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February 21, 2022

Via FedEx

Dr. Paulette Gaynor
Office of Food Additive Safety
CFSAN
Food and Drug Administration
5100 Campus Drive
College Park, MD 20740

Re: GRAS Notification for NABACO LLC's Use of Polyvinyl Alcohol (PVOH) as a Component of Coatings for Fruits and Vegetables

Dear Dr. Gaynor:

On behalf of NABACO LLC, I hereby submit the enclosed GRAS Notification for the use of polyvinyl alcohol (PVOH) as a component of fruit and vegetables coatings. The attached GRASN provides the information required under 21 CFR 170.220 *et seq.* Enclosed is both a paper copy and an electronic version on a thumb drive. The thumb drive has been scanned with Webroot and was found not to contain any electronic virus.

Should you have any questions regarding this submission, please do not hesitate to contact me.

Sincerely,

Mark L. Itzkoff

GRAS Notification for Polyvinyl Alcohol

Prepared for:

U.S. Food and Drug Administration
Office of Food Additive Safety
CFSAN
5001 Campus Drive
College Park, MD 20740

Prepared by:

Soni & Associates Inc.
749 46th Square
Vero Beach, FL 32968, USA

And

Mark L. Itzkoff
Attorney
1629 K St., NW
Suite 300
Washington, DC 2006

Date:

February 14, 2022

Table of Contents

PART 1 – SIGNED STATEMENTS AND CERTIFICATION

1.1.Applicability of 21 CFR Part 170, Subpart E

We submit this GRAS Notice in accordance with 21 CFR Part 170, Subpart E.

1.2.Name and Address of Notifier

Company:	NABACO LLC
Name:	Dr. Gary Beall, CEO
Address:	5040 SH 123 Bldg. 500 San Marcos, Texas 78666

1.3.Name of the Substance

The name of the substance of this GRAS assessment is polyvinyl alcohol (PVOH), CAS Number 9002-89-5. It is also known as vinyl alcohol polymer. The Notifier intends to use the substance as a component of the NABACO fruit and vegetable coating products marketed under the tradename NatuWrap PA™.

1.4.Intended Conditions of Use

NABACO intends to use polyvinyl alcohol as a surface-finishing agent and/or texturizer as defined at 21 CFR 170.3 (o)(30) and (32). Under the intended conditions of use the polymer will be one component of a product that will create a thin edible film that will function as a physical barrier on fruits and vegetables. This barrier will reduce moisture loss and oxidation to protect the freshness and extend the shelf-life of agricultural products. It will be applied to the surface of fruits (e.g., berries, grapes, stone fruit, citrus, bananas, mangoes, avocados) and vegetables (e.g., legumes, roots, tubers) at levels consistent with current Good Manufacturing Practice and is self-limiting for technological reasons. The maximum application will be 0.133 grams per pound of food.

1.5.Statutory Basis for GRAS Determination

This GRAS determination for the use of polyvinyl alcohol is based on scientific procedures in accordance with 21 CFR 170.30(a) and 170.30(b).

1.6.Exemption from Premarket Approval Requirements

It is the view of NABACO LLC that under the intended conditions of use, polyvinyl alcohol is not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on our conclusion that polyvinyl alcohol, meeting the specifications cited herein, and when used as a food ingredient and as a nutrient, is GRAS and is therefore exempt from the premarket approval requirements.

It is also our opinion that other qualified and competent scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Therefore, we have also concluded that polyvinyl alcohol, when used as described in this dossier, is GRAS based on scientific procedures.

1.7. Availability of Data and Information

The data and information that are the basis for this GRAS conclusion will be made available to the FDA upon request by contacting Mark Itzkoff, Counsel for NABACO, at the below address. The data and information will be made available to the FDA in a form in accordance with that requested under 21 CFR 170.225(c)(7)(ii)(A) or 21 CFR 170.225(c)(7)(ii)(B).

Mark L. Itzkoff
Counsel for NABACO, Inc.
1629 K St., NW
Suite 300
Washington, D.C. 20006

Tel: 202-600-7704
Email: Mark@Itzkofflaw.com

1.8. Applicability of FOIA exemptions

Parts 2 through 7 of the GRASN do not contain any privileged or confidential information such as trade secrets and/or commercial or financial information that would be exempt from disclosure under the Freedom of Information Act.

1.9. Certification

We certify that, to the best of our knowledge, this GRAS notice is a complete, representative, and balanced submission that includes unfavorable information, as well as favorable information, known to NABACO and pertinent to the evaluation of the safety and GRAS status of the use of the substance.

1.10. Name, position/title of responsible person who signs dossier and signature:

02/15/2022
Date

Dr. Gary Beall, CEO
CEO, NABACO

Please address correspondence to NABACO Counsel:

Mark Itzkoff
1629 K St., NW
Suite 300
Washington, DC 20006

Phone: 202-600-7704
Email: Mark@Itzkofflaw.com

1.11. USDA/FSIS

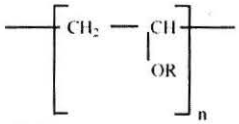
NABACO does not intend to use polyvinyl alcohol in any meat and/or poultry applications. Therefore, 21 CFR 170.270 does not apply.

PART II - IDENTITY AND TECHNICAL INFORMATION

2.1. Description

The subject of this GRAS assessment, polyvinyl alcohol, occurs as an odorless translucent, white, or cream-colored granular powder. The Food Chemicals Codex (FCC 2019; 11th Edition Third Supplement) has updated the monograph on polyvinyl alcohol and provides its description and specifications. Polyvinyl alcohol is soluble in water and sparingly soluble in ethanol. Commercially produced polyvinyl alcohol is a mixture of synthetic polymers produced by the polymerization of vinyl acetate and partial hydrolysis of the resulting esterified polymer. Physical and chemical properties of polyvinyl alcohol vary and depends on the degree of polymerization. Polyvinyl alcohol insoluble in aliphatic and aromatic hydrocarbons, esters, ketones, and oils. The general descriptive properties of polyvinyl alcohol, along with structural formula is provided in Table 1.

Table 1. General Descriptive Characteristics of Polyvinyl Alcohol*

Parameter	Description
Common name	Polyvinyl alcohol
Synonyms	Vinyl alcohol polymer; Poly(vinyl alcohol); Ethenol homopolymer; PVOH; Hydroxyethene
CAS Number	9002-89-5
EC Number	209-183-3; 618-340-9
Chemical/Molecular formula	$(C_2H_3OR)_n$ where R=H or $COCH_3$ (randomly distributed)
Structural formula	
Molecular weight	Ranges from 37,000 to 150,000 g/mol
Degree of Hydrolysis	Between 86.5 and 89%
Color	White or cream
Physical form	Granular powder
Solubility	Water; sparingly soluble in ethanol
Uses/Technical effects	Coating binder; sealing agent; surface finishing agent

*Based on publicly available information and provided by NABACO (2021)

2.2. Specifications and Identity

Food grade specifications for the polyvinyl alcohol used by NABACO have been established and are presented in Table 2. Where applicable these specifications comply with the polyvinyl alcohol monograph published in FCC (2019).[1] The functional use of polyvinyl alcohol in the food industry includes, among other uses, as a coating, binder, sealing agent, and surface finishing agent where polyvinyl alcohol is ingested (FCC, 2019).

[1] In the NABACO application, the polymer will dissolve in an aqueous solution. Therefore, the particle size is not relevant and is not measured in the quality control testing.

In addition to FCC, the chemical and physical characteristics of polyvinyl alcohol have also been reviewed in several other national and international official monographs, including the United States Pharmacopeia (USP, 2004) and the JECFA (2003; 2007). All analytical methods are validated for their intended use. Analytical results of three independently produced, representative batches are attached in Appendix I. The PVOH manufacturer, Kuraray, does not test every lot for lead levels. Rather, they monitor the lead level in their products on an ongoing basis and have determined that the level remains below 1 part per million.

Table 2. Specifications of Polyvinyl Alcohol

Parameter	Characteristics	Reference/Test Methodology
Description	Translucent, white or cream-colored granular powder	Visual inspection
Specific tests		
Acid value	NMT 3	FCC
Ester value	Between 125 and 153 mg KOH/g	FCC
Degree of hydrolysis	Between 86.5 and 89.0%	FCC
Loss on drying	NMT 5%	FCC
pH	5.0 - 6.5	FCC
Residue on ignition	NMT 1%	FCC
Viscosity	4.8–5.8 mPa·s (4% aqueous solution at 20°C)	FCC
Water insoluble substances	NMT 0.1%	FCC
Heavy metals		
Lead	NMT 2 ppm	FCC
Organic impurities		
Methanol	NMT 1%	FCC
Methyl acetate	NMT 1%	FCC

NMT = Not more than; ppm = part per million

2.3. Manufacturing Process

Polyvinyl alcohol is manufactured according to current good manufacturing practices (cGMP) and is essentially the same as the process described in GRAS Notice 767. PVOH is manufactured by polymerizing vinyl acetate monomer (VAM) to polyvinyl acetate and subsequent controlled hydrolysis (saponification) of the polyvinyl acetate to PVOH.

Polymerization of VAM takes place in methanol with a proprietary agent to initiate the polymerization reaction.

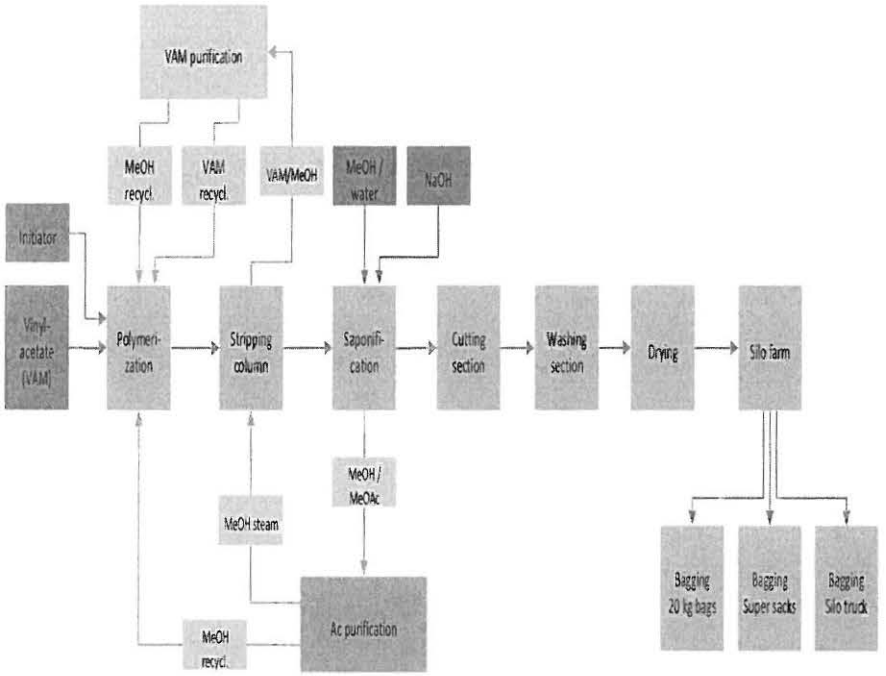
The saponification process is passed on the partial replacement of ester groups in vinyl acetate with hydroxyl groups using sodium hydroxide. Both the degree of polymerization and degree of saponification are controlled by modifying reaction conditions such as residence time, concentration of reaction agent and reaction temperature.

During saponification, the resulting PVOH precipitates from the methanol solution and forms a gel. The gel is subsequently cut into granules. Following this the PVOH is washed and dried.

In the production process two major solvent mixtures are generated. First, a mixture of VAM and methanol, and secondly, a mixture of methyl acetate in methanol. Both mixtures are recycled in separate distillation processes. The purified solvents are then reused in the production process.

Primary side components are sodium acetate, methanol and methyl acetate which are removed during the washing and drying production step. The final product is tested for compliance with Kuraray specifications.

The manufacturing process is set forth in Figure 1, below.



Effective as of November 2021

PART III - DIETARY EXPOSURE

3.1. Estimated Daily Intake from the Proposed Uses

Under the intended conditions of use, NABACO's NatuWrap PA™ containing polyvinyl alcohol will be used as a coating on fruits and vegetables. When used as directed, NatuWrap PA™ will be applied to the outside of the peel of fruits and vegetables. The quantity of NatuWrap PA™ recommended for use varies with the specific application, however the maximum application rate will result in a maximum of 0.133 g polyvinyl alcohol per pound of food (0.29 g/kg).

A. Fruit

NatuWrap PA™ will be applied to the peels of fruits that may be consumed with peels or without peels. Fruits where the peel or rind is removed or discarded before the food is consumed include bananas, citrus fruit, squash, and watermelon. The polyvinyl alcohol component of the NatuWrap PA™ coating is not expected to migrate through the fruit skin into the edible portions of these foods. While NatuWrap PA™ may be used on apples, oranges or grapes, it is expected that the product will remain on the peel and not present in juice extracted from these or other fruits. The primary source of consumer exposure to NatuWrap PA™ will be raw fruit with edible peels (RFEP).

In a recent report, Kimmons et al. (2009) reviewed data from the 2003-2004 National Health and Nutrition Examination Survey (NHANES) and determined the dietary contribution of fruits and vegetables from multiple sources. As shown in Table 3, below, the study reported on the ten most reported fruit and vegetable sources for adolescents, men over 19 years of age, and women over 19 years of age.

Table 3. Reported RFEP Fruit Sources as Percentage of Total Fruit Intake

Fruit	Adolescents Age 12 – 18 Years	Men Age ≥ 19 Years	Women Age ≥ 19 Years
Apples, raw	9.9	9.7	8.5
Grapes, raw	3.8	3.5	3.4
Strawberries, raw	Not Reported	1.6	2.2
Total	13.7	14.8	14.1
% total fruit intake represented by top 10	72.4	66.9	61.6
Percent RFEP in top 10	18.9	22.1	22.8

It is reasonable to assume that the percentage of RFEP in the total fruit intake is close to the percentage of RFEP in the top 10 fruit sources, *i.e.*, less than 25%. Thus, for the purpose of this estimate, we will use 25% as the percentage of RFEP in the diet.

The US Department of Agriculture (USDA) has reported the results on the intake of various fruits and vegetables (Smiciklas-Wright et al., 2002). The reported intake for apples, strawberries, and grapes among consumers who reported eating these fruits are presented in Table 4, below.

Table 4. Average Daily Intake of Apples, Strawberries, and Grapes Among Consumers Reporting (Grams)

	All Consumers	2-5	6-11	12 – 19		20 – 39		40 – 59		60 and Over	
				M	F	M	F	M	F	M	F
Apples	14	19	18	11	10	13	11	14	14	19	14
Grapes*	12	27	17	9	13	10	9	11	9	12	10
Strawberry*	3	2	3	2	3	2	4	4	4	8	7

* - Study reported only combined intake for raw fruit and fruit juice

As noted above, NatuWrap PA™ is intended to be applied to the raw fruit at levels so that the polyvinyl alcohol concentration will not exceed 0.29 g/kg of fruit or 29 g/100 kg. According to the USDA data presented above, the average daily consumption for apples, grapes, and strawberries was 14, 12 and 3 grams, respectively, with 60-year-old males reporting the highest average consumption level for both apples and strawberries at 19 and 8 grams, respectively.

Using 14 g per day of apples, 12 g per day of grapes, and 3 g per day of strawberries as the average daily consumption, the intake of the polyvinyl alcohol from the coating is calculated as follows:

i. Apples:

(14 g apples/day) (29 g polyvinyl alcohol/100 kg apples) = 4.1 mg/day

ii. Grapes

(12 g grapes/day) (29 g polyvinyl alcohol/100 kg grapes) = 3.5 mg/day

iii. Strawberries

(3 g strawberries/day) (29 g polyvinyl alcohol/100 kg strawberries) = 0.9 mg/day

The total intake from these sources would be 8.5 mg per day.

As shown in Table 3, these three fruits represent RFEP in the top 10 fruit sources and that the top 10 represent between 61.6% and 72.4% of daily fruit consumption. It is reasonable to assume that the percentage of RFEP in all fruit consumed is similar to the percentage in the top 10 sources. Using 61.6% as the minimum concentration of the top 10 sources, the daily intake of NatuWrap PA™ from all fruit would be:

$$(8.5 \text{ mg/day})/(61.6\%) = 14 \text{ mg/day}$$

Assuming that a high end consumer eats twice as much fruit as the average consumer, the daily intake for the high end consumer would be:

$$2 \times (14 \text{ mg/day}) = \underline{28 \text{ mg/day}}$$

B. Vegetables

A similar calculation can be used to determine the intake of polyvinyl alcohol from the use of NatuWrap PA™ on vegetables with edible peels (VEP). The Kimmons et al. (2009) report cited in Table 3 also includes data on the 10 most common vegetable sources. This information is set forth in Table 5, below.

Table 5. Reported VEP Vegetable Sources as Percentage of Total Vegetable Intake

Vegetables	Adolescents Age 12 – 18 Years	Men Age ≥ 19 Years	Women Age ≥ 19 Years
White potato, baked/boiled	13.1	8.8	8.6
Beans, various	4.6	5.3	3.7
Beans, string	Not Reported	2.0	2.3
Total	17.7	16.1	14.6
% total vegetable intake represented by top 10	70.1	57.4	54.9
Percent VEP in top 10	25.2	28.0	26.6

Thus, the top 10 vegetables represent 55% to 70% of the total amount of vegetables in the diet. Using an analogous assumption as was used to calculate the intake of polyvinyl alcohol due to the use of NatuWrap PA™ on fruit, it is reasonable to estimate that VEP will represent 30% of vegetable intake.

The USDA has also published data on the consumption of vegetables (Smiciklas-Wright et al., 2002). For potatoes and string (i.e., green) beans, the consumption levels are listed in Table 6 below.

Table 6. Average Daily Intake of Baked/Boiled Potatoes, String Beans, Among Consumers Reporting (Grams)

	All Consumers	2-5	6-11	12 – 19		20 – 39		40 – 59		60 and Over	
				M	F	M	F	M	F	M	F
Baked Potatoes	8	3	4	7	5	10	8	9	10	12	10
Boiled Potatoes	5	2	1	3	2	4	2	7	5	11	8
String Beans	7	5	5	4	3	7	6	9	7	10	9
Total	20	10	10	14	10	21	16	25	22	33	27

Using the same polyvinyl alcohol concentration used in the calculations for fruit exposure (29 g polyvinyl alcohol/100 kg vegetable) the average consumer's intake would be as follows:

(20 g vegetables/day) (29 g polyvinyl alcohol/100 kg vegetables) = 5.8 mg/day

Assuming that the top 10 reported vegetables are 55% of the total vegetables consumed and that the percentage of VEP in the diet is the same as the percentage of VEP in the top 10, then the amount of polyvinyl alcohol that may be consumed from its use on vegetables would be:

(5.8 mg/day)/(55%) = 10.5 mg/day

It is important to note that this estimate is very conservative since the use of NatuWrap PA™ on potatoes accounts for more than half of the amount consumed through vegetable consumption, and this estimate assumes that consumers eat the entire potato,

including the peel. In practice, the peel is often removed before or after frying or boiling potatoes and many consumers do not eat the peel when eating baked potatoes.

Assuming that a high end consumer would eat twice as much vegetables coated with NatuWrap PA™ as the average consumer, the quantity of polyvinyl alcohol per day for the high end consumer would be:

2 x (10.5 mg/day) = 21 mg/day

C. Total

The total amount of polyvinyl alcohol NatuWrap PA™ consumed by a high end consumer from both fruit and vegetable applications would be:

(28 mg/day) + (21 mg/day) = **49 mg/day**

For a 60 kg consumer, the dietary intake would be:

(49 mg/day)/(60 kg) = **0.82 mg/kg.**

3.2. Cumulative Intake from Existing and Proposed Uses

In addition to the proposed uses by NABACO, in three previous GRAS notices estimates of the polyvinyl alcohol from proposed and existing uses were provided. In the first GRAS notice (GRN 000141), Colorcon reported that the total maximum daily intake of polyvinyl alcohol from its intended use in dietary supplements and from its existing use in pharmaceutical products would be 360 mg/person/day, equivalent to 6 mg/kg bw/day for a 60 kg person. In the second GRAS notice (GRN 000767), Monosol estimated the dietary exposure to polyvinyl alcohol using consumption data from the USDA's 1994-1996 CSFII and reported that the cumulative dietary exposure, including that from GRN 000141, of polyvinyl alcohol for the total users only U.S. population is 45.16 mg/kg bw/day at the 90th percentile. In the subsequent GRAS notice (GRN, 927), Adept reported that there is no dietary exposure to polyvinyl alcohol or its constituents. Adept also noted that considering a worst-case scenario its intended use in edible film would result in the estimated daily intake of polyvinyl alcohol of 5.8 mg/person/day (0.1 mg/kg bw/day for a 60 kg individual) and the cumulative new estimated daily intake of polyvinyl alcohol of 45.26 mg/kg/day. As described above the proposed use of polyvinyl alcohol from its uses in fruits and vegetables will result in 49 mg/person/day. For a 60 kg consumer, the dietary intake of polyvinyl alcohol would be 0.82 mg/kg bw/day. The total cumulative intake from the proposed uses and previous existing uses will be 46.08 mg/kg bw/day. [2]

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[2] We note that in its response to GRASN 886 submitted by Apeel for "a mixture of mono-and diglycerides derived from grape seed" or "MDAG", the agency performed an independent estimate of the dietary exposure. FDA estimated that the daily exposure for high end consumers to be 281 mg/p/d.

MDAG is intended for use in the same applications as the polyvinyl alcohol in this Notice. However, polyvinyl alcohol will be used at a much lower concentration, 0.29 mg/kg of produce versus 1.52 mg/kg for MDAG. Using the FDE estimate, the daily exposure to polyvinyl alcohol from this application would be: ((0.29 mg/kg polyvinyl alcohol)/(1.52 mg/kg MDAG))(281 mg/p/d MDAG) = 54 mg/p/d polyvinyl alcohol

For the 60 kg consumer, this would be:

3.3. Consumption Summary

In summary, the proposed use of polyvinyl alcohol as a coating on fruits and vegetables for a high end consumer will result in 49 mg/person/day or 0.82 mg/kg bw/day for an individual weighing 60 kg. The existing uses of polyvinyl alcohol from dietary supplement products, pharmaceutical products, conventional food products, and from its use in abattoirs will result in a cumulative intake of 45.26 mg/kg bw/day. Thus the total intake of polyvinyl alcohol from the proposed uses by NABACO and the existing uses will be 46.08 mg/kg bw/day. For safety assessment purposes maximum intake of polyvinyl alcohol from all sources of 46.08 mg/kg bw/day is considered.

(54 mg/p/d)/(60 kg) = 0.90 mg/kg/day

The cumulative intake of polyvinyl alcohol using the FDA exposure estimate would be 46.16 mg/kg/day.

PART IV - SELF LIMITING LEVELS OF USE

The proposed use of polyvinyl alcohol on fresh (i.e., unprocessed) agricultural produce is self-limiting for technological reasons, such as appearance on produce and/or the effect on the produce's flavor profile, either of which could affect consumer acceptability. The quantity of polyvinyl alcohol to achieve the technical function is also inherently self-limiting given the unique characteristics of each fruit and vegetable and varies with the specific application. For example, over application of the substance may damage the fruit or vegetable, while under application will prohibit the maximum shelf life benefits from being achieved.

PART V - EXPERIENCE BASED ON COMMON USE IN FOOD BEFORE 1958

The statutory basis for the conclusion of the GRAS status of polyvinyl alcohol in this document is not based on common use in food before 1958. The GRAS assessment is based on scientific procedures.

PART VI - NARRATIVE

6.1. Data Pertaining to Safety

The safety of polyvinyl alcohol has been extensively investigated and reported in the published literature. The safety of polyvinyl alcohol has been studied in different species following both oral and non-oral routes, such as rectal, intra-vaginal, subcutaneous, intravenous, intra-peritoneal and dermal. As polyvinyl alcohol is very poorly absorbed following oral administration, the findings from non-oral studies are considered not to be predictive of oral toxicity. Given this, for the safety assessment of polyvinyl alcohol, emphasis is placed on the oral studies. The available safety related information on polyvinyl alcohol includes metabolism, genotoxicity, acute toxicity, subchronic toxicity and reproductive and developmental toxicity. Additionally, the carcinogenicity of polyvinyl alcohol has been studied following intra-vaginal administration to female mice. Additionally, polyvinyl alcohol has been approved for use in coatings applied to pharmaceutical products. Several national and international regulatory and other agencies have extensively evaluated the safety of polyvinyl alcohol. All these evaluations have concluded that polyvinyl alcohol is safe for use as a food or dietary supplement ingredient at the levels described in those assessments.

In a critical evaluation of the available safety data on polyvinyl alcohol, DeMerlis and Schoneker (2003) reported that orally administered polyvinyl alcohol is relatively harmless. The safety of polyvinyl alcohol is based on the following: (1) the acute oral toxicity of polyvinyl alcohol is very low, with LD_{50} in the range of 15-20 g/kg bw; (2) orally administered polyvinyl alcohol is very poorly absorbed from the gastrointestinal tract; (3) polyvinyl alcohol does not accumulate in the body when administered orally; (4) polyvinyl alcohol is not mutagenic or clastogenic; and (5) NOAELs of orally administered polyvinyl alcohol in male and female rats were 5000 mg/kg bw/day in the 90-day dietary study and 5000 mg/kg bw/day in the two-generation reproduction study, which was the highest dose tested.

6.2. Toxicological Studies

6.2.1. Toxicokinetics

Orally administered polyvinyl alcohol is poorly absorbed from the gastrointestinal tract (EFSA, 2005; Sanders and Matthews, 1990). Based on findings from animal study, Sanders and Matthews (1990) reported that greater than 98% of the radioactivity associated with a single oral dose of 0.01 mg/kg ^{14}C-labeled polyvinyl alcohol administered to 3 male rats was recovered in the feces within 48 hours of administration. In the urine, less than 0.2% of the total radioactivity was detected.

In an attempt to further assess potential for absorption and subsequent bioaccumulation, Sanders and Matthews (1990) administered 0.1 mg/kg ^{14}C-labeled polyvinyl alcohol by gavage to 3 male F344 rats for 10 consecutive days. The almost 100% recovery of orally dosed radioactivity in fecal materials supports the conclusion of Sanders and Matthews (1990), that polyvinyl alcohol is very poorly absorbed. These observations suggest that there is minimal amount of polyvinyl alcohol available for distribution to body tissues and only trace amounts are likely to be absorbed. This is not unexpected for a

degradation-resistant, high-molecular weight polymer. Thus, polyvinyl alcohol is not broken down or absorbed systemically to any significant extent in the gastrointestinal tract and that it passes through and is excreted in feces essentially intact and unabsorbed.

6.2.2. Acute Toxicity

In several studies, acute toxicity of polyvinyl alcohol has been investigated in rats, mice and dogs, following oral administration. As described in JECFA (2004) and EFSA (2005) assessment reports, the LD_{50} values of polyvinyl alcohol for mice, rats and dogs following oral administration have been reported to range from > 1.5 to approximately 22 g/kg bw. The oral LD_{50} of polyvinyl alcohol in different species has been reported as follows: mouse- >4000 mg/kg bw; rat- >21500 mg/kg bw; and dog- >20000 mg/kg bw, respectively. The findings from these studies suggest that polyvinyl alcohol is practically nontoxic following oral administration.

6.2.3. Subchronic Toxicity

In the 90-day oral toxicity study, Kelly et al. (2003) investigated the potential systemic and neurotoxic effects of polyvinyl alcohol in rats. In this GLP-compliant feeding study, male Sprague-Dawley rats (20/sex/group) were fed a diet containing polyvinyl alcohol that resulted in a dose level of 0, 2000, 3500 and 5000 mg/kg bw/day for 90 days. Rats in control group received untreated standard laboratory diet. Dose levels were selected on the basis of a preliminary 14-day range finding toxicity study. During the course of study and at termination rats were assessed for clinical observations, ophthalmology, body weight and feed consumption, hematology, coagulation, clinical chemistry, urinalyses, motor activity and functional observational battery, and gross and microscopic pathology. The only readily apparent polyvinyl alcohol treatment-related effect noted during the course of study was unformed stool with brown/black anogenital staining in rats fed polyvinyl alcohol at levels of 3500 and 5000 mg/kg bw/day. This finding was attributed to the consumption and excretion of high levels of polyvinyl alcohol. It was not accompanied by macroscopic or microscopic observations in these rats. The presence of loose stools and anogenital staining was considered to be the result of the large amount of unabsorbed polyvinyl alcohol in the stool. As a result, water is likely retained within the stool. The investigators concluded that this was a physiological process and not a toxic effect per se.

Besides above mentioned observations, no treatment-related changes were noted in mortality, ophthalmology, body weight and food consumption data, hematology, clinical chemistry, urinalysis data, functional observational assessments, motor activity, organ weight data and macroscopic and microscopic examinations. The investigators concluded that administration of polyvinyl alcohol as a dietary admixture to rats at doses of 2000, 3500 and 5000 mg/kg/day for up to 90 days did not result in any adverse, toxicological effects. The findings from this study suggest the no-observed-adverse-effect-level (NOAEL) of 5000 mg/kg bw/day.

6.2.4. Mutagenicity Genotoxicity

In addition to above described subchronic study, Kelly et al. (2003) also investigated the genotoxic potential of polyvinyl alcohol in a series of investigations as evaluated by: bacterial reverse mutation assay in *Salmonella typhimurium* and

Escherichia coli (Ames assay); *in vitro* forward mutation assay in a sub-line of mouse lymphoma L5178Y cells; and *in vivo* mouse micronucleus assay.

In the bacterial reverse mutation assay (Ames assay), polyvinyl alcohol at concentrations of up to 5000 µg/plate, both in the presence and absence of liver preparations from Aroclor 1254-induced rats (S9 mix), was not mutagenic to *S. typhimurium* strains TA1535, TA1537, TA98 and TA100, or to a tryptophan-dependent mutant of *E. coli* strain WP2*uvr*A/pKM101 (CM 891) (Kelly et al., 2003). In the *in vitro* mouse lymphoma assay, polyvinyl alcohol at concentrations up to 5000 µg/mL, in the presence and absence of metabolic activation (S9 mix), did not increase the incidence of forward mutations at the thymidine kinase locus (TK+/-). In the *in vivo* mouse micronucleus assay, administration of single doses of polyvinyl alcohol via oral gavage to male and female Swiss mice at doses of up to 2000 mg/kg bw did not show any evidence of causing chromosome damage or bone marrow cell toxicity at 24 to 48 hours following administration.

The above described observations from the genotoxicity studies of polyvinyl alcohol are further supported by the studies described in the JECFA (2004) and mentioned in EFSA (2005) evaluation of polyvinyl alcohol. As described in the JECFA and EFSA reports, negative results were noted in several strains of *S. typhimurium* in both the presence and absence of metabolic activation (Shibuya et al., 1985; Schweikl et al., 1996), as well as in an *in vitro* Chinese hamster V79 chromosomal aberration assay and *in vivo* in a female mouse bone marrow micronucleus test (Shibuya et al., 1985).

6.2.5. Chronic Toxicity and Carcinogenicity

No chronic toxicity or carcinogenicity studies were found following oral administration of polyvinyl alcohol, in the published literature. However, in a 2-year chronic toxicity study conducted by National Toxicology Program (NTP), intra-vaginal administration of polyvinyl alcohol to female B6C3F1 mice did not reveal compound-related neoplastic or non-neoplastic lesions (NTP, 1998). In this study, three groups (i.e., an untreated control, a vehicle control, and a dose group receiving 20 µL 25% polyvinyl alcohol [PVA] in de-ionized water) of 100 female B6C3F1 mice were administered polyvinyl alcohol. The only clinical finding noted in this study was vaginal irritation. The NTP report concluded that "under the conditions of this 2-year study, there was no evidence of carcinogenic activity..."

Based on the low absorption rate of polyvinyl alcohol through the mucosa of the gastrointestinal tract, the absence of genotoxicity concerns, and the results of the NTP study showing no neoplastic lesions in the internal and external organs of the intra-vaginally exposed mice, including on the directly exposed vaginal mucosal surface, it is concluded that there is no evidence that polyvinyl alcohol is carcinogenic and that polyvinyl does not pose a carcinogenic risk following dietary exposures.

6.2.6. Reproduction and Developmental Toxicity

In a 2-generation reproductive toxicity study, Rodwell et al. (2003) investigated the effects of polyvinyl alcohol on fertility, early embryonic development, growth and

subsequent development in rats. In this GLP-compliant study, groups of P_0 and F_1 parental Sprague-Dawley rats (26/sex/group) were fed diets containing polyvinyl alcohol at levels providing doses of 2000, 3500, or 5000 mg/kg bw/day for at least 70 consecutive days prior to mating. The treatment of male rats was continued during the 14-day mating period and throughout the post-mating period until euthanized. Female rats continued on their respective dietary exposure during the 14-day mating period, gestation, and lactation. Females were generally euthanized on lactation day 21.

Polyvinyl alcohol exposure via diet did not induce any treatment-related effects on P_0 or F_1 male reproductive performance, as evaluated by mating and fertility indices and sperm counts. Similarly, as assessed by mating, fertility and pregnancy indices, and estrous cycling data, there were no biologically significant effects attributable to polyvinyl alcohol treatment on P_0 or F_1 female reproductive performance. No polyvinyl alcohol related effects on litter parameters (litter size, pup sex distribution, pup survival, clinical observations, and body weights) in either the F_1 or F_2 generation were observed. Similarly, polyvinyl alcohol treatment in both F_1 and F_2 generations did not affect absolute organ weights, or organ to body weights and organ to brain weight ratios. Macroscopic and microscopic observations performed on the P_0 and F_1 parental animals and on the F_1 and F_2 pups did not reveal any adverse effects from polyvinyl alcohol exposure. The findings from this well-designed reproductive study suggest a NOAEL of 5000 mg/kg bw/day for both parental and offspring, the highest dose tested (Rodwell et al., 2003).

6.3. National and International Regulatory Agencies Assessments

6.3.1. GRAS Notification on Polyvinyl alcohol

Based on FDA GRAS Notices inventory website, the FDA has received three GRAS notices (Table 7) for use of polyvinyl alcohol as a food ingredient in a variety of conventional foods, all of which have received "no question" letters from the FDA. These GRAS notices include GRN 000141 (FDA, 2004), GRN 000767 (FDA, 2018) and GRN 000927 (FDA, 2021).

Table 7. GRAS Notices on Polyvinyl Alcohol Submitted to FDA and Received No Questions*

GRN No.	Substance	Date of closure	FDA's Letter
927	Polyvinyl alcohol	Feb 26, 2021	FDA has no questions (in PDF) (206 kB)
767	Polyvinyl alcohol	Sep 7, 2018	FDA has no questions (in PDF) (57 kB)
141	Polyvinyl alcohol	Apr 28, 2004	FDA has no questions

*Additional details of the complete GRAS notice and the FDA response letter is available by 'click' on the substance of the notice or FDA's no question letter.

The first GRAS notice (GRN 000141) on polyvinyl alcohol was submitted by Colorcon (2003). In this notice, the notifier informed the FDA that polyvinyl alcohol is GRAS, through scientific procedures, for use in aqueous film coating formulations applied to dietary supplement products (i.e., tablets or capsules), where the coating formulation is up to 4% (by weight) of the tablet or capsule, and polyvinyl alcohol is up to 45% (by weight) of the coating formulation. Assuming that a person consumes a maximum of ten 1

g dietary supplement tablets or capsules and ten 1 g pharmaceutical tablets or capsules with polyvinyl alcohol film coating formulations per day, the maximum daily intake of polyvinyl alcohol was estimated as 180 mg/person/day from dietary supplements and 180 mg/person/day from its use in film coatings applied to pharmaceutical products. The total maximum daily intake of polyvinyl alcohol from its intended use in dietary supplements and from its use in pharmaceutical products was estimated as 360 mg/person/day, equivalent to 6 mg/kg bw/day for a 60 kg person.

As regards safety of polyvinyl alcohol, the notifier reported that acute and subchronic oral toxicity studies conducted in animals including rats, mice, and dogs as well as a two-generation reproductive toxicity study conducted in rats fed polyvinyl alcohol showed no adverse toxicological or reproductive effects. *In vitro* and *in vivo* genotoxicity studies with polyvinyl alcohol also did not reveal any evidence of mutagenic or clastogenic effects. These studies suggest that polyvinyl alcohol is not mutagenic, genotoxic, or carcinogenic by the oral route. The notifier concluded that animal toxicology data (subchronic toxicity and reproductive toxicity study) support a NOAEL for polyvinyl alcohol of 5000 mg/kg bw/day, the highest dose tested. In a response letter to the notifier, the FDA did not question the conclusion that the ingredient polyvinyl alcohol is GRAS under the intended conditions of use.

In the second GRAS notice by Monosol (2018) the Notifier determined that polyvinyl alcohol is GRAS, through scientific procedures, for use as a component of water-soluble, edible film that may be used to form pouches containing pre-portioned aliquots of (1) certain dry ingredients (i.e., instant tea, instant coffee, hot chocolate mix, flavored drink powder, and whey protein supplement powder) to be used by the consumer in preparing ready-to-serve foods and beverages at a level up to 0.734 g polyvinyl alcohol/serving, (2) approved color additives to be used in manufacturing flavored beverages (non-dairy and non-alcohol) at a level up to 0.0006 g polyvinyl alcohol/serving, and (3) dry ingredients to be used by commercial establishments in making pizza dough at a level up to 0.0075 g polyvinyl alcohol/serving.

In this second GRAS notice, the total maximum daily intake (90^{th} percentile) of polyvinyl alcohol from its intended use in edible film was estimated for the total users only U.S. population as 45.16 mg/kg bw/day. The notifier discussed the safety of polyvinyl alcohol using the same published studies that were discussed in GRN 141. These published studies included animal toxicity studies (a subchronic toxicity study in rats and a two generation reproductive study), in which the authors reported no treatment-related effects at a dose of 5000 mg/kg bw/day. The notifier reported that a literature search was conducted through January 2018 and did not report any new data or information that would contradict their GRAS conclusion. In a September 19, 2018 response letter to the notifier, the FDA did not question the conclusion that polyvinyl alcohol is GRAS under the intended conditions of use.

The most recent and third GRAS notice was submitted by Adept Limited (2020) for the use of polyvinyl alcohol as a component of water-soluble anus plugs for use in abattoirs to block fecal material during processing of sheep, lambs, and hogs at levels up to 59% of the plug formulation. The notifier discussed publicly available data and

information supporting the safety of the intended use of polyvinyl alcohol, noting the previous GRAS conclusions from GRNs 000141 and 000767. In this GRAS notice, Adept Limited discussed published absorption, distribution and elimination studies of ^{14}C-labeled polyvinyl alcohol in rats and concludes that polyvinyl alcohol is not broken down or absorbed to any significant extent. Adept discussed a published subchronic study evaluating potential systemic or neurotoxic effects of dietary administration of polyvinyl alcohol to rats, concluding that there were no adverse effects up to the highest does of 5000 mg/kg bw/day for 90 days. The notifier also discussed a published two generation dietary study in rats and concluded that there were no effects on reproductive or developmental parameters evaluated up to the highest dose of 5000 mg/kg bw/day. Based on the published results from a standard battery of three genotoxicity studies, Adept concluded that polyvinyl alcohol is not genotoxic. Adept further describes the safety conclusions of polyvinyl alcohol by the JECFA and EFSA. Following its review, on February 26, 2021, the FDA responded to the notifier that the agency did not question the conclusion that polyvinyl alcohol is GRAS under the intended conditions of use.

6.3.2. JECFA Evaluation

In an extensive evaluation, The Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2004) reviewed number of studies related to the toxicity of polyvinyl alcohol following administration by different routes to a number of species. The Committee concluded that polyvinyl alcohol was very poorly absorbed following oral administration, that the acute oral toxicity was generally very low, and that, taken as a whole, the results were consistent with very low toxicity and showed no evidence for carcinogenicity. No adverse effects were noted in a two-generation reproductive toxicity study and a subchronic toxicity study in rats. There was no evidence for genotoxicity in a battery of tests undertaken with preparations of polyvinyl alcohol.

The Committee identified a No-Observed-Effect-Level (NOEL) of 5000 mg/kg bw/day for polyvinyl alcohol on the basis of the maximum dose tested in both the 90-day and the two-generation toxicity studies in rats. The Committee established an acceptable daily intake (ADI) for polyvinyl alcohol of 50 mg/kg bw/day, on the basis of the NOEL of 5000 mg/kg bw/day from the subchronic toxicity and two-generation studies in rats, with a safety factor of 100 (JECFA, 2004). These studies considered by JECFA were subsequently published and are described earlier in this GRAS document.

6.3.3. European Commission Evaluation

In 2005, the Scientific Panel of the European Food Safety Authority (EFSA, 2005) reviewed the safety of polyvinyl alcohol as a food additive when used as film coating agent for food supplements. Following a critical review of the relevant polyvinyl alcohol data, including physical/chemical properties, specifications, manufacturing process, proposed use levels, exposure, safety-related studies, etc., the EFSA Panel concluded that the consumption of polyvinyl alcohol, through its use as a coating agent for food supplement tablets and/or capsules at its intended use level and resulting in a total (cumulative) intake of 4.8 mg/kg bw from the proposed and existing food uses is not of safety concern.

The available evidence shows that polyvinyl alcohol is only minimally absorbed following oral administration. The Panel noted that the NOAEL of 5000 mg/kg bw/day (the highest dose tested) derived from the 90-day (subchronic) and two-generation reproductive dietary toxicity studies with polyvinyl alcohol indicates a low order of toxicity. The maximum assumed combined intakes of 4.8 mg/kg bw/day from the proposed uses plus existing uses from pharmaceutical products was over 1000-fold below the established NOAEL. The Panel concluded that the consumption of the polyvinyl alcohol through its use as a coating agent for food supplement tablets and/or capsules at its intended use level is not of safety concern.

6.3.4. Additional Regulatory Citations and Uses

In addition to food uses, polyvinyl alcohol is commonly used in pharmaceutical industry as part of film coating agents for ingestible tablets and capsules. As mentioned earlier, it is also used for coating ingestible dietary supplements as described in GRN 000141. Polyvinyl alcohol is approved for use as an indirect food additive in products that are intended for use in contact with food (21 CFR 177.1670), as a diluent in color additive mixtures for coloring shell eggs [21 CFR 73.1 (b)(2)] and for ophthalmic drug products for over the counter human use (21 CFR 349.12). It is also approved for use in cosmetic products (CIR, 1998) as well as in pharmaceutical products (Rothschild, 2004). In Europe, the specifications for the use of pharmaceutical grade polyvinyl alcohol are published in the European Pharmacopoeia (PhEur, 2002). In the UK, polyvinyl alcohol is allowed for use in non-parenteral licensed medicines (EFSA, 2005).

There exists an established history of use of polyvinyl alcohol in cosmetics and medical applications, as well as a component of food packaging materials (CIR, 1998; 21 CFR §175.105, §175.300, §175.320, §176.170, §176.180, §177.1200, §177.1670, §177.2260, §177.2800, §178.3910, §181.30).

6.4. Safety of Other Constituents

The subject of this GRAS polyvinyl alcohol contains residual solvents and by-products. Although the product used in toxicity studies also contains these constituents, the available additional information on some of these by-products generated during manufacturing is discussed here. The levels of these by-products and their levels are monitored by process control, individual specifications and analytical methods. The specifications of methanol and methyl acetate establish a limit of 1%. Considering that maximum cumulative intake of polyvinyl alcohol from all uses as 50 mg/kg bw/day, the resulting estimated daily intake of these manufacturing by-products (methanol as well as for methyl acetate) from the intended uses of polyvinyl alcohol as a food ingredient will be below 0.5 mg/kg bw/day (30 mg for an individual weighing 60 kg).

The residual solvent levels of methanol are permitted (21 CFR 173.250) from its use as secondary direct food additive in certain food for human consumption. As per this regulation, methanol may be present in the following foods under the conditions specified: (a) In spice oleoresins as a residue from the extraction of spice, at a level not to exceed 50 ppm. (b) In hops extract as a residue from the extraction of hops, at a level not to exceed 2.2% by weight; Provided, that: (1) The hops extract is added to the wort before or during

cooking in the manufacture of beer. (2) The label of the hops extract specifies the presence of methyl alcohol and provides for the use of the hops extract only as prescribed by paragraph (b)(1) of this section. Methanol uses are also recognized in the following 21 CFR citations with limits in parenthesis: 175.105 as an indirect food additive for use only as a component of adhesives; 172.589 for sucrose fatty acid esters (10 ppm); 172.560 for Modified hop extract (100 ppm); 173.250 for spice oleoresins (50 ppm); 172.867 for Olestra (300 ppm); and 73.615 for Turmeric oleoresin.

The available information also shows that dietary methanol can arise from fresh fruits and vegetables, where it occurs as free alcohol, methyl esters of fatty acids or methoxy group on polysaccharides such as pectin. Orange juice is a good example of fruit juice that contains approximately 500 mg methanol/liter. Thus, a typical serving of orange juice (200 ml or 6 oz) results in consumption of 100 mg of methanol. These observations suggest that the resulting intake of methanol (30 mg/day) from all the uses (cumulative) of polyvinyl alcohol is safe.

As per 21 CFR 172.515, methyl acetate, the other processing by-product, is a food additive permitted for direct addition to food for human consumption as a synthetic flavoring substance and adjuvant in accordance with the following conditions: 1) they are used in the minimum quantity required to produce their intended effect, and otherwise in accordance with all the principles of good manufacturing practice, and 2) they consist of one or more of the following, used alone or in combination with flavoring substances and adjuvants generally recognized as safe in food, prior-sanctioned for such use, or regulated by an appropriate section in this part. According to 21 CFR 175.105, methyl acetate is an indirect food additive for use only as a component of adhesives. The Flavor and Extract Manufacturer's Association (FEMA) has also approved food uses of methyl acetate (FEMA No. 2676) as a flavoring agent in beverages, ice cream, candy and baked goods at levels ranging from 11 to 29 ppm.

In summary, these regulatory citations for the by-products, and other safety related-information on methanol and methyl acetate, suggest that the resulting cumulative intake of these manufacturing by-products from the proposed and existing uses of polyvinyl alcohol is safe.

6.5. Summary, Discussion and Conclusion

NABACO Inc., intends to market NatuWrap PA™ containing polyvinyl alcohol as a food ingredient for use as a surface-finishing agent and/or texturizer as defined at 21 CFR 170.3 (o)(30) and (32).[3] When used in accordance with product instructions NatuWrap PA™ will be applied to the exterior of produce to form a thin and edible physical barrier against moisture loss and oxidation to protect the freshness and extend the shelf-life of agricultural products such as fruits (e.g., berries, grapes, stone fruit, citrus, bananas, mangoes, avocados) and vegetables (e.g., legumes, roots, tubers). It will be used at levels consistent with current Good Manufacturing Practice but not to exceed 0.29 g PVOH/kg

[3]*Surface-finishing agents*: Substances used to increase palatability, preserve gloss, and inhibit discoloration of foods, including glazes, polishes, waxes, and protective coatings. *Texturizers*: Substances which affect the appearance or feel of the food.

of food and is self-limiting for technological reasons. The intended use of polyvinyl alcohol on fruits and vegetables is estimated to result in a maximum daily (90^{th} percentile) intake of 49 mg/person/day or 0.82 mg/kg bw/day (for an individual weighing 60 kg). The cumulative intake of polyvinyl alcohol from the proposed uses and the existing uses is estimated as 46.08 mg/kg bw/day. The polyvinyl alcohol, subject of this GRAS assessment, meets appropriate food grade specifications, and is manufactured in compliance with current Good Manufacturing Practices.

For the present GRAS assessment, a comprehensive search of the scientific literature for safety and toxicity information on polyvinyl alcohol was conducted through September 2021 and used in the preparation of this dossier. The available information suggest that polyvinyl alcohol is commonly used in film coating formulations for pharmaceutical tablets and capsules. Similarly, it is also used for coating dietary supplements. Polyvinyl alcohol is also permitted for use in cosmetic products. As per FDA regulations, polyvinyl alcohol is approved for use as an indirect food additive in products that are in contact with food. In response to three GRAS Notification for polyvinyl alcohol use as a film coating for dietary supplements, as a component of water-soluble edible film, and as a component of water-soluble anus plugs, the FDA did not question the conclusion that the polyvinyl alcohol is GRAS for these intended conditions of use. The EFSA Panel evaluated the use of polyvinyl alcohol as a food additive film coating agent for food supplements and concluded that the consumption of the polyvinyl alcohol as a coating agent is safe. Similarly, JECFA also evaluated the safety of polyvinyl alcohol for use as a coating, binder, sealing or surface-finishing agent and established an ADI of 50 mg/kg bw for polyvinyl alcohol. There is no evidence that the existing uses of polyvinyl alcohol have resulted in any adverse effects in humans.

The safety of polyvinyl alcohol is supported by toxicity studies that include GLP-compliant studies (i.e., a subchronic oral toxicity study, a 2-generation reproductive toxicity study, and *in vitro* and *in vivo* genotoxicity assays). The available evidence suggests that following oral administration, polyvinyl alcohol is only minimally absorbed. The acute oral toxicity studies in rats, mice and dogs suggest that polyvinyl alcohol possesses a low order of acute toxicity. In the 90-day subchronic toxicity study, there was no evidence of systemic toxicity following dietary administration of polyvinyl alcohol at doses up to 5000 mg/kg bw/day, the highest dose tested. Similarly, in a 2-generation reproductive toxicity study, no adverse effects of polyvinyl alcohol administration occurred in parental, or first or second-generation rats. In this study also, the highest dose level of polyvinyl alcohol tested was 5000 mg/kg bw/day. The findings from a series of *in vitro* and *in vivo* mutagenicity and genotoxicity assays suggest that polyvinyl alcohol is neither mutagenic nor genotoxic. No oral chronic toxicity and carcinogenicity studies were available, however, in a topical carcinogenicity study, intravaginal administration of polyvinyl alcohol to female mice did not indicate any carcinogenic activity. The cumulative intake of polyvinyl alcohol of 46.08 mg/kg bw/day from all sources, including current proposed uses, is over 100 fold compared to the NOAEL of 5000 mg/kg bw/day determined from subchronic oral toxicity and 2-generation reproductive toxicity studies. The cumulative intake is also lower as compared to the JECFA established ADI of 50 mg/kg bw/day.

In summary, on the basis of scientific procedures[4] and common knowledge of exposure from existing uses, the consumption of polyvinyl alcohol as a food ingredient component when used as part of an edible film coating on fruits is considered safe at levels up to 50 mg/kg bw/day. The intended uses are compatible with current regulations, *i.e.,* polyvinyl alcohol-containing films will be used as a coating on fruits. Polyvinyl alcohol used in these applications is produced according to current good manufacturing practices (cGMP). The intended uses of the film along with other existing uses from all uses is estimated to result in maximum intake of 50 mg polyvinyl alcohol/kg bw/day using. Such exposure to polyvinyl alcohol is considered safe on the basis of the totality of the evidence, including the above described safety studies.

Based on a critical evaluation of the publicly available data, summarized herein, NABACO Inc. has concluded that polyvinyl alcohol, meeting the specifications cited herein, and when used as a surface-finishing agent and/or texturizer [21 CFR 170.3 (o)(30) and (32)], creating a thin and edible physical barrier against moisture loss and oxidation to protect the freshness and extend the shelf at levels consistent with current Good Manufacturing Practice as described in this monograph, and resulting in maximum cumulative estimated intake of 46.08 mg/kg bw/day, is safe. It is also the opinion of NABACO Inc. that other qualified and competent scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Therefore, we have also concluded that polyvinyl alcohol, when used as described, is Generally Recognized As Safe (GRAS) based on scientific procedures.

[4] 21 CFR §170.3 Definitions. (h) Scientific procedures include those human, animal, analytical, and other scientific studies, whether published or unpublished, appropriate to establish the safety of a substance.

Part VII- SUPPORTING LITERATURE AND REFERENCES

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Appendix I

Analytical results from three non-consecutive lots along with Data for Lead

kuraray

kuraray poval

Kuraray Europe GmbH
Philipp-Reis-Straße 4
65795 Hattersheim am Main

CERTIFICATE OF ANALYSIS

Order No.:
Delivery No.:
Cust Order No.:
Date of Print: 31.01.2022

These data do not release the customer from the obligation to carry out an inspection of goods received. All sales of this product shall be subject to our Standard Terms and Conditions of Sale.

PRODUCT QUALITY CONTROL DATA

Material: PV001245 KURARAY POVAL# 5-88 FA 500kg Big bag

Batch Number Characteristics	Test Method Test Method Description	Value	Unit	Min	Max
N122015126					
Methanol content		0,52	%	0,00	0,99
Viscosity 4% (DIN 53015)		5,2	mPa.s	4,8	5,8
pH		5,1		5,0	6,5
Degree of Hydrolysis		87,7	mole%	86,5	89,0
Ash Content		0,08	%	0,00	0,37
Solid content 105°C, 3h		98,3	%	95,0	100,0
Volatile Matter		1,7	%	0,0	5,0
Methylacetat content		0,02	%	0,00	0,99
Insoluble Matter POVAL		0,02	%	0,00	0,10

"This report is computer generated and valid without signature."

kuraray

kuraray poval

Kuraray Europe GmbH
Philipp-Reis-Straße 4
65795 Hattersheim am Main

CERTIFICATE OF ANALYSIS

Order No.:
Delivery No.:
Cust Order No.:
Date of Print: 31.01.2022

These data do not release the customer from the obligation to carry out an inspection of goods received. All sales of this product shall be subject to our Standard Terms and Conditions of Sale.

PRODUCT QUALITY CONTROL DATA

Material: PV001245 KURARAY POVAL# 5-88 FA 500kg Big bag

Batch Number

Characteristics	Test Method Test Method Description	Value	Unit	Min	Max
N122015118					
Methanol content		0,60	%	0,00	0,99
Viscosity 4% (DIN 53015)		5,2	mPa.s	4,8	5,8
pH		5,2		5,0	6,5
Degree of Hydrolysis		87,6	mole%	86,5	89,0
Ash Content		0,12	%	0,00	0,37
Solid content 105°C, 3h		98,4	%	95,0	100,0
Volatile Matter		1,6	%	0,0	5,0
Methylacetat content		0,02	%	0,00	0,99
Insoluble Matter POVAL		0,00	%	0,00	0,10

"This report is computer generated and valid without signature."

kuraray

kuraray poval

Kuraray Europe GmbH
Philipp-Reis-Straße 4
65795 Hattersheim am Main

CERTIFICATE OF ANALYSIS

Order No.:
Delivery No.:
Cust Order No.:
Date of Print: 31.01.2022

These data do not release the customer from the obligation to carry out an inspection of goods received. All sales of this product shall be subject to our Standard Terms and Conditions of Sale.

PRODUCT QUALITY CONTROL DATA

Material: PV001245 KURARAY POVAL# 5-88 FA 500kg Big bag

Batch Number Characteristics	Test Method Test Method Description	Value	Unit	Min	Max
N122015117					
Methanol content		0,53	%	0,00	0,99
Viscosity 4% (DIN 53015)		5,3	mPa.s	4,8	5,8
pH		5,2		5,0	6,5
Degree of Hydrolysis		87,4	mole%	86,5	89,0
Ash Content		0,12	%	0,00	0,37
Solid content 105°C, 3h		98,4	%	95,0	100,0
Volatile Matter		1,6	%	0,0	5,0
Methylacetat content		0,02	%	0,00	0,99
Insoluble Matter POVAL		0,04	%	0,00	0,10

"This report is computer generated and valid without signature."

Priifbericht

Auftraggeber Frau Dr. Shu-Hsien Li
D581, PVA/PVB - R&TS / PVB-Film
Eingangsdatum 28.10.2021

08.11.2021
Labor-Auftrags-Nr.: 2111252
bei Nachfragen bilte unbedingt angeben !!

Proben-Nr. **Parameter**	**Probenbezeichnung sample designation**	**Unit**	**analysis result**	**GW**
2111252-006	**Poval 5-88 FA N121085317** **Probenahme: 28.10.2021** **Probenfreigabe: 05.11.202115:25**			
	Determination of the original sample			
Aufschlussart*			DIN EN ISO 15587-2: 2002-07 Water quality - Information for the determination of selected elements in water - Part 2: nitric acid digestion (CEM)	
Blei*	Lead*	mg/kgOS	< 1,0	

Freigabe Priifbericht <lurch: Dr. Christoph Waller Fachlicher Leiter in Abteilung Umwelt- und Prozessanalyt

Telefonische Rlickfragen bitte an:
Dr. Kaltz 069/305-13801 (Achim.Kaltz@lnfraserv.com)
Dr. Waller 069/305-35056 (Christoph.Waller@lnfraserv.com) Dr. Alt 069/305-6774 (Christopher.Alt@lnfraserv.com)

You are welcome to give us feedback about our performance to the above-mentioned people.

This test report was created by an EDI system and is also valid without a signature!

test procedure

DIN EN ISO 17294-2

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Priifbericht

Auftraggeber **Frau Dr. Shu-Hsien Li**
D581, PVA/PVB - R&TS / PVB-Film
Eingangsdatum 28.10.2021

08.11.2021
Labor-Auftrags-Nr.: 2111252
bei Nachfragen bilte unbedingt angeben !!

Proben-Nr. / Parameter	Probenbezeichnung	Einheit	Analysenergebnis	GW
2111252-007	**Poval 5-88 FA N120075080** **Probenahme: 28.10.2021** **Probenfreigabe: 05.11.202115:26**			
	Bestimmung der Originalprobe			
Aufschlussart*			DIN EN ISO 15587-2: 2002-07 Wasserbeschaffenheit - Aufschluss for die Bestimmung ausgewiihlter Elemente in Wasser - Teil 2: Sal petersiiure- Aufsch luss (CEM)	
Blei*		mg/kgOS	< 1,0	

Freigabe Priifbericht <lurch: Dr. Christoph Waller Fachlicher Leiter in Abteilung Umwelt- und Prozessanalyt

Die vorliegenden Prlifergebnisse beziehen sich ausschlieBlich auf das untersuchte Probenmaterial.
Die Veroffentlichung und Vervielfaltigung unserer Prlifberichte sowie deren Verwendung zu Werbezwecken bedlirfen - auch auszu

Telefonische Rlickfragen bitte an:
Dr. Kaltz 069/305-13801 (Achim.Kaltz@Infraserv.com)
Dr. Waller 069/305-35056 (Christoph.Waller@lnfraserv.com) Dr. Alt 069/305-6774 (Christopher.Alt@lnfraserv.com)

Gerne konnen Sie uns eine Rlickmeldung Uber unsere Leistung an die oben genannten Personen geben.

Dieser Prlifbericht wurde durch ein EDY-System erstellt und ist auch ohne Unterschrift gliltig!

Priifverfahren

DIN EN ISO 17294-2

ik

igsweise - unserer schriftlichen Genehmigung.

Report Translation

Client: Dr. Shu-Hsien Liaaa
D581, PVA/PVB – R&TS/PVB Film
Date Received: 10/28/2021

Order # 2111252
Nov. 8, 2021

Sample No: 2111252-006
Sample Designation: Proval 5-88 FA N121085317
Sample received: 10/28/2021
Sample released: 11/05/2021 15:25

Determination of the original sample

Sample Preparation Method: ISO 15587-2:2002-07 *Water Quality – Information for the determination of selected elements in water – Part 2: nitric acid digestion.*

Analytical Test Method: ISO 17294-2

Results: Lead <1.0 mg/kg OS Test method ISO 17294-2

Test Report released by Dr. Christopher Waller

This test report was created by an EDI system and is valid without a signature

Report Translation

Client: Dr. Shu-Hsien Liaaa
D581, PVA/PVB – R&TS/PVB Film
Date Received: 10/28/2021

Order # 2111252
Nov. 8, 2021

Sample No: 2111252-007
Sample Designation: Proval 5-88 FA N120075080
Sample received: 10/28/2021
Sample released: 11/05/2021 15:25

Determination of the original sample

Sample Preparation Method: ISO 15587-2:2002-07 *Water Quality – Information for the determination of selected elements in water – Part 2: nitric acid digestion.*

Analytical Test Method: ISO 17294-2

Results: Lead <1.0 mg/kg OS Test method ISO 17294-2

Test Report released by Dr. Christopher Waller

This test report was created by an EDI system and is valid without a signature

From: Mark Itzkoff
To: Gaynor, Paulette M
Subject: Re: FW: [EXTERNAL] Re: GRN 001058 – items for clarification
Date: Tuesday, November 15, 2022 4:10:01 PM
Attachments: FDA Clarification Nov 15 2022 with app.pdf

Paulette,

I just finalized the clarification letter. It is attached.

Thank you for your patience.

Mark

On Tue, Nov 15, 2022 at 3:08 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Hi Mark,
>
> We are checking on the status of NABACO's providing the items for clarification as we have yet to receive any of these items. Please let us know.
>
> Thank you,
>
> Paulette
>
> ---
>
> **From:** Gaynor, Paulette M
> **Sent:** Wednesday, September 14, 2022 3:19 PM
> **To:** Mark Itzkoff <mark@itzkofflaw.com>
> **Subject:** RE: [EXTERNAL] Re: GRN 001058 – items for clarification
>
> Hi Mark,
>
> I can show the items for clarification (relating to the dietary exposure part of the notice) during the discussion tomorrow.

Also, I've shared your email below mentioning a "statistical analysis" with my fellow GRN 1058 review team members.

Regards,

Paulette

From: Mark Itzkoff <mark@itzkofflaw.com>
Sent: Wednesday, September 14, 2022 2:53 PM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Subject: Re: [EXTERNAL] Re: GRN 001058 – items for clarification

Paulette,

Please go ahead and share those points during our discussion. I have already provided copies of our dietary intake discussion and the questions from your email to all of our participants. However, I do not think that they are the main points that need clarification.

During our previous discussions, your toxicologist requested that we perform a "statistical analysis" of the intake data as part of the CEDI calculation. I did not understand what statistical analysis she was requesting and the conference call was suggested so that she and Intertek could speak directly to each other.

In terms of the points you have outlined, I believe we will shortly be able to provide the information in your email. We have retained Intertek to provide the dietary intake estimate using the more recent NHANES data and the 90th percentile consumer. We will ask them to include the NHANES food codes.

We are looking forward to the discussion tomorrow.

Mark

On Wed, Sep 14, 2022 at 2:30 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Hi Mark,
>
> I am following up about the items for clarification (relating to the dietary exposure part of the notice) as noted below in my email of September 1, 2022; please let me know whether you/NABACO would like us to show these during the meeting OR whether you/NABACO prefer to do so. Thank you.
>
> Regards,
>
> Paulette
>
> ---
>
> **From:** Mark Itzkoff <mark@itzkofflaw.com>
> **Sent:** Tuesday, September 6, 2022 11:49 AM
> **To:** Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
> **Cc:** rusty.phillips@nabacoinc.com
> **Subject:** Re: [EXTERNAL] Re: GRN 001058 – items for clarification
>
>
>
> Paulette,
>
> If it is still available, we would like to schedule the conference call for Thursday

Sept 15.

Mark

On Thu, Sep 1, 2022 at 4:56 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Hi Mark,
>
> A couple of options during that timeframe. Currently, we would be available – Wednesday, Sept 14th at 11:15 am (ET) for 30 minutes OR Thursday, Sept 15th at 11:00 am (ET) for 30 minutes. Please let me know which time would work and I can schedule the meeting.
>
> During the meeting, we advise showing the items for clarification (relating to the dietary exposure part of the notice). If you/NABACO would like, we can show these during the meeting; unless you/NABACO prefer to do so. Please let me know. And, the following are the items relating to the dietary exposure part of the notice (with the number listed as N):
>
> N. In Part 3 of the notice, the notifier discusses the approach used to estimate the dietary exposure to PVOH from the intended uses in fruits and vegetables. We note that the estimates of dietary exposure provided by the notifier were based on food consumption data from the 1994-1996 Continuing Survey of Food Intake by Individuals and the mean quantities of food consumed by both eaters and non-eaters. We note that there are more recent food consumption data available from the National Health and Nutrition Examination Survey (NHANES) and that typically the more conservative *eaters-only* dietary exposure is used for the safety assessment.
>
> Considering the above, we recommend that the notifier:
>
> - Conduct a dietary exposure assessment using the more recent food consumption data available from the NHANES.
> - Provide estimates of eaters-only dietary exposure to PVOH from the intended uses specified in GRN 001058 as well as eaters-only cumulative exposure (the intended uses specified in GRN 001058 and all current uses), at the mean and 90th percentile for the U.S. population 2 years and older.
> - Provide a list of all NHANES food codes considered in the dietary exposure

assessment.

N. In section 3.3 Consumption Summary (page 14) the notifier considers the total intake of PVOH from both intended uses and existing uses. It is not clear if this means the notifier considers the intended uses for PVOH to be additional and/or substitutional to existing uses of PVOH. Please clarify.

Regards,

Paulette

From: Mark Itzkoff <mark@itzkofflaw.com>
Sent: Tuesday, August 23, 2022 4:49 PM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>; Rusty Phillips <rusty.phillips@nabacoinc.com>
Subject: Re: [EXTERNAL] Re: GRN 001058 – items for clarification

Paulette,

We have discussed the dietary estimate conference call with Intertek. They are available from 9 a.m. to noon on Sept 13 through the 16th.

Please let me know if any of these dates and times is acceptable for you.

Best regards,

Mark

On Tue, Aug 16, 2022, 10:25 AM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Hi Mark, Thanks for the update. ~Paulette
>
> ---
>
> **From:** Mark Itzkoff <mark@itzkofflaw.com>
> **Sent:** Tuesday, August 16, 2022 10:03 AM
> **To:** Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
> **Subject:** Re: [EXTERNAL] Re: GRN 001058 – items for clarification
>
>
>
> Paulette,
>
> I have not yet heard back from NABACO on their availability for the conference call. It is unlikely they will respond in time for a phone call this morning. I will let you know as soon as I have heard back from them.
>
> Mark
>
> On Tue, Aug 16, 2022 at 7:34 AM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:
>
> > Hi Mark,
> >
> > A couple of options for this week. Currently, we would be available Today, August 16th at 11:30 am (ET) for 30 minutes OR Thursday, August 18th at 9:00 am (ET) for 30 minutes.
> >
> > Please let me know which time would work and I can schedule a call.

Regards,

Paulette

From: Mark Itzkoff <mark@itzkofflaw.com>
Sent: Monday, August 15, 2022 11:59 AM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Subject: Re: [EXTERNAL] Re: GRN 001058 – items for clarification

Dr. Gaynor,

I would like to schedule a brief phone call to discuss where we are in providing a responses to FDA's questions on GRN 1058. Please let me know when you are available.

Thank you,

Mark Itzkoff

On Wed, Jul 27, 2022 at 4:19 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Hi Mark,
>
> Currently, we would be available Friday, July 29th at 1 pm (ET) for 30 minutes.
>
> If that time would work for you/NABACO, I can schedule a call. Please let me know.

Regards,

Paulette

From: Mark Itzkoff <mark@itzkofflaw.com>
Sent: Wednesday, July 27, 2022 11:53 AM
To: Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 001058 – items for clarification

Dr. Gaynor,

We would appreciate the opportunity to speak with you and discuss your request. As you know, NABACO is not the manufacturer of the PVOH and we want to be sure that the information we obtain from the manufacturer will adequately respond to your request.

Please let me know if you are available for a conference call with NABACO sometime this week.

Mark Itzkoff

On Tue, Jul 26, 2022 at 3:24 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Mark Itzkoff
>
> *By email*: MARK@ITZKOFFLAW.COM
>
> Dear Mr. Itzkoff,

As we continue with our evaluation of GRN 001058, we have identified items that require clarification. These items follow; *note pages cited below are based on the numbering system in the Table of Contents in GRN 001058*:

1. The notifier (NABACO LLC (NABACO)) provides the analytical results from the representative batches in Appendix I ("Analytical results from three non-consecutive lots along with Data for Lead"). We note that two of the batches are identified by consecutive numbers (N122005117 and N122005118) indicating that these batches are also consecutive. Please confirm that these two batches are non-consecutive or provide the analytical results from an additional non-consecutive batch.

In addition, we note that Appendix I includes the analytical results for lead from only two batches (N120075080 and N121085317). We typically request analytical results from a minimum of three non-consecutive batches to demonstrate that the notified substance meets the proposed specifications. Please provide the analytical results for lead from an additional non-consecutive batch.

2. On page 8, the notifier states that polyvinyl alcohol (PVOH) is manufactured by polymerizing vinyl acetate monomer (VAM) to polyvinyl acetate and subsequent controlled hydrolysis of the polyvinyl acetate to PVOH. We note that the notifier did not discuss the potential for the presence of residual VAM in the final ingredient. Please provide a statement on whether residual VAM is expected to be present in the PVOH, supported by analytical results from a minimum of three non-consecutive representative batches, and discuss if its presence is expected to result in a safety concern. In addition, please specify the analytical method used to analyze for VAM and the limit of detection (LOD) of the method.

3. On page 8, the notifier states that the polymerization reaction of VAM is initiated with a proprietary agent. Please specify the type of the proprietary agent used in the polymerization reaction, provide a statement regarding whether the proprietary agent is expected to be present is the final PVOH, and if yes, please indicate the residual levels and discuss if exposure to those levels presents a safety concern. In addition, please provide LOD for the analytical method used to analyze

for the proprietary agent and a statement that the method was validated for the intended use.

4. On page 7, the notifier states that where applicable the proposed specifications for PVOH listed in Table 2 on page 8 comply with those in the monograph for PVOH published in the Food Chemicals Codex (FCC, 2019). We note that the specifications in Table 2 do not include the particle size and identification reactions listed in the FCC monograph. In footnote 1 on page 7, the notifier states that the particle size is not relevant and is not measured because "In the NABACO application, the polymer will dissolve in an aqueous solution."

We consider that PVOH particle size is important in understanding its physical and chemical properties. Further, we note that the subject of GRN 001058 is a PVOH powder, not a solution. In order to comply with the specifications in the FCC we request that the notifier 1) include the particle size and identification reactions in the proposed specifications for PVOH, 2) provide a revised Table 2, and 3) provided analytical results from a minimum of three non-consecutive representative batches to demonstrate that the ingredient meets the specifications for particle size and identification reactions.

5. The specifications provided in Table 2 on page 8 include limits for acid value and ester value. We note that the results of batch analyses in Appendix I do not include the results for acid value or ester value. Please provide the analytical results for these specification parameters from a minimum of three non-consecutive batches.

6. Please confirm that the unit for 0.29 and 1.52 in footnote 2 on page 13 should be g/kg instead of mg/kg.

7. In Part 3 of the notice, the notifier discusses the approach used to estimate the dietary exposure to PVOH from the intended uses in fruits and vegetables. We note that the estimates of dietary exposure provided by the notifier were based on food consumption data from the 1994-1996 Continuing Survey of Food Intake by Individuals and the mean quantities of food consumed by both eaters and non-eaters. We note that there are more recent food consumption data available from the National Health and Nutrition Examination Survey (NHANES) and that typically the more conservative *eaters-only* dietary exposure is used for the safety assessment.

Considering the above, we recommend that the notifier:

- Conduct a dietary exposure assessment using the more recent food consumption data available from the NHANES.
- Provide estimates of eaters-only dietary exposure to PVOH from the intended uses specified in GRN 001058 as well as eaters-only cumulative exposure (the intended uses specified in GRN 001058 and all current uses), at the mean and 90th percentile for the U.S. population 2 years and older.
- Provide a list of all NHANES food codes considered in the dietary exposure assessment.

8. In section 3.3 Consumption Summary (page 14) the notifier considers the total intake of PVOH from both intended uses and existing uses. It is not clear if this means the notifier considers the intended uses for PVOH to be additional and/or substitutional to existing uses of PVOH. Please clarify.

9. In support of the safety of PVOH, the notifier reports performing a comprehensive scientific literature search through September 2021 (page 25) but has not provided the details of this search. Please provide additional details of the literature search(es), including search engine(s) used, and search terms. Also, please confirm that no additional publicly available information were found since that last literature search that might contradict the current GRAS conclusion.

Please do not send a revised/completely rewritten notice (or any part of the notice, including any Appendix of the notice). As a reminder, confidential data and information cannot be determinant of safety. If you or NABACO have any questions about the items that require clarification, please let me know. FDA respectfully requests a complete response within 10 business days. If unable to complete the response within that timeframe, please contact me. Thank you.

Sincerely,

Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

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Mark L. Itzkoff

The Law Office of Mark L. Itzkoff
202 600-7704

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202 600-7704, MARK@ITZKOFFLAW.COM

November 15, 2022

Dr. Paulette Gaynor
Office of Food Additive Safety
CFSAN
Food and Drug Administration
5100 Campus Drive
College Park, MD 20740

Re: GRASN 001058 Clarifications

Dear Dr. Gaynor,

This letter is intended to supply the clarifications requested in your July 26 email for the NABACO GRAS Notice for polyvinyl alcohol, GRASN 001058. For clarity, the questions are reprinted below followed by our clarification.

1. The notifier (NABACO LLC (NABACO)) provides the analytical results from the representative batches in Appendix I ("Analytical results from three non-consecutive lots along with Data for Lead"). We note that two of the batches are identified by consecutive numbers (N122005117 and N122005118) indicating that these batches are also consecutive. Please confirm that these two batches are non-consecutive or provide the analytical results from an additional non-consecutive batch.

Analytical results from two additional non-consecutive batches, 22015129 and 120075080, are included in Appendix I to this letter. Please note that due to laboratory limitations, these tests were conducted in two separate labs. The initial tests were conducted by our supplier's laboratory in Germany. For those tests that could not be performed in Germany, we contracted with Element Materials Technology. The two laboratories tested different batches of PVOH but combined they performed all the tests in the Food Chemicals Codex Monograph.

2. On page 8, the notifier states that polyvinyl alcohol (PVOH) is manufactured by polymerizing vinyl acetate monomer (VAM) to polyvinyl acetate and subsequent controlled hydrolysis of the polyvinyl acetate to PVOH. We note that the notifier did not discuss the potential for the presence of residual VAM in the final ingredient. Please provide a statement on whether residual VAM is expected to be present in the PVOH, supported by analytical results from a minimum of three non-consecutive representative batches, and discuss if its presence is expected to result in a safety concern. In addition, please specify the

analytical method used to analyze for VAM and the limit of detection (LOD) of the method.

There is no reasonable expectation that vinyl acetate monomer will be present in the finished PVOH polymer. As detailed in Section 2.3 of the GRAS Notice, Manufacturing Process, PVOH is produced by first polymerizing the VAM to form polyvinyl acetate then hydrolyzing the polyvinyl acetate using sodium hydroxide to produce PVOH. Any residual VAM will react with the sodium hydroxide to form vinyl alcohol. Due to the smaller size of VAM when compared to polyvinyl acetate, the VAM is more highly reactive and will hydrolyze faster than the polyvinyl acetate. Thus, no residual VAM is expected.

We have asked our supplier for data confirming that no VAM is detected using a test method sensitive to the presence of the monomer at 1 part per million. We will forward the additional data from our supplier as soon as it is received. While we are waiting for that information, we arranged with Element to run residual monomer on the PVOH used in the analytical tests reported in Appendix I. The test method available to Element was sensitive to VAM at concentrations of 2.5 ppm or greater. As shown in the report attached as Appendix II, no residual VAM was detected.

Using the Element data and conservatively assuming that VAM might be present at the LOD we have calculated the potential consumer exposure from the NABACO applications. As shown in Appendix IV, we have calculated that the exposure to PVOH for the 90^{th} percentile adult consumer due to our application would be 75 mg/day. Assuming that the VAM is present at the limit of detection, the dietary concentration of VAM from this application would be:

(75 mg/day)(2.5 ppm)/(3000 g/day) = 0.063 parts per trillion (ppt)

This exposure is 4 orders of magnitude below the limit set forth in FDA's Threshold of Regulation, 21 CFR 170.39.

In addition, we note that there is no requirement for residual VAM testing in the FCC PVOH monograph. NABACO has determined that the Impurities and Specific Tests set forth in the monograph (with the exception of the particle size test as discussed in the response to question 4, below) are sufficient to establish that the PVOH used in the NABACO application is of a suitable purity for our application.

3. On page 8, the notifier states that the polymerization reaction of VAM is initiated with a proprietary agent. Please specify the type of the proprietary agent used in the polymerization reaction, provide a statement regarding

whether the proprietary agent is expected to be present is the final PVOH, and if yes, please indicate the residual levels and discuss if exposure to those levels presents a safety concern. In addition, please provide LOD for the analytical method used to analyze for the proprietary agent and a statement that the method was validated for the intended use.

The agent used to hydrolyze the polyvinyl alcohol is sodium hydroxide. When disassociated, the agent will form sodium (Na^+) and hydroxyl (OH^-) ions. These ions are commonly found in salt water and most aqueous foods.

The precise amount of sodium hydroxide (NaOH) used to produce the PVOH used in this application is a trade secret and was not provided by our supplier. However, assuming that the concentration does not exceed 1 percent of the polymer we can provide an estimate of the dietary contribution of sodium due to the proposed use of PVOH.

As shown on page 13 of the GRASN, the estimated daily intake of PVOH from this application is 75 mg/day. If sodium hydroxide is used at 1% of the polymer, the maximum quantity of NaOH in the polymer would be:

(75 mg)(1%) = 0.75 mg

Since sodium comprises approximately 58% of NaOH, the quantity of sodium in the polymer would be:

(0.75 mg)(58%) = 0.43 mg.

The 2020-2025 Dietary Guidelines for Americans[1] recommend a daily sodium intake for adults of less than 2,300 mg. However, most Americans consume significantly more sodium, more than 3,400 mg per day.[2] Thus, the potential dietary impact of sodium hydroxide in this application is 0.018% of the recommended maximum and less than 0.015% of the average daily sodium consumption.

4. On page 7, the notifier states that where applicable the proposed specifications for PVOH listed in Table 2 on page 8 comply with those in the monograph for PVOH published in the Food Chemicals Codex (FCC, 2019). We note that the specifications in Table 2 do not include the particle size and identification reactions listed in the FCC monograph. In footnote 1 on page 7, the notifier states that the particle size is not relevant and is not measured because "In the

[1] Available online at https://www.dietaryguidelines.gov/. Last accessed October 24, 2022.
[2] CDC, *About Sodium*, available online at https://www.cdc.gov/salt/index.htm. Last accessed on October 24, 2022.

> NABACO application, the polymer will dissolve in an aqueous solution." We consider that PVOH particle size is important in understanding its physical and chemical properties. Further, we note that the subject of GRN 001058 is a PVOH powder, not a solution. In order to comply with the specifications in the FCC we request that the notifier 1) include the particle size and identification reactions in the proposed specifications for PVOH, 2) provide a revised Table 2, and 3) provided analytical results from a minimum of three non-consecutive representative batches to demonstrate that the ingredient meets the specifications for particle size and identification reactions.

As noted in Section 1.4, intended Conditions of Use, in the NABACO application, PVOH will not be used in the powder form provided by our supplier. Rather, it will be dissolved in an aqueous solution that is then applied to the exterior of fruits and vegetables to form a continuous film. No PVOH powder will be present in the final application. Thus, the subject of the GRAS Notice is PVOH film, not PVOH powder. Under Section 201(s) of the Federal Food, Drug, and Cosmetic Act, the GRAS exclusion applies "generally recognized … to be safe under the conditions of its intended use; …"[3] Therefore, the GRAS evaluation should be made on the PVOH film rather than the PVOH powder.

We note that the Food Chemicals Codex monograph for PVOH includes a sieve screening test requiring that 99% of PVOH powder pass through a 100 mesh screen. NABACO has determined that this test is not applicable to PVOH used in our application in that the PVOH will be dissolved in water and the low viscosity solution will pass completely through a 100 mesh screen. Further, NABACO has determined that for substances that will be dissolved in solution, the particle size does not have any relevance to the substance's safety.[4]

Section 2.3 of the GRAS Notice describes the PVOH manufacturing process. Specifically it states that "[d]uring saponification, the resulting PVOH precipitates from the methanol solution and forms a gel. The gel is subsequently cut into granules. Following this the PVOH is washed and dried." Thus the particle size is a function of how the gel is cut into granules rather than a function of the polymerization process. While the equipment used to produce the PVOH used in this application results in a larger particle size that does not meet the particle size limit in the FCC Monograph, the Notifier has concluded that this difference does not impact the GRAS status.

---

[3] 21 USC §321(s).

[4] It should be noted that in addition to safety issues, the Food Chemicals Codex was originally used to help establish non-safety related parameters as well as purity. It appears that particle size was included in the PVOH monograph to ensure uniform processability rather than to address any consumer safety issue.

During our discussions with FDA one of the reviewers commented that the particle size information is needed to determine if the proposed use will introduce any nanoparticles into the diet. Our supplier has stated that "we confirm that Nano Materials are neither intentionally used to produce Kuraray Poval™ nor added after the manufacturing processes. In addition, Nano Materials are not handled in the production plant for Kuraray Poval™ and the production plant for Kuraray Poval™ is dedicated to polyvinyl alcohol production only." Further, our supplier has provided the following molecular weight data confirming that the amount of polymer with a molecular weight below 500 Newtons is less than 0.01%

Table 1
Molecular Weight Distribution

Grade Name	Mw	Mn	Mw/Mn	<Mw 1000	<Mw 500
6-88	83200	32000	2.6	~0.06%	<0.01%

5. The specifications provided in Table 2 on page 8 include limits for acid value and ester value. We note that the results of batch analyses in Appendix I do not include the results for acid value or ester value. Please provide the analytical results for these specification parameters from a minimum of three non-consecutive batches.

Notifier has had 4 lots of PVOH tested by Element for acid and ester values. This testing was performed in two phases. Phase one tested lots 22015118, 22015117 and 22015126. The second phase tested lot 120075080. These reports are attached in Appendix III. Results from all four lots demonstrate compliance with the acid value and ester value limits in the FCC monograph.

6. Please confirm that the unit for 0.29 and 1.52 in footnote 2 on page 13 should be g/kg instead of mg/kg.

We confirm the units for 0.29 and 1.52 in footnote 2 on page 13 should be g/kg instead of mg/kg.

7. In Part 3 of the notice, the notifier discusses the approach used to estimate the dietary exposure to PVOH from the intended uses in fruits and vegetables. We note that the estimates of dietary exposure provided by the notifier were based on food consumption data from the 1994-1996 Continuing Survey of Food Intake by Individuals and the mean quantities of food consumed by both eaters

and non-eaters. We note that there are more recent food consumption data available from the National Health and Nutrition Examination Survey (NHANES) and that typically the more conservative eaters-only dietary exposure is used for the safety assessment.

Considering the above, we recommend that the notifier:

- Conduct a dietary exposure assessment using the more recent food consumption data available from the NHANES.
- Provide estimates of eaters-only dietary exposure to PVOH from the intended uses specified in GRN 001058 as well as eaters-only cumulative exposure (the intended uses specified in GRN 001058 and all current uses), at the mean and 90th percentile for the U.S. population 2 years and older.
- Provide a list of all NHANES food codes considered in the dietary exposure assessment.

NABACO has contracted with Intertek Health Sciences, Inc. to perform the updated dietary exposure estimate as outline above. The report was prepared using data from the 2017 – 2018 NHANES. The key conclusions from the Intertek report are as follow:

- The EDI from the applications outlined in GRASN 1058 for adults at least 20 years old is 75 mg/day (1.04 mg/kg bw/day) for the 90th percentile consumer. The highest EDI was for infants at 3.34 mg/kg bw/day.[5]
- A new EDI for applications set forth in GRASN 767 for adults was determined to be 2.33 mg/kg bw/day, significantly less than the 45.16 mg/kg bw/day reported in GRASN 767.[6]
- The CEDI for all of the PVOH applications ranges from 1.56 mg/kg bw/day for teenagers to 4.25 mg/kg bw/day for children 2 to 5 years.[7]

The Intertek report detailing the results of this estimate are provided in Appendix IV. Intertek found that the EDI from the fruit and vegetable uses set forth in the NABACO Notice ranged from 1.04 mg/kg bw/day for adults 20 years and older to 3.34 mg/kg bw/day for children 2 to 5 years old. The level for the total population of consumers was calculated to be 1.39 mg/kg bw/day. These levels are substantially higher than the amount in the NABACO Notice. We believe that this is in part due to the fact that Intertek calculated the dietary exposure for each edible peel fruit and vegetable individually and then added them together. Clearly, this exaggerates the possible dietary consumption since it theorizes

[5] Intertek, *ESTIMATED CUMULATIVE DAILY INTAKE OF POLYVINYL ALCOHOL BY THE U.S. POPULATION FROM ALL DIETARY USES (2017 2018 NHANES)*, November 15, 2022, Table 4.1-1.
[6] *Id.* Table 4.2-1.
[7] Id. Table 4.3-1.

consumers who are 90th percentile eaters for every fruit and vegetable. Using the CEDI previously submitted to FDA in GRAS 767, the new CEDI for an adult 20 years and older[8] would be:

(46.08 mg/kg bw/day) + (1.04 mg/kg bw/day) = 47.12 mg/kg bw/day.

However, Intertek also prepared a revised CEDI for the applications set forth in GRASN 767 and the NABACO Notice which provides a more accurate estimate of consumer exposure to PVOH. Intertek calculated that the dietary exposure to PVOH to 90th percentile consumers resulting from the applications set forth in GRASN 767 using the most recent dietary survey, 2017 – 2018 NHANES. Intertek calculates that the consumer-only 90th percentile intake due to the applications in GRASN 767 would be only 1.04 mg/kg bw/day. This is less than 2.5% of the EDI estimated in GRASN 767, 45.16 mg/kg bw/day.[9] We believe that this may be due to more detailed data from NHANES that allowed Intertek to exclude non-relevant subcategories of the GRASN 767 applications.

Using the new dietary exposure for GRASN 767 Intertek estimates the CEDI from these two Notices would be 2.35 mg/kg bw/day. Factoring in the applications detailed in GRASN 000141 for the use of PVOH in dietary supplements and pharmaceuticals, 6 mg/kg bw/day, the CEDI would be 8.35 mg/kg bw/day.

8. In section 3.3 Consumption Summary (page 14) the notifier considers the total intake of PVOH from both intended uses and existing uses. It is not clear if this means the notifier considers the intended uses for PVOH to be additional and/or substitutional to existing uses of PVOH. Please clarify.

NABACO considers the dietary intake from the proposed would be additional to the GRASN 767 applications. There is no crossover between the two Notices.

9. In support of the safety of PVOH, the notifier reports performing a comprehensive scientific literature search through September 2021 (page 25) but has not provided the details of this search. Please provide additional details of the literature search(es), including search engine(s) used, and search terms. Also, please confirm that no additional publicly available information were found since that last literature search that might contradict the current GRAS conclusion.

[8] Monosol did not provide an EDI for populations other than adult. GRASN 767, Page 12.
[9] Monosol, GRASN 767, Page 12.

For the published studies we searched common databases, including PubMed, PubMed Central, MedlinePlus, European Chemical Agency (ECHA) and general internet searches, such as Google Scholar, etc. The key search terms used included: polyvinyl alcohol, vinyl alcohol polymer, PVOH, 9002-89-5, methanol, methyl acetate, toxicokinetics, toxicity. The refining search terms (depending on output of key term search) included absorption, distribution, metabolism, excretion, oral, ingestion, acute, subacute, subchronic, chronic, carcinogenicity, tumor promotion, genotoxicity, mutagenicity, reproductive, developmental, irritation, hypersensitivity, allergy, neurotoxicity.

In the search results, we primarily focused on publications or information that appeared since 2019, as we presumed that majority of the earlier relevant publication or information may have been considered and included in GRN 927 that was submitted in March 2020.

We have also performed a recent search for any new publication from September 2021 to August 1, 2022 and we confirm that no additional information or safety related any new publication was found that contradicts the current GRAS conclusion.

We trust this letter fully responds to your request for clarification. Should you have any additional questions, please do not hesitate to contact me.

Sincerely,

Mark L. Itzkoff

Attachments

APPENDIX I

Confidential Report

Prepared for:

Mark Itzkoff

Law office of Mark Itzkoff

mark@itzkofflaw.com

Project Code 22-93466-B
Issued 30 September 2022

Method Development for Quantifying Residual Vinyl Acetate Monomer in Polyvinyl Alcohol

Thank you for contacting Element Ann Arbor for the method development to quantify residual vinyl acetate monomer in polyvinyl alcohol. Following are the results, methodology, and data associated with our Method development.

Table 1: Sample Description

Element Ann Arbor Sample ID	Sample Description
06SEP22TH3986	Kurary, PVOH 5-88FA, Lot: 120075080, Plastic Pellets, White, 1 bag

Executive Summary

The goal of this analysis was to develop HPLC-DAD method for the quantitation of the residual vinyl acetate monomer in polyvinyl alcohol. The method was successfully developed and was tested the following parameters: System Suitability, Specificity, Linearity, Limit of Detection (LOD), Limit of Quantification (LOQ) and Accuracy. The detailed results of the development are shown in Table 2.

Table 2: Method Development, and Sample analysis Results

Qualification Parameter	Proposed Acceptance Criteria	Result		
System Suitability	The % RSD for the Vinyl acetate concentration in the six and all injections of Working vinyl acetate Standard (20 µg/mL) should be not more than 10 %	%RSD of first six injections: 2 %RSD of all replicate injections: 3 USP Tailing Factor: 1.02567		
	The USP tailing factor for the first injections of the Working Vinyl acetate peak Standard (20 µg/mL) should be not more than 2.0 for the Vinyl acetate peak			
Specificity	There should be no significant interference at the retention time of Vinyl acetate peak	There was no significant interference at the retention time of Vinyl acetate peak		
Linearity	The correlation coefficient ® should be not less than 0.99	Correlation Coefficient: 1.00		
Limit of Detection (2.5 ppm)	Average Signal to Noise should be ≥ 3.	Average S/N: 27.31008		
Limit of Quantification (5.0 ppm)	Average Signal to Noise should be ≥ 10.	Average S/N : 79.46681 %RSD: 3		
	%RSD (Concentration) ≤ 20%			
Accuracy 50% - 150% (10 ppm to 30 ppm)	Mean % Recovery at all levels must be 80 – 120% (n=3) RSD ≤ 20%	**Level**	**% Mean Recovery**	**% RSD**
		50%	89.1	7.5
		100%	91.5	3.1
		150%	90.1	3.1
Sample Analysis	Report the residual Vinyl acetate monomer content	None Detected		

Quality Statement

The work described in this report was conducted in compliance with the principles of current Good Manufacturing Practice. The following compliance exceptions were noted: results have been generated using method(s) that were not validated at this facility.

Analytical Testing

Initial Observations

The samples were received for analysis on 06 September 2022. The sample consisted of white plastic pellets in a transparent plastic bag. A photograph of the samples "As Received" can be found in Figure 1.

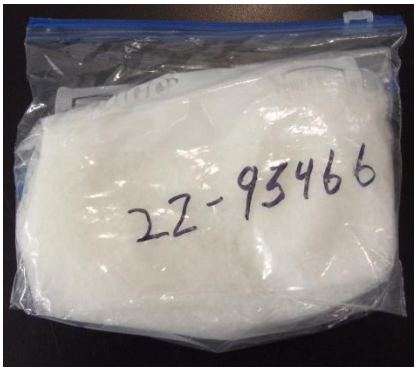

Figure 1: Photograph of the Sample "As Received"

Method Development

Solution Preparations

Solution Preparations

Mobile Phase A (100% purified water): Measured and transferred 2000 mL of purified water into a mobile phase container. The solution was sonicated to degas.

Mobile Phase B (100% ACN): Measured and transferred 2000 mL of Acetonitrile into suitable mobile phase container. The solution was mixed well and sonicated to degas.

Diluent (100% Methanol): Measured and transferred 1000 mL of methanol into a mobile phase container. The solution was sonicated to degas

Standard Preparations

Standard Stock Solution-1 (1000 ppm): Approximately 10 mL of diluent was added to a 100 mL volumetric flask. Accurately weighed 100.45 mg of vinyl acetate in a tarred 100 mL volumetric flask with the diluent. Diluted to volume with diluent and mixed well by vortexing.

Standard Stock Solution-2 (100 ppm): Using a glass pipette, 1mL of the standard stock solution (1000 ppm) was transferred into a 10 mL volumetric flask. Diluted to volume with diluent and mixed well by vortexing.

Working Standard (20 ppm): Using a glass pipette, 2.0 mL of the standard stock solution-2 (100 ppm) was transferred into a 10 mL volumetric flask. Diluted to volume with diluent 1 and mixed well by vortexing.

Linearity Standard Dilutions:
Using a glass pipette, following concentrations of Linearity standard and Limit of detection (2.5 ppm) dilutions were prepared using standard stock solution-2 into respective volumetric flasks as shown in Table 3.

Table 3: Preparation of Vinyl Acetate Standard Dilutions

Standard ID	Concentration (ppm)	Volume of standard (mL)	Final volumetric flask volume (mL)
1	30	3 mL of 100 ppm	10
2	20	2 mL of 100 ppm	10
3	15	1.5 mL of 10 ppm	10
4	10	5 mL of 20 ppm	10
5	7.5	5 mL of 15 ppm	10
6	5 (LOQ)	5 mL of 10 ppm	10
7	2.5 (LOD)	5 mL of 5 ppm	10

Sample stock solution (10,000 ppm):

Into a tared weigh boat, 502.22 mg of sample was weighed and transferred to a 50mL volumetric flask. Approximately 10mL of purified water was added to the volumetric flask and sonicated for about 30 minutes until the solid was completely dissolved. The solution was cooled to room temperature and diluted to volume with diluent.

Sample Control Solution (2000 ppm): Using a 2mL volumetric pipette, 2 mL of stock sample was transferred into a 10 mL volumetric flask. Diluted to volume with diluent.

Accuracy Preparations:
Using a glass pipette, following concentrations of accuracy preparation solutions were prepared using sample control solution and 10ppm standard stock and transferred into respective 10mL volumetric flasks as shown in Table 4.

Table 4: Preparation of Vinyl Acetate Accuracy Solutions

Concentration	Volume of standard (mL)		Final volume (mL)
	Sample stock solution (10,000 ppm)	Standard Stock Solution-2 (100 ppm)	
50% accuracy sample (2000 ppm sample + 10 ppm Vinyl acetate standard)	2	1	10
100% accuracy sample (2000 ppm sample + 20 ppm Vinyl acetate standard)	2	2	10
150% accuracy sample (2000 ppm sample + 30 ppm Vinyl acetate standard)	2	3	10

Instrument Conditions

Instrument:	Agilent 1100 Series HPLC with DAD Detector
Column:	Prodigy 5µm C8 150 Å, 250mm × 4.6mm
Flow Rate:	1 mL/minute
Column Temperature:	40 °C
Run Time:	15 minutes
Injection Volume:	20 µL
Detection:	DAD , 205 nm, 4 nm bandwidth
HPLC Gradient: isocratic	

Time (Minutes)	MPA (%)	MPB (%)
0.00	70	30
15	70	30

Results and Discussion

System Suitability

The system suitability was demonstrated by injecting six injections of the standard solution (20 ppm). The peak area of Vinyl acetate in each injection was analyzed for % RSD and the first six injections were analyzed for the USP tailing factor. The system suitability results are shown in Table 7 and the representative chromatography of vinyl acetate standard (20 ppm)) can be seen in Figure 2

Table 7: System Suitability Results

Injection	Vinyl acetate (20 ppm)		
	Area (mAU*s)	Concentration (ppm)	Tailing
1	1653.17594	21.9	1.02567
2	1614.94060	21.4	
3	1627.20613	21.6	
4	1583.53767	21.0	
5	1584.43928	21.1	
6	1605.81495	21.3	
Average	1611.51910	21.4	
STDEV	26.6	0.3	
%RSD	1.65	1.56	
7	1569.31600	20.9	
8	1633.64884	21.7	
9	1518.02078	20.2	
Average	1598.03566	21.2	
STDEV	43.2	0.5	
%RSD	2.7	2.6	

Conclusion: The % RSD for the vinyl acetate peak in the first six and all injections of standard solution (20 ppm) was not more than 10. The USP tailing factor for the first injection of the standard solution (20 ppm) was not more than 2. All system suitability criteria were met, establishing that the method and system are suitable for analyzing Vinyl acetate.

Specificity

The specificity of method was demonstrated by showing no interference from the Diluent at the retention time of vinyl acetate. The representative chromatography of the Diluent, Sample Solution (2000 ppm of vinyl acetate) and Working Standard (20 ppm) can be seen in Figures 2, 11, and 15.

Conclusion: There was no inference at the retention time of vinyl acetate in the blank preparation. The method was demonstrated to be specific for vinyl acetate.

Linearity

The linearity of the response of vinyl acetate was determined by analyzing vinyl acetate standard solution with concentrations ranging from 30 ppm to 5 ppm of vinyl acetate. The area response of the vinyl acetate Acid peak in the standards were plotted against the concentration of vinyl acetate standard, and the correlation coefficient (r) of the line was determined. The results are presented in Table 8. The graph of the linearity standards is shown in Figure 10, and the representative chromatography for each linearity solution can be seen in Figures 4– 10.

Table 8: Linearity Results

Linearity		
Level	**Concentration (ppm)**	**Area (mAU*s)**
25%	5.02	355.49377
38%	7.53	504.95319
50%	10.05	617.72556
75%	15.07	1120.26979
100%	20.09	1539.21684
150%	30.14	2302.07586
	Slope	79.7875
	Intercept	-95.5153
	Correlation	1.00
	R^2	1.00

Conclusion: The correlation coefficient of the vinyl acetate peak was not less than 0.98. The method was demonstrated to be linear between 5 ppm to 30 ppm vinyl acetate.

Limit of Detection (LOD)

The Limit of Detection was determined by injecting six replicates of the Limit of Detection solution (2.5 ppm) and measuring the signal-to-noise ratio (S/N) of the vinyl acetate peak. The S/N ratios for the vinyl acetate peaks in all injections are presented in Table 8. Representative chromatogram of vinyl acetate standard (2.5 ppm) can be seen in Figure 3.

Table 8: Limit of Detection Results

LOD (2.5 ppm)		
Replicate	**Area (mAU*s)**	**S/N**
1	196.33356	20.53879
2	208.15851	30.52422
3	199.20750	14.74359
4	237.87071	26.05188
5	169.90208	33.68621
6	198.14935	38.31581
Average	201.60362	27.31008

Conclusion: The S/N ratio of the vinyl acetate peak in the replicate injections of LOD samples was found to be in the range of 14 to 30 with an average S/N of 27.31008. The Limit of Detection for vinyl acetate peaks was determined to be 2.5 ppm.

Limit of Quantitation (LOQ)

The Limit of Quantitation was determined by injecting six replicates of the Limit of Quantitation Solution (5.0 ppm) and measuring the S/N ratio of the vinyl acetate peak. Additionally, the %RSD of the peak areas was calculated. The S/N ratios and peak areas for each injection are presented in Table 9. Representative chromatography of vinyl acetate standard (5 ppm) can be seen in Figure 4.

Table 9: Limit of Quantification Results

LOQ (5.0 ppm)			
Replicate	**Vinyl acetate area**	**Vinyl acetate (concentration in ppm)**	**S/N**
1	375.48161	5.9	201.40286
2	343.70041	5.5	61.53333
3	359.46350	5.7	51.59621
4	350.53843	5.6	31.90301
5	365.03345	5.8	75.53669
6	338.74522	5.4	54.82877
Average	355.49377	5.7	79.46681
STDEV	13.7872	0.1728	61.4029
%RSD	3.9	3.1	77.3

Conclusion: The S/N ratio of the vinyl acetate peak in the replicate injections of LOQ samples was found to be in the range of 31 to 201 with an average S/N of 79.46681 and the %RSD for the vinyl acetate peak areas was 4. The Limit of Quantitation for vinyl acetate peaks was determined to be 5.0 ppm.

Accuracy:

The accuracy of method was demonstrated by spiking the sample stock and standard solution (100 ppm) at three different levels; 50 % (10 ppm), 100 % (20 ppm), and 150 % (30 ppm). Each sample level was prepared in triplicate. Accuracy results for vinyl acetate are shown in Table 10. Representative chromatography for each sample preparation can be seen in Figures 11 – 14.

Table 10: Accuracy Results

Accuracy Results								
Level	**Level**	**Amount Added (ppm)**	**Area (mAU*s)**	**Amount Recovered (ppm)**	**%Recovery**	**Mean %Recovery**	**STDEV**	**%RSD**
50%	**10 ppm - 1**	10.05	760.73856	9.48	94	89.1	7	7.5
	10 ppm - 2	10.05	736.74587	9.18	91			
	10 ppm - 3	10.05	657.31030	8.19	82			
100%	**20 ppm - 1**	20.09	1494.19475	18.63	93	91.5	3	3.1
	20 ppm - 2	20.09	1507.87468	18.80	94			
	20 ppm - 3	20.09	1422.69652	17.74	88			
150%	**30 ppm - 1**	30.14	2104.67701	26.24	87	90.1	3	3.1
	30 ppm - 2	30.14	2187.14120	27.27	90			
	30 ppm - 3	30.14	2239.56314	27.92	93			

Conclusion: The % RSD of the vinyl acetate recovery in the triplicate preparations was not more than 20 % and the mean % recovery was between 80 % – 120 % for each level. The method was demonstrated to be accurate for vinyl acetate.

Figures

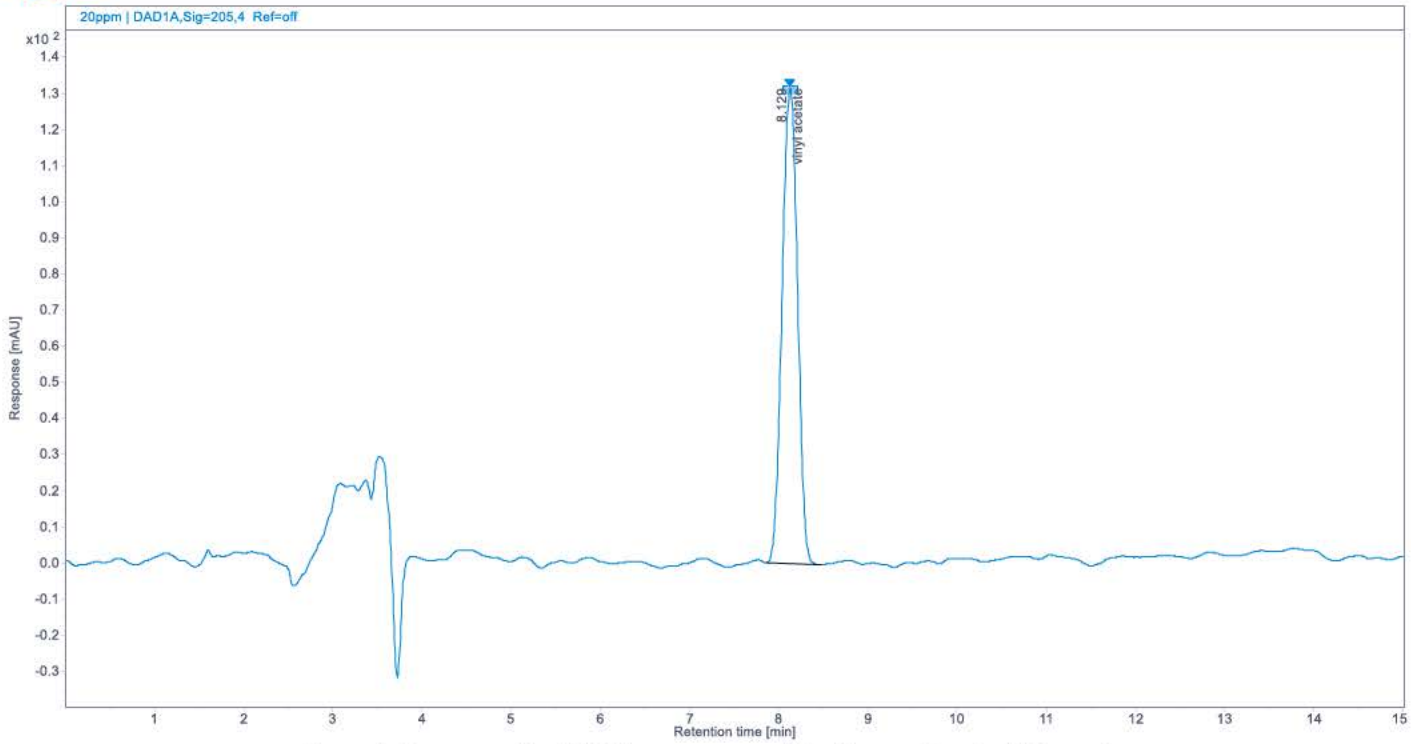

Figure 2: Representative HPLC Chromatogram of Vinyl Acetate Standard (20 ppm)

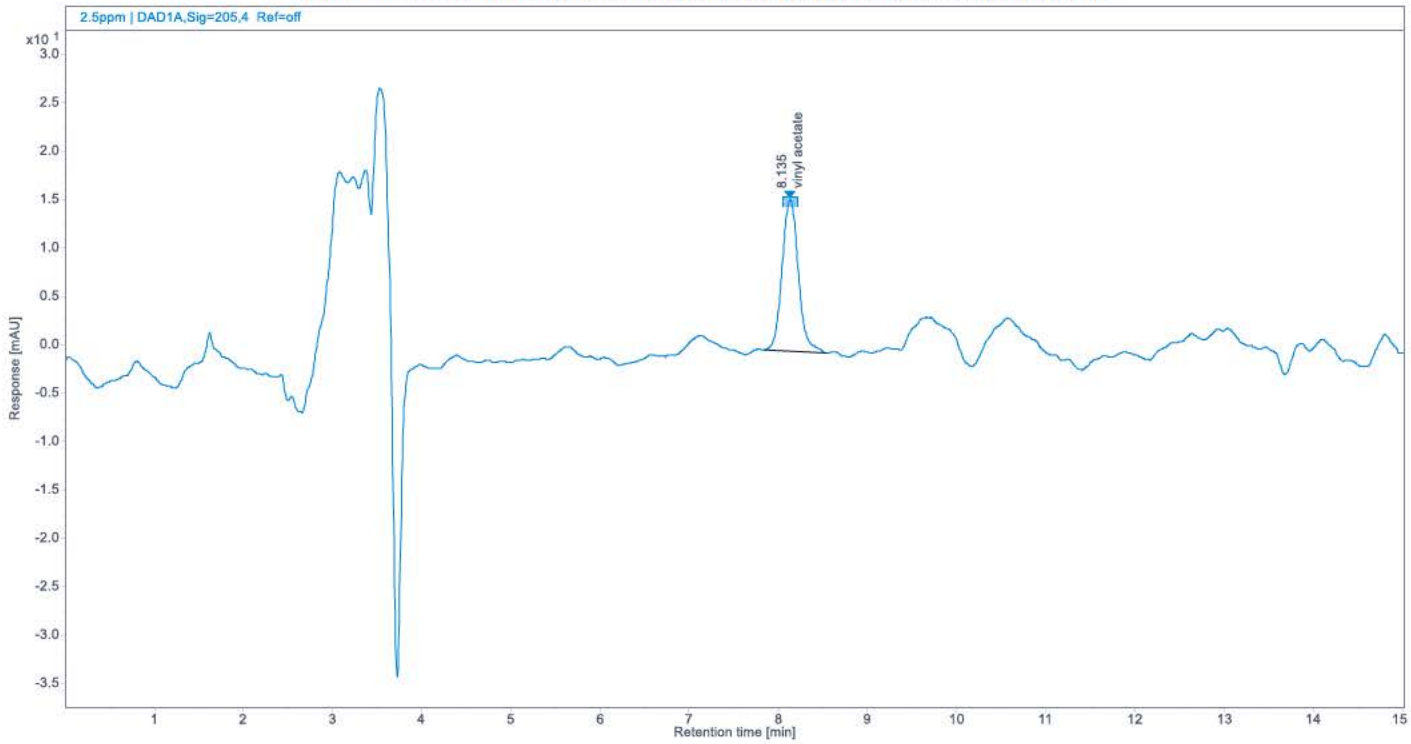

Figure 3: Representative HPLC Chromatogram of 2.5 ppm Linearity Solution

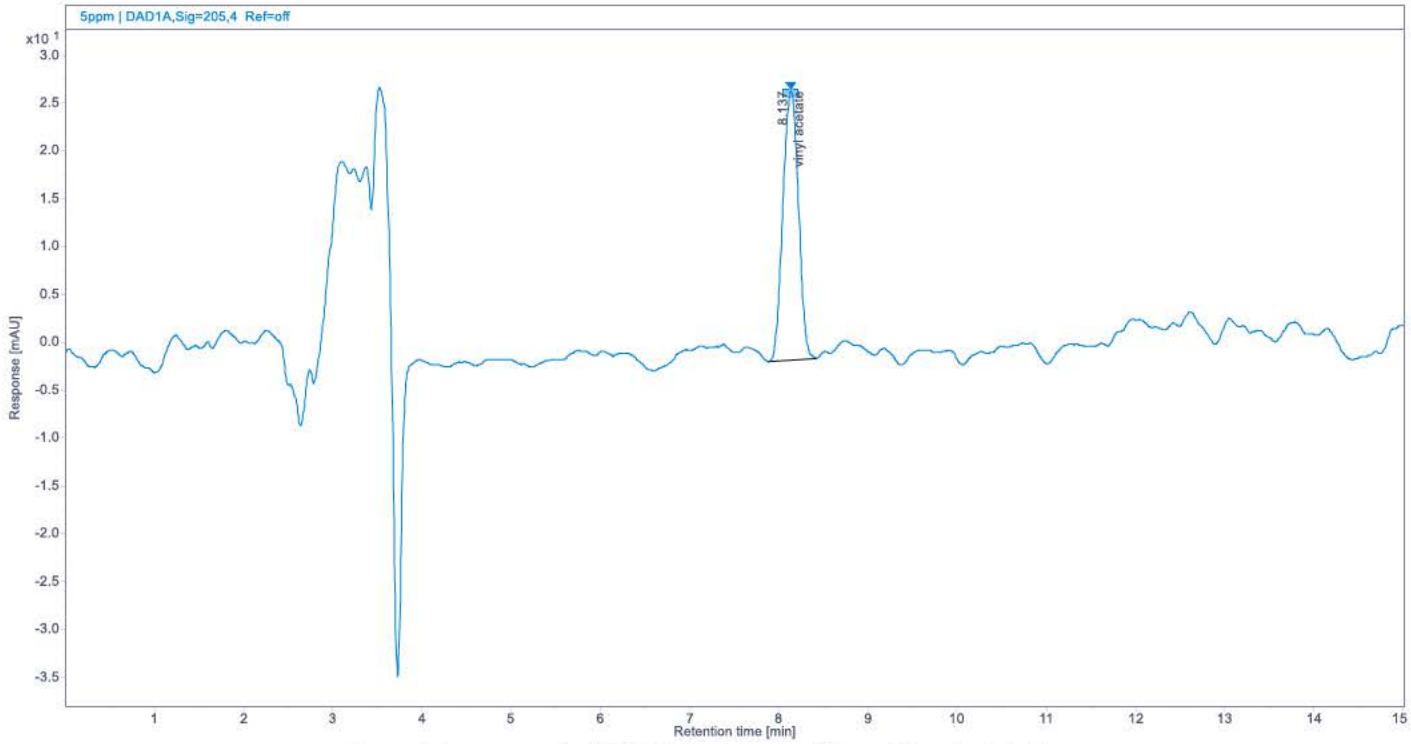

Figure 4: Representative HPLC Chromatogram of 5 ppm Linearity Solution

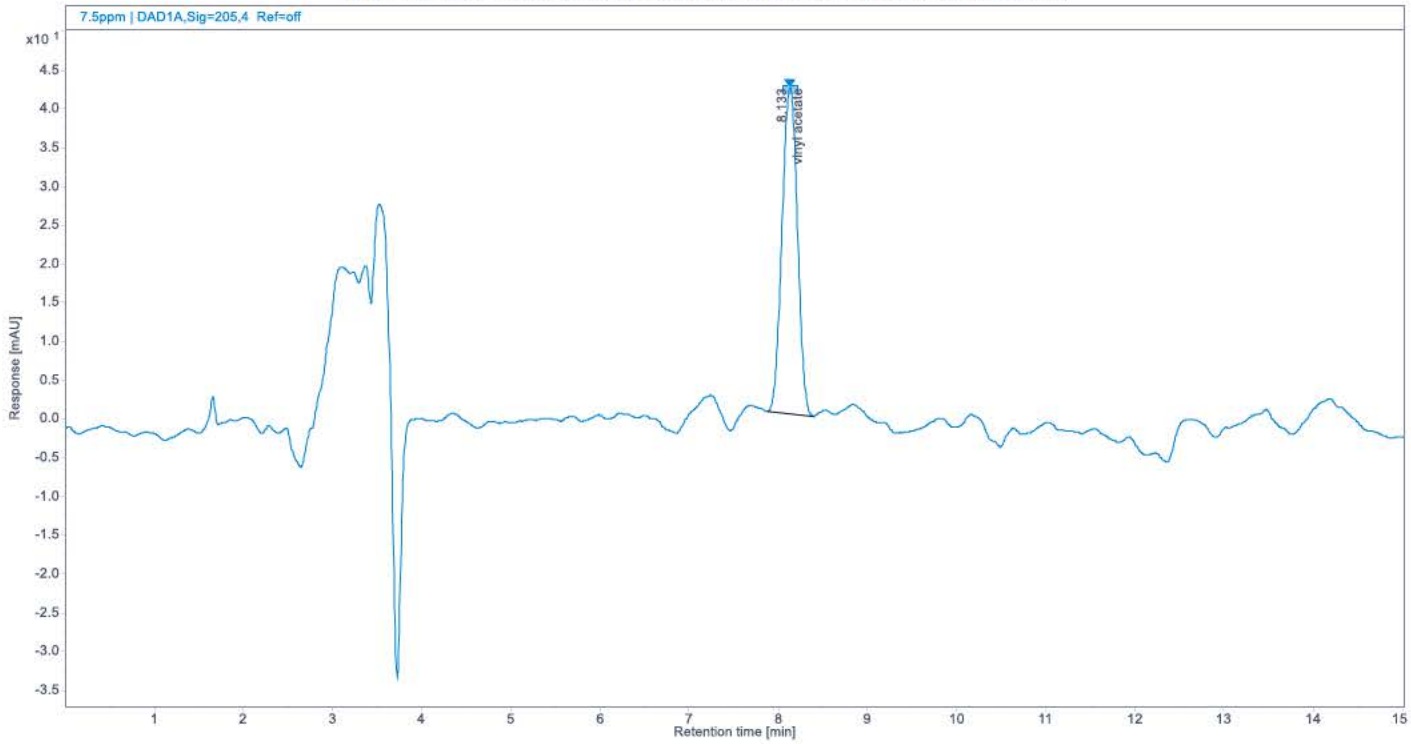

Figure 5: Representative HPLC Chromatogram of 7.5 ppm Linearity Solution

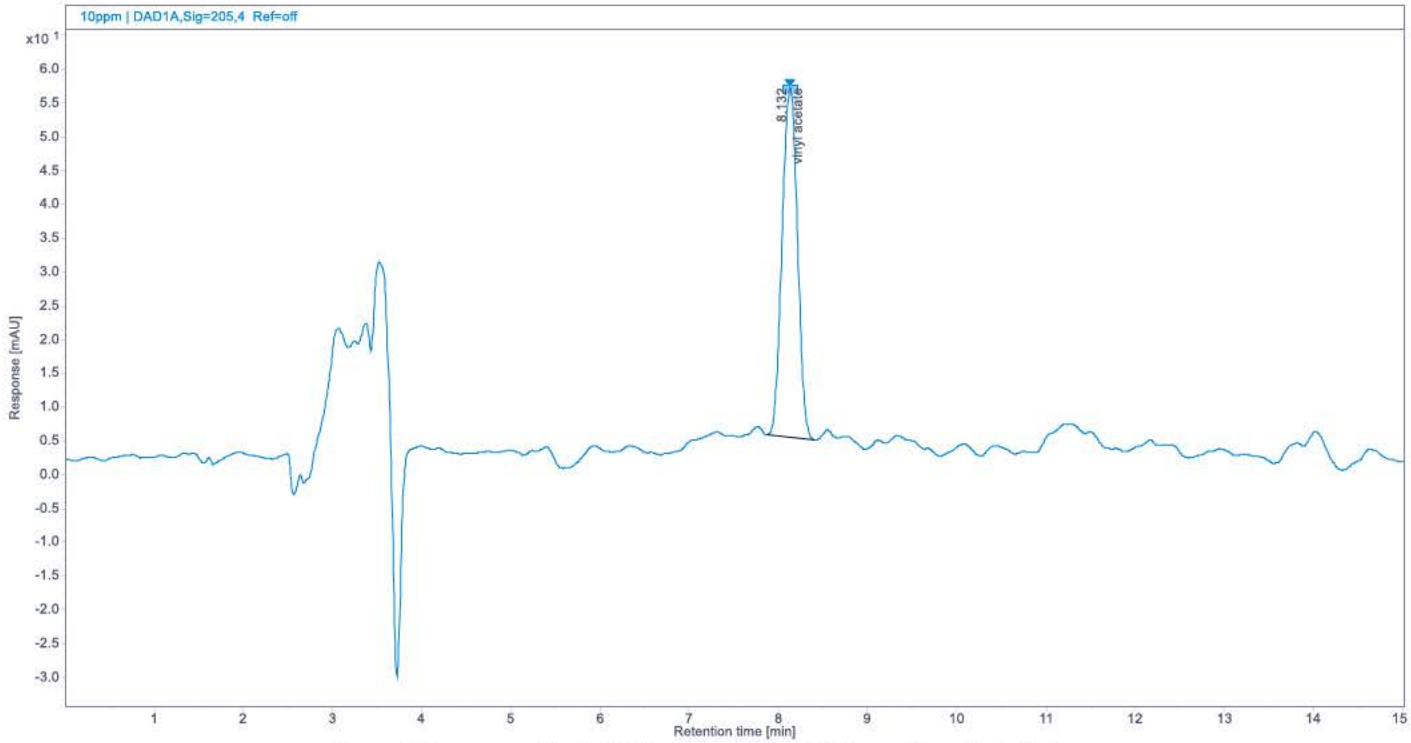

Figure 6: Representative HPLC Chromatogram of 10.0 ppm Linearity Solution

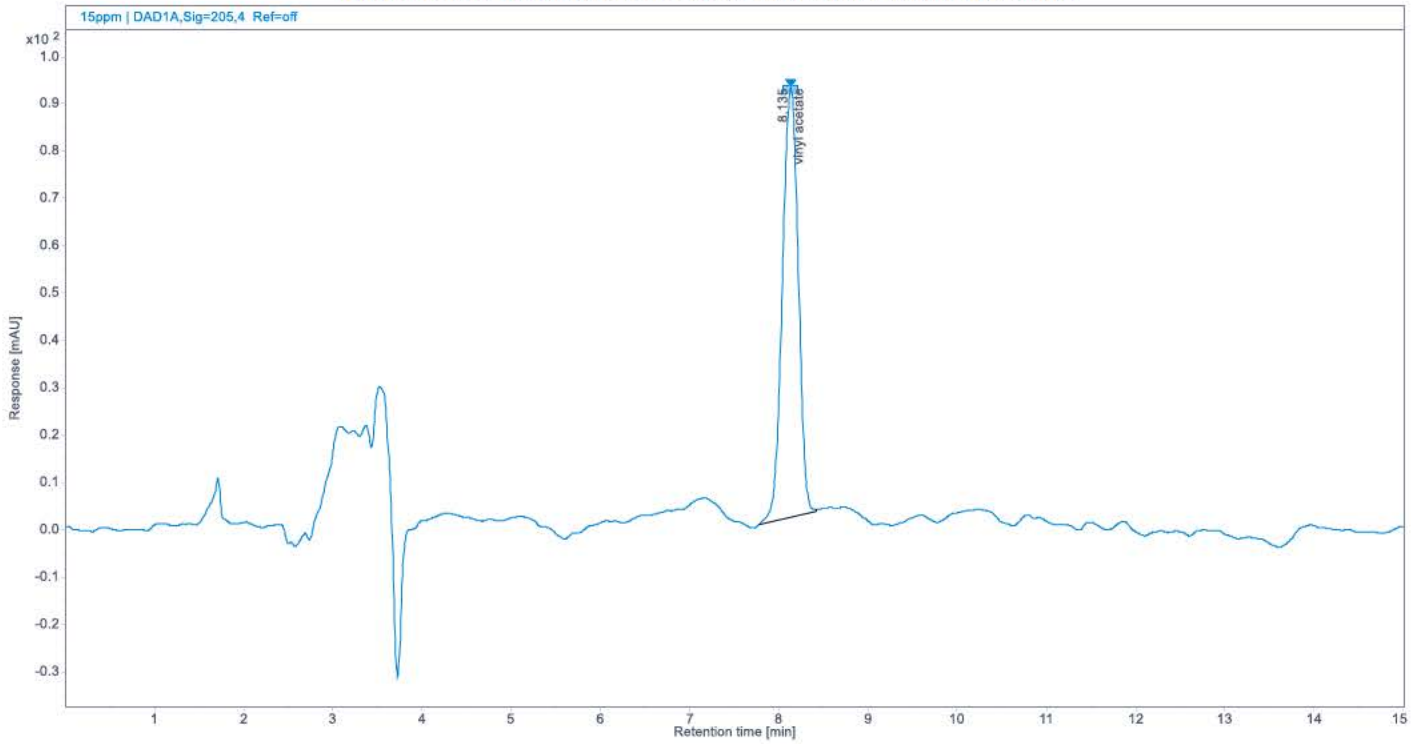

Figure 7: Representative HPLC Chromatogram of 15.0 ppm Linearity Solution

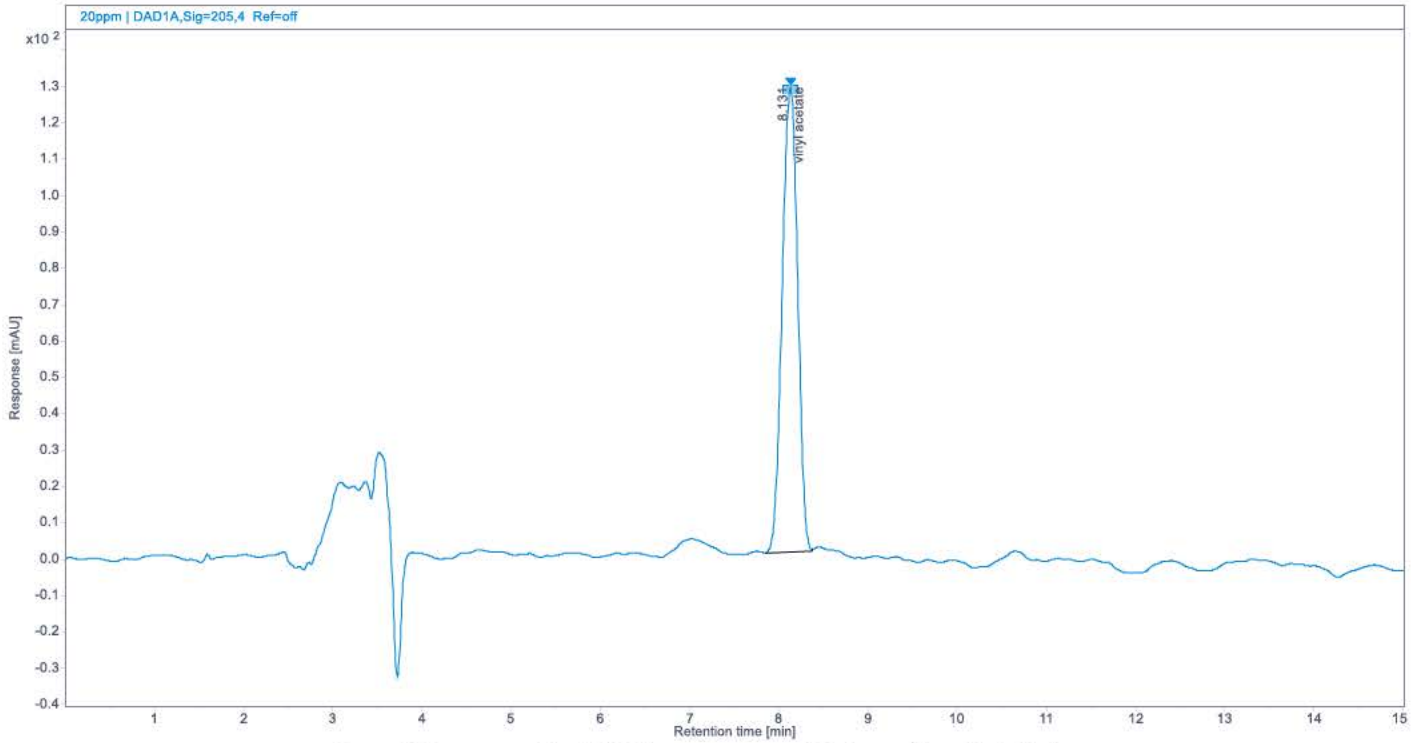

Figure 8: Representative HPLC Chromatogram of 20.0 ppm Linearity Solution

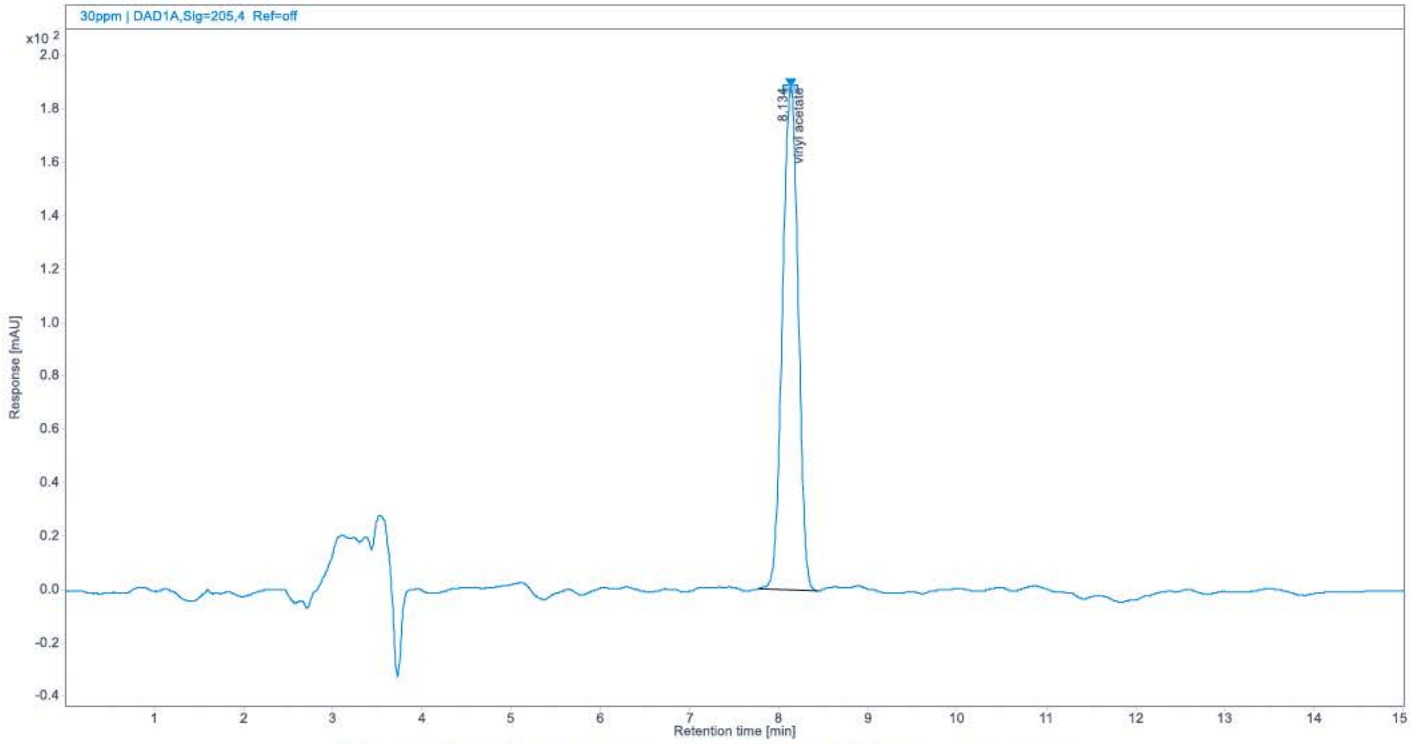

Figure 9: Representative HPLC Chromatogram of 30.0 ppm Linearity Solution

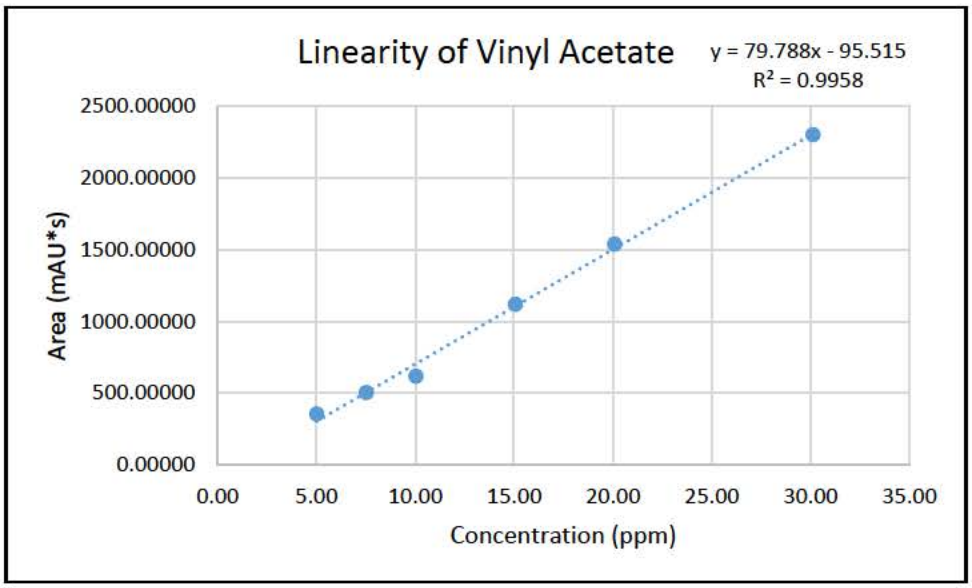

Figure 10: Linearity Plot

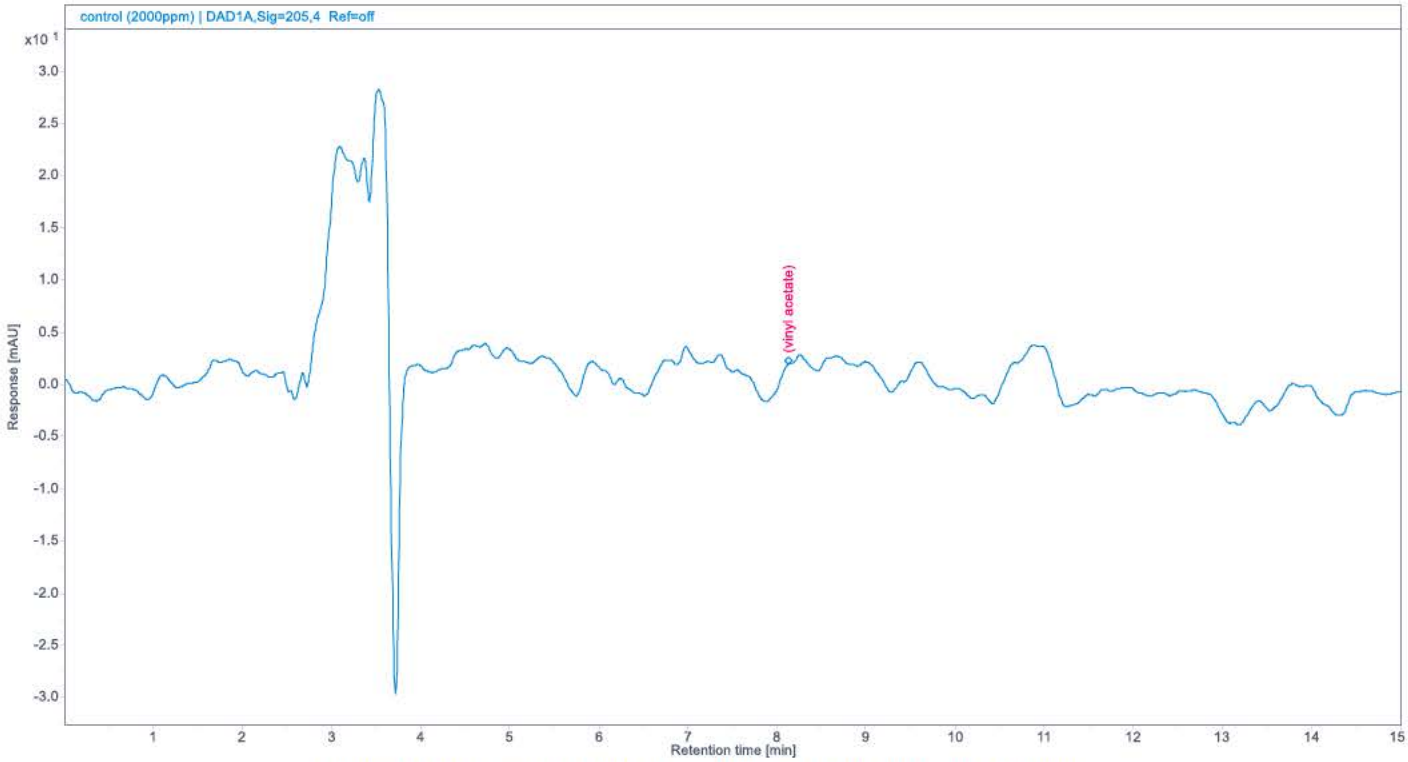

Figure 11: Representative HPLC Chromatogram of 2000 ppm Control Solution

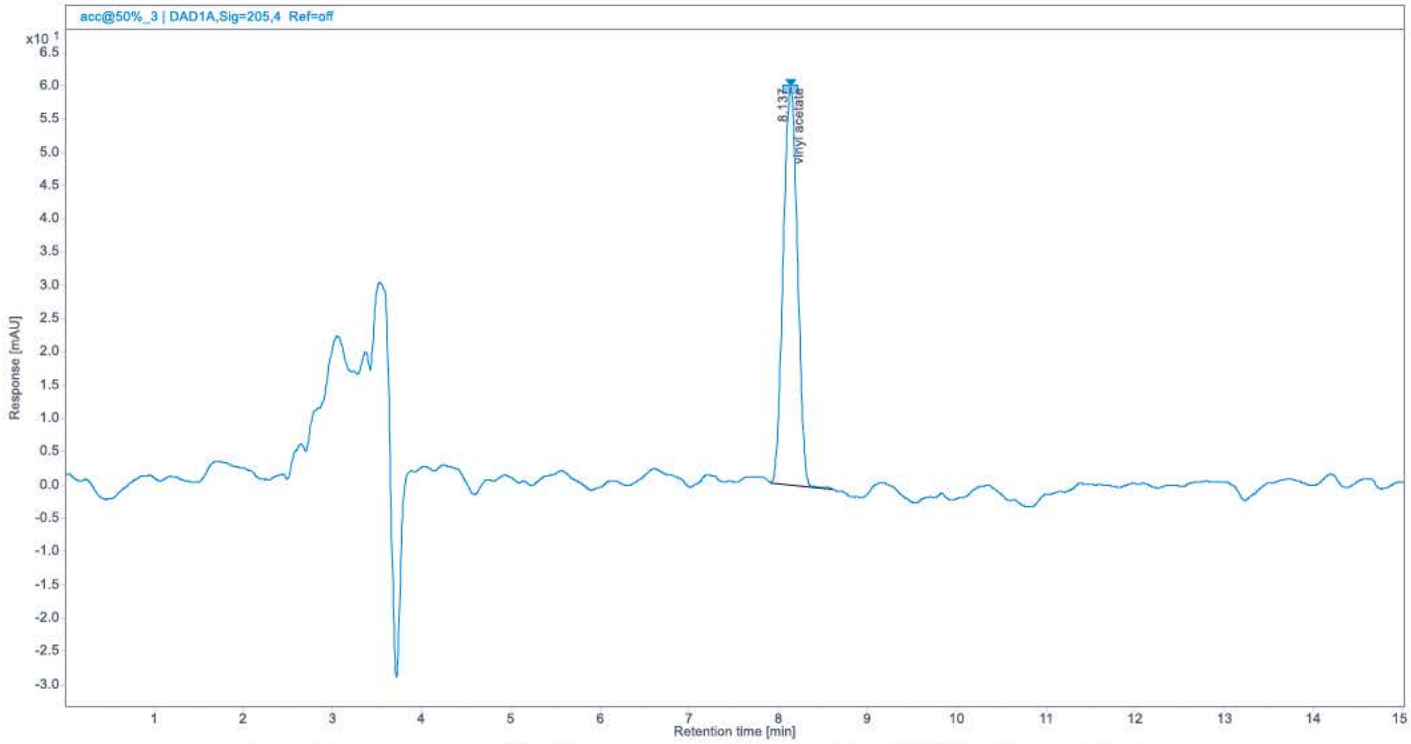

Figure 12: Representative HPLC Chromatogram of Accuracy- Level 50 % Vinyl Acetate Solution

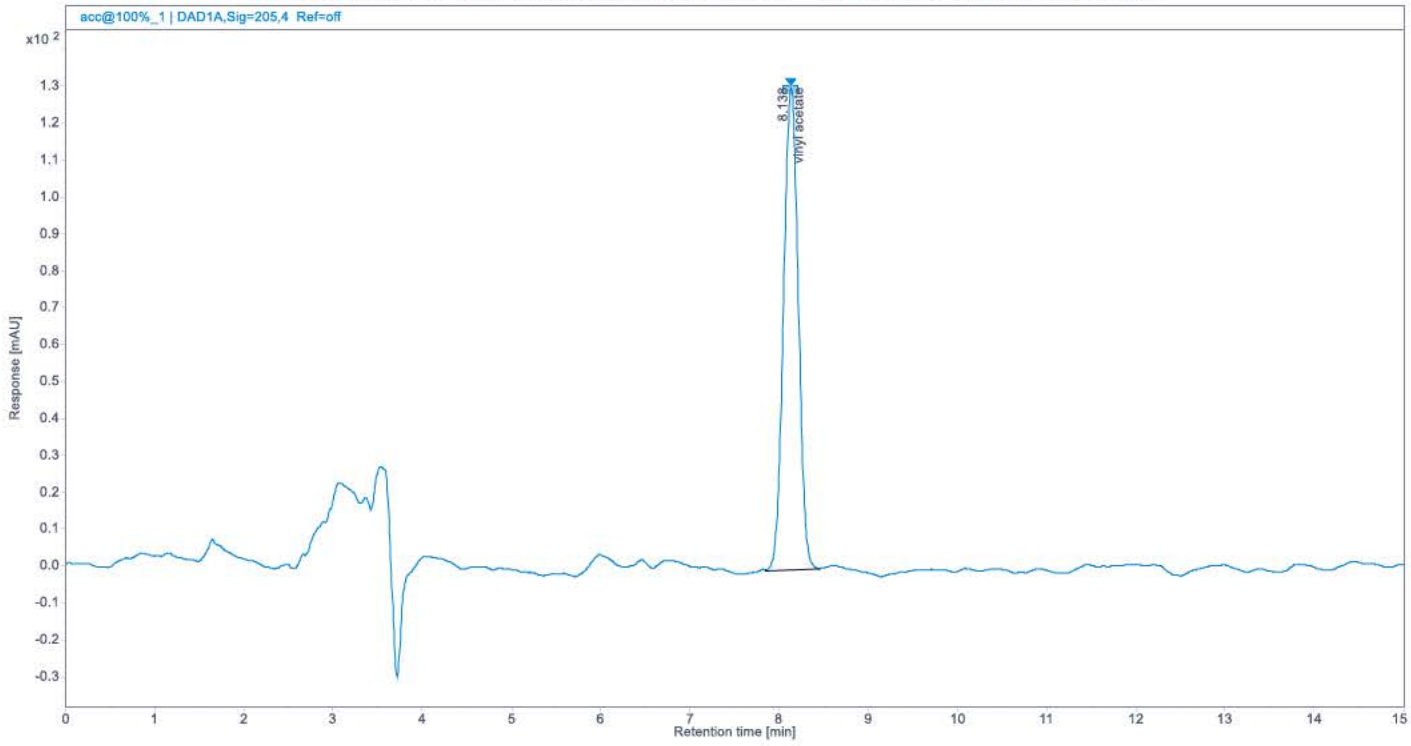

Figure 13: Representative HPLC Chromatogram of Accuracy- Level 100 % Vinyl Acetate Solution

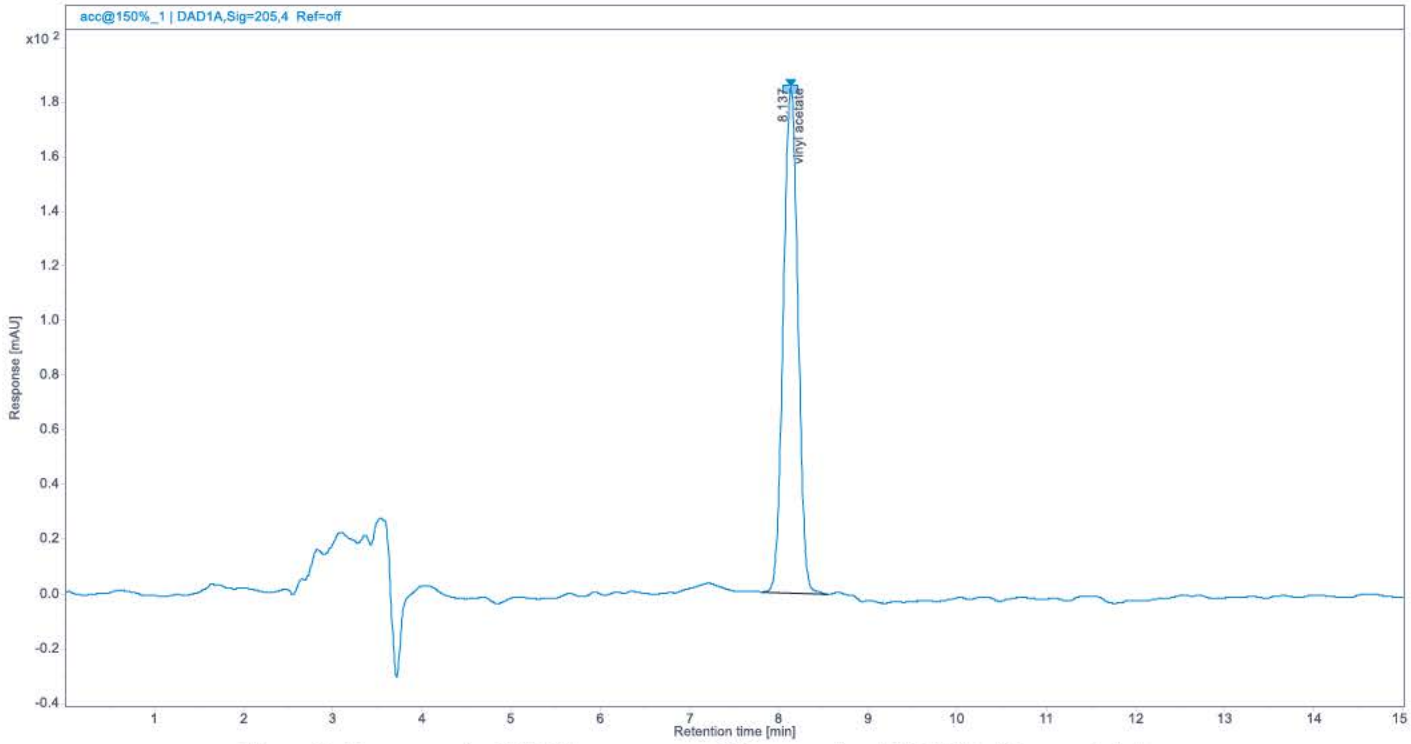

Figure 14: Representative HPLC Chromatogram of Accuracy- Level 150 % Vinyl Acetate Solution

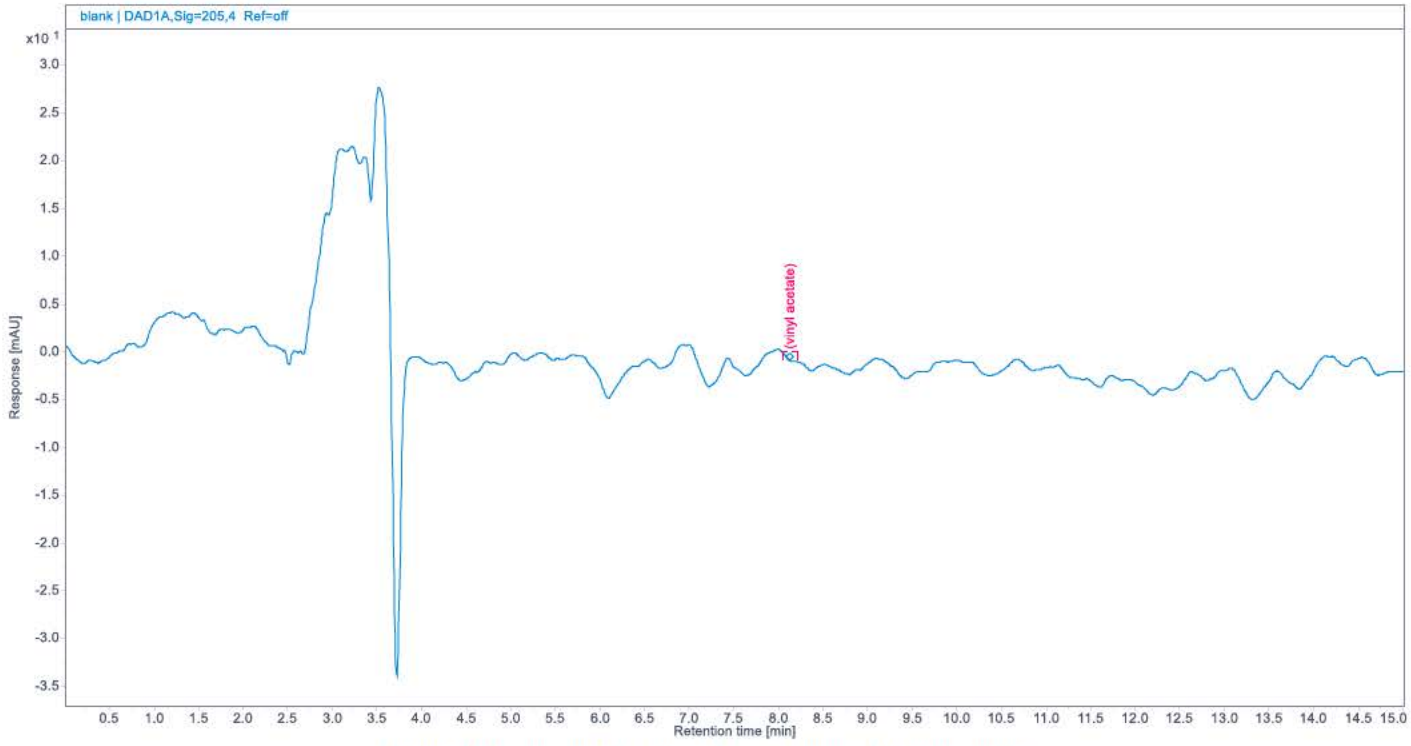

Figure 15: Representative HPLC Chromatogram of Blank Injection

Description of Instrumentation Used

Reverse Phase High Performance Liquid Chromatography (rpHPLC): Element Ann Arbor uses Agilent 1100 series instruments with quaternary pumps. Detection modules include Refractive Index, Evaporative Light Scattering, UV variable wavelength and UV Diode Array Detectors. The quaternary pumps allow the use of variable solvent chemistry to optimize resolution and run time. Diode Array detection allows for collection of data from multiple wavelengths simultaneously. The system is optimized for reverse phase chromatography, which allows the analyst to utilize a highly polar mobile phase solution that carries the compound of interest though the chromatography column. The column contains a non-polar stationary phase that interacts with the compound of interest as it is pumped through the column. The compound eventually is released from the column and travels to the detector where a signal arises based on the compound's characteristic absorbance and retention time. The analog signal is converted to a usable chromatogram where the information about the compound can be analyzed with high accuracy and precision.

History

Date	Revision	Changes
30SEP22	.00	New document

Wrap Up

Thank you for consulting with element Ann Arbor. Results relate only to items tested. If you have any questions regarding this analysis, or if we can be of any further assistance, please call us at (800) 930-5450. Following the receipt of this final report, a final invoice indicating the remaining payment will be sent to you. Reports shall not be reproduced, except in full, without approval from Element Ann Arbor in writing.

It has been a pleasure working with you and we look forward to serving you again.

Sincerely,

Kabita Gwachha
Kabita Gwachha, M.S.
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For questions or to arrange a teleconference, please contact your Project Manager, William Xue, at 800-930-5450 or william.xue@element.com.

APPENDIX II

Confidential Report

Prepared for:

Mark Itzkoff

Law office of Mark Itzkoff

mark@itzkofflaw.com

Project Code 22-93466-B
Issued 30 September 2022

Method Development for Quantifying Residual Vinyl Acetate Monomer in Polyvinyl Alcohol

Thank you for contacting Element Ann Arbor for the method development to quantify residual vinyl acetate monomer in polyvinyl alcohol. Following are the results, methodology, and data associated with our Method development.

Table 1: Sample Description

Element Ann Arbor Sample ID	Sample Description
06SEP22TH3986	Kurary, PVOH 5-88FA, Lot: 120075080, Plastic Pellets, White, 1 bag

Executive Summary

The goal of this analysis was to develop HPLC-DAD method for the quantitation of the residual vinyl acetate monomer in polyvinyl alcohol. The method was successfully developed and was tested the following parameters: System Suitability, Specificity, Linearity, Limit of Detection (LOD), Limit of Quantification (LOQ) and Accuracy. The detailed results of the development are shown in Table 2.

Table 2: Method Development, and Sample analysis Results

Qualification Parameter	Proposed Acceptance Criteria	Result		
System Suitability	The % RSD for the Vinyl acetate concentration in the six and all injections of Working vinyl acetate Standard (20 µg/mL) should be not more than 10 %	%RSD of first six injections: 2 %RSD of all replicate injections: 3 USP Tailing Factor: 1.02567		
	The USP tailing factor for the first injections of the Working Vinyl acetate peak Standard (20 µg/mL) should be not more than 2.0 for the Vinyl acetate peak			
Specificity	There should be no significant interference at the retention time of Vinyl acetate peak	There was no significant interference at the retention time of Vinyl acetate peak		
Linearity	The correlation coefficient ® should be not less than 0.99	Correlation Coefficient: 1.00		
Limit of Detection (2.5 ppm)	Average Signal to Noise should be ≥ 3.	Average S/N: 27.31008		
Limit of Quantification (5.0 ppm)	Average Signal to Noise should be ≥ 10.	Average S/N : 79.46681 %RSD: 3		
	%RSD (Concentration) ≤ 20%			
Accuracy 50% - 150% (10 ppm to 30 ppm)	Mean % Recovery at all levels must be 80 – 120% (n=3) RSD ≤ 20%	**Level**	**% Mean Recovery**	**% RSD**
		50%	89.1	7.5
		100%	91.5	3.1
		150%	90.1	3.1
Sample Analysis	Report the residual Vinyl acetate monomer content	None Detected		

Quality Statement

The work described in this report was conducted in compliance with the principles of current Good Manufacturing Practice. The following compliance exceptions were noted: results have been generated using method(s) that were not validated at this facility.

Analytical Testing

Initial Observations

The samples were received for analysis on 06 September 2022. The sample consisted of white plastic pellets in a transparent plastic bag. A photograph of the samples "As Received" can be found in Figure 1.

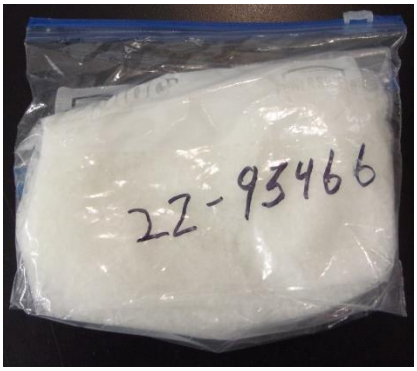

Figure 1: Photograph of the Sample "As Received"

Method Development

Solution Preparations

Solution Preparations

Mobile Phase A (100% purified water): Measured and transferred 2000 mL of purified water into a mobile phase container. The solution was sonicated to degas.

Mobile Phase B (100% ACN): Measured and transferred 2000 mL of Acetonitrile into suitable mobile phase container. The solution was mixed well and sonicated to degas.

Diluent (100% Methanol): Measured and transferred 1000 mL of methanol into a mobile phase container. The solution was sonicated to degas

Standard Preparations

Standard Stock Solution-1 (1000 ppm): Approximately 10 mL of diluent was added to a 100 mL volumetric flask. Accurately weighed 100.45 mg of vinyl acetate in a tarred 100 mL volumetric flask with the diluent. Diluted to volume with diluent and mixed well by vortexing.

Standard Stock Solution-2 (100 ppm): Using a glass pipette, 1mL of the standard stock solution (1000 ppm) was transferred into a 10 mL volumetric flask. Diluted to volume with diluent and mixed well by vortexing.

Working Standard (20 ppm): Using a glass pipette, 2.0 mL of the standard stock solution-2 (100 ppm) was transferred into a 10 mL volumetric flask. Diluted to volume with diluent 1 and mixed well by vortexing.

Linearity Standard Dilutions:
Using a glass pipette, following concentrations of Linearity standard and Limit of detection (2.5 ppm) dilutions were prepared using standard stock solution-2 into respective volumetric flasks as shown in Table 3.

Table 3: Preparation of Vinyl Acetate Standard Dilutions

Standard ID	Concentration (ppm)	Volume of standard (mL)	Final volumetric flask volume (mL)
1	30	3 mL of 100 ppm	10
2	20	2 mL of 100 ppm	10
3	15	1.5 mL of 10 ppm	10
4	10	5 mL of 20 ppm	10
5	7.5	5 mL of 15 ppm	10
6	5 (LOQ)	5 mL of 10 ppm	10
7	2.5 (LOD)	5 mL of 5 ppm	10

Sample stock solution (10,000 ppm):

Into a tared weigh boat, 502.22 mg of sample was weighed and transferred to a 50mL volumetric flask. Approximately 10mL of purified water was added to the volumetric flask and sonicated for about 30 minutes until the solid was completely dissolved. The solution was cooled to room temperature and diluted to volume with diluent.

Sample Control Solution (2000 ppm): Using a 2mL volumetric pipette, 2 mL of stock sample was transferred into a 10 mL volumetric flask. Diluted to volume with diluent.

Accuracy Preparations:
Using a glass pipette, following concentrations of accuracy preparation solutions were prepared using sample control solution and 10ppm standard stock and transferred into respective 10mL volumetric flasks as shown in Table 4.

Table 4: Preparation of Vinyl Acetate Accuracy Solutions

Concentration	Volume of standard (mL)		Final volume (mL)
	Sample stock solution (10,000 ppm)	Standard Stock Solution-2 (100 ppm)	
50% accuracy sample (2000 ppm sample + 10 ppm Vinyl acetate standard)	2	1	10
100% accuracy sample (2000 ppm sample + 20 ppm Vinyl acetate standard)	2	2	10
150% accuracy sample (2000 ppm sample + 30 ppm Vinyl acetate standard)	2	3	10

Instrument Conditions

Instrument:	Agilent 1100 Series HPLC with DAD Detector
Column:	Prodigy 5µm C8 150 Å, 250mm × 4.6mm
Flow Rate:	1 mL/minute
Column Temperature:	40 °C
Run Time:	15 minutes
Injection Volume:	20 µL
Detection:	DAD , 205 nm, 4 nm bandwidth
HPLC Gradient: isocratic	

Time (Minutes)	MPA (%)	MPB (%)
0.00	70	30
15	70	30

Results and Discussion

System Suitability

The system suitability was demonstrated by injecting six injections of the standard solution (20 ppm). The peak area of Vinyl acetate in each injection was analyzed for % RSD and the first six injections were analyzed for the USP tailing factor. The system suitability results are shown in Table 7 and the representative chromatography of vinyl acetate standard (20 ppm)) can be seen in Figure 2

Table 7: System Suitability Results

Injection	Vinyl acetate (20 ppm)		
	Area (mAU*s)	Concentration (ppm)	Tailing
1	1653.17594	21.9	1.02567
2	1614.94060	21.4	
3	1627.20613	21.6	
4	1583.53767	21.0	
5	1584.43928	21.1	
6	1605.81495	21.3	
Average	1611.51910	21.4	
STDEV	26.6	0.3	
%RSD	1.65	1.56	
7	1569.31600	20.9	
8	1633.64884	21.7	
9	1518.02078	20.2	
Average	1598.03566	21.2	
STDEV	43.2	0.5	
%RSD	2.7	2.6	

Conclusion: The % RSD for the vinyl acetate peak in the first six and all injections of standard solution (20 ppm) was not more than 10. The USP tailing factor for the first injection of the standard solution (20 ppm) was not more than 2. All system suitability criteria were met, establishing that the method and system are suitable for analyzing Vinyl acetate.

Specificity

The specificity of method was demonstrated by showing no interference from the Diluent at the retention time of vinyl acetate. The representative chromatography of the Diluent, Sample Solution (2000 ppm of vinyl acetate) and Working Standard (20 ppm) can be seen in Figures 2, 11, and 15.

Conclusion: There was no inference at the retention time of vinyl acetate in the blank preparation. The method was demonstrated to be specific for vinyl acetate.

Linearity

The linearity of the response of vinyl acetate was determined by analyzing vinyl acetate standard solution with concentrations ranging from 30 ppm to 5 ppm of vinyl acetate. The area response of the vinyl acetate Acid peak in the standards were plotted against the concentration of vinyl acetate standard, and the correlation coefficient (r) of the line was determined. The results are presented in Table 8. The graph of the linearity standards is shown in Figure 10, and the representative chromatography for each linearity solution can be seen in Figures 4– 10.

Table 8: Linearity Results

Linearity		
Level	**Concentration (ppm)**	**Area (mAU*s)**
25%	5.02	355.49377
38%	7.53	504.95319
50%	10.05	617.72556
75%	15.07	1120.26979
100%	20.09	1539.21684
150%	30.14	2302.07586
	Slope	79.7875
	Intercept	-95.5153
	Correlation	1.00
	R^2	1.00

Conclusion: The correlation coefficient of the vinyl acetate peak was not less than 0.98. The method was demonstrated to be linear between 5 ppm to 30 ppm vinyl acetate.

Limit of Detection (LOD)

The Limit of Detection was determined by injecting six replicates of the Limit of Detection solution (2.5 ppm) and measuring the signal-to-noise ratio (S/N) of the vinyl acetate peak. The S/N ratios for the vinyl acetate peaks in all injections are presented in Table 8. Representative chromatogram of vinyl acetate standard (2.5 ppm) can be seen in Figure 3.

Table 8: Limit of Detection Results

LOD (2.5 ppm)		
Replicate	**Area (mAU*s)**	**S/N**
1	196.33356	20.53879
2	208.15851	30.52422
3	199.20750	14.74359
4	237.87071	26.05188
5	169.90208	33.68621
6	198.14935	38.31581
Average	201.60362	27.31008

Conclusion: The S/N ratio of the vinyl acetate peak in the replicate injections of LOD samples was found to be in the range of 14 to 30 with an average S/N of 27.31008. The Limit of Detection for vinyl acetate peaks was determined to be 2.5 ppm.

Limit of Quantitation (LOQ)

The Limit of Quantitation was determined by injecting six replicates of the Limit of Quantitation Solution (5.0 ppm) and measuring the S/N ratio of the vinyl acetate peak. Additionally, the %RSD of the peak areas was calculated. The S/N ratios and peak areas for each injection are presented in Table 9. Representative chromatography of vinyl acetate standard (5 ppm) can be seen in Figure 4.

Table 9: Limit of Quantification Results

LOQ (5.0 ppm)			
Replicate	**Vinyl acetate area**	**Vinyl acetate (concentration in ppm)**	**S/N**
1	375.48161	5.9	201.40286
2	343.70041	5.5	61.53333
3	359.46350	5.7	51.59621
4	350.53843	5.6	31.90301
5	365.03345	5.8	75.53669
6	338.74522	5.4	54.82877
Average	355.49377	5.7	79.46681
STDEV	13.7872	0.1728	61.4029
%RSD	3.9	3.1	77.3

Conclusion: The S/N ratio of the vinyl acetate peak in the replicate injections of LOQ samples was found to be in the range of 31 to 201 with an average S/N of 79.46681 and the %RSD for the vinyl acetate peak areas was 4. The Limit of Quantitation for vinyl acetate peaks was determined to be 5.0 ppm.

Accuracy:

The accuracy of method was demonstrated by spiking the sample stock and standard solution (100 ppm) at three different levels; 50 % (10 ppm), 100 % (20 ppm), and 150 % (30 ppm). Each sample level was prepared in triplicate. Accuracy results for vinyl acetate are shown in Table 10. Representative chromatography for each sample preparation can be seen in Figures 11 – 14.

Table 10: Accuracy Results

Accuracy Results								
Level	**Level**	**Amount Added (ppm)**	**Area (mAU*s)**	**Amount Recovered (ppm)**	**%Recovery**	**Mean %Recovery**	**STDEV**	**%RSD**
50%	**10 ppm - 1**	10.05	760.73856	9.48	94	89.1	7	7.5
	10 ppm - 2	10.05	736.74587	9.18	91			
	10 ppm - 3	10.05	657.31030	8.19	82			
100%	**20 ppm - 1**	20.09	1494.19475	18.63	93	91.5	3	3.1
	20 ppm - 2	20.09	1507.87468	18.80	94			
	20 ppm - 3	20.09	1422.69652	17.74	88			
150%	**30 ppm - 1**	30.14	2104.67701	26.24	87	90.1	3	3.1
	30 ppm - 2	30.14	2187.14120	27.27	90			
	30 ppm - 3	30.14	2239.56314	27.92	93			

Conclusion: The % RSD of the vinyl acetate recovery in the triplicate preparations was not more than 20 % and the mean % recovery was between 80 % – 120 % for each level. The method was demonstrated to be accurate for vinyl acetate.

Figures

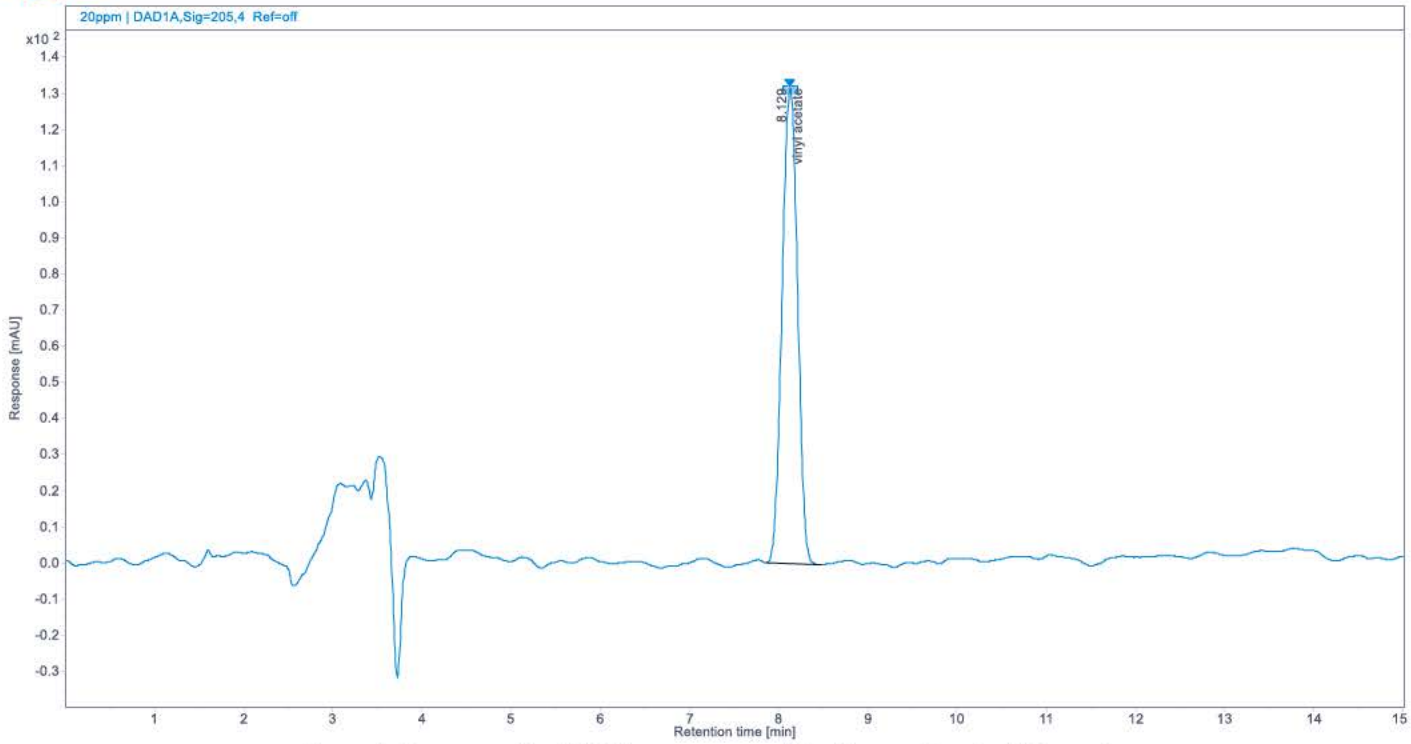

Figure 2: Representative HPLC Chromatogram of Vinyl Acetate Standard (20 ppm)

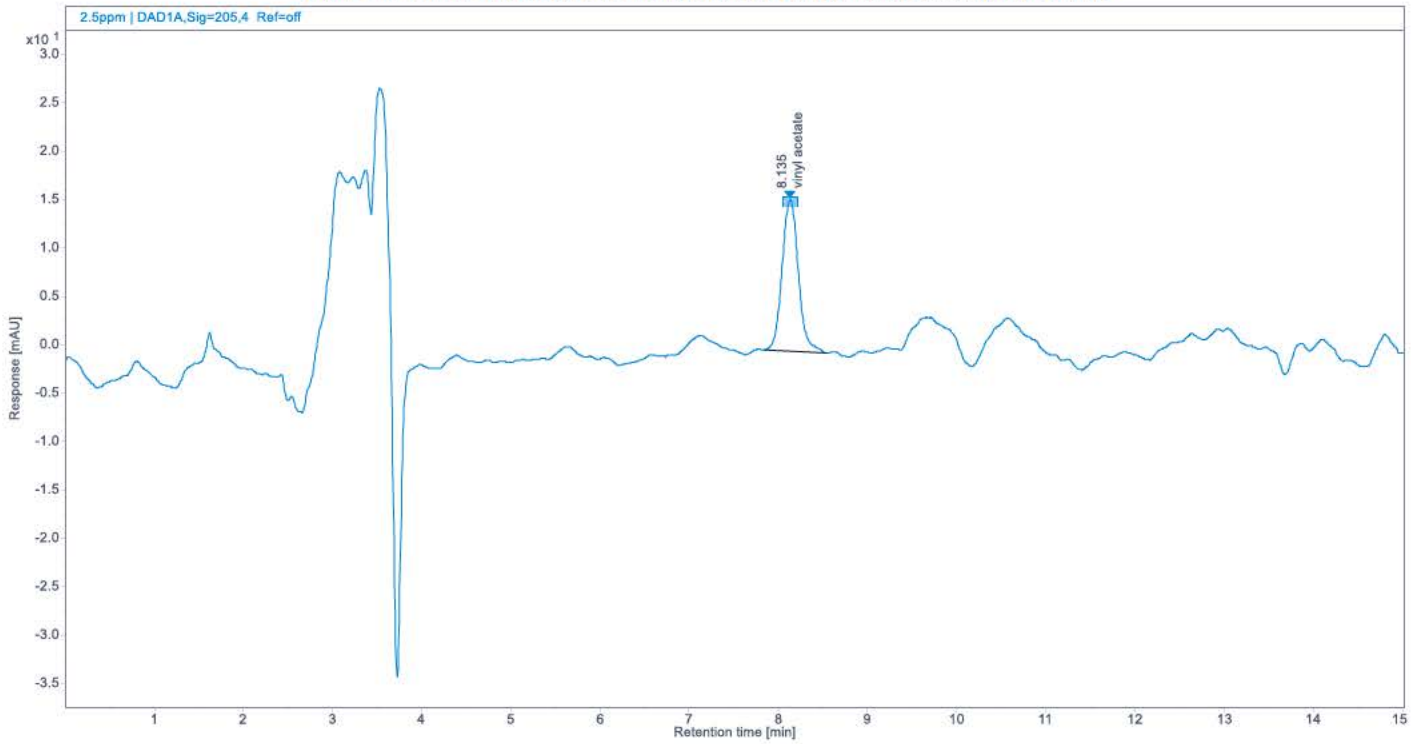

Figure 3: Representative HPLC Chromatogram of 2.5 ppm Linearity Solution

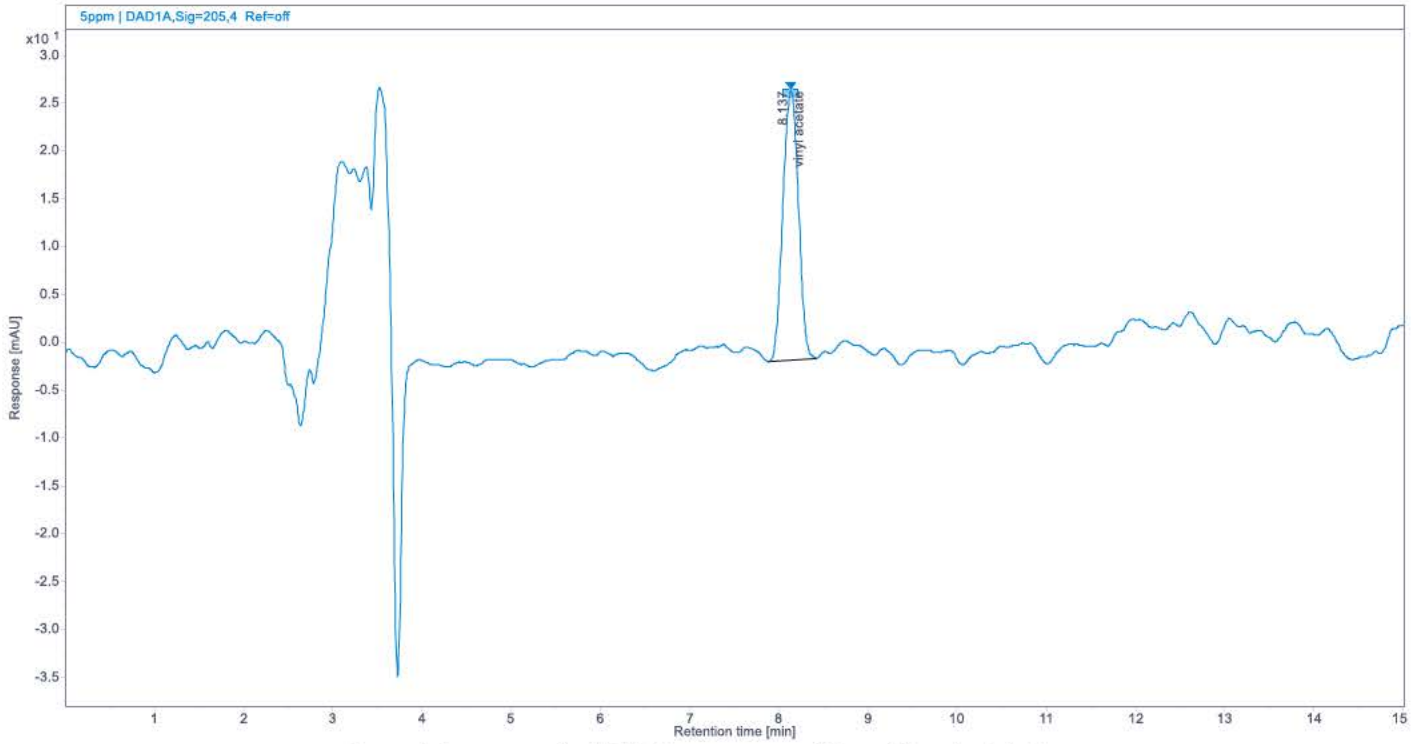

Figure 4: Representative HPLC Chromatogram of 5 ppm Linearity Solution

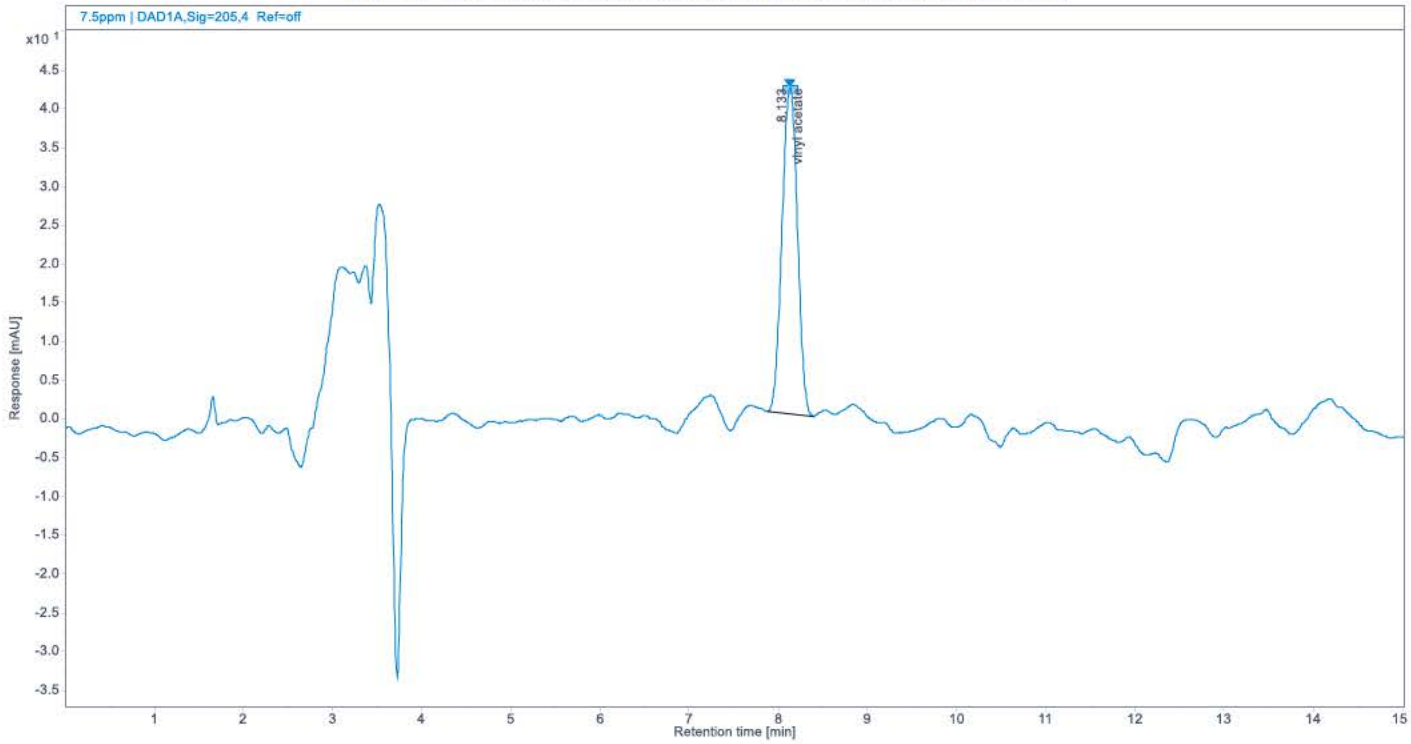

Figure 5: Representative HPLC Chromatogram of 7.5 ppm Linearity Solution

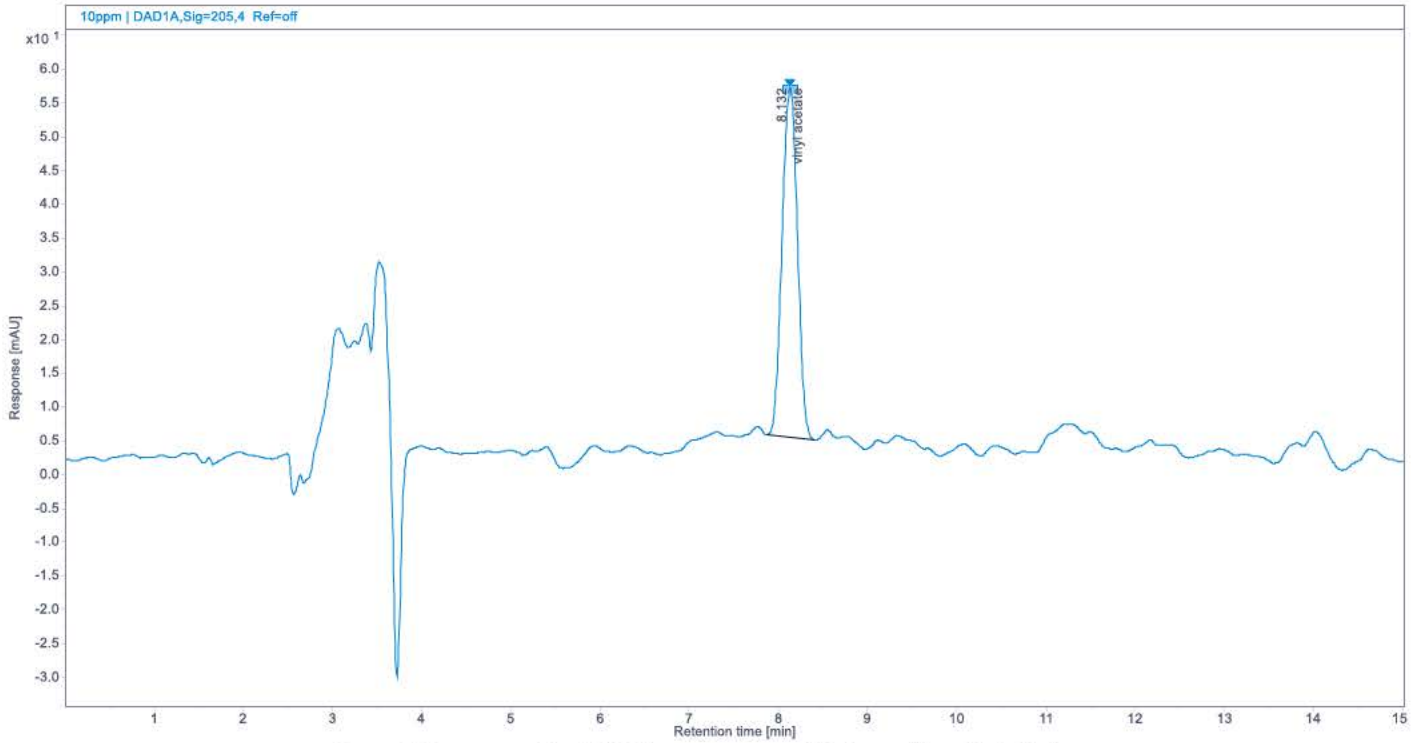

Figure 6: Representative HPLC Chromatogram of 10.0 ppm Linearity Solution

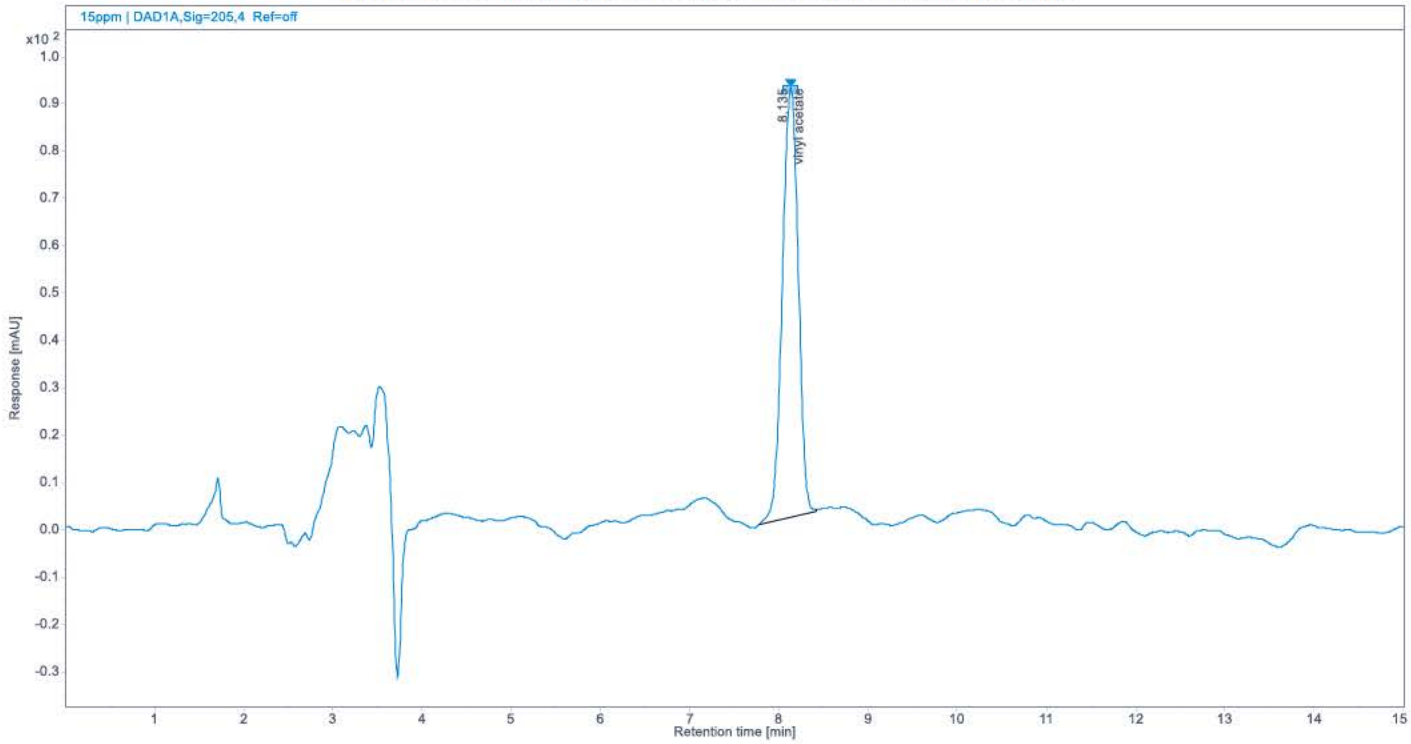

Figure 7: Representative HPLC Chromatogram of 15.0 ppm Linearity Solution

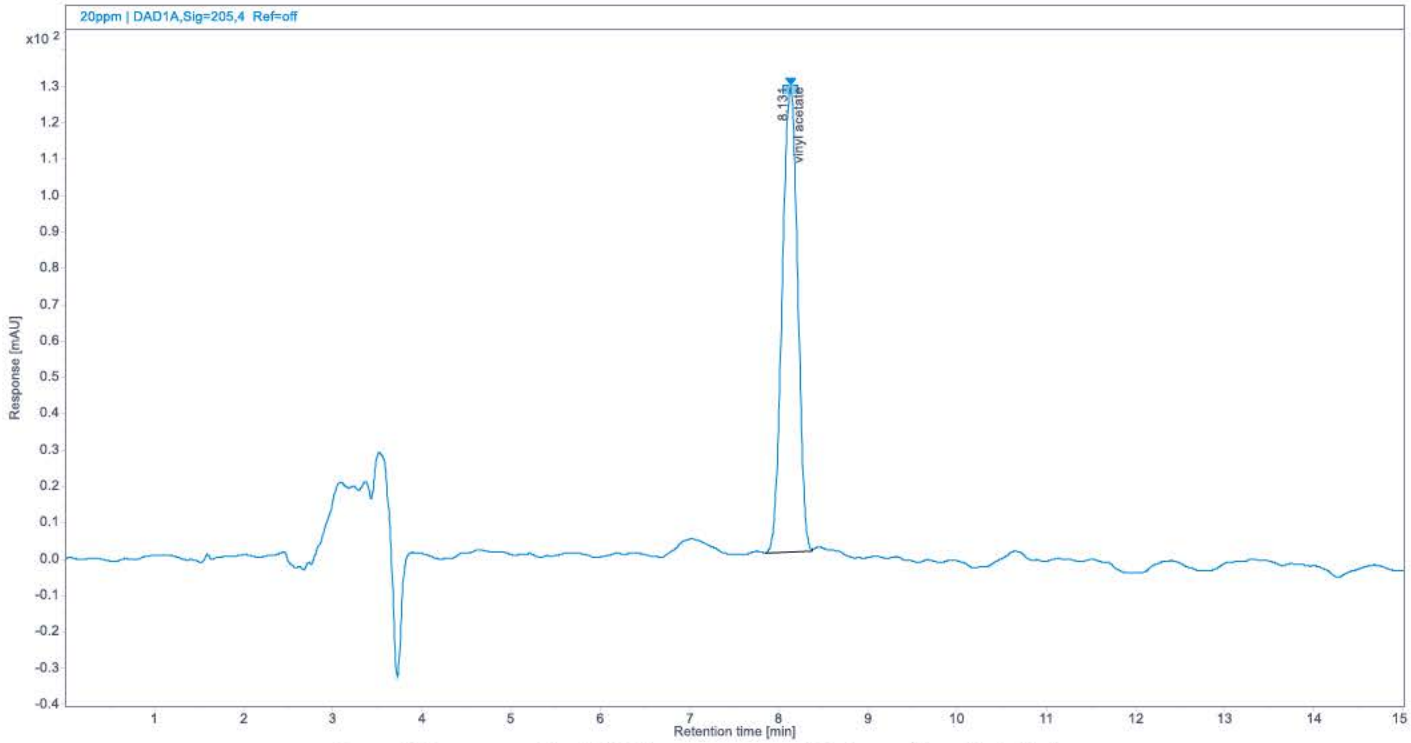

Figure 8: Representative HPLC Chromatogram of 20.0 ppm Linearity Solution

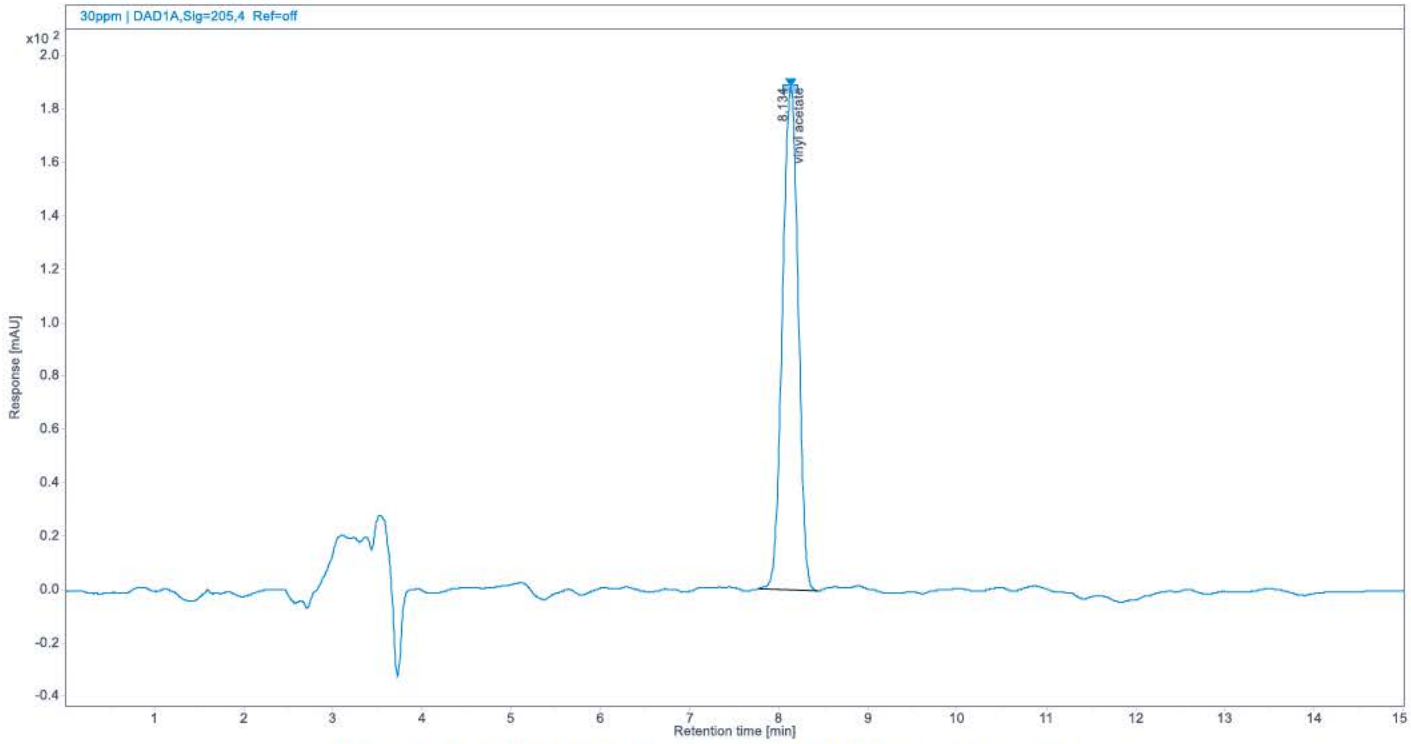

Figure 9: Representative HPLC Chromatogram of 30.0 ppm Linearity Solution

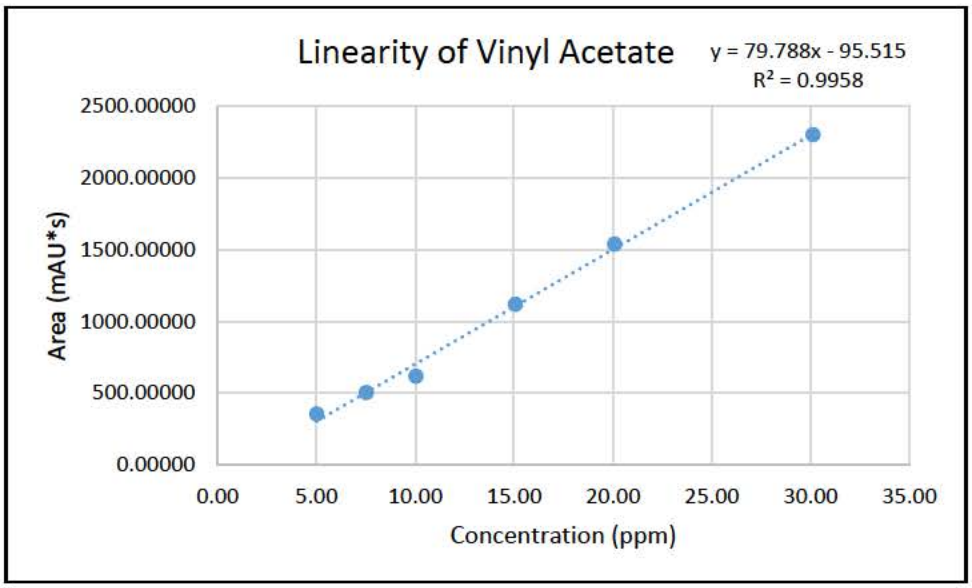

Figure 10: Linearity Plot

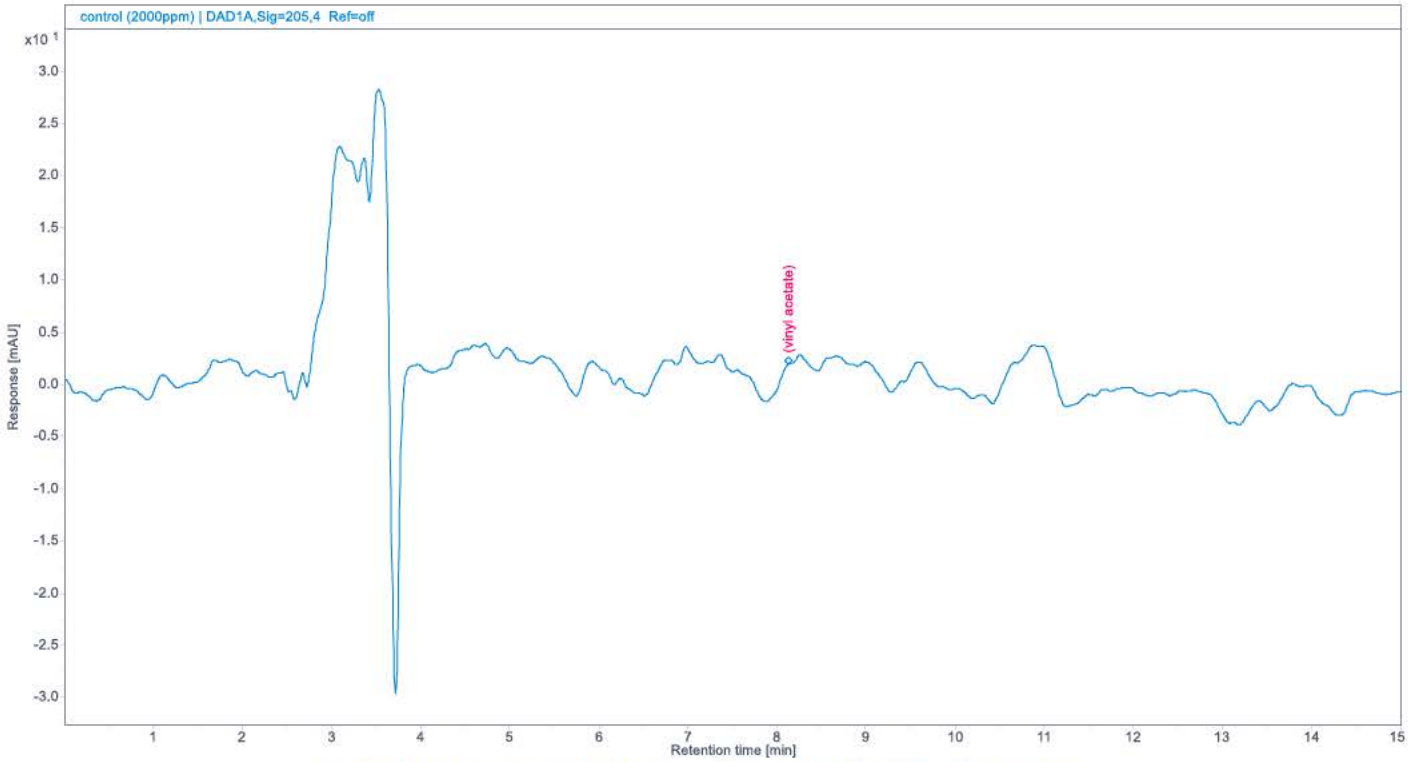

Figure 11: Representative HPLC Chromatogram of 2000 ppm Control Solution

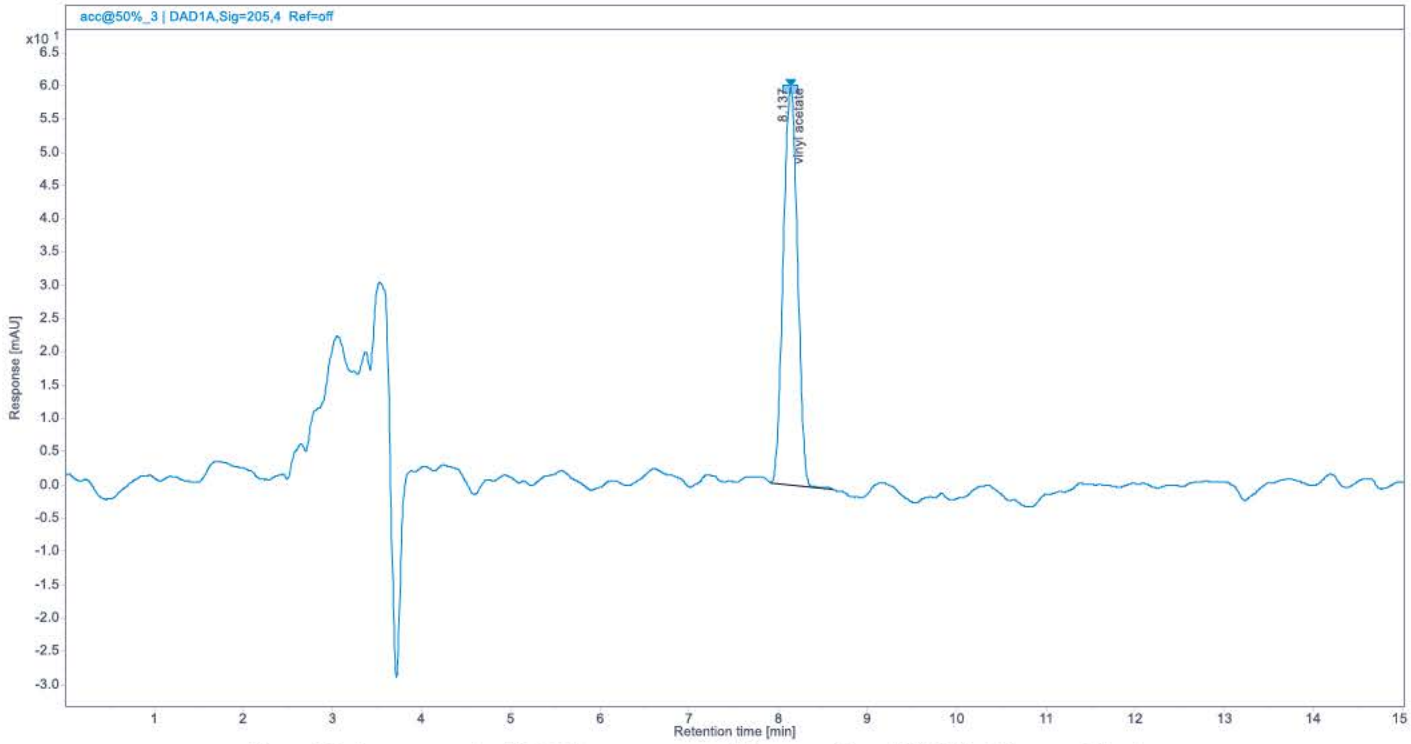

Figure 12: Representative HPLC Chromatogram of Accuracy- Level 50 % Vinyl Acetate Solution

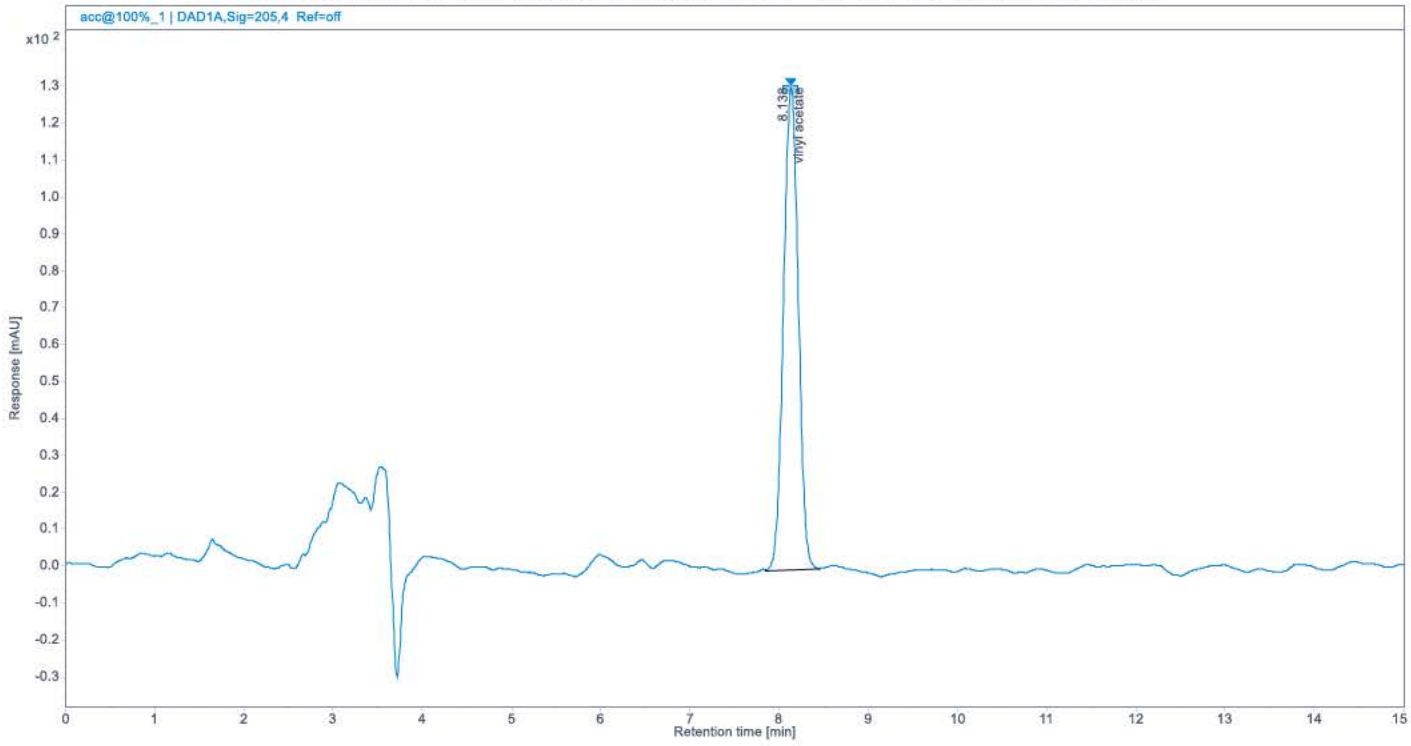

Figure 13: Representative HPLC Chromatogram of Accuracy- Level 100 % Vinyl Acetate Solution

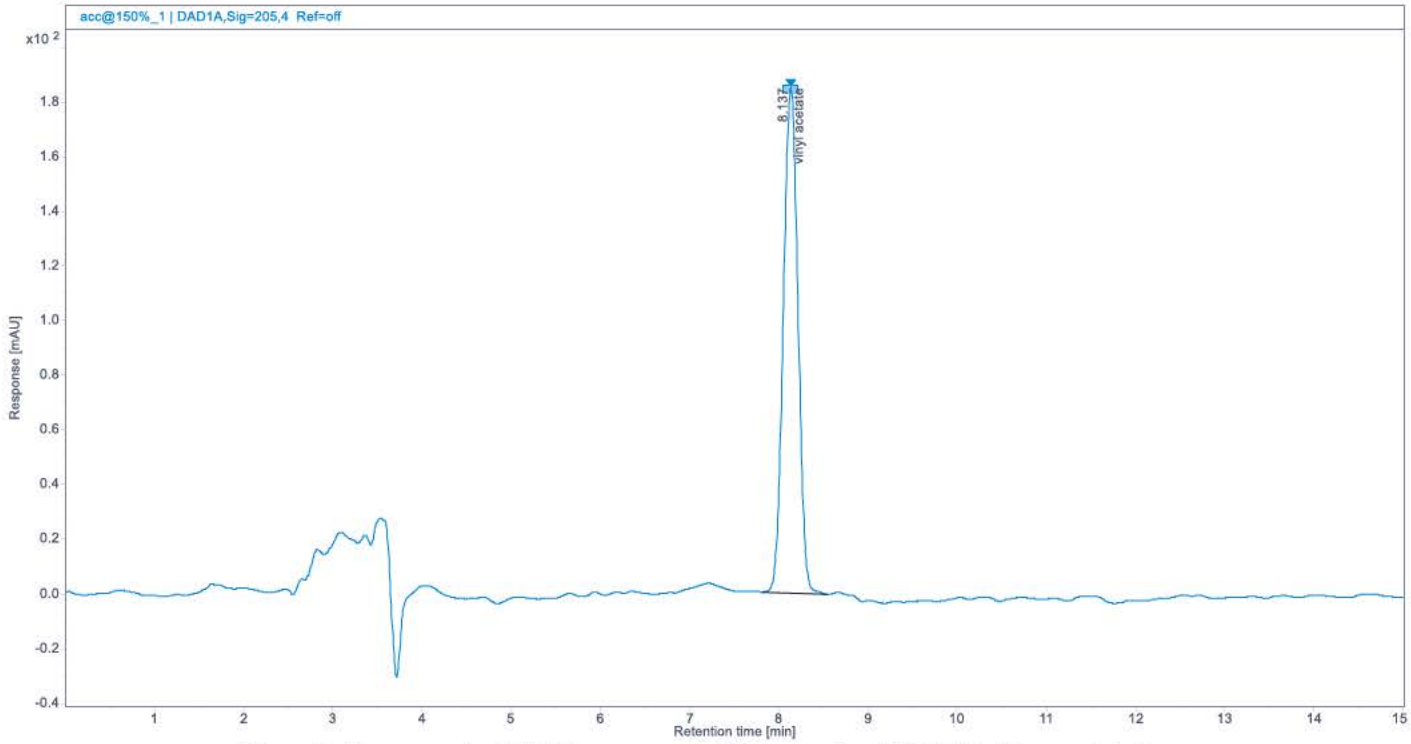

Figure 14: Representative HPLC Chromatogram of Accuracy- Level 150 % Vinyl Acetate Solution

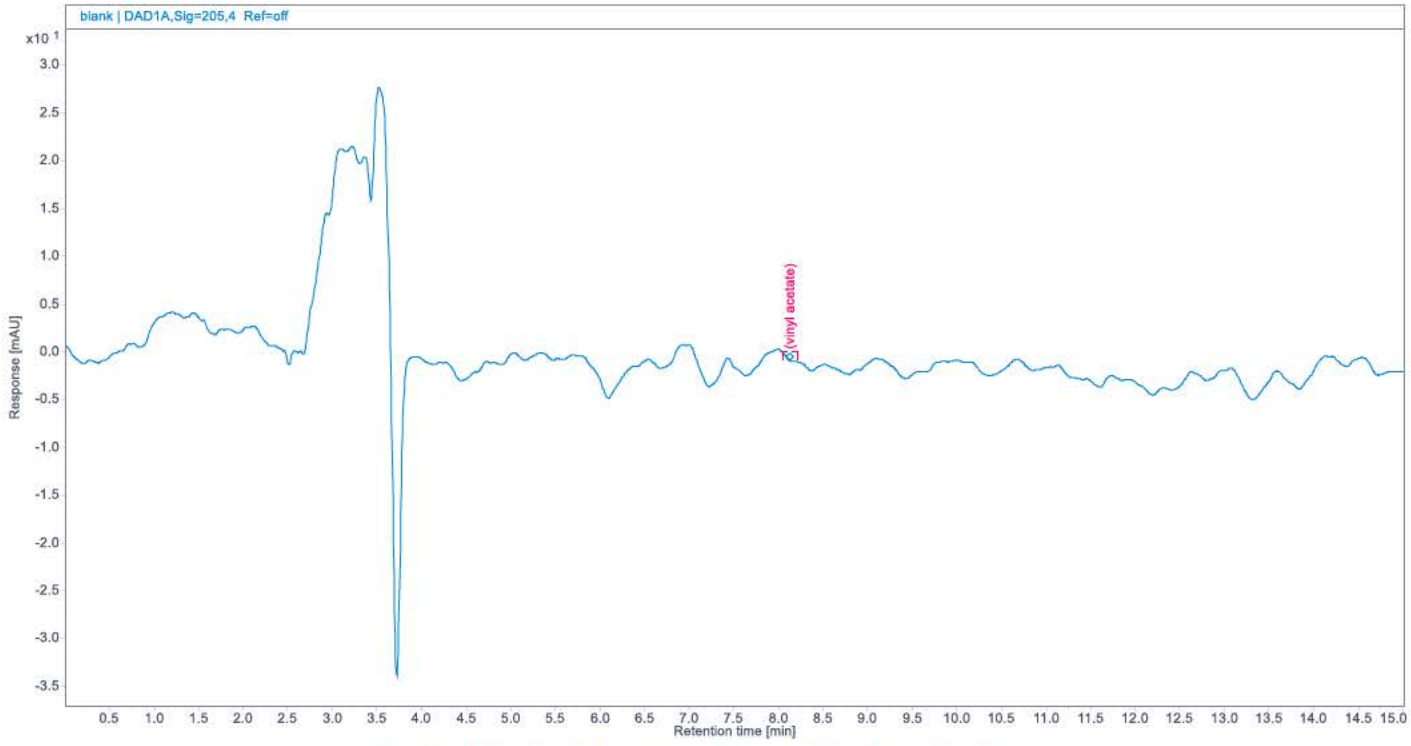

Figure 15: Representative HPLC Chromatogram of Blank Injection

Description of Instrumentation Used

Reverse Phase High Performance Liquid Chromatography (rpHPLC): Element Ann Arbor uses Agilent 1100 series instruments with quaternary pumps. Detection modules include Refractive Index, Evaporative Light Scattering, UV variable wavelength and UV Diode Array Detectors. The quaternary pumps allow the use of variable solvent chemistry to optimize resolution and run time. Diode Array detection allows for collection of data from multiple wavelengths simultaneously. The system is optimized for reverse phase chromatography, which allows the analyst to utilize a highly polar mobile phase solution that carries the compound of interest though the chromatography column. The column contains a non-polar stationary phase that interacts with the compound of interest as it is pumped through the column. The compound eventually is released from the column and travels to the detector where a signal arises based on the compound's characteristic absorbance and retention time. The analog signal is converted to a usable chromatogram where the information about the compound can be analyzed with high accuracy and precision.

History

Date	Revision	Changes
30SEP22	.00	New document

Wrap Up

Thank you for consulting with element Ann Arbor. Results relate only to items tested. If you have any questions regarding this analysis, or if we can be of any further assistance, please call us at (800) 930-5450. Following the receipt of this final report, a final invoice indicating the remaining payment will be sent to you. Reports shall not be reproduced, except in full, without approval from Element Ann Arbor in writing.

It has been a pleasure working with you and we look forward to serving you again.

Sincerely,

Kabita Gwachha
Kabita Gwachha, M.S.
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For questions or to arrange a teleconference, please contact your Project Manager, William Xue, at 800-930-5450 or william.xue@element.com.

APPENDIX III

element

Certificate of Analysis

Date Received:	Client:	Method:
06SEP22	Mark Itzkoff Law Office of Mark Itzkoff mark@itzkofflaw.com	FCC Monograph: Polyvinyl Alcohol ICP-MS
Test Date: 15SEP22	**Sample Description:** Kuraray, PVOH 5-88 FA, Lot: 120075080, Plastic Pellets, White, 1 bag	**Element ID:** 06SEP22TH3986
Issued Date: 26Sep22		**Element Project Code:** 22-93466-A

Table 1: Sample Results

Test	Acceptance Criteria	Result			Pass/Fail
Color Reaction A	A blue color is produced upon addition of boric acid	A blue color was produced upon addition of boric acid			Pass
Color Reaction B	A dark red or blue color is produced after addition of iodine TS	A dark red color was produced after addition of iodine TS			Pass
Infrared Absorption	The spectrum of the sample exhibits maxima at the same wavelengths as those in the spectrum of the Reference Standard	The spectrum of the sample exhibits maxima at the same wavelengths as those in the spectrum of the Reference Standard			Pass
Acid Value	No more than 3.0 KOH/g	1.1 mg KOH/g			Pass
Ester Value	Between 125 and 153 mg KOH/g	143 mg KOH/g			Pass
Water-Insoluble Substances	No more than 0.1 %	0.07476% or 0.1%			Pass
Inorganic Impurities – Lead by ICP-MS	Lead (Pb) is no more than 2 mg/kg	**Pb Mass (amu)**	**LOQ (mg/kg)**	**Result (mg/kg)**	Pass
		206	0.2460	< LOQ	
		207		< LOQ	
		208		< LOQ	

Luke Bryant
Luke Bryant, B.A.
Analytical Chemist I

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Ramkumar Varadharajan, Ph.D.
Manager, Pharmaceutical Analysis and Testing

Khanh Ngo Courtney
Khanh Ngo Courtney, Ph.D.
Head of Laboratory Operations

History

Date	Revision	Changes
26Sep22	.00	New document

The work described in this report was conducted in compliance with the principles of current Good Manufacturing Practice. The following compliance exceptions were noted: results have been generated using method(s) that were not validated at this facility.

element

Certificate of Analysis

Date Received:	Client:	Method:
22Mar22	Mark Itzkoff Law Office of Mark Itzkoff mark@itzkofflaw.com	FCC Monograph: Polyvinyl Alcohol
Test Date: 13Apr22	**Sample Description:** *Refer to Table 1	**Element ID:** *Refer to Table 1
Issued Date: 29Apr22		**Element Project Code:** 22-92209

Table 1: Sample Info

Element ID	Sample Description
22MAR22LA1179	Polyvinyl alcohol powder, Kuraray Poval, 5-88 FA, Lot: NA22015118, 1 container
22MAR22LA1180	Polyvinyl alcohol powder, Kuraray Poval, 5-88 FA, Lot: NA22015117, 1 container
22MAR22LA1181	Polyvinyl alcohol powder, Kuraray Poval, 5-88 FA, Lot: NA22015126, 1 container

Table 2: ID Color Reaction A

Sample	Acceptance Criteria	Result	Pass/Fail
22MAR22LA1179	A blue color is produced upon addition of boric acid	A blue color was produced upon addition of boric acid	Pass
22MAR22LA1180		A blue color was produced upon addition of boric acid	Pass
22MAR22LA1181		A blue color was produced upon addition of boric acid	Pass

Table 3: ID Color Reaction B

Sample	Acceptance Criteria	Result	Pass/Fail
22MAR22LA1179	A dark red or blue color is produced after addition of iodine TS	A dark red color was produced after addition of iodine TS	Pass
22MAR22LA1180		A dark red color was produced after addition of iodine TS	Pass
22MAR22LA1181		A dark red color was produced after addition of iodine TS	Pass

The work described above was conducted in compliance with the principles of ISO 17025. The results reported accurately reflect the raw data.

Table 4: Acid Value

Sample	Acceptance Criteria	Result	Pass/Fail
22MAR22LA1179	NMT 3.0 mg KOH/g	1.1 mg KOH/g	Pass
22MAR22LA1180		1.0 mg KOH/g	Pass
22MAR22LA1181		1.0 mg KOH/g	Pass

Table 5: Ester Value

Sample	Acceptance Criteria	Result	Pass/Fail
22MAR22LA1179	Between 125 and 153 mg KOH/g	135 mg KOH/g	Pass
22MAR22LA1180		129 mg KOH/g	Pass
22MAR22LA1181		143 mg KOH/g	Pass

Table 6: Water Insoluble Substances

Sample	Acceptance Criteria	Result	Pass/Fail
22MAR22LA1179	NMT 0.1%	0.0062189% or 0.0%	Pass
22MAR22LA1180		0.0075714% or 0.0%	Pass
22MAR22LA1181		0.011431% or 0.0%	Pass

element

[redacted]

Aaron Lindstrom, B.S.
Manager, Pharma Analysis & Testing

29APR22
Date

[redacted]

Melinda Place, B.S.
Quality Assurance Specialist

29 APR 22
Date

The results detailed within this COA have been generated and reviewed by the following:

Name	Title
Khanh Ngo Courtney, Ph.D.	Head of Laboratory Operations
Aaron Lindstrom, B.S.	Technical Manager
Luke Byrant, B.A.	Analytical Chemist I

History

Date	Revision	Changes
29Apr22	.00	New document

APPENDIX IV

ESTIMATED CUMULATIVE DAILY INTAKE OF POLYVINYL ALCOHOL BY THE U.S. POPULATION FROM ALL DIETARY USES (2017-2018 NHANES)

CONFIDENTIAL

PREPARED FOR:
Mark L. Itzkoff
Counsel for NABACO, Ltd.
805 Valley View West Road
San Marcos, TX 78666

DATE:
15 November 2022

Estimated Cumulative Daily Intake of Polyvinyl Alcohol by the U.S. Population from All Dietary Uses (2017-2018 NHANES)

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Estimated Cumulative Daily Intake of Polyvinyl Alcohol by the U.S. Population from All Dietary Uses (2017-2018 NHANES)

1.0 INTRODUCTION

NABACO is proposing that the current conditions of use of polyvinyl alcohol be extended to include use as a fine protective coating for fruits and vegetables with edible peels in the United States (U.S.). Polyvinyl alcohol has previously been concluded to be Generally Recognized as Safe (GRAS) in a number of food applications (pizza dough packs, color packs in flavored beverages, flavored water drinks, hot chocolate, instant coffee and tea, and whey protein supplements) (GRAS Notice [GRN] 767) (U.S. FDA, 2004, 2018), as well as in dietary supplements and pharmaceutical products (GRN 141); therefore, background and cumulative exposure were also considered in the current assessment. Of note, polyvinyl alcohol has also been GRAS for use as the primary component in water-soluble plugs intended for use in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs (GRN 927) (Adept Limited, 2020; U.S. FDA, 2021a). However, this was not considered relevant as the proposed use is not for direct human consumption (see further details in Section 4.2).

As such, 3 different dietary exposure assessments were conducted to determine the impact of extending the food uses of polyvinyl alcohol to include a protective coating for fruit and vegetables under the proposed conditions of use, while also taking into consideration the background exposure to polyvinyl alcohol from the food and supplement uses included in GRN 141 and GRN 767 (Colorcon, 2003; U.S. FDA, 2004, 2018; MonoSol LLC, 2018):

1. Intake of polyvinyl alcohol from proposed conditions of use as a protective coating for fruits and vegetables;

2. Background exposure of polyvinyl alcohol from current uses based on GRN 141 and GRN 767; and

3. Cumulative intake of polyvinyl alcohol from the proposed use as a protective coating to fruit and vegetables, and background exposure from GRN 141 and GRN 767.

Estimates for the intake of polyvinyl alcohol were based on the food uses and use levels for polyvinyl alcohol in conjunction with food consumption data included in the U.S. National Center for Health Statistics' National Health and Nutrition Examination Surveys (NHANES) 2017-2018 (CDC, 2022a,b; USDA, 2022). As polyvinyl alcohol is GRAS in whey protein supplements (GRN 767 – MonoSol LLC, 2018; U.S. FDA, 2018), supplement composition data from the same NHANES survey was also applied in the exposure estimates. Calculations for the mean and 90th percentile consumer-only intakes were performed for each of the 3 exposure assessments described above, and the percentage of consumers were determined. In both cases, the per person and per kilogram body weight intakes were reported for the following population groups:

- Children, ages 2 to 5 years;
- Children, ages 6 to 11 years;
- Teenagers, ages 12 to 19 years;
- Adults, ages 20 years and older; and
- Total population (ages 2 years and older, and both gender groups combined).

2.0 FOOD CONSUMPTION SURVEY DATA

2.1 Survey Description

The NHANES are conducted as continuous, annual surveys, and they are released in 2-year cycles. During each year of the ongoing NHANES program, individuals from the U.S. are sampled from up to 30 different study locations in a complex multi-stage probability design intended to ensure the data are a nationally representative sample of the U.S. population.

NHANES 2017-2018 dietary survey data were collected from individuals and households *via* 24-hour dietary recalls administered on 2 non-consecutive days (Day 1 and Day 2) throughout all 4 seasons of the year. Day 1 data were collected in-person, and Day 2 data were collected by telephone in the following 3 to 10 days, on different days of the week, to achieve the desired degree of statistical independence. The data were collected by first selecting primary sampling units (PSUs), which were counties throughout the U.S., of which 30 PSUs are visited per year. Smaller contiguous counties were combined to attain a minimum population size. These PSUs were segmented, and households were chosen within each segment. One or more participants within a household were interviewed. For NHANES 2017-2018, 16,211 individuals were selected for the sample, 9,254 were interviewed (51.9%), and 8,704 were examined (48.8%).

Participants who completed the dietary intake data collection were also asked to complete a similar recall in which they documented the supplement products consumed within the previous 24 hours on 2 non-consecutive days. The participants were asked to record the name and manufacturer of the supplement, which is visually confirmed by the interviewer if possible. The amounts of individual ingredients present in the supplement are then itemized and entered into the NHANES database, which allows the data to be incorporated into the dietary intake estimates.

In addition to collecting information on the types and quantities of foods being consumed, NHANES 2017-2018 collected socio-economic, physiological, and demographic information from individual participants in the survey, such as sex, age, body weight, and other variables (such as height and race-ethnicity) that may be useful in characterizing consumption. The inclusion of this information allows for further assessment of food intake based on consumption by specific population groups of interest within the total population. The primary sample design for NHANES 2017-2018 includes an oversample of non-Hispanic Asian persons, Hispanic persons, non-Hispanic black persons, non-Hispanic white and “other” older persons (≥80 years), and non-Hispanic low income white and ”others” persons (≤185% of the Department of Health and Human Services poverty guidelines); however, sample weights were incorporated to allow estimates from these subgroups to be combined to obtain national estimates that reflect the relative proportions of these groups in the population as a whole (CDC, 2022a,b; USDA, 2022).

2.2 Statistical Methods

For the intake assessment, consumption data from individual dietary records, detailing food items ingested by each survey participant, were collated by computer and used to generate estimates for the intake of polyvinyl alcohol by the U.S. population.[1] Estimates for the daily intake of polyvinyl alcohol represent projected 2-day averages for each individual from Day 1 and Day 2 of NHANES 2017-2018 (*i.e.*, a value was established for each person). From these average amounts, a distribution was established from which the mean and percentile intake estimates for the cohort of interest were determined, which incorporated survey weights in order to provide representative intakes for the entire U.S. population. "Consumer-only" intake refers to the estimated intake of polyvinyl alcohol by only those individuals who reported consuming food products of interest on either Day 1 or Day 2 of the survey. The consumer-only estimates are more relevant to risk assessments as they represent exposures in the target population; consequently, only consumer-only intake results are presented herein.

3.0 FOOD USAGE DATA

The food uses and use levels for polyvinyl alcohol applied in the current exposure assessment are summarized in Table 3-1. Food codes representative of each food use were chosen from the NHANES 2017-2018 (CDC, 2022b). Food codes were grouped in food use categories according to Title 21, Section §170.3 of the *Code of Federal Regulations* (U.S. FDA, 2021b). If necessary, product-specific adjustment factors were developed for composite foods/mixtures based on data provided in the Food and Nutrient Database for Dietary Studies (USDA ARS, 2022a,b). All food codes included in the current intake assessment are listed in Appendix B.

One of the previously GRAS food uses of polyvinyl alcohol was "whey protein supplements" (GRN 767; U.S. MonoSol LLC, 2018; U.S. FDA, 2018). In order to fully account for the intakes of this food use, food codes for nutritional protein beverages (whey/protein nutritional drinks and shakes in both powder and ready-to-drink formats; see Appendix B for further details) from the NHANES 2017-2018 were included. In addition, the NHANES 2017-2018 supplements database was searched for dietary supplements containing "whey" in the product supplement name. The relevant supplement products were included in the intakes assessment (see Section 4.2 and Appendix B for further details).

Table 3-1 Summary of the Individual Food Uses and Use Levels for Polyvinyl Alcohol in the U.S.

Food Category (21 CFR §170.3 – U.S. FDA, 2021b)	Food Uses[a]	Polyvinyl Alcohol Use Levels (mg/100 g)
Proposed Uses		
Fresh Fruits and Fruit Juices	Coating of fruits with edible peels (*e.g.*, apples, pears, peaches *etc.*)	29
Fresh Vegetables, Tomatoes, and Potatoes	Coating of vegetables with edible peels (*e.g.*, zucchini, cucumber, eggplant, *etc.*)	29
Processed Fruits and Fruit Juices	Coating of fruits with edible peels (*e.g.*, canned apricots, canned peaches, *etc.*)	29
Processed Vegetables and Vegetable Juices	Coating of vegetables with edible peels (*e.g.*, canned tomatoes, pickled zucchini *etc.*)	29

[1] Statistical analysis and data management were conducted in DaDiet Software (Dazult Ltd., 2018). DaDiet Software is a web-based software tool that allows accurate estimate of exposure to nutrients and to substances added to foods, including contaminants, food additives and novel ingredients. The main input components are concentration (use level) data and food consumption data. Data sets are combined in the software to provide accurate and efficient exposure assessments.

Table 3-1 Summary of the Individual Food Uses and Use Levels for Polyvinyl Alcohol in the U.S.

Food Category (21 CFR §170.3 – U.S. FDA, 2021b)	Food Uses[a]	Polyvinyl Alcohol Use Levels (mg/100 g)
GRAS Food Uses[b]		
Baked Goods and Baking Mixes	Pizza dough packs[c]	5.36
Beverages and Beverage Bases	Color packs in flavored beverages[d] (non-dairy and non-alcohol)	0.176
	Flavored water drinks	11
	Hot chocolate	114
Coffee and Tea	Instant coffee	28
	Instant tea	28
Milk Products	Whey protein supplement[e]	142

CFR = *Code of Federal Regulations*; GRAS = Generally Recognized as Safe; U.S. = United States.

[a] Polyvinyl alcohol is intended for use in unstandardized products and not in foods where standards of identity exist and do not permit its addition.

[b] Based on food uses previously notified in GRAS Notice (GRN) 767 (U.S. FDA, 2018).

[c] The use level of 5.36 mg/100 g is reflective of the amount per pizza (based on the information provided in GRN 767); therefore, all pizza food codes were selected to represent this food use.

[d] Soft drinks were used to represent this category of flavored beverages as a worst-case scenario based on the information provided in GRN 767.

[e] Whey/protein nutritional beverages (powder and ready-to-drink formats) as well as whey protein dietary supplements were selected to represent this food use (see further details in Appendix B).

4.0 FOOD SURVEY RESULTS

Estimates for the total daily intakes of polyvinyl alcohol from proposed food uses are provided in Section 4.1. Estimates for the total background daily intakes of polyvinyl alcohol from GRAS food uses as presented in GRN 767 are provided in Section 4.2 (MonoSol LLC, 2018; U.S. FDA, 2018). Estimates for the total cumulative daily intakes of polyvinyl alcohol based on both proposed uses and GRAS food uses are provided in Section 4.3. Estimates for the daily intake of polyvinyl alcohol from individual food uses in the U.S. are summarized in Section 4.4 and are presented in Appendix A for the total population aged 2 years and older.

4.1 Estimated Daily Intake of Polyvinyl Alcohol from All Proposed Uses in the U.S.

Table 4.1-1 summarizes the estimated total intake of polyvinyl alcohol on both an absolute basis (mg/person/day) and a per body weight basis (mg/kg body weight/day) from all proposed uses in the U.S. population. The percentage of consumers was moderate among all age groups evaluated in the current intake assessment; more than 49.9% of the population groups consisted of consumers of food products in which polyvinyl alcohol is currently proposed for use (see Table 4.1-1). Children (2 to 5 years old) had the greatest proportion of consumers at 76.1%.

Among the total population (ages 2 years and older), the mean and 90th percentile consumer-only intakes of polyvinyl alcohol based on proposed uses were determined to be 34 and 73 mg/person/day, respectively. Of the individual population groups, adults were determined to have the greatest mean and 90th percentile consumer-only intakes of polyvinyl alcohol on an absolute basis, at 34 and 75 mg/person/day, respectively, while children (2 to 5 years old) had the lowest mean and 90th percentile consumer-only intakes of 30 and 57 mg/person/day, respectively.

On a body weight basis, the total population (ages 2 years and older) mean and 90th percentile consumer-only intakes of polyvinyl alcohol were determined to be 0.58 and 1.39 mg/kg body weight/day, respectively. Among the individual population groups, children (2 to 5 years old) were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 1.79 and 3.34 mg/kg body weight/day, respectively. Adults had the lowest mean and 90th percentile consumer-only intakes of 0.44 and 1.04 mg/kg body weight/day, respectively (see Table 4.1-1).

Table 4.1-1 Summary of the Estimated Daily Intake of Polyvinyl Alcohol from Proposed Food Uses in the U.S. by Population Group (2017-2018 NHANES Data)

Population Group	Age Group	Consumer-Only Intake					
		Percentage of Population (%)	n	Absolute Basis (mg/day)		Body Weight Basis (mg/kg bw/day)	
				Mean	90th Percentile	Mean	90th Percentile
Children	2 to 5 yrs	76.1	348	30	57	1.79	3.34
Children	6 to 11 yrs	70.2	449	33	66	1.07	2.23
Teenagers	12 to 19 yrs	49.9	431	32	66	0.56	1.16
Adults	20 and older yrs	67.8	2,735	34	75	0.44	1.04
Total Population	2 and older yrs	66.5	3,963	34	73	0.58	1.39

bw = body weight; n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States; yrs = years.

4.2 Dietary Exposure of Polyvinyl Alcohol from GRAS Food Uses in the U.S.

As previously mentioned, polyvinyl alcohol was determined to be GRAS for specific uses in GRN 141, GRN 767, and GRN 927 (U.S. FDA, 2004; 2018, 2021a); however, the use of polyvinyl alcohol in GRN 927 was not considered relevant to the current intakes assessment, as direct human consumption is not a proposed use (U.S. FDA, 2021a). In GRN 927, polyvinyl alcohol was proposed for use as the primary component in water-soluble plugs intended for use in abattoirs to plug the anus of slaughtered sheep, lambs, and hogs. As part of GRN 927, it was determined that:

> *"No dietary exposure to polyvinyl alcohol or its constituents is expected because less than 1% (by weight) of the plug will dissolve under the intended conditions of use and any low levels of polyvinyl alcohol that do dissolve will be removed from animal tissues during the extensive washing steps that accompany breakdown of the animal"* (U.S. FDA, 2021a).

In GRN 767, polyvinyl alcohol was determined to be GRAS for use as an edible film in a variety of food uses, specifically the use:

> "[...] *to form pouches containing pre-portioned aliquots of (1) certain dry ingredients (i.e., instant tea, instant coffee, hot chocolate mix, flavored drink powder, and whey protein supplement powder) to be used by the consumer in preparing ready-to-serve foods and beverages, (2) approved color additives to be used in manufacturing flavored beverages (non-dairy and non-alcohol), and (3) dry ingredients to be used by commercial establishments in making pizza dough*"[2] (U.S. FDA, 2018).

[2] Table 3-1 for all uses and use levels.

Therefore, an exposure assessment was conducted to determine the intakes of polyvinyl alcohol based on these GRAS food uses and use levels using data from the NHANES 2017-2018 database (using the same methodology as discussed in Sections 2.1 and 2.2). It should be noted that the use of polyvinyl alcohol as an aqueous film coating in dietary supplement and pharmaceutical products (based on GRN 141 – Colorcon, 2003; U.S. FDA, 2004) will be considered in the cumulative assessment (see Section 4.3).

Table 4.2-1 summarizes the estimated total intake of polyvinyl alcohol from all GRAS food uses (based on GRN 767 – MonoSol LLC, 2018; U.S. FDA, 2018) in the U.S. population groups on an absolute (mg/person/day) and per body weight basis (mg/kg body weight/day). The percentage of consumers was moderate among all age groups evaluated in the current intake assessment; more than 52.1% of the population groups consisted of consumers of food products in which polyvinyl alcohol is currently proposed for use (see Table 4.2-1). Teenagers had the greatest proportion of consumers at 71.3%.

Among the total population (ages 2 years and older), the mean and 90th percentile consumer-only intakes of polyvinyl alcohol were determined to be 50 and 151 mg/person/day, respectively. Of the individual population groups, adults were determined to have the greatest mean and 90th percentile consumer-only intakes of polyvinyl alcohol on an absolute basis, at 57 and 184 mg/person/day, respectively, while children (2 to 5 years old) had the lowest mean and 90th percentile consumer-only intakes of 15 and 28 mg/person/day, respectively.

On a body weight basis, the total population (ages 2 years and older) mean and 90th percentile consumer-only intakes of polyvinyl alcohol were determined to be 0.72 and 2.13 mg/kg body weight/day, respectively. Among the individual population groups, children (2 to 5 years old) were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 0.93 and 2.09 mg/kg body weight/day, respectively. Teenagers had the lowest mean and 90th percentile consumer-only intakes of 0.57 and 1.15 mg/kg body weight/day, respectively (see Table 4.2-1).

Table 4.2-1 Summary of the Estimated Daily Intake of Polyvinyl Alcohol from GRAS Uses in the U.S. by Population Group (2017-2018 NHANES Data)

Population Group	Age Group	Consumer-Only Intake					
		Percentage of Population (%)	n	Absolute Basis (mg/day)		Body Weight Basis (mg/kg bw/day)	
				Mean	90th Percentile	Mean	90th Percentile
Children	2 to 5 yrs	52.1	226	15	28	0.93	2.09
Children	6 to 11 yrs	66.3	445	20	38	0.61	1.15
Teenagers	12 to 19 yrs	71.3	638	34	72	0.57	1.15
Adults	20 and older yrs	64.1	2,705	57	184	0.74	2.33
Total Population	2 and older yrs	64.4	4,014	50	151	0.72	2.13

bw = body weight; GRAS = Generally Recognized as Safe; n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States; yrs = years.

4.3 Cumulative Dietary Exposure from Proposed Uses and Background GRAS Uses

Table 4.3-1 summarizes the estimated cumulative total intake of polyvinyl alcohol on both an absolute basis (mg/person/day) and on a per body weight basis (mg/kg body weight/day) from all proposed and GRAS uses in the U.S. population. The percentage of consumers was high among all age groups evaluated in the current intake assessment; more than 90.1% of the population groups consisted of consumers of food products in which polyvinyl alcohol is currently proposed for use or from previous GRAS food uses (see Table 4.3-1). Children (2 to 5 years old) had the greatest proportion of consumers at 92.2%.

Among the total population (ages 2 years and older), the mean and 90th percentile consumer-only intakes of polyvinyl alcohol based on proposed and GRAS uses were determined to be 61 and 142 mg/person/day, respectively. Of the individual population groups, adults were determined to have the greatest mean and 90th percentile consumer-only intakes of polyvinyl alcohol on an absolute basis, at 66 and 159 mg/person/day, respectively, while children (2 to 5 years old) had the lowest mean and 90th percentile consumer-only intakes of 34 and 69 mg/person/day, respectively.

On a body weight basis, the total population (2 years and older) mean and 90th percentile consumer-only intakes of polyvinyl alcohol were determined to be 0.94 and 2.35 mg/kg body weight/day, respectively. Among the individual population groups, children (2 to 5 years old) were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 2.00 and 4.25 mg/kg body weight/day, respectively. Teenagers had the lowest mean and 90th percentile consumer-only intakes of 0.78 and 1.56 mg/kg body weight/day, respectively (see Table 4.3-1).

Table 4.3-1 Summary of the Estimated Cumulative Daily Intake of Polyvinyl Alcohol from Proposed and GRAS Food Uses in the U.S. by Population Group (2017-2018 NHANES Data)

Population Group	Age Group	Consumer-Only Intake					
		Percentage of Population (%)	n	Absolute Basis (mg/day)		Body Weight Basis (mg/kg bw/day)	
				Mean	90th Percentile	Mean	90th Percentile
Children	2 to 5 yrs	92.2	420	34	69	2.00	4.25
Children	6 to 11 yrs	91.5	605	40	86	1.26	2.81
Teenagers	12 to 19 yrs	87.4	775	46	94	0.78	1.56
Adults	20 and older yrs	90.2	3,733	66	159	0.86	2.08
Total Population	2 and older yrs	90.1	5,533	61	142	0.94	2.35

bw = body weight; GRAS = Generally Recognized as Safe; n = sample size; NHANES = National Health and Nutrition Examination Survey; U.S. = United States; yrs = years.

In addition, polyvinyl alcohol has been GRAS for use in aqueous film coating formulations applied to tablets or capsules belonging to dietary supplements and pharmaceutical products based on GRN 141 (Colorcon, 2003; U.S. FDA, 2004). The coating formulation was reported at up to 4% (by weight) of the tablet or capsule, and polyvinyl alcohol is comprised of up to 45% (by weight) of the coating formulation. Using a very conservative estimation of exposure to polyvinyl alcohol, it was estimated that the maximum intakes of polyvinyl alcohol would be ten 1-g tablets or capsules from both pharmaceutical products and dietary supplements, which provides an intakes estimation of 360 mg/person/day (or equivalent to 6 mg/kg body weight/day based on a 60-kg individual) (Colorcon, 2003; U.S. FDA, 2004). In order to determine the worst-case cumulative intakes of polyvinyl alcohol, this additional 6 mg/kg body weight/day from the use of

polyvinyl alcohol in dietary supplements and pharmaceutical products was summed with the highest 90th percentile cumulative intakes of polyvinyl alcohol (proposed food uses and GRAS uses based on GRN 767 and 141 – Colorcon, 2003; U.S. FDA, 2004, 2018; MonoSol LLC, 2018). For example, the highest 90th percentile intake of polyvinyl alcohol was observed in children at 4.25 mg/kg body weight/day (as shown in Table 4.3-1); therefore, the worst-case cumulative daily intake of polyvinyl alcohol was calculated to be 10.25 mg/kg body weight/day (*i.e.*, 4.25 + 6 mg/kg body weight/day).

4.4 Estimated Cumulative Daily Intake of Polyvinyl Alcohol from Individual Food Uses in the U.S.

Estimates for the mean and 90th percentile cumulative daily intakes of polyvinyl alcohol from each individual food category are summarized in Appendix A for the total population (ages 2 years and older). The total U.S. population was identified as being significant consumers of color packs (46.0% consumers), fresh fruit (35.5% consumers), processed vegetables (31.2 % consumers), fresh vegetables (29.0% consumers), and pizza dough (22.1% consumers).

In terms of contribution to total mean intake of polyvinyl alcohol, whey protein supplement (which contributed 34.0% to total mean intakes) and fresh fruit (which contributed 20.0% to total mean intakes) were the 2 main sources of intake across the total U.S. population. The remaining food uses all individually contributed ≤10.7% to the total mean polyvinyl alcohol intakes among the total population group.

5.0 DISCUSSION OF EXPOSURE ASSESSMENT RESULTS

In the current assessment, it should be noted that the intake results (from Section 4.2) based on GRAS food uses (GRN 767; MonoSol LLC, 2018) were significantly lower than the results reported in GRN 767 (MonoSol LLC, 2018). A comparison of the intake results from GRN 767 and the current assessment are summarized below in Table 5-1. There are a number of reasons for this difference. For example, the methodology applied to estimate the daily intakes of polyvinyl alcohol in GRN 767 differed from the methodology utilized in this assessment (as discussed in Sections 2.1 and 2.2). Firstly, in GRN 767 the estimated intakes of each food use (pizza dough packs, color packs, *etc*.) were summed together (as shown in Table 5-1) to determine the estimated polyvinyl alcohol intake of 39.16 mg/kg body weight/day, whereas the current assessment applied statistical modeling to generate a distribution curve from which the mean and percentile intake estimates for the cohort of interest were determined and survey weights were incorporated in order to provide representative intakes for the entire U.S. population. The summation of intakes produces a crude estimate, as it assumes an individual could be a consumer of all of the food uses in a given day, which is unrealistic. For example, the largest difference in intake results was observed in the "whey protein supplement" category (see Table 5-1). The intake results of whey protein supplement from GRN 767 were estimated to be 24.47 mg/kg body weight/day, which is about 3-fold higher than the intakes from the current assessment. The calculated value based on the NHANES 2017-2018 data is considerably lower than the value obtained in GRN 767, which assumed that the whole population consumed a whey protein supplement; however, in reality, based on the 2017-2018 NHANES data only 5.7% of the U.S. population consumed a whey protein supplement. Furthermore, GRN 767 applied food consumption data from 1994 to 1996 (Continuing Survey of Food Intakes [CSFII] 1994-96), which is now outdated. The current assessment applied the most up-to date food consumption data for the U.S. population (NHANES 2017-2018); therefore, the current assessment is more reflective of the current patterns of consumption.

Table 5-1 Comparison of the Estimated Daily Intake of Polyvinyl Alcohol between the Current Assessment and GRN 767 (MonoSol LLC, 2018; U.S. FDA, 2018)

Food Use	Current Assessment Based on GRAS food uses from GRN 767 using the NHANES 2017-2018		Estimate in GRN 767[a] (mg/kg bw/day)
	Mean (mg/kg bw/day)	90th Percentile (mg/kg bw/day)	
Pizza dough packs	0.11	0.23	0.625
Color packs in flavored beverages (non-dairy and non-alcohol)	0.01	0.02	0.03
Flavored water drinks	0.54	0.89	1.87
Hot chocolate	3.51	7.65	6.72
Instant coffee	1.04	1.86	5.45
Instant tea	1.22	2.71	
Whey protein supplement	4.57	7.72	24.47
Total intakes	**0.72[b]**	**2.13[b]**	**39.16[c]**

bw = body weight; GRN = GRAS Notice.
[a] Details based on GRN 767 (U.S. FDA, 2018).
[b] Based on the methodology described in Section 2.1 and 2.2.
[c] Total intakes were summed, according to the methodology described in GRN 767 (MonoSol LLC, 2018; U.S. FDA, 2018).

6.0 CONCLUSION

Consumption data and information pertaining to the individual proposed and GRAS food uses of polyvinyl alcohol were used to estimate the consumer-only intakes of polyvinyl alcohol for specific demographic groups and for the total U.S. population. There were a number of assumptions included in the assessment, rendering exposure estimates that may be considered suitably conservative. For example, it has been assumed in the above exposure assessments that all food products within a food category contain polyvinyl alcohol at the maximum specified level of use. In reality, the levels added to specific foods will vary depending on the nature of the food product and it is unlikely that polyvinyl alcohol will have 100% market penetration in all identified food categories.

In summary, among the total population (ages 2 years and older), the mean and 90th percentile intakes of polyvinyl alcohol based on proposed uses were determined to be 34 and 73 mg/person/day, respectively. On a body weight basis, the total population (ages 2 years and older) mean and 90th percentile consumer-only intakes of polyvinyl alcohol were determined to be 0.58 and 1.39 mg/kg body weight/day, respectively.

When considering all dietary sources of polyvinyl alcohol (proposed uses and GRAS uses based on GRN 767 and 141 – U.S. FDA, 2004, 2018), the cumulative daily intake of polyvinyl alcohol was estimated to be up to 10.25 mg/kg body weight/day, which is substantially below the acceptable daily intake of 50 mg/kg body weight/day for polyvinyl alcohol (JECFA, 2004).

7.0 REFERENCES

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APPENDIX A
Estimated Daily Intake of Polyvinyl Alcohol from Individual Food Uses in the Total U.S. Population Aged 2 Years and Older (2017-2018 NHANES Data)

Table A-1 Estimated Cumulative Daily Intake of Polyvinyl Alcohol from Individual Food Uses by the U.S. Population Aged 2 Years and Older (2017-2018 NHANES Data)

Food Use Category	% Contribution to Total Mean Intake	Consumer-Only Intake					
		Percentage of Population (%)	n	Absolute Basis (mg/day)		Body Weight Basis (mg/kg bw/day)	
				Mean	90th Percentile	Mean	90th Percentile
All	***100***	***90.1***	***5,533***	***61***	***142***	***0.94***	***2.35***
Proposed Uses							
Fresh Fruit Peels	20.0	35.5	2,226	31	58	0.60	1.36
Processed Fruit Peels	1.8	8.1	475	12	31	0.22	0.53
Fresh Vegetable Peels	8.5	29.0	1,603	16	36	0.25	0.57
Processed Vegetable Peels	10.7	31.2	1,756	19	46	0.27	0.66
GRN 767 GRAS Uses							
Pizza Dough Packs	2.7	22.1	1,374	7	12	0.11	0.23
Color Packs	0.6	46.0	2,835	1	2	0.01	0.02
Flavored Drink	1.7	2.5	120	37	59	0.54	0.89
Hot Chocolate	5.9	1.7	118	194	362	3.51	7.65
Instant Coffee	9.5	6.5	577	80	143	1.04	1.86
Instant Tea	4.6	2.7	135	94	206	1.22	2.71
Whey Protein Supplement	34.0	5.7	262	326	576	4.57	7.72

bw = body weight; GRAS = Generally Recognized as Safe; GRN = GRAS Notice; n = sample size; na = not available; NHANES = National Health and Nutrition Examination Surveys; U.S. = United States.

APPENDIX B
Representative Food Codes for All Uses (Proposed Uses and GRAS Uses) of Polyvinyl Alcohol in the U.S. (2017-2018 NHANES Data)

Representative Food Codes for Proposed Uses and GRAS Uses of Polyvinyl Alcohol in the U.S. (2017-2018 NHANES Data)

Proposed Food Uses

Coatings of Fresh Fruits with Edible Peels
[Polyvinyl Alcohol] = 29 mg/100 g

63101000	Apple, raw
63123000	Grapes, raw
63131010	Nectarine, raw
63135010	Peach, raw
63137010	Pear, raw
63137050	Pear, Asian, raw
63201010	Blackberries, raw
63203010	Blueberries, raw
63207010	Cranberries, raw
63219000	Raspberries, raw
63223020	Strawberries, raw
63103010	Apricot, raw
63109700	Starfruit, raw
63115010	Cherries, raw
63119010	Fig, raw
63125010	Guava, raw
63126500	Kiwi fruit, raw
63139010	Persimmon, raw
63143010	Plum, raw

Coatings of Fresh Vegetables with Edible Peels
[Polyvinyl Alcohol] = 29 mg/100 g

73101010	Carrots, raw
73302010	Winter squash, raw
74101000	Tomatoes, raw
75101800	Green beans, raw
75102500	Beets, raw
75111000	Cucumber, raw
75111200	Eggplant, raw
75112000	Kohlrabi, raw
75115000	Mushrooms, raw
75121400	Pepper, poblano, raw
75121500	Pepper, Serrano, raw
75122000	Pepper, raw, NFS
75122100	Pepper, sweet, green, raw

75122200 Pepper, sweet, red, raw
75124000 Pepper, banana, raw
75125000 Radish, raw
75127000 Rutabaga, raw
75128000 Summer squash, yellow, raw
75128010 Summer squash, green, raw
75129000 Turnip, raw
73101110 Carrots, raw, salad
73101210 Carrots, raw, salad with apples
75121000 Pepper, hot chili, raw
75127750 Snowpeas, raw

Coatings of Processed Fruits with Edible Peels
[Polyvinyl Alcohol] = 29 mg/100 g

62101100 Apple, dried
62104100 Apricot, dried
62105000 Blueberries, dried
62106000 Cherries, dried
62108100 Currants, dried
62109100 Cranberries, dried
62110100 Date
62113100 Fig, dried
62116100 Peach, dried
62119100 Pear, dried
62120000 Persimmon, dried
62122100 Prune, dried
62125100 Raisins
63101310 Apple, baked
63135620 Peach, frozen
63200100 Berries, NFS
63201600 Blackberries, frozen
63203110 Bluberries, canned
63203600 Blueberries, frozen
63219610 Raspberries, frozen
63223110 Strawberries, canned
63223610 Strawberries, frozen
63103110 Apricot, canned
63111010 Cherries, maraschino
63115110 Cherries, canned
63115200 Cherries, frozen
63119110 Fig, canned
63135110 Peach, canned, NFS
63135140 Peach, canned, in syrup
63135170 Peach, canned, juice pack

63137110 Pear, canned, NFS
63137140 Pear, canned, in syrup
63137170 Pear, canned, juice pack
63143110 Plum, canned
63401060 Apple, candied

Coatings of Processed Vegetables with Edible Peels
[Polyvinyl Alcohol] = 29 mg/100 g

71000100 Potato, NFS
71100100 Potato, baked, NFS
71101000 Potato, baked, peel not eaten
71102980 Potato, boiled, NFS
71102990 Potato, boiled, ready-to-heat
71103105 Potato, boiled, from fresh, peel eaten, NS as to fat
71103115 Potato, boiled, from fresh, peel eaten, fat added, NS as to fat type
71103125 Potato, boiled, from fresh, peel eaten, no added fat
71103135 Potato, boiled, from fresh, peel eaten, made with oil
71103140 Potato, boiled, from fresh, peel eaten, made with butter
71103150 Potato, boiled, from fresh, peel eaten, made with margarine
71104040 Potato, roasted, from fresh, peel eaten, NS as to fat
71104050 Potato, roasted, from fresh, peel eaten, no added fat
71104060 Potato, roasted, from fresh, peel eaten, fat added, NS as to fat type
71104070 Potato, roasted, from fresh, peel eaten, made with oil
71104080 Potato, roasted, from fresh, peel eaten, made with butter
71104090 Potato, roasted, from fresh, peel eaten, made with margarine
71508001 Potato, baked, peel eaten
71508005 Potato, baked, peel eaten, with butter
71508010 Potato, baked, peel eaten, with sour cream
71508020 Potato, baked, peel eaten, with cheese
71508025 Potato, baked, peel eaten, with meat
71508030 Potato, baked, peel eaten, with chili
71508035 Potato, baked, peel eaten, with vegetables
73102190 Carrots, cooked, from restaurant
73102211 Carrots, fresh, cooked, no added fat
73102212 Carrots, frozen, cooked, no added fat
73102217 Carrots, fresh, cooked with oil
73102218 Carrots, fresh, cooked with butter or margarine
73102220 Carrots, NS as to form, cooked
73102221 Carrots, fresh, cooked, fat added, NS as to fat type
73102222 Carrots, frozen, cooked, fat added, NS as to fat type
73102224 Carrots, frozen, cooked with oil
73102225 Carrots, frozen, cooked with butter or margarine
73102241 Carrots, glazed, cooked
73303010 Winter squash, cooked, no added fat

73303020	Winter squash, cooked, fat added
73401000	Sweet potato, NFS
73402000	Sweet potato, baked, peel eaten, NS as to fat
73402010	Sweet potato, baked, peel eaten, no added fat
73402020	Sweet potato, baked, peel eaten, fat added, NS as to fat type
73402021	Sweet potato, baked, peel eaten, made with oil
73402022	Sweet potato, baked, peel eaten, made with butter
73402023	Sweet potato, baked, peel eaten, made with margarine
74201000	Tomatoes, NS as to form, cooked
74201001	Tomatoes, fresh, cooked
74205010	Fried green tomatoes
74205020	Tomato, green, pickled
74206000	Sun-dried tomatoes
75205005	Green beans, cooked, from restaurant
75205021	Green beans, fresh, cooked, no added fat
75205022	Green beans, frozen, cooked, no added fat
75205023	Green beans, canned, cooked, no added fat
75205030	Green beans, NS as to form, cooked
75205031	Green beans, fresh, cooked, fat added, NS as to fat type
75205032	Green beans, frozen, cooked, fat added, NS as to fat type
75205033	Green beans, canned, cooked, fat added, NS as to fat type
75205044	Green beans, fresh, cooked with oil
75205045	Green beans, fresh, cooked with butter or margarine
75205047	Green beans, frozen, cooked with oil
75205048	Green beans, frozen, cooked with butter or margarine
75208011	Beets, fresh, cooked, no added fat
75208020	Beets, NS as to form, cooked
75208021	Beets, fresh, cooked, fat added
75217010	Eggplant, cooked, no added fat
75217020	Eggplant, cooked, fat added
75219011	Mushrooms, fresh, cooked, no added fat
75219020	Mushrooms, NS as to form, cooked
75219021	Mushrooms, fresh, cooked, fat added, NS as to fat type
75219023	Mushrooms, canned, cooked
75219033	Mushrooms, fresh, cooked with oil
75219034	Mushrooms, fresh, cooked with butter or margarine
75219100	Mushroom, Asian, cooked, from dried
75220011	Okra, fresh, cooked, no added fat
75220012	Okra, frozen, cooked, no added fat
75220020	Okra, NS as to form, cooked
75220021	Okra, fresh, cooked, fat added
75220022	Okra, frozen, cooked, fat added
75222020	Parsnips, cooked
75226020	Peppers, green, cooked
75226060	Peppers, red, cooked

75227110	Daikon radish, cooked
75231011	Snowpea, fresh, cooked, no added fat
75231012	Snowpea, frozen, cooked, no added fat
75231020	Snowpea, NS as to form, cooked
75231021	Snowpea, fresh, cooked, fat added
75231022	Snowpea, frozen, cooked, fat added
75233011	Summer squash, yellow or green, fresh, cooked, no added fat
75233012	Summer squash, yellow or green, frozen, cooked, no added fat
75233013	Summer squash, yellow or green, canned, cooked, no added fat
75233020	Summer squash, yellow or green, NS as to form, cooked
75233021	Summer squash, yellow or green, fresh, cooked, fat added, NS as to fat type
75233022	Summer squash, yellow or green, frozen, cooked, fat added, NS as to fat type
75233023	Summer squash, yellow or green, canned, cooked, fat added, NS as to fat type
75233027	Summer squash, yellow or green, fresh, cooked with oil
75233028	Summer squash, yellow or green, fresh, cooked with butter or margarine
75233030	Summer squash, yellow or green, frozen, cooked with oil
75233031	Summer squash, yellow or green, frozen, cooked with butter or margarine
75233033	Summer squash, yellow or green, canned, cooked with oil
75233034	Summer squash, yellow or green, canned, cooked with butter or margarine
75234021	Turnip, cooked
75412010	Fried eggplant
75414030	Fried mushrooms
75510000	Olives, NFS
75510010	Olives, green
75510020	Olives, black
75511100	Pickles, NFS
71103300	Potato, canned, NS as to fat
71103310	Potato, canned, fat added, NS as to fat type
71103320	Potato, canned, no added fat
71104030	Potato, roasted, NFS
71104200	Potato, roasted, ready-to-heat
71106000	Stewed potatoes, Puerto Rican style
71106010	Potato only from Puerto Rican mixed dishes, gravy and other components reported separately
71106020	Potato from Puerto Rican style stuffed pot roast, with gravy
71106050	Potato from Puerto Rican beef stew, with gravy
71106070	Potato from Puerto Rican chicken fricassee, with sauce
71410000	Potato skins without topping
71410500	Potato skins, with cheese
71411000	Potato skins, with cheese and bacon
71411100	Potato skins, NFS
71703990	Stewed potatoes
71704000	Stewed potatoes with tomatoes
73201020	Pumpkin, cooked
73210010	Calabaza, cooked

73405000	Sweet potato, boiled, NS as to fat
73405010	Sweet potato, boiled, no added fat
73405020	Sweet potato, boiled, fat added, NS as to fat type
73405021	Sweet potato, boiled, made with oil
73405022	Sweet potato, boiled, made with butter
73405023	Sweet potato, boiled, made with margarine
74201003	Tomatoes, canned, cooked
74204500	Tomatoes, canned, reduced sodium, cooked
75205050	Green beans, canned, cooked with oil
75205051	Green beans, canned, cooked with butter or margarine
75205120	Green beans, canned, reduced sodium, cooked, no added fat
75205130	Green beans, canned, reduced sodium, cooked, fat added, NS as to fat type
75205131	Green beans, canned, reduced sodium, cooked with oil
75205132	Green beans, canned, reduced sodium, cooked with butter or margarine
75205200	Fried green beans
75206020	Yellow string beans, cooked
75216720	Cucumber, cooked
75226111	Hot peppers, cooked
75226700	Pimiento
75511020	Peppers, pickled
75511040	Pepper, hot, pickled
75535000	Zucchini, pickled

GRAS Food Uses

Baked Goods and Baking Mixes

Pizza Dough Packs

[Polyvinyl Alcohol] = 5.36 mg/100 g

58106200	Pizza, cheese, from frozen, thin crust
58106205	Pizza, cheese, from frozen, thick crust
58106210	Pizza, cheese, from restaurant or fast food, NS as to type of crust
58106220	Pizza, cheese, from restaurant or fast food, thin crust
58106225	Pizza, cheese, from restaurant or fast food, medium crust
58106230	Pizza, cheese, from restaurant or fast food, thick crust
58106233	Pizza, cheese, stuffed crust
58106234	Pizza, cheese, from school lunch, medium crust
58106235	Pizza, cheese, from school lunch, thin crust
58106236	Pizza, cheese, from school lunch, thick crust
58106250	Pizza, extra cheese, thin crust
58106260	Pizza, extra cheese, thick crust
58106300	Pizza, cheese, with vegetables, from frozen, thin crust
58106305	Pizza, cheese with vegetables, from frozen, thick crust
58106320	Pizza, cheese, with vegetables, from restaurant or fast food, thin crust

58106325 Pizza, cheese, with vegetables, from restaurant or fast food, medium crust
58106330 Pizza, cheese, with vegetables, from restaurant or fast food, thick crust
58106345 Pizza with cheese and extra vegetables, thin crust
58106347 Pizza with cheese and extra vegetables, medium crust
58106350 Pizza with cheese and extra vegetables, thick crust
58106358 Pizza, cheese, with fruit, thin crust
58106359 Pizza, cheese, with fruit, medium crust
58106360 Pizza, cheese, with fruit, thick crust
58106512 Pizza with pepperoni, from frozen, thin crust
58106514 Pizza with pepperoni, from frozen, medium crust
58106516 Pizza with pepperoni, from frozen, thick crust
58106540 Pizza with pepperoni, from restaurant or fast food, NS as to type of crust
58106550 Pizza with pepperoni, from restaurant or fast food, thin crust
58106555 Pizza with pepperoni, from restaurant or fast food, medium crust
58106560 Pizza with pepperoni, from restaurant or fast food, thick crust
58106565 Pizza with pepperoni, stuffed crust
58106570 Pizza with pepperoni, from school lunch, thin crust
58106578 Pizza, with pepperoni, from school lunch, medium crust
58106580 Pizza with pepperoni, from school lunch, thick crust
58106602 Pizza with meat other than pepperoni, from frozen, thin crust
58106604 Pizza with meat other than pepperoni, from frozen, medium crust
58106606 Pizza with meat other than pepperoni, from frozen, thick crust
58106610 Pizza with meat other than pepperoni, from restaurant or fast food, NS as to type of crust
58106620 Pizza with meat other than pepperoni, from restaurant or fast food, thin crust
58106625 Pizza with meat other than pepperoni, from restaurant or fast food, medium crust
58106630 Pizza with meat other than pepperoni, from restaurant or fast food, thick crust
58106633 Pizza, with meat other than pepperoni, stuffed crust
58106634 Pizza, with meat other than pepperoni, from school lunch, medium crust
58106635 Pizza, with meat other than pepperoni, from school lunch, thin crust
58106636 Pizza, with meat other than pepperoni, from school lunch, thick crust
58106650 Pizza with extra meat, thin crust
58106655 Pizza with extra meat, medium crust
58106660 Pizza with extra meat, thick crust
58106700 Pizza with meat and vegetables, from frozen, thin crust
58106702 Pizza with meat and vegetables, from frozen, medium crust
58106705 Pizza with meat and vegetables, from frozen, thick crust
58106720 Pizza with meat and vegetables, from restaurant or fast food, thin crust
58106725 Pizza with meat and vegetables, from restaurant or fast food, medium crust
58106730 Pizza with meat and vegetables, from restaurant or fast food, thick crust
58106736 Pizza with extra meat and extra vegetables, thin crust
58106737 Pizza with extra meat and extra vegetables, thick crust
58106738 Pizza with extra meat and extra vegetables, medium crust
58106750 Pizza with meat and fruit, thin crust
58106755 Pizza with meat and fruit, medium crust

58106760 Pizza with meat and fruit, thick crust
58106820 Pizza with beans and vegetables, thin crust
58106830 Pizza with beans and vegetables, thick crust
58107050 Pizza, no cheese, thin crust
58107100 Pizza, no cheese, thick crust
58107205 White pizza, cheese, thin crust
58107207 White pizza, cheese, thick crust
58107212 White pizza, cheese, with vegetables, thin crust
58107214 White pizza, cheese, with vegetables, thick crust
58107222 White pizza, cheese, with meat, thin crust
58107224 White pizza, cheese, with meat, thick crust
58107232 White pizza, cheese, with meat and vegetables, thin crust
58107234 White pizza, cheese, with meat and vegetables, thick crust
58109015 Pizza, cheese, whole wheat thin crust
58109020 Pizza, cheese, whole wheat thick crust
58109030 Pizza, with meat, whole wheat thin crust
58109040 Pizza, with meat, whole wheat thick crust
58109050 Pizza, cheese and vegetables, whole wheat thin crust
58109060 Pizza, cheese and vegetables, whole wheat thick crust
58109100 Pizza, cheese, gluten-free thin crust
58109110 Pizza, cheese, gluten-free thick crust
58109120 Pizza, with meat, gluten-free thin crust
58109130 Pizza, with meat, gluten-free thick crust
58109140 Pizza, cheese and vegetables, gluten-free thin crust
58109150 Pizza, cheese and vegetables, gluten-free thick crust

Beverages and Beverage Bases

Color Packs in Flavored Beverages (non-dairy and non-alcohol)
[Polyvinyl Alcohol] = 0.176 mg/100 g

92400000 Soft drink, NFS
92400100 Soft drink, NFS, diet
92410110 Carbonated water, sweetened
92410210 Carbonated water, unsweetened
92410250 Carbonated water, sweetened, with low-calorie or no-calorie sweetener
92410310 Soft drink, cola
92410315 Soft drink, cola, reduced sugar
92410320 Soft drink, cola, diet
92410340 Soft drink, cola, decaffeinated
92410350 Soft drink, cola, decaffeinated, diet
92410360 Soft drink, pepper type
92410370 Soft drink, pepper type, diet
92410390 Soft drink, pepper type, decaffeinated
92410400 Soft drink, pepper type, decaffeinated, diet

92410410 Soft drink, cream soda
92410420 Soft drink, cream soda, diet
92410510 Soft drink, fruit flavored, caffeine free
92410520 Soft drink, fruit flavored, diet, caffeine free
92410550 Soft drink, fruit flavored, caffeine containing
92410560 Soft drink, fruit flavored, caffeine containing, diet
92410610 Soft drink, ginger ale
92410620 Soft drink, ginger ale, diet
92410710 Soft drink, root beer
92410720 Soft drink, root beer, diet
92410810 Soft drink, chocolate flavored
92410820 Soft drink, chocolate flavored, diet
92411510 Soft drink, cola, fruit or vanilla flavored
92411520 Soft drink, cola, chocolate flavored
92411610 Soft drink, cola, fruit or vanilla flavored, diet
92411620 Soft drink, cola, chocolate flavored, diet
92432000 Fruit juice drink, citrus, carbonated
92433000 Fruit juice drink, noncitrus, carbonated

Flavoured Water Drinks
[Polyvinyl Alcohol] = 11 mg/100 g

94100200 Water, bottled, sweetened, with low calorie sweetener
94100300 Water, bottled, flavored (Capri Sun Roarin' Waters)
94210100 Water, bottled, flavored (Propel Water)
94210200 Water, bottled, flavored (Glaceau Vitamin Water)
94210300 Water, bottled, flavored (SoBe Life Water)
94220215 Water, bottled, flavored, sugar free (Glaceau Vitamin Water)
94220310 Water, bottled, flavored, sugar free (SoBe)

Hot Chocolate
[Polyvinyl Alcohol] = 114 mg/100 g

11512010 Hot chocolate / Cocoa, ready to drink
11512020 Hot chocolate / Cocoa, ready to drink, made with nonfat milk
11512030 Hot chocolate / Cocoa, ready to drink, made with non-dairy milk
11512100 Hot chocolate / Cocoa, ready to drink, with whipped cream
11512110 Hot chocolate / Cocoa, ready to drink, made with nonfat milk and whipped cream
11512120 Hot chocolate / Cocoa, ready to drink, made with non-dairy milk and whipped cream
11514100 Hot chocolate / Cocoa, made with dry mix and water
11514110 Hot chocolate / Cocoa, made with dry mix and whole milk
11514120 Hot chocolate / Cocoa, made with dry mix and reduced fat milk
11514130 Hot chocolate / Cocoa, made with dry mix and low fat milk
11514140 Hot chocolate / Cocoa, made with dry mix and fat free milk

11514150	Hot chocolate / Cocoa, made with dry mix and non-dairy milk
11514310	Hot chocolate / Cocoa, made with no sugar added dry mix and water
11514320	Hot chocolate / Cocoa, made with no sugar added dry mix and whole milk
11514330	Hot chocolate / Cocoa, made with no sugar added dry mix and reduced fat milk
11514340	Hot chocolate / Cocoa, made with no sugar added dry mix and low fat milk
11514350	Hot chocolate / Cocoa, made with no sugar added dry mix and fat free milk
11514360	Hot chocolate / Cocoa, made with no sugar added dry mix and non-dairy milk

Coffee and Tea

Instant Coffee
[Polyvinyl Alcohol] = 28 mg/100 g

92103000	Coffee, instant, reconstituted
92104000	Coffee, instant, 50% less caffeine, reconstituted
92114000	Coffee, instant, decaffeinated, reconstituted
92121000	Coffee, instant, pre-lightened and pre-sweetened with sugar, reconstituted
92121001	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, reconsitituted
92121010	Coffee, instant, pre-sweetened with sugar, reconstituted
92121020	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, reconstituted
92121030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
92121040	Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
92121041	Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted
92121050	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, reconstituted

Foods adjusted for being present in dried form
Reconstitution factor of 9.7

92192000	Coffee, mocha, instant, pre-lightened and pre-sweetened with sugar, not reconstituted
92192030	Coffee, mocha, instant, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted
92192040	Coffee, mocha, instant, decaffeinated, pre-lightened and pre-sweetend with low calorie sweetener, not reconstituted

Foods adjusted for being present in dried form
Reconstitution factor of 46

92191100	Coffee, instant, not reconstituted
92191105	Coffee, instant, 50% less caffeine, not reconstituted
92191200	Coffee, instant, decaffeinated, not reconstituted
92191400	Coffee, instant, pre-sweetened with sugar, not reconstituted
92193000	Coffee, instant, pre-lightened and pre-sweetened with sugar, not reconstituted

92193005 Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with sugar, not reconstituted
92193020 Coffee, instant, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted
92193025 Coffee, instant, decaffeinated, pre-lightened and pre-sweetened with low calorie sweetener, not reconstituted

Mixed foods containing instant coffee
Adjusted for instant coffee content of 50%

92100500 Coffee, NS as to brewed or instant
92111000 Coffee, NS as to brewed or instant, decaffeinated

Instant Tea
[Polyvinyl Alcohol] = 28 mg/100 g

92305010 Tea, iced, instant, black, unsweetened
92305040 Tea, iced, instant, black, pre-sweetened with sugar
92305050 Tea, iced, instant, black, decaffeinated, pre-sweetened with sugar
92305090 Tea, iced, instant, black, pre-sweetened with low calorie sweetener
92305110 Tea, iced, instant, black, decaffeinated, pre-sweetened with low calorie sweetener
92305180 Tea, iced, instant, black, decaffeinated, unsweetened
92305900 Tea, iced, instant, green, unsweetened
92305910 Tea, iced, instant, green, pre-sweetened with sugar
92305920 Tea, iced, instant, green, pre-sweetened with low calorie sweetener

Foods adjusted for being present in dried form
Reconstitution factor of 15.4

92307000 Tea, iced, instant, black, unsweetened, dry
92307400 Tea, iced, instant, black, pre-sweetened, dry

Milk Products

Whey Protein Supplement
[Polyvinyl Alcohol] = 142 mg/100 g

NHANES 2017-2018 Food Codes

11825000 Whey, sweet, dry
95101000 Nutritional drink or shake, ready-to-drink (Boost)
95101010 Nutritional drink or shake, ready-to-drink (Boost Plus)
95102000 Nutritional drink or shake, ready-to-drink (Carnation Instant Breakfast)
95103000 Nutritional drink or shake, ready-to-drink (Ensure)
95103010 Nutritional drink or shake, ready-to-drink (Ensure Plus)
95104000 Nutritional drink or shake, ready-to-drink, sugar free (Glucerna)
95105000 Nutritional drink or shake, ready-to-drink (Kellogg's Special K Protein)

95106000 Nutritional drink or shake, ready-to-drink (Muscle Milk)
95106010 Nutritional drink or shake, ready-to-drink, light (Muscle Milk)
95110000 Nutritional drink or shake, ready-to-drink (Slim Fast)
95110010 Nutritional drink or shake, ready-to-drink, sugar free (Slim Fast)
95110020 Nutritional drink or shake, high protein, ready-to-drink (Slim Fast)
95120000 Nutritional drink or shake, ready-to-drink, NFS
95120010 Nutritional drink or shake, high protein, ready-to-drink, NFS
95120020 Nutritional drink or shake, high protein, light, ready-to-drink, NFS
95120050 Nutritional drink or shake, liquid, soy-based

Foods adjusted for being present in dried form
Reconstitution factor of 6.5 to 9.3

95201000 Nutritional powder mix (Carnation Instant Breakfast)
95201010 Nutritional powder mix, sugar free (Carnation Instant Breakfast)
95201200 Nutritional powder mix (EAS Whey Protein Powder)
95201300 Nutritional powder mix (EAS Soy Protein Powder)
95201500 Nutritional powder mix, high protein (Herbalife)
95201600 Nutritional powder mix (Isopure)
95201700 Nutritional powder mix (Kellogg's Special K20 Protein Water)
95202000 Nutritional powder mix (Muscle Milk)
95202010 Nutritional powder mix, light (Muscle Milk)
95210000 Nutritional powder mix (Slim Fast)
95210010 Nutritional powder mix, sugar free (Slim Fast)
95210020 Nutritional powder mix, high protein (Slim Fast)
95220000 Nutritional powder mix, NFS
95220010 Nutritional powder mix, high protein, NFS
95230000 Nutritional powder mix, whey based, NFS
95230010 Nutritional powder mix, protein, soy based, NFS
95230020 Nutritional powder mix, protein, light, NFS
95230030 Nutritional powder mix, protein, NFS

NHANES 2017-2018 Whey Protein Dietary Supplement Codes

311 TWINLAB TRIPLE WHEY FUEL
333 VHT ONLY WHEY
1417 XRATED COMPLETE WHEY PROTEIN
1419 NATROL PROLAB NUTRITION WHEY PROTEIN
1493 EAS SIMPLY PROTEIN COMPLETE WHEY CHOCOLATE
1663 OPTIMUM NUTRITION NATURAL 100% WHEY PROTEIN CHOCOLATE
2263 GNC PRO PERFORMANCE 100% WHEY PROTEIN INSTANTIZED, CHOCOLATE POWDER
2922 SCI FIT WHEY PROTEIN ICE CREAM STRAWBERRY FLAVOR ASPARTAME FREE
3523 DEFAULT WHEY PROTEIN
4455 NATURE'S BEST PERFECT WHEY VANILLA POWDER
4456 NATURE'S BEST PERFECT ISOPURE WITH 50 GRAMS OF 100% PURE ION EXCHANGE WHEY PROTEIN ISOLATE PACKETS

5049 SPORTPHARMA JUST-WHEY
5663 GNC PRO PERFORMANCE 100% WHEY PROTEIN STRAWBERRY
5703 ESSENTIAL PROTEIN 100% PURE WHEY IRON-TEK
6111 GENERIC8 WHEY PROTEIN POWDER WITH 21 VITAMINS & MINERALS CHOCOLATE FLAVORED
6227 CHAMPION NUTRITION PURE WHEY PROTEIN STACK 26 G OF PROTEIN PER SERVING VANILLA
6234 EAS ADVANT EDGE HP WHEY PROTEIN CHOCOLATE
6722 GNC PRO PERFORMANCE 100% WHEY PROTEIN INSTANTIZED, CHOCOLATE POWDER
6989 ABB HARDCORE ESSENTIALS PURE PRO WHEY PROTEIN
7056 CYTOSPORT COMPLETE WHEY PROTEIN PARTIALLY PRE-DIGESTED WHEY PEPTIDES NO TRANS FATTY ACIDS 50.3% BRANCHED-CHAIN AMINOS!
7082 HIGHER POWER NUTRITION 100% WHEY POWER
7266 PROLAB PURE WHEY CHOCOLATE
7795 DESIGNER WHEY PROTEIN
8627 BODY FORTRESS SUPER ADVANCED WHEY PROTEIN 52 G PREMIUM PROTEIN 100% PREMIUM WHEY PROTEIN OVER 7 GRAMS OF BCAAS CRYSTALLI
8855 NOW SPORTS PREMIUM WHEY PROTEIN ENHANCED FORMULA WITH HIGHER ISOLATE CONTENT MICROFILTERED ION-EXCHANGED HIGH IN BRANCH
9123 GNC PRO PERFORMANCE 100% WHEY PROTEIN POWDERED DRINK MIX NATURAL SOURCE OF BCAA 20 GRAMS OF HIGH-QUALITY PROTEIN SOURCE
9205 PROLAB N-LARGE2 52G MASS GAINER WHEY PROTEIN ULTIMATE MUSCLE MASS FORMULA
9243 GENERIC3 SHOW ME THE WHEY NO ADDED SUGAR
9336 GOLD STANDARD 100% WHEY WHEY PROTEIN ISOLATES PRIMARY SOURCE ON 24 G PROTEIN 5.5 G BCAAS 4 G GLUTAMINE & PRECURSORS
9690 DEFAULT WHEY PROTEIN
9918 GNC PRO PERFORMANCE AMP AMPLIFIED WHEYBOLIC EXTREME 60
10605 JAY ROBB WHEY PROTEIN
11705 DYMATIZE NUTRITION ELITE WHEY PROTEIN ISOLATE
12224 BODY FORTRESS SUPER ADVANCED WHEY PROTEIN 52 G PREMIUM PROTEIN PREMIUM WHEY PROTEIN OVER 8 GRAMS OF BCAAS CRYSTALLINE TAURINE GLUTAMINE PROTEIN
12372 GASPARI NUTRITION INTRAPRO PURE WHEY PROTEIN ISOLATE PRECISION ANABOLIC / ANTI-CATABOLIC FORMULA 25 GRAMS OF PROTEIN PER SERVING UNDENATURED PURE WHEY PROTEIN ISOLATE
12616 GNC PRO PERFORMANCE AMP ADVANCED MUSCLE PERFORMANCE AMPLIFIED WHEYBOLIC EXTREME 60 PREMIER WHEY + LEUCINE FORMULA
13633 DEFAULT WHEY PROTEIN
13970 MRI PERFORMANCE PRO-NOS 100% PREMIUM WHEY FRACTIONS! 42 GRAMS OF PROTEIN PER SERVING MULTI-FRACTIONATED WHEY ISOLATE COMPLEX
14513 DYMATIZE NUTRITION ISO-100 HYDROLYZED 100% WHEY PROTEIN ISOLATE PROTEIN 24G CARBS 1 GRAM FAT 0 LACTOSE 0 RATIO 86% PROTEIN
14616 SOLGAR WHEY TO GO CROSS-FLOW MICRO-FILTERED WHEY PROTEIN POWDER 20 GRAMS OF PROTEIN PER SERVING RBGH FREE
14618 GENERIC42 WHEY PROTEIN
14690 IMMUNOTEC IMMUNOCAL PLATINUM WHEY PROTEIN ISOLATE POWDER WITH MINERALS AND CREATINE
14815 SIX STAR PRO NUTRITION WHEY PROTEIN +PLUS ELITE SERIES FROM THE MAKERS OF MUSCLETECH
15004 GENERIC3 SHOW ME THE WHEY

15190 MUSCLETECH PREMIUM 100% WHEY PROTEIN+ PLUS
15214 BPI SPORTS WHEY HD ULTRA PREMIUM WHEY PROTEIN POWDER 25 G PROTEIN PER SCOOP
15296 BODY FORTRESS SUPER ADVANCED WHEY PROTEIN FEATURES 100% PREMIUM WHEY ZERO ADDED SOY PROTEIN 60 G PROTEIN 12 G BCAAS
17169 ARNOLD SCHWARZENEGGER SERIES ARNOLD IRON WHEY ULTRA-MICROFILTERED WHEY PROTEIN MP MUSCLEPHARM
17416 WHEY PROTEIN JAY ROBB 25 GRAMS PROTEIN PER SERVING! EASY TO MIX! MADE WITH STEVIA!
17720 DEFAULT WHEY PROTEIN
18360 BODY FORTRESS SUPER ADVANCED WHEY PROTEIN FEATURES 100% PREMIUM WHEY ZERO ADDED SOY PROTEIN 60 G PROTEIN 12 G BCAAS
18362 DEFAULT WHEY PROTEIN
18517 IMMUNOTEC IMMUNOCAL PLATINUM GLUTATHIONE PRECURSOR WITH EXCLUSIVE CMP AND RMF WHEY PROTEIN ISOLATE WITH BONDED CYSTEINE
18609 GNC PRO PERFORMANCE AMP AMPLIFIED WHEYBOLIC EXTREME 60 POWER 60G PROTEIN/ 18G BCAA/ 2G SUGAR/ 3G CREATINE
18610 GNC PRO PERFORMANCE AMP PURE ISOLATE 25G PROTEIN/ >5G BCAA/ 1G SUGAR MICRO-FILTERED WHEY PROTEIN ISOLATE
19003 ALLMAX ALLWHEY CLASSIC 100% WHEY PROTEIN SOURCE 30G PROTEIN 0MG GLUTEN 0MG TRANS-FAT PROTEIN
19217 MUSCLETECH PERFORMANCE SERIES NITRO-TECH 100% WHEY GOLD WHEY PROTEIN PEPTIDES & ISOLATE-PRIMARY SOURCES 24G PROTEIN 5.5G BCAAS 4G GLUTAMINE & PRECURSOR
19255 TOPCARE WHEY & SOY PROTEIN

From:	Mark Itzkoff
To:	Gaynor, Paulette M
Cc:	Martin Jacobvitz
Subject:	[EXTERNAL] Re: GRN 001058, question about materials designated confidential in the amendment of November 15, 2022
Date:	Friday, February 3, 2023 8:58:43 PM
Attachments:	image001.png image002.png image003.png image004.png image005.png image006.png

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Dr. Gaynor,

No, the appendices are not intended to be confidential. These appendices are reports from independent laboratories that performed services for NABACO. We are releasing the information as part of the GRAS Notice.

Best Regards,
Mark Itzkoff

On Fri, Feb 3, 2023 at 4:09 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Hi Mr. Itzkoff,
>
> In the amendment of November 15, 2022, there are materials designated as confidential; these are Appendices I, II, and IV. Are Appendices I, II, and IV intended to be confidential?
>
> Please let us know.
>
> Thank you,
>
> Paulette Gaynor
>
> **Paulette M. Gaynor, Ph.D.**
> *Senior Policy Advisor*
>
> **Center for Food Safety and Applied Nutrition**
> **Office of Food Additive Safety, Division of Food Ingredients**
> **U.S. Food and Drug Administration**
> Tel: 240-402-1192
> Paulette.Gaynor@fda.hhs.gov

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MARK L. ITZKOFF

THE LAW OFFICE OF MARK L. ITZKOFF
202 600-7704

From: Mark Itzkoff
To: Gaynor, Paulette M
Subject: [EXTERNAL] Re: GRN 001058 amendment of November 15, 2022 – items for clarification
Date: Tuesday, March 7, 2023 3:06:32 PM
Attachments: image001.png
image002.png
image003.png
image004.png
image005.png
image006.png
GRN 001058 Clarification March 7 2023 rev.pdf

Dr. Gaynor,

The revised letter is attached.

Sincerely,
Mark Itzkoff

On Tue, Mar 7, 2023 at 2:31 PM Mark Itzkoff <mark@itzkofflaw.com> wrote:

> Dr. Gaynor
>
> My earlier letter was sent in error. I will send a corrected copy later today.
>
> Mark Itzkoff
>
> On Wed, Feb 22, 2023 at 4:36 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:
>
> > Dear Mr. Itzkoff,
> >
> > In response to our question about Appendices I, II, and IV, we have the amendment of February 3, 2023, that the appendices are not intended to be confidential. This email, however, follows up on the February 14, 2023, discussion with FDA staff about the amendment of November 15, 2022. We have identified items in the amendment of November 15, 2022, that require clarification. These items follow:
> >
> > 1. In the response to Question 1 (amendment dated November 15, 2022), the notifier states that *"analytical results from two additional non-consecutive batches, 22015129 and 120075080, are included in Appendix I"*. We note that Appendix I contains no analytical results for the specification parameters from either batch 22015129 or 120075080. We note that some analytical results for batch 120075080 are reported in Table 1 of Appendix III (page 42 of the amendment dated November 15, 2022); however, these results do not include the results for all specification parameters.

a. Please provide the missing analytical results for batch 22015129 (and 12007580 if necessary) to ensure that you provide a minimum of three results total for each specification parameter listed in Table 2 on p. 8 of the notice. For the clarity, we suggest that you provide a summary of the analytical results in a table that includes the specification parameters, reference analytical methods, applicable batch numbers, and the analytical results corresponding to each batch.
b. We note that in the amendment dated November 15, 2022, Appendix I and Appendix II seem to be the same. Please clarify.

2. In the response to Question 2 (amendment dated November 15, 2022), the notifier indicates that the additional data on the residual levels of vinyl acetate monomer (VAM) generated using an analytical method with the limit of detection (LOD) of 1 mg/kg will be provided. Please provide those additional analytical data or explain why they are not necessary to reach a GRAS conclusion.

3. In the response to Question 3 (amendment dated November 15, 2022), the notifier states that *"the agent used to hydrolyze the polyvinyl alcohol is sodium hydroxide"*. Please note that in Question 3 we requested additional information regarding the proprietary agent used to initiate the polymerization reaction, not the agent used in the hydrolysis reaction that was already identified as sodium hydroxide on p. 8 of GRN 001058. To clarify, we are requesting information on the proprietary agent mentioned on p. 8 of GRN 001058 (*"Polymerization of VAM takes place in methanol with a proprietary agent to initiate the polymerization reaction."*) and described as the "Initiator" in Figure 1 on p. 9 of GRN 001058.

To reiterate, we request that the notifier specify the chemical class of the proprietary agent used to initiate the polymerization reaction and provide a statement on whether this agent is expected to be present in the final PVOH, and if yes, indicate the residual levels and discuss if those levels present a safety concern. In addition, we request that the notifier provide the limit of detection (LOD) for the analytical method used to analyze for the proprietary agent and a statement that the method is validated for the intended use.

4. In the response to Question 4 (amendment dated November 15, 2022), the notifier refers to data in Table 1 and states that "supplier has provided the following molecular weight data confirming that the amount of polymer with a molecular weight below 500 Newtons is less than 0.01%". We note that molecular weight is usually expressed in grams per mole (g/mol) or Daltons (Da), not Newtons (N). Please clarify the unit for the molecular weights provided in Table 1.

5. In the response to Question 4 (amendment dated November 15, 2022), the notifier states that the subject of GRN 001058 is PVOH film, not PVOH powder, because

the powder will be dissolved in an aqueous solution prior to applying to food. We note that according to Part 1.3 and Part 2.1 of GRN 001058, the identity of the substance that is the subject of the notice is described as PVOH or PVOH powder, respectively, not an edible film containing PVOH. This is consistent with the description of PVOH in the previous GRAS notices (GRNs 000141 and 000767) submitted for its use as a component of edible films/coatings. Please confirm that the subject of GRN 001058 is PVOH powder.

6. In the response to Question 7 (amendment dated November 15, 2022), the notifier discusses the dietary exposure assessment provided in Appendix IV. We have the following comments:

    a. The notifier states that *"The highest EDI was for infants at 3.34 mg/kg bw/day"*. We note that according to Table 4.1-1 in Appendix IV this estimate is listed for the population of children aged 2-5 years, not infants. Please confirm that the correct population in this sentence is children aged 2-5 years.
    b. The notifier notes that the 90th percentile eaters-only dietary exposure estimates from the intended uses of PVOH provided in Appendix IV (1.04 mg/kg bw/day for adults aged 20 years and older to 3.34 mg/kg bw/day for children aged 2-5 years) are substantially higher than the initial estimate provided in GRN 001058 (i.e., 0.82 mg/kg bw/day) and states that the difference is *"in part due to the fact that Intertek calculated the dietary exposure for each edible peel fruit and vegetable individually and then added them together*". Please confirm that by this statement the notifier means that the estimates of dietary exposure were determined from the distribution of 2-day average consumptions of all fruits and vegetables that may contain PVOH by individuals who consumed one or more of these fruits and vegetables during the 2-day survey.
    c. The notifier states that *"Intertek calculates that the consumer-only 90th percentile intake due to the application in GRASN 767 would be only 1.04 mg/kg bw/day*". Please confirm that the correct estimate value in this sentence is 2.33 mg/kg bw/day (Appendix IV, Table 4.2-1).
    d. The notifier states that the updated dietary exposure to PVOH from the current uses (Appendix IV) is significantly lower than the estimate provided in GRN 000767 and that this may be due to *"more detailed data from NHANES that allowed Intertek to exclude non-relevant subcategories of the GRASN 767 applications".* While we do not disagree with this statement, we note that there are other reasons why the updated dietary exposure from the current uses of PVOH (Appendix IV, Table 4.2-1) is significantly lower than the dietary exposure reported in GRN 000767. For example, as explained in Section 5 of Appendix IV, the updated exposure was estimated using a different and more appropriate methodology. Please confirm that the use of a different and more appropriate methodology is one of the reasons why the updated estimate is significantly lower than that reported in GRN 000767.

FDA respectfully requests a complete response within 10 business days. Thank you.

Sincerely,

Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

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March 7, 2023

Dr. Paulette Gaynor
Office of Food Additive Safety
CFSAN
Food and Drug Administration
5100 Campus Drive
College Park, MD 20740

Re: GRASN 001058 Clarifications

Dear Dr. Gaynor,

On behalf of NABACO LLC, I am hereby submitting this letter is intended to respond to your February 22, 2023 email requesting further clarifications to NABACO's GRAS Notification for polyvinyl alcohol (PVOH), GRN 001058. As an initial matter, I am confirming that Appendices I, II and IV to our November 15, 2022 letter are not intended to be confidential. These appendices are report of work performed under confidentiality agreements for NABACO by independent laboratories. NABACO acknowledges that as part of the GRAS Notification, these reports are no longer confidential.

1. In the response to Question 1 (amendment dated November 15, 2022), the notifier states that "analytical results from two additional non-consecutive batches, 22015129 and 120075080, are included in Appendix I". We note that Appendix I contains no analytical results for the specification parameters from either batch 22015129 or 120075080. We note that some analytical results for batch 120075080 are reported in Table 1 of Appendix III (page 42 of the amendment dated November 15, 2022); however, these results do not include the results for all specification parameters.

    a. Please provide the missing analytical results for batch 22015129 (and 12007580 if necessary) to ensure that you provide a minimum of three results total for each specification parameter listed in Table 2 on p. 8 of the notice. For the clarity, we suggest that you provide a summary of the analytical results in a table that includes the specification parameters, reference analytical methods, applicable batch numbers, and the analytical results corresponding to each batch.

Attached as Table 1 are analytical results from testing on six lots of PVOH, N12201516, N122015117, N122015118, N121085317, N122015129, and N120075080. Included in the table are references to the report where the results are reported. The specific analytical method is provided in the referenced reports.

b. We note that in the amendment dated November 15, 2022, Appendix I and Appendix II seem to be the same. Please clarify.

Appendix I should have been a new Certificate of Analysis from Kuraray. The correct Appendix I is attached. In addition, we note that in the second paragraph on Page 2 of the November 15 letter, Appendix II is initially referred to as Appendix I.

2. In the response to Question 2 (amendment dated November 15, 2022), the notifier indicates that the additional data on the residual levels of vinyl acetate monomer (VAM) generated using an analytical method with the limit of detection (LOD) of 1 mg/kg will be provided. Please provide those additional analytical data or explain why they are not necessary to reach a GRAS conclusion.

Our supplier has notified us that they are unable to provide the additional analytical data on residual VAM. As discussed in our November 15, 2022 letter, there is no reasonable expectation that vinyl acetate monomer will be present in the finished PVOH polymer. PVOH is produced by first polymerizing the VAM to form polyvinyl acetate then hydrolyzing the polyvinyl acetate using sodium hydroxide to produce PVOH. Any residual VAM will react with the sodium hydroxide to form vinyl alcohol. Due to the smaller size of VAM when compared to polyvinyl acetate, the VAM is more highly reactive and will hydrolyze faster than the polyvinyl acetate. Thus, no residual VAM is expected.

In support of this Notification, NABACO submitted a sample of PVOH to Element Laboratory for residual VAM testing. This report was submitted as Appendix II to the November 15, 2022 letter. The analysis showed no detectable VAM using a method with an LOD of 2.5 parts per million (ppm). Assuming for the purpose of calculating the "worst case" exposure to VAM that may result from this application that the monomer is present at the LOD, we have calculated the maximum dietary concentration to be 0.063 parts per trillion (ppt) or 3.15×10^{-6} mg/kg of body weight. This exposure is 4 orders of magnitude below the limit set forth in FDA's Threshold of Regulation, 21 CFR 170.39.

We also note that there is no requirement for residual VAM testing in the FCC or JECFA PVOH monographs.

3. In the response to Question 3 (amendment dated November 15, 2022), the notifier states that "the agent used to hydrolyze the polyvinyl alcohol is sodium hydroxide". Please note that in Question 3 we requested additional information regarding the proprietary agent used to initiate the polymerization reaction, not the agent used in the hydrolysis reaction that was already identified as sodium hydroxide on p. 8 of GRN 001058. To clarify, we are requesting information on the proprietary agent

mentioned on p. 8 of GRN 001058 ("Polymerization of VAM takes place in methanol with a proprietary agent to initiate the polymerization reaction.") and described as the "Initiator" in Figure 1 on p. 9 of GRN 001058.

Our supplier has informed us that the initiator used in the production of polyvinyl acetate is a peroxide. They have not provided further information stating that the specific chemical identity is a trade secret.

4. In the response to Question 4 (amendment dated November 15, 2022), the notifier refers to data in Table 1 and states that "supplier has provided the following molecular weight data confirming that the amount of polymer with a molecular weight below 500 Newtons is less than 0.01%". We note that molecular weight is usually expressed in grams per mole (g/mol) or Daltons (Da), not Newtons (N). Please clarify the unit for the molecular weights provided in Table 1.

The units for the molecular weight data in Table of our November 15, 2022 letter is Daltons.

5. In the response to Question 4 (amendment dated November 15, 2022), the notifier states that the subject of GRN 001058 is PVOH film, not PVOH powder, because the powder will be dissolved in an aqueous solution prior to applying to food. We note that according to Part 1.3 and Part 2.1 of GRN 001058, the identity of the substance that is the subject of the notice is described as PVOH or PVOH powder, respectively, not an edible film containing PVOH. This is consistent with the description of PVOH in the previous GRAS notices (GRNs 000141 and 000767) submitted for its use as a component of edible films/coatings. Please confirm that the subject of GRN 001058 is PVOH powder.

The subject of GRN 001058 is a PVOH film that will be used on the exterior of fruits and vegetables. The PVOH is supplied to the Notifier as a powder. The Notifier will dissolve the PVOH along with other materials used in compliance with FDA regulations and the Federal Food, Drug and Cosmetic Act in water. This aqueous solution is then diluted at a farm or food processing facility and applied to produce either as a spray or as a dip. Following application, the water will evaporate leaving a thin PVOH film on the produce. Thus it is the film that is the subject of this Notification.

6. In the response to Question 7 (amendment dated November 15, 2022), the notifier discusses the dietary exposure assessment provided in Appendix IV. We have the following comments:
    a. The notifier states that "The highest EDI was for infants at 3.34 mg/kg bw/day". We note that according to Table 4.1-1 in Appendix IV this

estimate is listed for the population of children aged 2-5 years, not infants. Please confirm that the correct population in this sentence is children aged 2-5 years.

That is correct. The highest EDI was for children 2-5 years.

b. The notifier notes that the 90th percentile eaters-only dietary exposure estimates from the intended uses of PVOH provided in Appendix IV (1.04 mg/kg bw/day for adults aged 20 years and older to 3.34 mg/kg bw/day for children aged 2-5 years) are substantially higher than the initial estimate provided in GRN 001058 (i.e., 0.82 mg/kg bw/day) and states that the difference is "in part due to the fact that Intertek calculated the dietary exposure for each edible peel fruit and vegetable individually and then added them together". Please confirm that by this statement the notifier means that the estimates of dietary exposure were determined from the distribution of 2-day average consumptions of all fruits and vegetables that may contain PVOH by individuals who consumed one or more of these fruits and vegetables during the 2-day survey.

The estimated dietary exposures were calculated by adding the 90th percentile exposures for 2-day average consumption for individuals who consumed any of the individual fruits and vegetables. This would be the same population as "individuals who consumed one or more of these fruits and vegetables during the 2-day survey."

c. The notifier states that "Intertek calculates that the consumer-only 90th percentile intake due to the application in GRASN 767 would be only 1.04 mg/kg bw/day". Please confirm that the correct estimate value in this sentence is 2.33 mg/kg bw/day (Appendix IV, Table 4.2-1).

This is correct. As stated on page 6 of the November 15, 2022 letter, "A new EDI for applications set forth in GRASN 767 for adults was determined to be 2.33 mg/kg bw/day, significantly less than the 45.16 mg/kg bw/day reported in GRASN 767." The relevant portions of the first paragraph on page 7 should be amended to read "Intertek calculates that the consumer-only 90th percentile intake due to the applications in GRASN 767 would be only <u>2.33</u> mg/kg bw/day. This is <u>approximately 5.2%</u> of the EDI estimated in GRASN 767, 45.16 mg/kg bw/day." (Changes are underlined.)

d. The notifier states that the updated dietary exposure to PVOH from the current uses (Appendix IV) is significantly lower than the estimate provided in GRN 000767 and that this may be due to "more detailed data from NHANES that allowed Intertek to exclude non-relevant subcategories of the

> GRASN 767 applications". While we do not disagree with this statement, we note that there are other reasons why the updated dietary exposure from the current uses of PVOH (Appendix IV, Table 4.2-1) is significantly lower than the dietary exposure reported in GRN 000767. For example, as explained in Section 5 of Appendix IV, the updated exposure was estimated using a different and more appropriate methodology. Please confirm that the use of a different and more appropriate methodology is one of the reasons why the updated estimate is significantly lower than that reported in GRN 000767.

NABACO agrees with this statement.

Please let me know if you have any additional questions.

Sincerely,

Mark L. Itzkoff

Attachment

Table 1

Compilation of PVOH Testing
For Compliance with
FCC Monograph

FCC Test	Test Limit	Lot Numbers					
		N122015126[i]	N122015118[i]	N122015117[i]	N122015129[ii]	N121085317[iii]	N120075080[iv]
Color Reaction A	Blue color is produced	Pass[v]	Pass[v]	Pass[v]			Pass
Color Reaction B	A dark red to blue color is produced color produced	Pass[v]	Pass[v]	Pass[v]			Pass
Solid content	95.0 – 100%	98.3%	98.4%	98.4%		98.3%	
IR Absorption							Pass
Lead	NMT 2.0 mg/kg	ND[vi]	ND	ND		<1.0 mg/kg	<1.0 mg/kg[vii]
Methanol and Methyl Acetate	Methanol NMT 1.0% Methyl acetate NMT 1.0%	0.52% 0.02%	0.60% 0.02%	0.53% 0.02%	0.57% 0.04%		
Acid Value	NMT 3.0 KOH/g	1.0 KOH/g[v]	1.1 KOH/g[v]	1.0 KOH/g[v]			1.1 KOH/g
Ester Value	NMT Between 125 and 153 mg KOH/g	143 mg KOH/g[v]	135 mg KOH/g[v]	129 mg KOH/g[v]			143 KOH/g
Degree of Hydrolysis	Between 86.5 and 89.0%	87.7%	87.6%	87.4%	87.9		
Loss on Drying	NMT 5.0%	1.7%	1.6%	1.6%			
pH	5.0 – 6.5	5.1	5.2	5.2	5.4		
Residue on Ignition	NMT 1.0%	0.08%	0.12%	0.12%	0.25		
Viscosity	4.8 – 5.8 mPa	5.2	5.2	5.3	5.2		

Water Insoluble Substances	NMT 0.1%	0.02%	0.00%	0.05	0.00		0.075%

[i] Kuraray Certificate of Analysis, Jan. 31, 2022. Submitted in Appendix I to original GRASN, except where noted.
[ii] Kurraray Certificaqte of Analysis, printed Jan 31, 2022. Attached as Appendix I to this letter.
[iii] Results for August 11, 2021 Report from Dr. Shu-Hsien Liaa. Appendix I to original Submission.
[iv] Results reported on Element Certificate of Analysis dated Sept 6, 2022. Project Code 22-93466-A. Appenix III to November 15, 2022 Letter.
[v] Kuraray Certificate of Analysis, Jan. 31, 2022. Submitted in Appendix I to original GRASN, except where noted.
[vi] None Detected. Results reported on Element Certificate of Analysis dated March 22, 2022. Project Code 22-92209-CO1
[vii] Results from Element Laboratory Certificate of Analysis 22-93455-A, Appendix III to November 15, 2022 to Dr. Paulette Gaynor.

Appendix I

Kuraray Europe GmbH
Philipp-Reis-Straße 4
65795 Hattersheim am Main

CERTIFICATE OF ANALYSIS

Order No.:
Delivery No.:
Cust Order No.:
Date of Print: 31.01.2022

These data do not release the customer from the obligation to carry out an inspection of goods received. All sales of this product shall be subject to our Standard Terms and Conditions of Sale.

PRODUCT QUALITY CONTROL DATA

Material: PV001245 KURARAY POVAL# 5-88 FA 500kg Big bag

Batch Number

Characteristics	Test Method Test Method Description	Value	Unit	Min	Max
N122015129					
Methanol content		0,57	%	0,00	0,99
Viscosity 4% (DIN 53015)		5,2	mPa.s	4,8	5,8
pH		5,4		5,0	6,5
Degree of Hydrolysis		87,9	mole%	86,5	89,0
Ash Content		0,25	%	0,00	0,37
Solid content 105°C, 3h		98,3	%	95,0	100,0
Volatile Matter		1,7	%	0,0	5,0
Methylacetat content		0,04	%	0,00	0,99
Insoluble Matter POVAL		0,00	%	0,00	0,10

"This report is computer generated and valid without signature."

From: Mark Itzkoff
To: Gaynor, Paulette M
Subject: [EXTERNAL] Re: Items for follow-up clarification (GRN 001058)
Date: Wednesday, April 19, 2023 1:13:18 PM
Attachments: image001.png
image002.png
image003.png
image004.png
image005.png
image006.png
April 19 reply to FDA w att.pdf

Dear Dr. Gaynor,

On behalf of NABACO, I am hereby submitting the attached letter in response to your April 5, 2023 email.

Please let me know if there are any further questions.

Sincerely,
Mark Itzkoff

On Wed, Apr 5, 2023 at 1:20 PM Gaynor, Paulette M <Paulette.Gaynor@fda.hhs.gov> wrote:

> Dear Mr. Itzkoff,
>
> This email follows the March 30, 2023, discussion with FDA staff. We have identified items for follow-up clarification. These items follow:
>
> 1. In the response to Question 5 (amendment dated March 7, 2023), the notifier disagrees with our statement that the subject of GRN 001058 is PVOH powder and not a film containing the PVOH powder. However, the notice states (p. 8) "The subject of this GRAS assessment, polyvinyl alcohol, occurs as an odorless translucent, white, or cream-colored granular **powder**." In addition, the notifier states that the film contains not only PVOH but also *"other materials used in compliance with FDA regulations and the Federal Food, Drug and Cosmetic Act in water"*. Please note that the film as the notifier describes would be considered to be a physical mixture of PVOH powder and substances that are already authorized for their respective uses. We typically do not evaluate GRAS notices for physical mixtures (i.e., formulations) but rather for individual ingredients that are then used as components of the mixtures (formulations) added to foods. Therefore, we reiterate our request that the notifier confirm that the subject of GRN 001058 is the PVOH powder.
>
> 2. In the response to Question 1 (amendment dated March 7, 2023), the notifier provides a summary of the results from the batch analyses (Table 1). We request the following

additional information and/or clarifications:

a. The lead test results for batches N122015126, N122015118, and N122015117 are reported as "ND" (not detected). Please provide the limit of detection (LOD) of the analytical method used to test for lead.
b. The notifier states that the certificates of analyses (COAs) with the results for lead from the analyses of the above-mentioned batches were provided in either Appendix I of GRN 001058 or in "Element Certificate of Analysis dated March 22, 2022. Project Code 22-92209-CO1". We note that the results for lead from those batches are not included in either of the sources specified by the notifier. Please clarify that the COAs with the results for lead from the above-mentioned batches were not provided in GRN 001058 or the subsequent amendments. We note that the results were summarized in Table 1, so therefore, it is not necessary to provide the COAs, but rather clarify that they have not been provided.
c. For the lead test results reported as < 1 mg/kg (batches N121085317 and N120075080), please provide the actual measured levels of lead if the limit of quantitation (LOQ) is below 1 mg/kg or state that the measured levels are below the specified LOD.
d. Furthermore, we note that the limit for lead (≤ 2 mg/kg) specified in the monograph for PVOH in the Food Chemical Codex was established in 2008. Considering FDA's recent "Closer to Zero" initiative that focuses on reducing dietary exposure to heavy metals, we request that the notifier lower the specification limit for lead in the finished PVOH, which is the subject of GRN 001058, based on the results of batch analyses. The revised limit for lead should be reflective of the measured lead levels and be as low as possible.

3. According to Table 2 (page 8 of GRN 001058), the FCC method was used to test for lead in the finished PVOH. We note that the FCC monograph for PVOH lists an atomic absorption spectrophotometric (AAS) method whereas the certificates of analysis provided in GRN 001058 and the amendment dated March 7, 2023 (in response to Question 1), specify the methods used as ISO 17294-2 and ICP-MS, respectively. Please clarify this discrepancy. In addition, please confirm that all the remaining methods listed in Table 2 are the methods that were used to generate the provided results of the batch analyses. If different methods were used, please provide the appropriate references and state that the methods are validated for their intended use.

4. In the response to Question 3 (amendment dated March 7, 2023), the notifier states that a peroxide is used as a polymerization initiator in the production of PVOH. However, the notifier does not address the potential presence of the peroxide in the finished PVOH that was also part of this question. Please state whether the peroxide or its decomposition products are expected to be present in the finished PVOH, and either discuss how the notifier ensures that these substances are removed from the finished PVOH or indicate the residual levels and discuss why those levels would not present a safety concern.

5. In the response to Question 6b (amendment dated March 7, 2023), the notifier states that *"the estimated dietary exposures were calculated by adding the 90th percentile exposures for 2-day average consumption…"*. In our view, this statement is incorrect because according to the information provided in Appendix IV (page 5) of the amendment dated November 15, 2023, the mean and 90th percentile estimates were determined from a distribution of the 2-day average consumptions and not by *"adding the 90th percentile for 2-day average consumption"*. Therefore, we reiterate our request that the notifier confirm that the mean and 90th percentile estimates were determined from the distribution of the 2-day average consumptions.

If you or NABACO LLC (the notifier) have any questions about the items for follow-up clarification, please let me know. FDA respectfully requests a complete response within 10 business days. Thank you.

Sincerely,

Paulette Gaynor

Paulette M. Gaynor, Ph.D.
Senior Policy Advisor

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety, Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-1192
Paulette.Gaynor@fda.hhs.gov

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April 19, 2023

Dr. Paulette Gaynor
Office of Food Additive Safety
CFSAN
Food and Drug Administration
5100 Campus Drive
College Park, MD 20740

Re: GRASN 001058 Clarifications

Dear Dr. Gaynor,

On behalf of NABACO LLC, I am hereby submitting this letter which is intended to respond to your April 5, 2023 email regarding GRAS Notification GRN001058.

1. In the response to Question 5 (amendment dated March 7, 2023), the notifier disagrees with our statement that the subject of GRN 001058 is PVOH powder and not a film containing the PVOH powder. However, the notice states (p. 8) "The subject of this GRAS assessment, polyvinyl alcohol, occurs as an odorless translucent, white, or cream-colored granular powder." In addition, the notifier states that the film contains not only PVOH but also "other materials used in compliance with FDA regulations and the Federal Food, Drug and Cosmetic Act in water". Please note that the film as the notifier describes would be considered to be a physical mixture of PVOH powder and substances that are already authorized for their respective uses. We typically do not evaluate GRAS notices for physical mixtures (i.e., formulations) but rather for individual ingredients that are then used as components of the mixtures (formulations) added to foods. Therefore, we reiterate our request that the notifier confirm that the subject of GRN 001058 is the PVOH powder.

NABACO LLC hereby confirms that the subject of GRN 0010508 is PVOH powder.

2. In the response to Question 1 (amendment dated March 7, 2023), the notifier provides a summary of the results from the batch analyses (Table 1). We request the following additional information and/or clarifications:

    a. The lead test results for batches N122015126, N122015118, and N122015117 are reported as "ND" (not detected). Please provide the limit of detection (LOD) of the analytical method used to test for lead.

Attached is the Certificate of Analysis (COA) from Element for Project Code 22-92209-CO1. This COA states that the levels of lead were below the limit of quantification (LOQ)

for each of the lots identified above. The samples were tested using the ICP-MS method also used for lot N120075080. Specifically, the LOQ's for the individual lots were:

N122015126	0.2373 mg/kg
N122015118	0.2465 mg/kg
N122015117	0.2467 mg/kg

b. The notifier states that the certificates of analyses (COAs) with the results for lead from the analyses of the above-mentioned batches were provided in either Appendix I of GRN 001058 or in "Element Certificate of Analysis dated March 22, 2022. Project Code 22-92209-CO1". We note that the results for lead from those batches are not included in either of the sources specified by the notifier. Please clarify that the COAs with the results for lead from the above-mentioned batches were not provided in GRN 001058 or the subsequent amendments. We note that the results were summarized in Table 1, so therefore, it is not necessary to provide the COAs, but rather clarify that they have not been provided.

The COAs were not previously been provided.

c. For the lead test results reported as < 1 mg/kg (batches N121085317 and N120075080), please provide the actual measured levels of lead if the limit of quantitation (LOQ) is below 1 mg/kg or state that the measured levels are below the specified LOD.

For both lots, no lead was detected using a method with an LOD of 1.0 mg/kg.

d. Furthermore, we note that the limit for lead (≤ 2 mg/kg) specified in the monograph for PVOH in the Food Chemical Codex was established in 2008. Considering FDA's recent "Closer to Zero" initiative that focuses on reducing dietary exposure to heavy metals, we request that the notifier lower the specification limit for lead in the finished PVOH, which is the subject of GRN 001058, based on the results of batch analyses. The revised limit for lead should be reflective of the measured lead levels and be as low as possible.

We have discussed the lead limit with our supplier, Kuraray. It is our understanding that they are discussing internally reducing the lead limit to "no more than 1 mg/kg." At this point no final decision has been made and they have not provided a date when this decision will be finalized.

3. According to Table 2 (page 8 of GRN 001058), the FCC method was used to test for lead in the finished PVOH. We note that the FCC monograph for PVOH lists an atomic absorption spectrophotometric (AAS) method whereas the certificates of analysis provided in GRN 001058 and the amendment dated March 7, 2023 (in response to Question 1), specify the methods used as ISO 17294-2 and ICP-MS, respectively. Please clarify this discrepancy. In addition, please confirm that all the remaining methods listed in Table 2 are the methods that were used to generate the provided results of the batch analyses. If different methods were used, please provide the appropriate references and state that the methods are validated for their intended use.

The lead testing reported in the original Notice, lots N121085317 and N120075080 were performed using the ISO 17294-2 test method. The lead analysis reported in our March 7, 2023 amendment, was analyzed using ICP-MS.

4. In the response to Question 3 (amendment dated March 7, 2023), the notifier states that a peroxide is used as a polymerization initiator in the production of PVOH. However, the notifier does not address the potential presence of the peroxide in the finished PVOH that was also part of this question. Please state whether the peroxide or its decomposition products are expected to be present in the finished PVOH, and either discuss how the notifier ensures that these substances are removed from the finished PVOH or indicate the residual levels and discuss why those levels would not present a safety concern.

Kuraray has informed us that the polymerization initiator used to produce the polyvinyl acetate (PVA) precursor is an organic peroxide. They have also stated that the decomposition products of the initiator are organic alcohols that are soluble in methanol. The PVA is dissolved in methanol during the subsequent hydrolysis. Kuraray expects that all of the decomposition byproducts are removed in either the hydrolysis step ot the subsequent washing and drying.

5. In the response to Question 6b (amendment dated March 7, 2023), the notifier states that "the estimated dietary exposures were calculated by adding the 90th percentile exposures for 2-day average consumption…". In our view, this statement is incorrect because according to the information provided in Appendix IV (page 5) of the amendment dated November 15, 2023, the mean and 90th percentile estimates were determined from a distribution of the 2-day average consumptions and not by "adding the 90th percentile for 2-day average consumption". Therefore, we reiterate our request that the notifier confirm that the mean and 90th percentile estimates were determined from the distribution of the 2-day average consumptions.

We have consulted with Intertek, the consultants who performed the dietary exposure analysis. They have confirmed that the "the mean and 90th percentile estimates were determined from the distribution of the 2-day average consumptions."

Please let me know if you have any additional questions.

Sincerely,

Mark L. Itzkoff

Attachment

element

Certificate of Analysis

Date Received:	Client:	Method:
22Mar22	Mark Itzkoff Law Office of Mark Itzkoff mark@itzkofflaw.com	Polyvinyl Alcohol, ICP-MS
Test Date: 28Apr22	**Sample Description:** *Refer to Table 1	**Element ID:** *Refer to Table 1
Issued Date: 29Apr22		**Element Project Code:** 22-92209-CO1

Table 1: Sample Info

Element ID	Sample Description
22MAR22LA1179	Polyvinyl alcohol powder, Kuraray Poval, 5-88 FA, Lot: NA22015118, 1 container
22MAR22LA1180	Polyvinyl alcohol powder, Kuraray Poval, 5-88 FA, Lot: NA22015117, 1 container
22MAR22LA1181	Polyvinyl alcohol powder, Kuraray Poval, 5-88 FA, Lot: NA22015126, 1 container

Table 2: Pb Limit Test

Sample	Acceptance Criteria (FCC Monograph)	Pb Mass (amu)	LOQ (mg/kg)	Result (mg/kg)	Pass/Fail
22MAR22LA1179	Pb is NMT 2 mg/kg	206	0.2465	<LOQ	Pass
		207		<LOQ	
		208		<LOQ	
22MAR22LA1180		206	0.2467	<LOQ	Pass
		207		<LOQ	
		208		<LOQ	
22MAR22LA1181		206	0.2373	<LOQ	Pass
		207		<LOQ	
		208		<LOQ	

The work described in this report was conducted in compliance with the principles of current Good Manufacturing Practice. The following compliance exceptions were noted: results have been generated using method(s) that were not validated at this facility.

William Wood
William Wood, B.S.
Analytical Chemist II

Aaron Lindstrom
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Aaron.lindstrom@element.com

Khanh Ngo Courtney
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History

Date	Revision	Changes
29Apr22	.00	New document