and other information deemed appropriate, the Expert Panel unanimously concluded that the proposed uses of Ingredion's DSP, manufactured consistent with current good manufacturing practice (cGMP) and meeting appropriate food-grade specifications presented in the Keller and Heckman opinion, are safe and suitable, and Generally Recognized As Safe (GRAS) based on scientific procedures.

Ingredion's DSP is intended for use in various processed food products, including bread, ready-to-eat cereals, cereal bars, and other foods to contribute enough dietary fiber to support a "good source of fiber" claim (10% of the 28 gram daily value of dietary fiber, which is 2.8 grams) or an "excellent source of fiber" claim (20% of the 28 gram daily value for dietary fiber, which is 5.6 grams). DSP will be used as a source of dietary fiber and as a functional ingredient such as a thickener or texturizing agent.

Modified food starch is an approved food additive as described at 21 C.F.R. § 172.892. Section 172.892 sets forth the various treatments that can be used to modify the starch including the esterification of starch by phosphorus oxychloride (POCl3); however, the level of POCl3 to be used is limited to 0.1% whereas Ingredion is interested in using higher levels of POCl3. Thus, Ingredion's product technically falls outside the scope of the food additive regulation, and must be reviewed to determine if it is generally recognized as safe on a self-determined basis so that it can be lawfully used as an ingredient in food.

The Expert Panel critically evaluated the GRAS Notification prepared by Keller and Heckman LLP, that summarized the characteristics, manufacturing process, proposed uses, digestibility (including resistance to digestion, based on the in vitro Englyst procedure), safety studies applicable to Ingredion's DSP, and other information deemed appropriate.

The Expert Panel also critically evaluated reports of expert committees including the European Food Safety Authority (EFSA), the Joint FAO/WHO Expert Committee on Food Additives (JECFA), and the Scientific Committee for Food (SCF) who evaluated the safety of phosphated

starches and concluded that they are safe without any limitation on use. In 1979, the Select Committee on GRAS Substances (SCOGS) concluded that phosphated starches are safe but that unlimited use was not justified based on one report of adverse effects in the kidneys of rats. Subsequent studies demonstrated that these adverse effects are not relevant to human safety. It was also reported that similar renal effects occurred in rats fed lactose and other non-digestible ingredients at high dietary levels. Further, there are numerous published animal and human safety/toxicity studies that support the safety of phosphated starches. These findings are corroborated by unpublished studies. Published animal studies on modified starches and human studies on resistant starches are summarized in the Appendix to the GRAS Notification. These animal studies include: (1) acute studies in mice, rats, guinea pigs, rabbits and cats; (2) a long term multi-generational chronic study in rats; and (3) multigeneration reproductive and developmental studies. The human studies that support the safety of type 4 resistant starches like DSP are also summarized in the Appendix to the GRAS Notification.

The Expert Panel considered the residual phosphorus that is present in the DSP and concluded that the amount of bioavailable phosphorus in the DSP is very low. If all of the phosphorus in the resistant starch were bioavailable, the total amount would result in a small fraction of the level of phosphorus that is tolerable in the human diet (0.2 g/day phosphorus from DSP v. 4.0 g/day phosphorus that is upper level established by the Food and Nutrition Board of the Institute of Medicine).

Conclusion

Following its independent and critical evaluation of the GRAS Notification prepared by Keller and Heckman LLP and other materials deemed appropriate, the Expert Panel convened by telephone, and independently, jointly, and unanimously concluded that the proposed uses in multiple food applications, including bread, ready-to-eat cereals, cereal bars, and other foods, with no limitations on its use other than current good manufacturing practice (cGMP) that may typically provide up to 5.6 grams of dietary fiber in a serving of food of Ingredion's Distarch Phosphate modified food starch, manufactured consistent with current good manufacturing practice (cGMP) and meeting appropriate food-grade specifications presented in the Keller and Heckman GRAS Notification, are safe and suitable.

The Expert Panel further unanimously concluded that the proposed uses in multiple food applications, including bread, ready-to-eat cereals, cereal bars, and other foods, with no limitations on its use other than current good manufacturing practice (cGMP) that may typically provide up to 5.6 grams of dietary fiber in a serving of food of Ingredion's Distarch Phosphate modified food starch, manufactured consistent with current good manufacturing practice (cGMP) and meeting appropriate food-grade specifications presented in the Keller and Heckman GRAS Notification, are Generally Regarded As Safe (GRAS) based on scientific procedures.

It is the opinion of this Expert Panel that other qualified experts would concur with these conclusions.

(b) (6)

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APPENDIX IV:

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SUBMISSION END