Toxicological profile for

Polyvinyl acetate

This ingredient has been assessed to determine potential human health effects for the consumer. It was considered not to increase the inherent toxicity of the product and thus is acceptable under conditions of intended use.

1. Name of substance and physico-chemical properties

1.1. IUPAC systematic name

Not applicable.

1.2. Synonyms

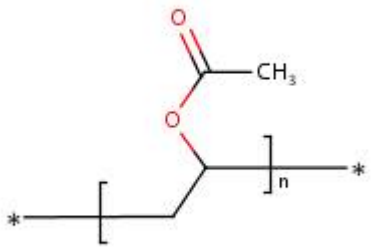
Acetic acid, ethenyl ester, homopolymer; Ethenyl acetate, homopolymer; Polyvinyl acetate; 76 Res; ASB 516; AYAA; AYAF; AYJV; Acetic acid vinyl ester, polymers; Asahisol 1527; Bakelite AYAA; Bakelite AYAF; Bakelite AYAT; Bakelite LP 90; Bond CH 1200; Bond CH 18; Bond CH 3; Booksaver; Borden 2123; Cascorez; Cemedine 196; Cevian 380; Cevian A 678; D 50; D 50 (Polymer); D 50 M; DCA 70; Danfirm; Daratak; Duvilax; Duvilax BD 20; Duvilax HN; Duvilax LM 52; EP 1208; EP 1436; EP 1437; EP 1463; Elmer's Glue All; Elvacet 81-900; Emultex F; En-cor; Esnil P 18; Ethenyl acetate homopolymer; Everflex B; Formvar 1285; Gelva; Gelva 25; Gelva CSV 16; Gelva GP 702; Gelva S 55H; Gelva TS 22; Gelva TS 23; Gelva TS 30; Gelva TS 85; Gelva V 100; Gelva V 15; Gelva V 25; Gelva V 800; Gohensil E 50Y; Gohsenyl E 50 Y; HSDB 1250; Kurare OM 100; Lemac; Lemac 1000; Meikatex 5000NG60; Merckogel OR; Merckogen 6000; Mokotex D 2602; Movinyl; Movinyl 114; Movinyl 50M; Movinyl 801; Mowilith 30; Mowilith 50; Mowilith 70; Mowilith 90; Mowilith D; Mowilith DV; Mowilith M70; NS 2842; National 120-1207; National starch 1014; OM 100; OR 1500; P-170; PS 3h; PVAE; Pioloform F; Plyamul 40-155; Plyamul 40-350; Polisol S-3; Poly(vinyl acetate); Poly(vinylacetate); Polyco 117FR; Polyco 2116; Polyco 2134; Polyco 953; Polyfox P 20; Polyfox PO; Polysol 1000; Polysol 1000AX; Polysol 1200; Polysol PS 10; Polysol S 5; Polysol S 6; Polyvinyl acetate resin; Protex (polymer); R 10688; RV225-5B; Raviflex 43; Resyn 25-1014; Resyn 25-1025; Rhodopas; Rhodopas 010; Rhodopas 5000SMR; Rhodopas 5425; Rhodopas A 10; Rhodopas AM 041; Rhodopas B; Rhodopas BB; Rhodopas HV 2; Rhodopas M; S-Nyl-P 42; SP 60; SP 60 (Ester); Sakunol SN 08; Soloid; Soviol; TS2; Toabond 2; Toabond 40H; Toabond 6; UK 131; Ucar 130; Ucar 15; V 501; VA 0112; Vinac; Vinac ASB 10; Vinac B 7; Vinac RP251; Vinacet D; Vinalite D 50N; Vinalite DS 41/11; Vinamul 9300; Vinapol A 16; Vinipaint 555; Vinnapas B; Vinnapas B 100; Vinnapas B 17; Vinnapas UW 50; Vinyl acetate homopolymer; Vinyl acetate polymer; UNII-32K497ZK2U; Vinyl acetate, homopolymer; Acetic acid, vinyl ester, polymer (ChemIDplus)

1.3. Molecular formula

$(C_4H_6O_2)x$- (ChemIDplus)

1.4. Structural Formula

(ChemIDplus)



1.5. Molecular weight (g/mol)

Polymer, so variable; 11,000 – 1,500,000 (HSDB, 2002)

1.6. CAS registration number

9003-20-7

1.7. Properties

1.7.1. Melting point

35-50ºC (with softening) (HSDB, 2002)

1.7.2. Boiling point

Degrades at 220-250ºC (IARC, 1979)

1.7.3. Solubility

Practically insoluble in water. Soluble in methanol, ethanol, propan-2-ol and a variety of other organic solvents; insoluble in higher alcohols, aliphatic hydrocarbons, carbon disulfide and cyclohexane (CIR, 1992,1996; IARC, 1979)

1.7.4. pKa

No data available to us at this time.

1.7.5. Flashpoint

No data available to us at this time.

1.7.6. Flammability limits (vol/vol%)

No data available to us at this time.

1.7.7. (Auto)ignition temperature

550ºC (cloud)

1.7.8. Decomposition temperature

220-250ºC (HSDB, 2002)

1.7.9. Stability

Stable at normal temperatures and pressure; Softens at relatively low temperatures but is relatively stable in light and oxygen (HSDB, 2002)

1.7.10. Vapor pressure

Not found (as a polymer likely to be extremely low).

1.7.11. log Kow

Not applicable.

2. General information

2.1. Exposure

“The available results of occupational exposure to vinyl acetate have been well documented (NIOSH, 1978). Some minor skin and eye irritations to airborne vinyl acetate were noted.”

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

A recent US EPA risk assessment concluded that no mammalian toxicity would be anticipated from inhalation exposure to vinyl acetate polymers (EPA, 2001).

Cosmetics	Yes (CosIng; Cosmetics Bench Ref, 1996).
Environment	No evidence
Food	Yes (Sheftel, 2000; US FDA, 2021a,b)
Pharmaceuticals	No evidence
Tobacco: In the burned part	Yes
In tobacco naturally	No evidence

Used in cosmetics in the EU as an antistatic, binding, emulsion stabilising and film forming agent. As taken from CosIng, undated..

Polyvinyl acetate (CAS RN 9003-20-7) is listed (at given concentrations, where specified) as an ingredient in home maintenance (up to 25%), “old” auto (3-7%), hobby/craft and inside the home (>1-60%, includes “old” products) products by the CPID.

Polyvinyl acetate is reported used in water-based coatings (paints and lacquers), adhesives (paper, wood, glass, metals, and porcelain), sealants, textile finishes, fabric binders and inks.

Industrial Processes with risk of exposure: Painting (Pigments, Binders, and Biocides), Textiles (Printing, Dyeing, or Finishing), Working with Glues and Adhesives

As taken from Haz-Map, 2020.

A Cosmetic Ingredient Rereview confirmed that polyvinyl acetate is “safe in the present practices of use and concentration” (ranging from 0.4-47% in certain cosmetic products).

As taken from Burnett CL. 2017. Int. J. Toxicol. 36(Suppl. 2), 48S-49S. Available at https://online.personalcarecouncil.org/ctfa-static/online/lists/cir-pdfs/PR758.pdf

Polyvinyl acetate (CAS RN 9003-20-7) is used as a binder and film former in non-medicinal natural health products (Health Canada, 2022).

2.2. Combustion products

No data available to us at this time.

2.3. Ingredient(s) from which it originates

No data available to us at this time.

3. Status in legislation and other official guidance

States approving use in tobacco	Approved in Belgium, France, Germany and UK.			
Food	EU	No	USA	Yes
ADI	None identified.			
Codex Alim.	Not listed.			
C of E no.	Not listed.		FEMA no.	None identified.
TLV (ACGIH)	Not listed.			
Cosmetics (UK)	Not listed in Schedule 1.			

FDA Requirements:

“US fda permits use of polyvinyl acetate homopolymers & copolymers as components of adhesives, resinous & polymeric coatings, & paper & paperboard (for aq, fatty or dry food) when they are intended for use in contact with food (US FDA, 1977). [IARC (1979). Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/index.php p. V19 350] **PEER REVIEWED**”

“8.390; limitations: diluent in ink for marking gum, confectionery, & food supplements in tablet form; minimum molecular wt of 2000. [Furia, T.E. (ed.). CRC Handbook of Food Additives. 2nd ed. Cleveland: The Chemical Rubber Co., 1972., p. 922] **PEER REVIEWED**”

As taken from HSDB, 2002

Polyvinyl acetate is included on the FDA’s inventory of Food Contact Substances Listed in 2 CFR under color additive regulations, food additive and GRAS regulations as below. As taken from US FDA, 2022d.

Polyvinyl acetate is included on the FDA’s inventory of “Substances Added to Food (formerly EAFUS)” as a masticatory substance and is included under 21 CFR sections:

172.615 (chewing gum base),

175.105 (adhesives),

175.300 (resinous and polymeric coatings),

175.320 (resinous and polymeric coatings for polyolefin films),

176.170 (components of paper and paperboard in contact with aqueous and fatty foods),

176.180 (components of paper and paperboard in contact with dry food),

177.1200 (cellophane),

177.2260 (filters, resin-bonded),

177.2800 (textiles and textile fibers),

181.30 (substances used in the manufacture of paper and paperboard products used in food packaging) and

73.1 (diluents in color additive mixtures for food use exempt from certification)

As taken from US FDA, 2022a,b.

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is listed in the US EPA InertFinder Database (2022) as approved for food and non-food use pesticide products. For food use, it is listed under 40 CFR Part 180.960 (TOLERANCES AND EXEMPTIONS FOR PESTICIDE CHEMICAL RESIDUES IN FOOD: Polymers; exemptions from the requirement of a tolerance) (US EPA, 2022).

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is pre-registered under REACH ("envisaged registration deadline 31 May 2013") (ECHA).

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is not classified for packaging and labelling under Regulation (EC) No. 1272/2008 (ECHA, 2022).

Polyvinyl acetate is listed in the US EPA Toxic Substances Control Act (TSCA) inventory, 2020 CDR TSCA Inventory and is fully exempt from reporting under the US EPA Chemical Data Reporting (CDR) rule..

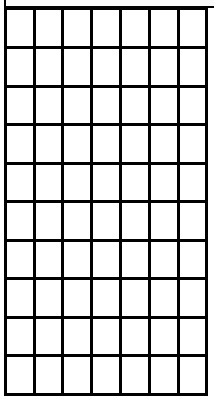
The TSCA inventory and 2020 CDR Exempt List are available at: https://sor.epa.gov/sor_internet/registry/substreg/searchandretrieve/advancedsearch/externalSearch.do?p_type=SRSITN&p_value=161406

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is included on the New Zealand Inventory of Chemicals and does not have an individual approval but may be used under an appropriate group standard (NZ EPA, 2006).

Polyvinyl acetate (CAS RN 9003-20-7) is included on the US FDA's list of inactive ingredients for approved drug products. It is permitted for use as an ingredient in various products, at the following maximum potencies per unit dose and maximum daily exposures:

POLYVINYL ACETATE	ORAL	SUSPENSION	9003207	32K497ZK2U
POLYVINYL ACETATE	ORAL	SUSPENSION, EXTENDED RELEASE	9003207	32K497ZK2U
POLYVINYL ACETATE	ORAL	TABLET	9003207	32K497ZK2U
POLYVINYL ACETATE	ORAL	TABLET, CHEWABLE	9003207	32K497ZK2U
POLYVINYL ACETATE	ORAL	TABLET, CHEWABLE, EXTENDED RELEASE	9003207	32K497ZK2U
POLYVINYL ACETATE	ORAL	TABLET, EXTENDED RELEASE	9003207	32K497ZK2U
POLYVINYL ACETATE	ORAL	TABLET, ORALLY DISINTEGRATING	9003207	32K497ZK2U
POLYVINYL ACETATE	SUBLINGUAL	TABLET	9003207	32K497ZK2U
POLYVINYL ACETATE	TRANSDERMAL	SYSTEM	9003207	32K497ZK2U
POLYVINYL ACETATE PHTHALATE	ORAL	CAPSULE	34481486	58QVG85GW3
POLYVINYL ACETATE	ORAL	CAPSULE, EXTENDED	34481486	58QVG85GW3

PHTHALATE		RELEASE		
POLYVINYL ACETATE PHTHALATE	ORAL	TABLET, DELAYED RELEASE	34481486	58QVG85GW3
POLYVINYL ACETATE PHTHALATE	ORAL	TABLET, EXTENDED RELEASE	34481486	58QVG85GW3
POLYVINYL CHLORIDE-POLYVINYL ACETATE COPOLYMER	TRANSDERMAL	FILM, EXTENDED RELEASE		NA



As taken from US FDA, 2022c

Acetic acid, ethenyl ester, homopolymer (CAS RN 9003-20-7) “pose np unreasonable risk to human health based on Tier I assessment under the NICNAS IMAP assessment framework” and has been “identified as low concern to human health by application of expert validated rules” by the Australian Department of Health (AICIS, 2012).

Acetic acid, ethenyl ester, homopolyme (CAS RN 9003-20-7) is listed on Australian Inventory of Industrial Chemicals (AICIS, formerly NICNAS). As taken from AICIS, undated.

4. Metabolism/Pharmacokinetics

4.1. Metabolism/metabolites

No data available to us at this time.

4.2. Absorption, distribution and excretion

“An aqueous emulsion of PVAc was administered to rabbits by the following routes: subcutaneous (s.c.) in 2 rabbits, intratracheally in 3 rabbits, and intravenously (i.v.) in 131 rabbits (Miyasaki, 1975). In the s.c. study, 2 rabbits were injected with 0.3 ml of 30% PVAc. The PVAc remained localized at the site of injection with little absorption. When 1 mllkg of a 3% solution of PVAc was injected intratracheally in 3 rabbits every fourth day for a total of four injections, the PVAc was phagocytized by alveolar phagocytes. Six groups of rabbits received i.v. injections. The first group of 41 rabbits received 1 ml/kg injections of 5% PVAc daily for 1, 2, 4, 8, 12, 16, or 24 weeks; a second group of 60 rabbits reccived daily injections of 2 ml/kg of 5% PVAc for 3 days, or 1, 2, 3, 6, 12, or 24 weeks; a third group of 5 rabbits received daily injections of 3 ml/kg of 5% PVAc for 26 weeks; a fourth group of 2 rabbits received injections for 26 weeks as did the third group, followed by a 12-week nontreatment period; a fifth group of 18 rabbits received daily injections of 4 ml/kg of 5% PVAc for 1,2,4, or 6 weeks; and a sixth group of 5 pregnant rabbits each received a 5 rnllkg-injection of 5% PVAc. A small amount of the i.v. injected PVAc was excreted in the urine; the remainder was retained in the body.” As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176

4.3. Interactions

"This study investigated the non-sink in vitro dissolution behavior and in vivo performance in rats of celecoxib (CCX) amorphous solid dispersions with polyvinyl acetate (PVA), polyvinylpyrrolidone (PVP) and hydroxypropyl methylcellulose (HPMC) at different drug doses. Both in vitro and in vivo, the amorphous solid dispersions with the hydrophilic polymers PVP and HPMC led to higher areas under both, the in vitro dissolution and the plasma concentration-time curves (AUC) compared to crystalline and amorphous CCX for all doses. In contrast, the amorphous solid dispersion with the hydrophobic polymer PVA showed a lower AUC both in vitro and in vivo than crystalline CCX. For crystalline CCX and CCX:PVA, the in vitro AUC was limited by the low solubility of the drug and the slow release of the drug from the hydrophobic polymer, respectively. For the supersaturating formulations, amorphous CCX, CCX:PVP and CCX:HPMC, the in vitro performance was mainly dependent on the dissolution rate and precipitation/crystallization inhibition of the polymer. As expected, the crystallization tendency increased with increasing dose, and therefore the in vitro AUCs did not increase proportionally with dose. Even though the in vivo AUC for all formulations increased with increasing dose, the relative bioavailability decreased significantly, indicating that the supersaturating formulations also crystallized in vivo and that the absorption of CCX was solubility-limited. These findings underline the importance of evaluating relevant in vitro doses, in order to rationally assess the performance of amorphous solid dispersions and avoid confusion in early in vivo studies. " As taken from Knopp MM et al. 2016. Eur. J. Pharm. Biopharm. 105, 106-14. PubMed, 2017 available at: https://www.ncbi.nlm.nih.gov/pubmed/27212472

5. Toxicity

5.1. Single dose toxicity

“PVAc, 25 g/kg as a single dose, was administered orally to rats and mice (strain unspecified) (IARC, 1979). Effects due to oral administration of PVAc included lymphoid infiltration of the liver, depigmented epithelial cells of the renal tubules, and a slight increase in the number of polynucleated cells in the spleen.” As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

Type of Test	Route of Exposure or Administration	Species / Test System	Dose Data	Reference
LD - Lethal dose	Oral	Rodent - rat	>25 gm/kg	JACTDZ Journal of the American College of Toxicology. (Mary Ann Liebert, Inc., 1651 Third Ave., New York, NY 10128) V.1-12, 1982-1993. Discontinued. Volume(issue)/page/year: 11,465,1992
LD - Lethal dose	Oral	Rodent - mouse	>25 gm/kg	JACTDZ Journal of the American College of Toxicology. (Mary Ann Liebert, Inc., 1651 Third Ave., New York, NY 10128) V.1-12, 1982-1993. Discontinued. Volume(issue)/page/year: 11,465,1992
LD50 - Lethal dose, 50	Oral	Rodent -	>25	ENTOX* Encyclopedia of Toxicology: Reference Book, Elsevier, 2005 Volume(issue)/page/year: -

percent kill		rat	gm/kg	,516,2005

As taken from RTECS, 2007.

5.2. Repeated dose toxicity

“The PVAc injected daily over a long period of time caused enlargement of the spleen, lymph nodes, and liver. The monocyte-macrophage system of the liver, spleen, bone marrow, lymph nodes, adrenal glands, and lungs phagocytosed the injected PVAc, forming foam cells. The cellular storage of PVAc remained unchanged 3 months after treatment.”

“Extracts of a commercial hair spray containing polyvinyl pyrrolidine (PVP)/polyvinyl acetate (PVAc) were dissolved in isotonic saline and injected s.c. in the scapular area of adult mice, rats, and guinea pigs (Gebbers et al., 1979); polymer concentrates were not stated. PVP and PVAc alone in saline were also injected s.c. in the scapular area of mice, rats, and guinea pigs. Control animals received injections of saline. The animals were killed 4, 10, or 30 days after injection and the injection site was biopsied; samples from the liver, spleen, and kidneys were obtained for electron microscopic evaluation. A strong s.c. foreign body reaction with granulomas was seen in the animals injected with hair spray extracts and with PVP/PVAc 4 and 10 days postinjection. No reaction was noted at 30 days. The foreign body reaction consisted of many monocytes, large macrophagcs, multi-nucleated giant cells with periodic acid-Schiff (PAS)-positive inclusions, and many foam cells. Lamellar lysosomal inclusions were observed in the macro-phages and giant cells. The Kupffer's cells of the liver and macrophages of the spleen contained PAS-positive cytoplasmic inclusiuns 4 weeks after injection of hair spray extract and PVP/PVAc.”

“When PVAc, 250 mg/kg, was administered orally for 12 months to rats and mice, fluctuations in weight, changes in blood composition, changes in liver-to-body weight ratios, and changes in cholinesterase and catalase activities were observed (IARC, 1979). No other details were given.”

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176

5.3. Reproduction toxicity

“No studies have reported effects of PVAc on reproduction, leratology, or other developmental toxicity. However, data from pregnant rabbits (Miyasaki, 1975) indicate that PVAc was not transferred to the fetus in appreciable amounts, even when administered by the i.v. route, thus suggesting that no developmental effects could be produced by the usual dermal application of cosmetic ingredients.” As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

“Male rats were given 250 mg/kg unplasticized polyvinyl acetate (pvad) & pvad plasticized with 15% aq soln dibutylphthalate in food (dry residue equivalent to 125 mg/kg= 0.5% of diet) & paired with females at end of 11 mo. only male progeny revealed disturbances in orientation response.”

As taken from HSDB, 2002

“A brief abstract reported a study where male rats received unplasticised polyvinyl acetate, dispersed in the feed (apparently at a concentration that gave a dose level of 125 mg/kg bw), probably for 11 months before mating with untreated females. Duration of pregnancy was not affected, and the pups showed no external defects or abnormalities in body weight or length. However the males (but not the females) were reported to have an altered “orientation response” (Shcherbak, 1977).

“A review cited that polyvinyl acetate is not transferred to foetuses in “appreciable amounts” following applications (not further specified, but including intravenous administration) in

[presumably pregnant] rabbits. This was said to suggest that no developmental effects could be produced by the dermal application of cosmetics containing this ingredient. Polyvinyl acetate as used in cosmetic products was said to be an emulsion “containing 55-60% resin” (CIR, 1992).

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is suspected to be toxic for reproduction. The CAESAR developmental toxicity model in VEGA (Q)SAR platform predicts that the chemical is a toxicant (good reliability).

As taken from ECHA, 2021

The reliability and applicability of this QSAR prediction as standalone source of toxicological information is limited and inappropriate for some complex endpoints like reprotoxicity or carcinogenicity. Nevertheless, for the toxicological assessment of this ingredient, this result was still taken into consideration and used within the WoE approach as a supportive tool, in combination with other sources of information when available, like experimental data or appropriate read-across

5.4. Mutagenicity

“PVAc was tested for mutagenic potential in the Ames test using Salmonella Typhimurium strains TA92, TA1535, TA100, TA1537, TA94, and TA98, with metabolic activation (Ishidate et al., 1984). PVAc, 98.6% pure and dissolved in acetone, at a maximum dose of 5.0 mg/plate, was not mutagenic under the conditions of the study.”

“PVAc was also tested for mutagenic potential in the chromosomal aberration test using a Chinese hamster fibroblast cell line (Ishidate et al., 1984). No metabolic activation system was used. The test cells were exposed to three concentrations of the test substance; the maximum concentration was 200 mg/ml. Polyploid cells, as well as cells with chromosomal structural aberrations, were recorded. A result was considered positive if >10% aberrations were found, equivocal if 5.0 to 9.9% aberrations were detected, and negative if there were <4.9% aberrations. The negative controls, consisting of untreated and solvent-treated cells, contained <3.0% aberrations. The maximum incidence of polyploid cells in the treated groups was 2.0%; no chromosomal aberrations were observed at 24 and 48 h. PVAc was negative for mutagenicity under the conditions of the study.”

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

“Polyvinyl acetate was nonmutagenic in the Ames assay, with and without activation and in the Chinese hamster fibroblast cell assay. Several carcinogenic implantation studies using mice gave negative results”. As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176

In vivo				
Species	**Test conditions**	**Endpoint**	**Result**	**Reference**
According to a short English abstract, a small group of workers involved in the production of polyvinyl acetate production had higher levels of chromosome damage (aberrations) in the white blood cells (lymphocytes) than workers not involved in production (Shirinian & Arutyunyan, 1980). It is not clear how closely matched the two groups were, or what other exposures the production workers had. Therefore, the results are not interpretable. However, it seems unlikely that a high-molecular weight polymer would have any significant genotoxicity potential.				

In vitro					
Test system	**Test conditions**	**Endpoint**	**Activation**	**Result**	**References**

Chinese hamster lung fibroblast cells	Incubated for 48 hr at up to 200 mg/ml. Cells examined for chromosome aberrations and polyploidy.	Chromosome damage and changes in chromosome number	Without	-ve Limited assay as not tested in the presence of metabolic activation.	Ishidate, 1987; Ishidate et al. 1984
Salmonella typhimurium, strains TA92, TA94, TA98, TA100, TA1535, TA1537 (and possibly TA2637)	Ames assay. Tested up to 5 mg/plate.	Mutation	With and without S9	-ve Good quality study.	Ishidate et al. 1984
+ve, positive; ve, negative; ?, equivocal; with, with metabolic activation; without, without metabolic activation					

5.5. Cytotoxicity

No data available to us at this time.

5.6. Carcinogenicity

Evidence for Carcinogenicity:

“No data are available in humans. Inadequate evidence of carcinogenicity in animals. OVERALL EVALUATION: Group 3: The agent is not classifiable as to its carcinogenicity to humans. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: http://monographs.iarc.fr/index.php p. S7 70 (1987)] **QC REVIEWED**”

As taken from HSDB, 2002

“In a single inhalation study, 96 rats were exposed 6 h/day, 5 dayslweek, to vinyl acetate at a concentration of 8,750 mg/ml for 1 year and observed until death. There was no evidence that vinyl acetate influenced the incidence of neoplasms (Maltoni, 1976).”

“Vinyl chloride-vinyl acetate (VC/VA) polymer was tested for strain response differences to s.c. implantation of the polymer in 18 strains of mice (Brand et al., 1977). There was a 90 to 100% incidence of neoplasms in female mice of the CBA/H, CBA/H-T6, BALB/cJ, BALB/cWAT, 657BL/10ScSn strains, in males of the AKR/J strain, and in both sexes of the (C57BL/10ScSnxCBA/H)FI strain mice. All other strains had intermediate responses, with incidence of neoplasms in males lower than that in females, with the exception aP male AKR mice.”

“VC/VA powder, equivalent to two films 15 x 22 x 0.2 mrn (as in the previous study), was injected s.c. in 30 male and 46 female 6-week-old CBA mice; the mice were observed until death (Brand et al., 1975). One female mouse developed a sarcoma possibly due to the clumping of the powder after administration. No other treatment-related neoplasms were observed. Clayssn (1962) concluded that the induction of local sarcomas after the sc, injection of a substance cannot be regarded as sufficient to state that the substance is a chemical carcinogen.”

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

Species	Test conditions	Evidence of carcinogenicity	Reference
Rat (100) and mouse (100)	Polyvinyl acetate powder was implanted [presumably subcutaneously], animals were examined [presumably regularly] for local tumours appearing within 16-20 months. No further details provided in the citing source, but it was noted that these results were presented, without details, as a footnote to another study.	No local tumours within 16-20 months of implantation. This early study is very limited. Modern carcinogenicity study guidelines recommend that groups of 50 animals/sex be exposed, at several dose levels, on 5-7 days/week, for 2 yr, followed by microscopic examination of a comprehensive range of tissues and organs.	Nothdurft, 1956
One publication reported that polyvinyl actetate has demonstrated equivocal (“?”) carcinogenic activity (Ishidate et al. 1988). No further details were given and no studies supporting this statement were identified.			

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is a suspected carcinogen. The CAESAR Carcinogenicity model in VEGA (Q)SAR platform predicts that the chemical is a carcinogen (moderate reliability).

As taken from ECHA, 2021

The reliability and applicability of this QSAR prediction as standalone source of toxicological information is limited and inappropriate for some complex endpoints like reprotoxicity or carcinogenicity. Nevertheless, for the toxicological assessment of this ingredient, this result was still taken into consideration and used within the WoE approach as a supportive tool, in combination with other sources of information when available, like experimental data or appropriate read-across.

5.7. Irritation/immunotoxicity

“Polyvinyl acetate caused moderate inflammatory reaction when injected sc in rats and peaked at day 7 and minimal at day 42. Histological appearance of hamster cheek pouch was not significantly altered from topical application to pouche. [CARPENTER WM ET AL; ORAL SURG; ORAL MED ORAL PATHOL 42(4) 461 (1976)] **PEER REVIEWED** “

As taken from HSDB, 2002

“A dose of 0.1 ml of a solution of 1.25% PVAc in ethanol saline was injected s.c. into the shaved posterior dorsal skin of 24 adult albino rats to determine the irritation potential of the PVAc (Carpenter et al., 1976). Twelve negative vehicle controls and 24 positive controls (carrageenan) were included in the study program. Two rats from the negative control group and four rats from the positive control group and four from the test group were killed on days 3,7, 14, 21, 28, and 42. The injection sites were removed and preserved for microscopic examination. Tissue samples obtained from the test rats killed on day 3 had a moderate subacute inflammatory infiltrate of lymphocytes and plasma cells. Ulceration, accompanied by edema and tissue destruction, was frequently observed. Tissue samples from the rats killed on day 7 had retained PVAc surrounded by a severe inflammatory response. Ulceration, accompanied by abscesses and necrosis, was present in almost all the rats. In addition to lymphocytes and plasma cells, neutrophils were also present in abundance. The inflammatory response had reduced in severity by day 14, although many plasma cells and lymphocytes were still present. Many areas of granulation tissue were evident, as well as foci of necrosis with ulceration and an accompanying acute response. The tissue samples from the rats killed on day 21 had a moderate inflammatory response, with inflammatory cells and granulation tissue in abundance. By day 28, a minimal inflammatory response was evident, with cicatrization and early maturation of collagen fibrils. By day 42, inflammatory response was

minimal, with the epithelium intact and cicatrization of the dermis. The PVAc response was similar to that of the positive control through day 14, at which time the PVAc response was much reduced compared to the positive control. PVAc was considered very irritating when injected s.c., with an initial response similar to that of the positive control except for granuloma formation, which did not occur in the PVAc-treated animals. The adverse irritation reactions to the i.v. injection of PVAc cited in this section are similar to that previously reported as a foreign body reaction by Gebbers et al. (1979) in their short-term toxicity i.v. studies of PVAc using mice, rats, and guinea pigs."

"An occlusive skin irritation test (CTFA, 1994) was conducted using 54 female volunteers and an aqueous PVAc solution (50% concentration). Approximately 0.05 ml was placed on a patch test plaster that was applied to the intact forearm area for 24 h. On removal of the plaster, the skin response was immediately scored on a six-point scale: 0 (-), no reaction; 1 (+/-), faint or minimal erythema; 2(+), distinct erythema; 3(+ +), distinct erythema with infiltration, edema, or papules; 4 (+ + +), edema or papules, with vesicles; and 5 (+ + + +), crust or necrosis. All 54 subjects had no reaction."

"A repeat insult patch test (CTFA, 1994) was conducted using 159 volunteers (26 males and 133 females; aged 16-65 years). Aqueous PVAc emulsions at 50% concentration were used for induction and challenge. Induction was done using 0.2 ml of the PVAc solution placed onto an occlusive patch and then applied to the back of each subject. Patches were left on for 24 h, removed for 24 h, and a new patch applied after examination of the induction site. This sequence was continued through nine applications and varied only by allowing 48 h between applications of the patch on weekends. Two weeks after the last patch was removed, a challenge patch was applied to a previously unexposed site. All challenge sites were evaluated at 24 and 72 h after application, and subjects were instructed to report any delayed skin reactivity occurring at a later time. Thirteen subjects discontinued the study for reasons unrelated to the conduct of the study. Of the 146 subjects completing the study, none had any skin irritation or allergic contact sensitization at any time."

"No significant skin or eye irritation due to occupational exposure has been reported. Polyvinyl acetate at concentration of 50% in a cosmetic product showed no irritation reaction ain 54 female volunteers tested with occlusive patches and no irritation or allergic contact sensitisation in 146 volunteers in a repeat insult patch".

"No sensitization potential was observed in a repeat insult protocol, involving nine 24-hr applications (on alternate days) of a 50% aqueous solution to the skin of 159 volunteers, followed 2 weeks later by a similar challenge application".

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

Acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is a suspected skin sensitizer. The CAESAR skin sensitization model in VEGA (Q)SAR platform predicts that the chemical is a sensitizer (good reliability).

As taken from ECHA, 2021

The reliability and applicability of this QSAR prediction as standalone source of toxicological information is limited and inappropriate for some complex endpoints like reprotoxicity or carcinogenicity. Nevertheless, for the toxicological assessment of this ingredient, this result was still taken into consideration and used within the WoE approach as a supportive tool, in combination with other sources of information when available, like experimental data or appropriate read-across.

5.8. All other relevant types of toxicity

"Other in vitro test"

Sustained release capsules of nifedipine containing an initial rapidly available loading dose in a solid dispersion and sustained action polyvinyl acetate coated microparticles were prepared and evaluated for in vitro release and stability. The capsules provided release of the initial therapeutic dose in less than 45 min and sustained release for over 11-12 h. In addition, they were stable over 3.23 yr.

As taken from Ali A ; Sharma SN . Indian Drugs; VOL 33 ISS Jan 1996, P30-35.

6. Functional effects on

6.1. Broncho/pulmonary system

“Chemical factors operating in the manufacture of vinyl acetate and its derivatives cause pathologic changes in the bronchopulmonary system reflected in ventilatory disturbances (overt or latent) with or without clinical manifestations of chronic bronchitis. The boundary zone of normality and latent or overt ventilatory disturbances, which represent different stages of changes in pulmonary function, were encountered more frequently than clinical manifestations of bronchitis in workers.”

As taken from Amatuni VG et al., GIG TR PROF ZABOL; 0 (2). 1980. 14-16.

6.2. Cardiovascular system

“To assess blood compatibility of artificial materials, the blood of human donors was passed through columns containing various materials, including PVAc beads (Lindon et al., 1978). The PVAc was observed for signs of platelet retention and release of platelet constituents due to lysis. Platelet aggregation and adhesion to the PVAc resulted in retention of platelets in the test column. When various blood sample parameters of the donors were examined to assess the causes of donor-to-donor variability, it was reported that the amount of platelet retention by PVAc increased as the sedimentation rate increased. The use of birth control pills by female blood donors increased platelet retention by PVAc. PVAc did not adsorb serotonin from platelet-free plasma, and did not cause lysis of erythrocytes.”

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176

6.3. Nervous system

Abstracts cited in Toxline have reported nervous system, lung and liver enzyme effects in workers involved in polyvinyl acetate production. It is likely that the workers were exposed to a number of chemicals, including the monomer vinyl acetate. Further details of these publications could be provided if required.

6.4. Other organ systems, dependent on the properties of the substance

The PVAc injected daily over a long period of time caused enlargement of the spleen, lymph nodes, and liver. The monocyte-macrophage system of the liver, spleen, bone marrow, lymph nodes, adrenal glands, and lungs phagocytosed the injected PVAc, forming foam cells. The cellular storage of PVAc remained unchanged 3 months after treatment.”

As taken from CIR (1996). Amended final safety assessment of polyvinyl acetate. Journal of the American College of Toxicology, 15, 166-176.

7. Addiction

JTI is not aware of any information that demonstrates that this ingredient has any addictive effect.

8. Burnt ingredient toxicity

Endpoint	Tested level (ppm)	Reference
Smoke chemistry	- -	JTI Internal Report Coggins (2013)
In vitro genotoxicity	- -	JTI Internal Report Coggins (2013)
In vitro cytotoxicity	-	Coggins (2013)
90 days inhalation	-	Coggins (2013)

In comparison with a CSC of a reference cigarette with sideseam adhesives/cigarette paper corresponding to representative specifications for the majority of commercial cigarettes no differences were observed either in the bacterial mutagenicity, cytotoxicity or mammalian cell genotoxicity of the smoke condensate prepared from cigarettes with sideseam adhesives/cigarette paper containing Polyvinyl acetate at 1.62 mg/cig. The smoke chemistry data between test and reference cigarette revealed small changes towards both higher and lower yields per cigarette over all analytical groups. These differences were well within the variability of the analytical methods (JTI NTM Study Report(s)).

“CONTEXT: Adhesives are used in several different manufacturing operations in the production of cigarettes. The use of new, "high-speed-manufacture" adhesives (e.g. vinyl acetate based) could affect the smoke chemistry and toxicology of cigarettes, compared with older "low-speed-manufacture" adhesives (e.g. starch based). OBJECTIVE: This study was conducted to determine whether the inclusion of different levels of three adhesives (ethylene vinyl acetate, polyvinyl acetate and starch) in experimental cigarettes results in different smoke chemistry and toxicological responses in in vitro and in vivo assays. MATERIALS AND METHODS: A battery of tests (analytical chemistry, in vitro and in vivo assays) was used to compare the chemistry and toxicology of smoke from experimental cigarettes made with different combinations of the three adhesives. Varying levels of the different side-seam adhesives, as well as the transfer of adhesives from packaging materials, were tested. RESULTS: There were differences in some mainstream cigarette smoke constituents as a function of the level of adhesive added to experimental cigarettes and between the tested adhesives. None of these differences translated into statistically significant differences in the in vitro or in vivo assays. CONCLUSION: The use of newer "high-speed-manufacture" vinyl acetate-based adhesives in cigarettes does not produce toxicological profiles that prevent the adhesives from replacing the older "low-speed-manufacture" adhesives (such as starch).” As taken from Coggins CR et al. 2013. Inhal. Toxicol. 25(Suppl. 2), 6-18. PubMed, 2014 available at http://www.ncbi.nlm.nih.gov/pubmed/24341843

9. Heated/vapor emissions toxicity

Aerosol from heated tobacco stick(s) containing Polyvinyl Acetate was tested in aerosol chemistry and a battery of in vitro test(s). Under the test conditions and within the sensitivity and specificity of the bioassay(s), the activity of the total particulate matter (TPM) and/or gas vapor phase (GVP) were not increased by the addition of this ingredient when compared to TPM and/or GVP from reference combustible cigarettes. The table below provides the highest tested level(s) and specific endpoint(s):

Endpoint	Tested level (mg/stick)	Reference
Aerosol chemistry	0.20	Labstat International Inc. (2021a)
In vitro genotoxicity	0.20	Labstat International Inc. (2021b)
In vitro cytotoxicity	0.20	Labstat International Inc. (2021b)

10. Ecotoxicity

10.1. Environmental fate

The Ecological Categorization Results from the Canadian Domestic Substances List simply state that acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is persistent in the environment.

Data accessed June 2017 on the OECD website: http://webnet.oecd.org/CCRWeb/Search.aspx

10.2. Aquatic toxicity

The Ecological Categorization Results from the Canadian Domestic Substances List simply state that acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is not inherently toxic to aquatic organisms and give a pivotal value for inherent toxicity of 14 mg/l.

Data accessed June 2017 on the OECD website: http://webnet.oecd.org/CCRWeb/Search.aspx

10.3. Sediment toxicity

No data available to us at this time.

10.4. Terrestrial toxicity

No data available to us at this time.

10.5. All other relevant types of ecotoxicity

The Ecological Categorization Results from the Canadian Domestic Substances List simply state that acetic acid ethenyl ester, homopolymer (CAS RN 9003-20-7) is not bioaccumulative in the environment.

Data accessed June 2017 on the OECD website: http://webnet.oecd.org/CCRWeb/Search.aspx

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13. Last audited

April 2022

VINYL ACETATE, POLYVINYL ACETATE AND POLYVINYL ALCOHOL

VOL.: 19 (1979) (p. 341)

Vinyl acetate
CAS No.: 108-05-4
Chem. Abstr. Name: Acetic acid ethenyl ester

Polyvinyl acetate
CAS No.: 9003-20-7
Chem. Abstr. Name: Acetic acid ethenyl ester homopolymer

Polyvinyl alcohol
CAS No.: 9002-89-5
Chem. Abstr. Name: Ethenol homopolymer

5. Summary of Data Reported and Evaluation

5.1 Experimental data

In the only study available, vinyl acetate was tested in rats by inhalation exposure; it produced no evidence of carcinogenicity.

Vinyl acetate was non-mutagenic in the only test system used.

Subcutaneous or intraperitoneal implantation of polyvinyl acetate powder in mice and rats did not result in local sarcomas. Subcutaneous implantation of polyvinyl alcohol sponges in rats produced local sarcomas, whereas negative results were obtained with polyvinyl alcohol powder.

5.2 Human data

No case reports or epidemiological studies relating to the carcinogenicity of either vinyl acetate or polyvinyl acetate were available to the Working Group. One case of haemangiopericytoma was reported in a man exposed to polyvinyl alcohol.

The high levels of production of vinyl acetate, polyvinyl acetate and polyvinyl alcohol indicate that occupationally exposed groups could be identified for epidemiological investigation. The widespread use of polyvinyl acetate and polyvinyl alcohol in diverse applications indicates that the general population is also exposed.

5.3 Evaluation

No case reports or epidemiological studies concerning vinyl acetate were available to the Working Group. Animal studies involving implantation of polyvinyl acetate and

polyvinyl alcohol powder in rats did not result in local sarcomas, whereas in similar experiments with polyvinyl alcohol sponges, local sarcomas were produced. Both polyvinyl acetate and polyvinyl alcohol have substantial commercial applications. Further studies are required before an evaluation can be made of the carcinogenicity of these compounds.

Subsequent evaluation: Suppl. 7 (1987) (Polyvinyl acetate, p. 70: **Group 3**) (Polyvinyl alcohol, p. 70: **Group 3**); Vol. 63 (1995) (Vinyl acetate)

For definition of Groups, see Preamble Evaluation.

Synonyms for Vinyl acetate

- Acetic acid vinyl ester
- 1-Acetoxyethylene
- 2,4-Diisocyanatotoluene
- Vinyl A monomer
- VAc
- VyAc

Synonyms for Polyvinyl acetate

- Acetic acid vinyl ester polymers
- Asahisol 1527
- ASB 516
- AYAA
- AYAF
- AYJV
- Bakelite AYAA
- Bond CH 3
- Borden 2123
- Cemedine 196
- Cevian 380
- D 50
- D 50(polymer)
- DCA 70
- Duvilax
- Elvacet 81-900
- Emultex F
- En-Cor
- EP 1208
- Esnil P 18
- Everflex B
- Formvar 1285
- Gelva
- Gohensil E 50Y

- Kurare OM 100
- Lemac
- Meikatex 5000NG60
- Merckogel OR
- Merckogen 6000
- Mokotex D 2602
- Movinyl
- Movinyl 801
- Movinyl 50M
- Mowilith 30
- National 120-1207
- National Starch 1014
- NS 2842
- OM 100
- OR 1500
- P-170
- Pioloform F
- Plyamul 40-155
- Plyamul 40-350
- Polisol S-3
- Polyco 953
- Polyfox P 20
- Poly(vinylacetate)
- Protex
- PS 3h
- PVAE
- R 10688
- Resyn 25-1025
- Rhodopas
- RV 225-5B
- S-nyl-p 42
- Soloid
- Soviol
- SP 60
- SP 60 (ester)
- Toabond 2
- TS2
- Ucar 15
- UK 131
- V 501
- VA-0112
- Vinac ASB 10
- Vinalite D 50N
- Vinamul 9300
- Vinapol A 16
- Vinnapas B

- Vinyl acetate homopolymer
- Vinyl acetate polymer
- Vinyl acetate resin
- Vinylite AYAF
- Vinyl Products R 10688
- Winacet D

Synonyms for Polyvinyl Alcohol

- Poly(vinyl alcohol)
- PVA
- vinyl alcohol polymer
- Alcotex 88/05
- Alkotex
- Alvyl
- Aracet A-PV
- Cipoviol W 72
- Covol
- Elvanol
- EP 160
- Gelvatol
- GH 20
- GL 02
- GL 03
- GLO 5
- GM 14
- Gohsenol AH 22
- Kuralon VP
- Kurare Poval 120
- Lemol
- M 13/20
- Mowiol
- NH 18
- Polydesis
- Polysizer 173
- Polyvinol
- Polyviol
- Polyviol M 13/140
- Poval 117
- PVA 008
- PVS 4
- Resistoflex
- Rhodoviol
- Solvar
- Sumitex H 10
- Vibatex S

- Vinacol MH
- Vinalak
- Vinarol
- Vinavilol 2-98
- Vinnarol
- Vinol
- Vinylon Film 2000

Last updated: 30 March 1998

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REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS

1. REPORT NUMBER: 51-077-73/75

2. GOVT ACCESSION NO.:

4. TITLE (and Subtitle): Special Study No. 51-077-73/75, Toxicological Evaluation of Polyvinyl Acetate (PVA) Emulsion Dust Control Material

5. TYPE OF REPORT & PERIOD COVERED: May 1973 - March 1974

6. PERFORMING ORG. REPORT NUMBER: 51-077-73/75

7. AUTHOR(s)

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8. CONTRACT OR GRANT NUMBER(s):

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18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Polyvinyl Acetate	Flexol 4GO	Inhalation
PVA	Eye Irritation	Aerosol
Dust Control	Santicizer 140	DCA 1295
Clinical Chemistry	Approximate Lethal Dose	Hematology
Skin Irritation	Cholinesterase	Subchronic Inhalation

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The relative toxicity of polyvinyl acetate (PVA) emulsion dust control material was investigated using laboratory animals. PVA emulsion is a mixture composed of a base latex plasticized with cresyl diphenyl phosphate (Santicizer 140) and tetraethylene glycol di-(2-ethylhexanoate) (Flexol 4GO). The PVA emulsion, base latex, and Flexol 4GO produced moderate to severe primary irritation when applied to the intact and abraded skin of rabbits. Santicizer 140 did not produce eye or skin irritation but did cause a reduction in blood plasma cholinesterase activity of squirrel monkeys and coturnix quail 24 hours after a

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

Block 19. Histopathology
Toxicity
rats
New Zealand White rabbits
Dogs
Quail
Squirrel Monkeys

Block 20. single intraperitoneal injection. Data indicate little acute toxic hazard from ingestion of PVA emulsion or its component compounds. No clinically significant changes occurred in groups of dogs or rats as a result of repeated exposures to aerosols of PVA emulsion 4 hours per day, 5 days per week for 6 weeks at concentrations of 90 mg/M^3 and 380 mg/M^3.

It was recommended that personnel potentially exposed to PVA emulsion, either as the liquid or aerosol, wear gloves, coveralls and goggles. Medical surveillance of workers involved with the field dispersion of the material should take cognizance of the potential for primary irritation of the skin. Plasma and erythrocyte cholinesterase activity should be monitored in the event of accidents involving the exposure of large areas of the skin.

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

USAEHA-LT

6 SEP 1974

SPECIAL STUDY NO. 51-077-73/75
TOXICOLOGICAL EVALUATION OF POLYVINYL ACETATE (PVA) EMULSION
DUST CONTROL MATERIAL
MAY 1973 - MARCH 1974

ABSTRACT

The relative toxicity of polyvinyl acetate (PVA) emulsion dust control material was investigated using laboratory animals. PVA emulsion is a mixture composed of a base latex plasticized with cresyl diphenyl phosphate (Santicizer 140) and tetraethylene glycol di-(2-ethylhexanoate)(Flexol 4G0). The PVA emulsion, base latex, and Flexol 4G0 produced moderate to severe primary irritation when applied to the intact and abraded skin of rabbits. Santicizer 140 did not produce eye or skin irritation but did cause a reduction in blood plasma cholinesterase activity of squirrel monkeys and coturnix quail 24 hours after a single intraperitoneal injection. Data indicate little acute toxic hazard from ingestion of PVA emulsion or its component compounds. No clinically significant changes occurred in groups of dogs or rats as a result of repeated exposures to aerosols of PVA emulsion 4 hours per day, 5 days per week for 6 weeks at concentrations of 90 mg/M^3 and 380 mg/M^3.

It was recommended that personnel potentially exposed to PVA emulsion, either as the liquid or aerosol, wear gloves, coveralls and goggles. Medical surveillance of workers involved with the field dispersion of the material should take cognizance of the potential for primary irritation of the skin. Plasma and erythrocyte cholinesterase activity should be monitored in the event of accidents involving the exposure of large areas of the skin.

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

USAEHA-LT

SPECIAL STUDY NO. 51-077-73/75
TOXICOLOGICAL EVALUATION OF POLYVINYL ACETATE (PVA) EMULSION
DUST CONTROL MATERIAL
MAY 1973 - MARCH 1974

1. REFERENCES.

a. Letter, DASG-HEO, Office of The Surgeon General, Washington, DC, 27 February 1973, subject: Request for Toxicological Hazard Evaluation of Polyvinyl Acetate Emulsion Dust Control Material.

b. Letter, WESDV, Waterways Experimental Station, 2 November 1970, subject: Request for Toxic Hazard Analysis and Toxicology Report.

c. Occupational Safety and Health Administration of 1970, Title 29, Code of Federal Regulations, Part 1910.93, 18 October 1972.

d. Letter, MEDPS-PO, Office of The Surgeon General, Washington, DC, 25 June 1971, subject: Request for Toxic Hazard Analysis and Toxicology Report.

e. Report, USAEHA-OI, Environmental Hygiene Special Study No. 99-019-72/73, 24 October 1972, subject: Particle Size Analysis from Engineering Test of Dust Control Material and Liquid Distribution for Dust Control.

f. Procedural Guide for the Toxicology Division, US Army Environmental Hygiene Agency, 1970.

g. Contract Report S-71-9, Union Carbide Corporation, subject: Development of An Improved Dust Control System Based on Polyvinyl Acetate Latex for US Army Engineer Waterways Experimental Station, October 1971.

2. PURPOSE. The purpose of this study was to acquire information concerning the toxicity of a polyvinyl acetate (PVA) emulsion. This information provides a basis for advising on possible hazards associated with the use of this emulsion and safety precautions to be observed in its application as a dust control material.

3. BACKGROUND. The polyvinyl acetate emulsion* dust control material is composed of 90.9 percent base latex (98 percent vinylacetate homopolymer,

* Manufactured by Union Carbide Corporation, South Charleston, West Virginia.

1.5 percent hydroxy ethyl cellulose plus small traces of a catalyst) plasticized with 3.2 percent cresyl diphenyl phosphate (Santicizer 140) and 5.9 percent tetraethylene glycol di(2-ethylhexanoate) (Flexol 4G0)[1]. Bulk samples of PVA come in liquid form in 55 gallon steel drums. Field application is accomplished from a distributor located on a motor vehicle. The distributor is loaded with the material by removing the lids from the drums and inserting a hose which is connected to a pump on the distributor. The material is then pumped into the distributor tank, diluted using three parts PVA to one part water; transported to the desired location where it is sprayed upon the ground surface through nozzles. The nozzles are located at the rear of the distributor approximately 12 inches above the ground. The sprayed material is then air cured for 4 hours. The operator of the spray apparatus stands on a platform at the rear of the vehicle located about 6 inches above the exit of the spray nozzles (refer to para 1b). Personnel may work with this material for periods of time varying from 1 to 10 hours per day for several consecutive days.

4. SUMMARY OF FINDINGS. The relative toxicity of polyvinyl acetate emulsion dust control material was invesigated by this Agency using quail, rats, rabbits, monkeys, and dogs. The PVA emulsion and two of its components, base latex and Flexol 4G0, were found to cause moderate to severe erythema and very slight edema when applied to the intact and abraded skin of rabbits. Santicizer 140 did not produce eye or skin irritation but did cause a significant decrease in plasma cholinesterase activity of coturnix quail and squirrel monkeys 24 hours after an intraperitoneal injection. Base latex and Flexol 4G0 did not affect the plasma cholinesterase activity of these animals. Groups of 3 dogs and 30 rats, each were exposed to PVA aerosol concentrations of 90 mg/M^3 and 380 mg/M^3, 4 hours per day, 5 days per week for a total of 30 days. The mean particle diameter of the aerosol at each concentration was 1.22 $\mu \pm 0.16 \mu$. No significant changes occurred in hematology, clinical chemistry and histopathology of dogs exposed to PVA aerosols. Histopathological examination of organs and tissues from exposed and control rats showed no abnormalities attributable to inhalation of PVA aerosols. Definitions of selected terms and abbreviations used in this report are found in Appendix A. Numerical data presented in the appendices are expressed as the mean plus or minus one standard deviation. Statistical significance in this report has been selected at the 0.01 level of probability. A detailed tabular presentation of toxicity data follows:

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[1] FONECON between Dr. R. Stickle, Union Carbide Chemical Corp., South Charleston, West Virginia and Joseph Macko, Toxicology Division, USAEHA, 8 May 1974.

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application of PVA and each of its components (Base Latex, Flexol 4G0 and Santicizer 140) to intact and abraded skin of New Zealand White rabbits.		
0.5 ml PVA Emulsion was applied to each of six rabbits.	Slight edema and very slight redness to well defined erythema of intact skin was present 24 hours after application. Seven days after application only very slight erythema remained. Individual erythema scores ranged from 0 to 2 with a mode of 1 and edema scores ranged from 0 to 1 with a mode of 0 (ref Appendix B). Slight edema and well defined and moderate to severe erythema of abraded skin was present after 24 hours. Well defined erythema and slight edema was seen after 72 hours. Swelling diminished after 7 days but slight erythema remained. Individual erythema scores ranged from 1 to 3 with a mode of 2 and edema scores ranged from 0 to 1 with a mode of 0 (ref Appendix B).	The PVA emulsion produced moderate primary irritation of intact skin and moderate to severe irritation on skin surrounding an abrasion. If compound comes in contact with the skin it should be washed off immediately with water.

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES (cont)		
0.5 ml Base Latex was applied to each of six rabbits.	Slight edema and well defined redness to well defined erythema of intact skin was present 24 hours after application. Swelling was absent after 72 hours. After 7 days well defined erythema of intact skin was still present. Individual erythema scores ranged from 2 to 3 with a mode of 2 and individual edema scores ranged from 0 to 1 with a mode of 0 for intact skin. (ref Appendix B) Very slight edema and moderate to severe erythema of abraded skin occurred after 24 hours. Edema diminished after 72 hours. Well defined to moderate to severe erythema remained after 7 days. Individual erythema scores ranged from 2 to 3 with a mode of 3 and edema from 0 to 1 with a mode of 0 for abraded skin. (ref Appendix B)	The base latex produced moderate to severe irritation of intact and abraded skin. If compound should come in contact with the skin it should be washed off immediately with water.

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES (cont)		
0.5 ml Flexol 4G0 was applied to each of six rabbits.	Very slight edema and well defined erythema of intact skin was present after 24 hours. Redness increased after 72 hours. Swelling diminised and erythema decreased to very slight after 7 days. Individual erythema scores ranged from 0 to 3 with a mode of 1 and individual edema scores ranged from 0 to 1 with a mode of 0 for intact skin. (ref Appendix B) Well defined and moderate to severe erythema of abraded skin occurred 24 hours after application. Swelling disappeared after 72 hours and redness disappeared after 7 days. Individual erythema scores ranged from 0 to 3 with a mode of 1 and edema from 0 to 1 with a mode of 0 for abraded skin. (ref Appendix B)	Flexol 4G0 produced moderate to severe irritation of intact and abraded skin. If compound comes in in contact with the skin, it should be washed off immediately.
0.5 ml Santicizer 140 was applied to each of six rabbits.	Compound produced no primary irritation of the intact skin at 24 hours, 72 hours and 7 days. Very slight erythema of the skin surrounding an abrasion was observed in one rabbit at 24 hours but the skin appeared normal at 72 hours and 7 days. Individual irritation scores ranged from 0 to 1 with a mode of 0 (ref Appendix B).	Compound produced no primary irritation of the intact skin and no greater than mild primary irritation of the skin surrounding an abrasion. If compound comes in contact with the skin, it should be washed off immediately.

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
EYE IRRITATION STUDIES		
Rabbits		
Santicizer 140		
Single 24-hour application of 0.1 ml technical grade compound applied to one eye of each of six rabbits.	Compound produced no irritation to the cornea, iris, or conjunctivae of six rabbits.	Irritation of human eye is not expected if the compound should accidentally get into the eyes, provided it is washed out immediately.

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
APPROXIMATE LETHAL DOSE		
PVA EMULSION (DCA 1295)		
Intraperitoneal		
Quail (female) water diluent	ALD - >4311 mg/kg	
Quail (male) water diluent	ALD - >4311 mg/kg	
Rat (male) water diluent	ALD - >4311 mg/kg	
Oral		
Rat (male) water diluent	ALD - >9699 mg/kg	PVA emulsion would probably present little hazard from acute accidental ingestion.
SANTICIZER 140		
Intraperitoneal		
Quail (female) 95 percent ethanol diluent	ALD - >4311 mg/kg Ataxia occurred at 4311 mg/kg dose of compound.	
Rat (female) corn oil diluent	ALD - >1272 mg/kg	
Rat (male) corn oil diluent	ALD - >851 mg/kg	
Oral		
Rat (male) corn oil diluent	ALD - >4311 mg/kg	Santicizer 140 would probably present little hazard from acute accidental ingestion.
Rat (female) corn oil diluent	ALD - >4311 mg/kg	

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
APPROXIMATELY LETHAL DOSE (cont)		
FLEXOL 4GO		
Intraperitoneal		
Quail (female) 95 percent ethanol diluent	ALD - >1916 mg/kg	
Rat (female) peanut oil diluent	ALD - >1916 mg/kg	
Rat (male) peanut oil diluent	ALD - >1916 mg/kg	
Oral		
Rat (male) peanut oil diluent	ALD - >9699 mg/kg	Flexol 4GO would probably present little hazard from acute accidental ingestion.
Rat (female) peanut oil diluent	ALD - >9699 mg/kg	
BASE LATEX		
Intraperitoneal		
Quail (female) water diluent	ALD - >6473 mg/kg	
Quail (male) water diluent	ALD - >2874 mg/kg	
Rat (male) water diluent	ALD - >6466 mg/kg	
Oral		
Rat (male) water diluent	ALD - >9699 mg/kg	Base latex would probably present little hazard from acute accidental ingestion.

TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
CHOLINESTERASE ACTIVITY STUDIES		
Intraperitoneal (IP) Administration		
Studies were made to determine the effect on erythrocyte and plasma cholinesterase activity in squirrel monkeys of Santicizer 140 and Flexol 4G0, diluted with 95 percent ethanol, 24 hours following IP administration.		
Squirrel Monkey		
Four animals per dose level of 1000 mg/kg.	A dosage of 1000 mg/kg of ethanol and Flexol 4G0 produced no effect on the erythrocyte and plasma cholinesterase activity of squirrel monkeys 24 hours after an IP injection. Santicizer 140 caused an 89 percent reduction in plasma cholinesterase activity 24 hours after an IP injection. No change in erythrocyte cholinesterase activity following IP injection of Santicizer 140 was observed (ref Appendix C).	Santicizer 140 produced a decrease in plasma cholinesterase activity in squirrel monkeys suggesting a potential hazard from Santicizer 140.

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
CHOLINESTERASE ACTIVITY STUDIES (cont) Intraperitoneal (IP) Administration Studies were made to determine the effect of Santicizer 140 on the plasma cholinesterase activity in quail 24 hours following IP administration. Quail (male and female) Ten animals per dose level of 50, 250, 1000, 4000 mg/kg of Santicizer 140.	Santicizer 140 caused a decrease in plasma cholinesterase activity in male and female quail 24 hours after IP injections of 250, 1000, and 4000 mg/kg (ref Appendix D).	Santicizer 140 produced a decrease in plasma cholinesterase activity in male and female quail suggesting a potential hazard from Santicizer 140.

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SUBCHRONIC INHALATION AEROSOL STUDIES PVA EMULSION (DCA 1295) Two groups of 30 rats and 3 dogs each were exposed to aerosols of PVA emulsion, for 4 hours per day 5 days a week for 6 weeks. The emulsion was dispersed by a Spraying Systems Aerosol nozzle #2050/64 at 24°C. Input pressure of the compressed air source was controlled to produce two different rates of aerosol delivery. The chamber concentrations were determined by measuring weight changes on type A glass filters after collecting known amounts of chamber air from the 1000L dynamic exposure chamber. Animals were exposed to two different aerosol concentrations of PVA emulsion. Particle sizes were determined microscopically by examining cellulose acetate filter samples. The mean particle diameter was 1.22 μ ± 0.16 μ for both chamber concentrations.	Synopses of data are found in Appendix E, Tables 1-8.	

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TABULAR PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SUBCHRONIC INHALATION AEROSOL STUDIES		
PVA EMULSION (DCA 1295)(cont)		
Dogs and rats exposed to 90 mg/M^3 (S.D.±20)(4 hours daily, 5 days a week, 6 weeks)	Dogs and rats exposed to aerosols of PVA emulsion at a concentration of 90 mg/M^3 exhibited gasping and excessive preening during and immediately after each exposure period of the first week. Signs were absent 24 hours after each exposure. Body weight gain was normal. No statistically significant changes in erythrocyte and serum ChE values were found. No clinically significant changes were noted in alkaline phosphatase and BUN. Values for hematocrit, total erythrocyte count and mean cell value did not change significantly during the test period. Organ to body weight ratios of exposed rats compared to control rats were not significantly different. No histopathology due to the chemical compound was noted in examination of the liver, kidney, spleen, lung and testes of test animals 1 hour, 30 days or 4 months after final exposure.	Aerosols of PVA emulsion DCA 1295 at concentrations of 90 mg/M^3 present little inhalation hazard. Gasping and some initial eye irritation are commonly observed in rats exposed to this concentration of many different types of aerosols.
Dogs and rats exposed to 380 mg/M^3 (S.D.±45) (4 hours daily, 5 days a week, 6 weeks)	Dogs and rats exposed to aerosols of PVA emulsion at a concentration of 380 mg/M^3 exhibited gasping and excessive preening during and immediately after each exposure period of the first week. Signs were absent 24 hours after each exposure. Body weight gain was normal. No statistically significant changes in erythrocyte and serum ChE values were found. No clinically significant changes were noted in alkaline phosphatase and BUN. Values for hematocrit, total leukocyte and erythrocyte count and mean cell value did not change significantly during the test period. Organ to body weight ratios of exposed rats compared to control rats, except for liver, were not significantly different. No histopathology due to the chemical compound was noted in examination of the liver, kidney, spleen, lung and testes of the test animals 1 hour, 30 days or 4 months after final exposure.	Aerosols of PVA emulsion (DCA 1295) at concentrations of 380 mg/M^3 present little acute inhalation hazard. Gasping and initial eye irritation are commonly observed in rats exposed to this concentration of many different types of aerosols. No explanation for statistical differences in liver to terminal body weight ratios could be determined from gross or histological examination of these organs.

5. DISCUSSION.

a. Animal data from skin irritation studies indicate that the liquid PVA emulsion should be handled with caution, using skin and eye protective equipment.

b. Single oral ingestion studies of PVA emulsion and its components with male and female rats showed that little hazard would be expected from acute accidental ingestion.

c. Santicizer 140, comprising 3.2 percent of the total PVA emulsion, has been reported to be a mild cholinesterase inhibitor in chickens (reference paragraph 1b). Our studies showed a reduction in plasma cholinesterase activity in quail and squirrel monkeys after intraperitoneal (IP) injection of Santicizer 140. However, no reduction in plasma or erythrocyte cholinesterase activity was observed in dogs undergoing 6 weeks of exposure to aerosols of the PVA emulsion. Comparison of the responses from rats and dogs during and following subchronic inhalation exposure to PVA emulsion aerosols did not indicate any potential inhalation hazard at the concentrations 90 and 380 mg/M^3.

6. CONCLUSIONS. Evaluation of toxicity data on rabbits, rats, quail, monkeys and dogs indicate that with appropriate safety precautions PVA emulsion (DCA 1295) will probably present little toxicological hazard when used as a dust control material.

7. RECOMMENDATIONS. The following recommendations are based upon toxicological data generated by this Agency subsequent to previous guidance (reference paragraph 1e) relevant to the use of this material as a dust control agent.

a. Personnel potentially exposed to the formulated PVA emulsion either as a liquid or aerosol must wear gloves, coveralls and goggles.

b. Medical surveillance of workers involved with the field dispersion of the PVA emulsion should take cognizance of the potential for primary irritation of the skin.

c. In the event of accidents involving the exposure of large areas of the skin and/or ingestion, the attending physician should take cognizance of the potential for depression of cholinesterase activity.

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APPENDIX A

GLOSSARY OF RECURRING DEFINITIONS, ABBREVIATIONS AND SYMBOLS USED BY THE TOXICOLOGY DIVISION, USAEHA

Definitions of medical terms and abbreviations used in this report are in agreement with the New Gould Medical Dictionary, Second Edition, published by the Blakiston Division of McGraw-Hill Book Company, Inc. Statistical terms and abbreviations are in agreement with those found in J. Maxwell Little's, An Introduction to the Experimental Method, 1961, Burgess Publishing Company, Minneapolis, Minn. The following terms and abbreviations are either not found in the above references or have been modified to fit the special purposes of this report. Some of the terms have been included below for special emphasis.

DEFINITIONS

WORD	DEFINITION
Acute Exposure	One exposure to exogenous test material for no longer than 8 hours. Animals are normally observed for 14 days after exposure.
Approximate Lethal Dose	In range finding the first dose of the lowest series of three ascending doses (each being 50% higher in concentration than the previous) all of which produce fatalities.
Garry & Routh Units	Micromoles sulfhydryl groups liberated at 37 degrees centigrade per milliliter of serum, plasma or packed red blood cells at a calculated incubation time of 3 minutes.
Hazard Evaluation	A study performed to estimate the degree of danger associated with the use of a material under specified conditions of use.
International Unit	An international unit is defined as that amount of enzyme activity responsible for the conversion of one micromole of substrate per minute at 37°C.
Primary Irritation	A local inflammatory reaction of the skin, produced by a compound, which does not produce destruction or irreversible change at the site of contact.
Subchronic Exposure	Repeated daily or constant exposure to a test material for no longer than 59 days or less than 2 days. Post observation period will vary.
Technical Grade Compound	As produced by the manufacturers of the commercial compound; definition dependent upon manufacturers' criteria.

ABBREVIATIONS

ABBREVIATION	MEANING
ALD	approximate lethal dose
BUN	blood urea nitrogen
ChE	cholinesterase
df	degrees of freedom
IU	international unit
ip	intraperitoneal
iv	intravenous
mg/M^3	milligrams per cubic meter
P	probability
$p = <.01$	The probability of the change from normal or control being due to chance alone is less than 1 out of 100.
SD or $(S_{\bar{x}})$	standard deviation
w/v	weight-to-volume ratio
w/w	weight-to-weight ratio

SYMBOLS

SYMBOLS	MEANING
>	is greater than
<	is less than

APPENDIX B

EVALUATION OF SKIN REACTIONS

Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness to slight eschar formation)	4

Edema Formation

No edema	0
Very slight (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

An individual irritation score is equal to the sum of the scores for edema formation and erythema and eschar formation.

APPENDIX C

Summary of Erythrocyte and Plasma Cholinesterase Activity of Squirrel Monkeys Following Intraperitoneal Injection of Santicizer 140 and Flexol 4GO (Garry and Routh Units)

Treatment	Pretreatment		24-Hour Post Treatment	
	Erythrocyte	Plasma	Erythrocyte	Plasma
Santicizer 140				
1000 mg/kg	37.4	10.0	32.0	1.1*
Diluent ethanol	±2.0	±1.2	±4.8	±0.4
Flexol 4GO				
1000 mg/kg	35.8	8.2	37.1	8.8
Diluent ethanol	±4.1	±0.7	±11.3	±1.4
Control				
Ethanol	34.9	15.6	41.5	14.6
1000 mg/kg	±5.2	±4.2	±10.8	±3.5

* Significantly different from pretreatment control value at .01 level of probability.

APPENDIX D

Summary of Plasma Cholinesterase Activity of Coturnix Quail Following Intraperitoneal Injection of Santicizer 140 (Garry and Routh Units)

	Ethanol Control	Santicizer 140			
	3 ml/kg	50 mg/kg	250 mg/kg	1000 mg/kg	4000 mg/kg
Quail (female)	8.3 ±7.3	7.2 ±3.3	4.1* ±2.5	3.2* ±2.1	0.1* ±0.1
Quail (male)	8.7 ±4.0	7.5 ±2.7	5.3* ±1.6	2.2* ±1.5	1.0* ±1.1

* Significantly different from ethanol control treatment group value at .01 level of probability.

APPENDIX E
TABLE 1
Subchronic Inhalation Aerosol Exposures
Erythrocyte Cholinesterase Activity Values of Male Dogs
Exposed 4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols
(Garry and Routh Units)

Treatment Group	Preexposure	Treatment Periods							
		Exposure						Post Exposure	
	4 Week	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 1	Week 2
Chamber Control	9.17 ±2.67	8.23 ±3.37	9.67 ±3.72	9.33 ±3.25	9.67 ±3.66	11.40 ±1.70	8.83 ±3.22	8.65 ±3.32	9.10 ±1.84
Exposed 90 mg/M^3 PVA Aerosols	9.58 ±2.67	8.20 ±2.35	9.60 ±3.52	9.03 ±3.25	9.40 ±3.24	8.27 ±2.77	8.77 ±2.95	8.55 ±1.48	8.00 ±1.27
Exposed 380 mg/M^3 PVA Aerosols	6.94 ±0.78	6.37 ±0.76	6.43 ±0.64	6.43 ±0.90	6.87 ±0.59	6.23 ±0.50	6.10 ±0.85	6.45 ±0.92	6.90 ±0.57

APPENDIX E
Table 2
Subchronic Inhalation Aerosol Exposures
Plasma Cholinesterase Activity Values of Male Dogs
Exposed 4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols
(Garry and Routh Units)

Treatment Group	Preexposure	Treatment Periods							
		Exposure						Post Exposure	
	4 Week	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 1	Week 2
Chamber Control	7.97 ±1.61	7.83 ±2.47	7.97 ±2.00	7.23 ±1.71	8.07 ±1.85	7.47 ±1.91	7.73 ±1.97	9.40 ±1.56	8.50 ±0.85
Exposed 90 mg/M^3 PVA Aerosols	8.10 ±2.50	7.70 ±2.49	7.47 ±2.75	7.47 ±2.52	7.67 ±2.57	6.87 ±2.15	7.07 ±2.60	7.00 ±2.26	6.90 ±2.26
Exposed 380 mg/M^3 PVA Aerosols	8.84 ±0.96	7.87 ±1.11	7.80 ±1.50	8.60 ±1.49	8.20 ±1.15	7.57 ±1.50	7.97 ±1.10	8.05 ±1.63	8.50 ±0.99

APPENDIX E
Table 3
Subchronic Inhalation Aerosol Exposures
Clinical Chemistry Values of Male Dogs
Exposed 4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols

Clinical Chemistry Determination	Treatment Group	Preexposure	Treatment Periods							
			Exposure						Post Exposure	
		4 Week	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 1	Week 2
BUN (mg %)	Chamber Control	13.1 ±4.3	10.5 ±0.7	11.0 ±1.8	13.5 ±0.8	12.1 ±0.8	11.5 ±4.5	13.4 ±0.8	11.4 ±1.0	11.3 ±3.5
	Exposed 90 mg/M^3	12.7 ±5.5	9.9 ±0.5	9.6 ±1.4	16.2 ±4.9	11.9 ±0.3	14.9 ±1.0	14.9 ±3.6	10.8 ±2.1	13.1 ±2.9
	Exposed 380 mg/M^3	13.9 ±3.4	14.5 ±1.7	15.6 ±0.9	15.5 ±1.9	14.5 ±2.2	19.1 ±2.8	16.9 ±2.0	17.6 ±1.0	21.0 ±2.1
Alkaline Phosphatase (IU)	Chamber Control	24.6 ±11.1	27.9 ±9.0	36.9 ±10.6	32.9 ±2.9	28.4 ±4.7	24.2 ±2.5	34.6 ±13.1	26.8 ±0.2	28.9 ±2.6
	Exposed 90 mg/M^3	22.5 ±11.0	31.8 ±0.4	26.0 ±10.6	26.2 ±6.9	29.3 ±12.0	20.6 ±6.2	23.3 ±6.9	24.2 ±4.7	23.5 ±8.9
	Exposed 380 mg/M^3	24.1 ±8.6	30.2 ±4.2	32.3 ±6.1	33.4 ±2.5	30.3 ±3.6	25.5 ±2.0	28.0 ±2.6	15.1 ±13.3	22.5 ±14.3

APPENDIX E
Table 4
Subchronic Inhalation Aerosol Exposures
Hematology Values of Male Dogs Exposed
4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols

Hematological Determination	Treatment Group	Preexposure 4 Week	Treatment Periods: Exposure Week 1	Exposure Week 2	Exposure Week 3	Exposure Week 4	Exposure Week 5	Exposure Week 6	Post Exposure Week 1	Post Exposure Week 2
Hematocrit (%)	Chamber Control	44.8 ±8.3	47.3 ±4.3	44.3 ±1.6	44.0 ±2.6	43.7 ±2.0	45.8 ±3.6	46.7 ±3.3	46.0 ±5.9	45.1 ±3.9
	Exposed 90 mg/M^3	45.1 ±2.5	45.1 ±3.3	45.2 ±3.0	44.3 ±4.5	43.6 ±3.0	44.0 ±1.7	45.5 ±2.7	42.9 ±2.8	45.7 ±0.2
	Exposed 380 mg/M^3	45.7 ±4.5	53.1 ±15.6	43.6 ±4.7	43.9 ±5.2	42.6 ±2.8	45.0 ±2.8	47.3 ±6.2	46.6 ±0.6	44.2 ±5.5
RBC X 10^6/mm^3	Chamber Control	6.44 ±0.67	6.73 ±0.76	6.75 ±0.46	6.60 ±0.17	6.65 ±0.56	6.81 ±0.78	6.72 ±0.58	6.75 ±0.81	6.64 ±0.56
	Exposed 90 mg/M^3	6.50 ±0.40	6.55 ±0.37	6.64 ±0.27	6.54 ±0.47	6.69 ±0.21	6.55 ±0.10	6.53 ±0.29	6.35 ±0.30	6.47 ±0.17
	Exposed 380 mg/M^3	6.63 ±0.59	7.73 ±1.93	6.52 ±0.62	6.70 ±0.74	6.31 ±0.42	6.94 ±0.36	6.90 ±0.74	6.95 ±0.06	6.98 ±0.25
Mean Corpuscular Volume (μ^3)	Chamber Control	69.6 ±2.0	70.7 ±2.1	70.0 ±2.0	68.7 ±1.5	68.3 ±1.5	68.3 ±0.6	70.0 ±1.0	68.5 ±0.7	67.5 ±0.7
	Exposed 90 mg/M^3	68.6 ±1.6	69.0 ±2.0	68.3 ±1.5	67.7 ±2.5	68.0 ±2.0	67.3 ±2.1	69.0 ±1.0	68.0 ±1.4	68.5 ±0.7
	Exposed 380 mg/M^3	66.8 ±1.8	68.3 ±3.2	67.3 ±1.5	66.0 ±1.0	67.3 ±2.0	65.0 ±1.7	68.7 ±2.1	67.5 ±0.7	66.5 ±2.1
WBC X 10^3/mm^3	Chamber Control	13.4 ±4.1	16.5 ±4.6	19.7 ±9.8	15.0 ±2.2	12.3 ±0.9	16.2 ±7.9	11.7 ±2.2	9.8 ±2.2	11.3 ±2.8
	Exposed 90 mg/M^3	11.5 ±4.3	10.6 ±1.3	8.6 ±5.3	12.1 ±1.0	11.9 ±2.8	9.1 ±1.4	8.0 ±1.1	8.0 ±0.0	10.7 ±2.5
	Exposed 380 mg/M^3	11.7 ±2.5	12.9 ±1.1	13.0 ±3.6	12.8 ±2.1	12.2 ±0.6	11.0 ±2.2	10.9 ±0.6	12.2 ±2.1	11.3 ±0.9
Prothrombin Time (sec)	Chamber Control	6.7 ±0.5	6.4 ±0.5	6.4 ±0.5	7.1 ±0.3	7.2 ±0.3	6.7 ±1.0	6.7 ±0.3	6.9 ±0.7	7.4 ±0.0
	Exposed 90 mg/M^3	6.9 ±0.9	6.6 ±0.3	7.4 ±1.3	7.2 ±0.3	6.7 ±0.6	6.7 ±0.3	6.9 ±0.5	7.4 ±0.4	6.9 ±0.7
	Exposed 380 mg/M^3	6.7 ±0.4	6.7 ±0.3	7.7 ±1.0	7.6 ±0.7	6.9 ±0.0	7.2 ±0.3	7.2 ±0.6	6.9 ±0.7	6.9 ±1.4

APPENDIX E
Table 5
Subchronic Inhalation Aerosol Exposures
Body Weights of Male Rats Exposed
4 Hour/Day, 5 Days/Week for 6 Weeks to PVA Aerosols
(Grams)

Treatment Group	Preexposure		Treatment Periods: Exposure						Post Exposure			
	Week 2	Week 1	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 1	Week 4	Week 8	Week 16
Chamber Control	94 ±13	123 ±14	150 ±16	192 ±18	234 ±19	262 ±21	293 ±25	324 ±26	360 ±28	399 ±29	448 ±37	486 ±52
Exposed 90 mg/M^3 PVA Aerosols	100 ±14	132 ±15	157 ±15	198 ±18	234 ±28	261 ±33	295 ±22	327 ±22	351 ±23	404 ±27	446 ±27	484 ±33
Exposed 380 mg/M^3 PVA Aerosols	101 ±13	135 ±15	159 ±16	205 ±20	242 ±23	273 ±30	297 ±28	326 ±31	352 ±35	400 ±40	422 ±42	469 ±41

APPENDIX E
Table 6
Subchronic Inhalation Aerosol Exposures
Body and Organ Weights of Male Rats Necropsied 1-Hour Post Exposure
(Exposure 4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols)

Treatment Group	Mean Terminal Body Weight (gm)	Mean Organ Weights per 100 gms Body Weight				
		Liver (gm)	Spleen (gm)	Kidney (gm)	Lung (gm)	Testes (gm)
CONTROLS						
Chamber Controls	345 ±29	4.48 ±0.41	0.24 ±0.03	0.70 ±0.04	0.51 ±0.08	0.92 ±0.08
EXPOSED						
Exposed 90 mg/M^3 PVA Aerosols	352 ±23	4.03 ±0.29	0.23 ±0.03	0.72 ±0.04	0.49 ±0.04	0.86 ±0.10
Exposed 380 mg/M^3 PVA Aerosols	357 ±21	3.87* ±0.24	0.23 ±0.03	0.69 ±0.06	0.49 ±0.03	0.88 ±0.08

* Statistically significant from chamber controls at .01 level of probability.

APPENDIX E
Table 7
Subchronic Inhalation Aerosol Exposures
Body and Organ Weights of Male Rats Necropsied 30 Days Post Exposure
(Exposure 4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols)

Treatment Group	Mean Terminal Body Weight (gm)	Mean Organ Weights per 100 gms Body Weight				
		Liver (gm)	Spleen (gm)	Kidney (gm)	Lung (gm)	Testes (gm)
CONTROLS						
Chamber Controls	395 ±33	3.91 ±0.25	0.22 ±0.04	0.68 ±0.04	0.47 ±0.03	0.82 ±0.06
EXPOSED						
Exposed 90 mg/M^3 PVA Aerosols	438 ±28	4.09 ±0.26	0.21 ±0.03	0.68 ±0.05	0.47 ±0.05	0.77 ±0.10
Exposed 380 mg/M^3 PVA Aerosols	431 ±30	4.31* ±0.27	0.21 ±0.03	0.66 ±0.05	0.46 ±0.04	0.70 ±0.12

* Statistically significant from chamber controls at .01 level of probability.

APPENDIX E
Table 8
Subchronic Inhalation Aerosol Exposures
Body and Organ Weights of Male Rats Necropsied 4 Months Post Exposure
(Exposure 4 Hours/Day, 5 Days/Week for 6 Weeks to PVA Aerosols)

Treatment Group	Mean Terminal Body Weight (gm)	Mean Organ Weights per 100 gms Body Weight				
		Liver (gm)	Spleen (gm)	Kidney (gm)	Lung (gm)	Testes (gm)
CONTROLS						
Chamber Controls	479 ±57	3.40 ±0.38	0.16 ±0.01	0.58 ±0.06	0.46 ±0.10	0.77 ±0.09
EXPOSED						
Exposed 90 mg/M^3 PVA Aerosols	487 ±58	3.27 ±0.26	0.19 ±0.03	0.61 ±0.07	0.41 ±0.05	0.70 ±0.05
Exposed 380 mg/M^3 PVA Aerosols	484 ±37	3.79 ±0.30	0.17 ±0.02	0.60 ±0.07	0.43 ±0.06	0.66 ±0.11

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Amended Final Safety Assessment of Polyvinyl Acetate[1]

Abstract: The polymer Polyvinyl Acetate (PVAc) is used in cosmetics as a binder, emulsion stabilizer, and hair fixative. Current reported uses are limited to a few eye makeup formulations. As used in cosmetic formulations, PVAc is an emulsion containing 55 to 60% resin. The Cosmetic Ingredient Review (CIR) Expert Panel had previously published a review of the safety of this ingredient in *J Am Coll Toxicol* (1992;11:465–74) concluding that the available data were not sufficient to support safety. The report included mutagenesis and carcinogenesis studies with negative findings. Data from pregnant rabbits indicated that PVAc was not transferred to the fetus, even when administered by the i.v. route, suggesting that present cosmetic use practices preclude any reproduction or developmental toxicity hazard to humans. Composition and impurities data and human skin irritation and sensitization data, however, were not available. Data received since that assessment include the nature of the ingredient as used in cosmetics, the identity of many of the impurities, and the test results of human exposure to aqueous emulsions containing ≤50% PVAc. Less than 2 ppm of arsenic and <20 ppm of heavy metals reportedly will be in a typical emulsion. The clinical testing of an aqueous emulsion with 50% PVAc produced no irritation or sensitization. Based on the recent information, this ingredient is found to be safe for use as a cosmetic ingredient in the present practices of use. **Key Words:** Polyvinyl Acetate—Cosmetic use—Impurity—Human.

In an earlier evaluation (Elder, 1992), the Cosmetic Ingredient Review (CIR) Expert Panel found that there were insufficient data to support the safety of Polyvinyl Acetate (PVAc) and cited three missing pieces of data: (a) composition of the PVAc as used in cosmetic formulations, including impurities and additives; (b) skin irritation (human); and (c) skin sensitization (human). Data received since that evaluation have been reviewed, incorporated into the original report, and used as the basis for an amended conclusion.

PVAc as used in cosmetic products and reviewed in this report is the emulsion rather than the solid form. All available safety test data on PVAc are included in this report. Some safety test data on films and polymers of vinyl acetate in an earlier report (Elder, 1983) are also included.

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[1] Reviewed by the Cosmetic Ingredient Review Expert Panel.

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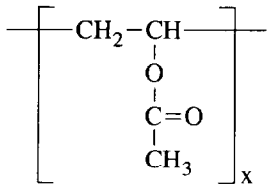
CHEMISTRY

Definition and Structure

PVAc (CAS No. 9003-20-7) is the homopolymer of vinyl acetate (Wenninger and McEwen, 1993). It conforms to the general formula:



PVAc is also known as the homopolymer of ethenyl acetate (Wenninger and McEwen, 1993), vinyl acetate homopolymer, vinyl acetate polymer, and vinyl acetate resin (IARC, 1979).

Properties

PVAc is a clear white to pale yellow solid (Food Chemicals Codex, 1981). The melting range (softening range) of PVAc is between 30° and 50°C (Lindemann, 1971); the softening point of various PVAc resins ranged from 43 to 141°C, depending on molecular weight (Union Carbide Corporation, 1989*a*). The refractive index of PVAc has been reported as 1.4669 (Lindemann, 1971) and 1.4665 at 20°C (Union Carbide Corporation, 1989*a*). PVAc has reported specific gravities of 1.19 at 15°C (Hawley, 1971), 1.177 (temperature unspecified) (Matharu and Lalla, 1985), and 1.18 (temperature unspecified) (Union Carbide Corporation, 1989*a*). A saponification value of 260 to 270 has been recorded for PVAc (Matharu and Lalla, 1985). PVAc is insoluble in water (Hawley, 1971; Grant, 1972), gasoline, oils, fats (Hawley, 1971), mineral oil (Grant, 1972), high-molecular-weight alcohols, aliphatic hydrocarbons, carbon disulfide, and cyclohexane. It is soluble in low-molecular-weight alcohols, esters, chlorinated hydrocarbons, and benzene and in acetone, chloroform, carbon tetrachloride, trichloroethylene, and methylene chloride (Hawley, 1971; Lindemann, 1971). PVAc is tasteless and odorless (Hawley, 1971) or may have a slight characteristic odor (Union Carbide Corporation, 1989*b*). It is not known if PVAc, used as a cosmetic ingredient, contains plasticizers or emulsifiers.

Method of Manufacture

PVAc is manufactured by the polymerization of vinyl acetate using peroxide catalysts (Hawley, 1971) or other initiators (Lindemann, 1971). Most commercial production of PVAc is made by an emulsion polymerization reaction carried out in aqueous solution, in the presence of emulsifiers or protective colloids and an initiator as well as a neutralizer (Lindemann, 1971). Chemicals identified from

patents and the trade literature to be used as emulsifiers, protective colloids, neutralizers, and initiators are shown below in Table 1.

Another process, suspension polymerization, is conducted in the same manner as emulsion polymerization, with the use of more water and the addition of a suspending agent such as partially hydrolyzed polyvinyl alcohol. That process results in the solid resin as small pearls (IARC, 1979; Lindemann, 1971). After completion of polymerization, the resin is purified by the removal of residual catalyst, vinyl acetate, and solvent by vacuum drying, steam sparging, and/or washing (Food Chemicals Codex, 1981); as noted previously, commercial forms of PVAc contain small amounts of residual monomer (Union Carbide Corporation, 1989*b*). PVAc may be produced as a co-polymer and referred to as PVAc if it contains ≥60% vinyl acetate (IARC, 1979), but PVAc as defined for cosmetic use is a homopolymer (CTFA, 1994). If the PVAc is supplied as an emulsion, it generally contains 55% resin (IARC, 1979).

Impurities

PVAc intended for use as a food chemical may contain not more than 3 ppm arsenic, not more than 0.05% free acetic acid, not more than 0.004% heavy metals, and not more than 3 ppm lead (Food Chemicals Codex, 1981). PVAc contains residual vinyl acetate, usually <0.02% of the total polymer (Union Carbide Corporation, 1989*a*). Depending on whether the PVAc is supplied as a solid or as an emulsion, it may contain hardeners, plasticizers (typically, dialkyl-phthalate), emulsifiers, thickeners, biocides, pigments, and other additives used to impart desired characteristics in the final product (IARC, 1979; Union Carbide Corporation, 1989*a;* CTFA, 1994). Purification steps are taken to remove residual plasticizers, emulsifiers, and antifreezing agents for PVAc intended for cosmetic use (CTFA, 1994). One typical PVAc composition included (a) no plasticizer; (b) 0.2% dihydroxy acetic acid as a preservative; (c) arsenic <2 ppm; and (d) heavy metals

TABLE 1. *Components used in commercially produced Polyvinyl Acetate*

Component function	Specific component
Emulsifiers	Sodium lauryl sulfate
	Alkylarenesulfonates
	Ethylene oxide adducts of alkylphenols
	Ethylene oxide-propylene oxide copolymers
	Poly(ethylene oxide)-fatty acid esters and ethers
Protective colloids	Polyvinyl alcohol
	Hydroxyethylcellulose
	Maleic anhydride-alkyl vinyl ether copolymers
	Gum arabic
Initiators	Alkali peroxysulfites
	Hydrogen peroxide
	t-Butyl hydroperoxide
	Cumene hydroperoxide

Data adapted from Lindemann (1971).

<20 ppm (CTFA, 1994). Another formulation was identical except for the use of 2% ethanol as a preservative (CTFA, 1994).

Chemical Reactivity

PVAc is a stable compound (Union Carbide Corporation, 1989*b*) resistant to weathering (Hawley, 1971). PVAc is resistant to heat and light, and will swell and soften on continuous immersion in water (Union Carbide Corporation, 1989*a*). Vinyl acetate in liquid form polymerizes on exposure to light (Sax, 1979; Windholz, 1983).

Analytical Methods

PVAc may be identified through its infrared absorption spectrum (Food Chemicals Codex, 1981). Pyrolysis gas chromatography may also be used to identify PVAc in various plastics, rubbers, and adhesives (IARC, 1979). PVAc may also be identified by liquid chromatography, ultraviolet-visible spectrophotometry, and by hydrolysis followed by potentiometric titration or gas chromatographic analysis of the acid. Colorimetry of the iodine complex of PVAc may also be used to identify the compound. The method of determination used depends on the form in which the PVAc is present (i.e., adhesive, paint, paper coating).

USE

Cosmetic

United States

PVAc is used in cosmetics as a binder, emulsion stabilizer, film former, and hair fixative (Wenninger and McEwen, 1992). The PVAc used in cosmetics is an emulsion containing 55 to 60% resin rather than the solid form of PVAc (Eiermann, personal communication)[2].

Data submitted to the Food and Drug Administration (FDA) indicate that PVAc is used in a total of seven eye makeup formulations (FDA, 1994). As reported to the FDA in 1989 and confirmed in 1994, PVAc is used in cosmetics at concentrations <25% (FDA, 1989; CTFA, 1994).

International

PVAc is listed in the Japanese Cosmetic Ingredient Dictionary, a compilation of cosmetic ingredients previously approved for products marketed in Japan (Rempe and Santucci, 1992).

Noncosmetic

PVAc has a variety of noncosmetic uses. In veterinary medicine, it is used as an adhesive film former in antibiotic aerosol sprays for teat treatments in cattle (Rossoff, 1974). It is also used as a diluent for inks used to mark gum, confections, and food supplements in tablet form (Furia, 1977), and as a base for chewing gums

[2]Available for review from: Director, Cosmetic Ingredient Review, 1101 17th Street NW, Suite 310, Washington, D.C. 20036, U.S.A.

(Food Chemicals Codex, 1981). PVAc is used as an adhesive for paper, wood, glass, metal, and porcelain (Hawley, 1971). It is also approved as an adjuvant for pesticide chemicals; as a substance in the manufacture of paper and paperboard products that come in contact with aqueous, fatty, and dry foods, and in resinous and polymeric coatings, in closures with sealing gaskets for foods, in cellophane, and in water-insoluble hydroxyethyl cellulose film (Food Chemical News Guide, 1988). Other noncosmetic uses of PVAc include sealants, latex paints, shatterproof photographic bulbs, bookbinding, and textile finishing; as a component of lacquers, inks, and plastic wood; and as a strengthening agent for cement (Hawley, 1971). PVAc may also be used as an intermediate for the conversion into polyvinyl alcohol and acetals (Hawley, 1971). PVAc is also used for binding bag seams, laminations, tube winding, remoistenable labels, and in smoothing plasterboard tape joints, in spackling paste, and in secondary furniture gluing (IARC, 1979). Mixtures containing 18 to 24% PVAc have been reported suitable for mouth protection during sports activities (Bishop et al., 1985). Mixtures of polyethylene glycols and PVAc may be used as tissue-embedding media, with the PVAc adding tensile strength and ease of handling of sections on water (Reid and Sarantakos, 1966). PVAc has also been used as a component of chemical protective clothing (Coletta, 1985).

GENERAL BIOLOGY

Effects on Blood

To assess blood compatibility of artificial materials, the blood of human donors was passed through columns containing various materials, including PVAc beads (Lindon et al., 1978). The PVAc was observed for signs of platelet retention and release of platelet constituents due to lysis. Platelet aggregation and adhesion to the PVAc resulted in retention of platelets in the test column. When various blood sample parameters of the donors were examined to assess the causes of donor-to-donor variability, it was reported that the amount of platelet retention by PVAc increased as the sedimentation rate increased. The use of birth control pills by female blood donors increased platelet retention by PVAc. PVAc did not adsorb serotonin from platelet-free plasma, and did not cause lysis of erythrocytes.

Absorption, Distribution, and Excretion

An aqueous emulsion of PVAc was administered to rabbits by the following routes: subcutaneous (s.c.) in 2 rabbits, intratracheally in 3 rabbits, and intravenously (i.v.) in 131 rabbits (Miyasaki, 1975). In the s.c. study, 2 rabbits were injected with 0.3 ml of 30% PVAc. The PVAc remained localized at the site of injection with little absorption. When 1 ml/kg of a 3% solution of PVAc was injected intratracheally in 3 rabbits every fourth day for a total of four injections, the PVAc was phagocytized by alveolar phagocytes. Six groups of rabbits received i.v. injections. The first group of 41 rabbits received 1 ml/kg injections of 5% PVAc daily for 1, 2, 4, 8, 12, 16, or 24 weeks; a second group of 60 rabbits received daily injections of 2 ml/kg of 5% PVAc for 3 days, or 1, 2, 3, 6, 12, or 24

weeks; a third group of 5 rabbits received daily injections of 3 ml/kg of 5% PVAc for 26 weeks; a fourth group of 2 rabbits received injections for 26 weeks as did the third group, followed by a 12-week nontreatment period; a fifth group of 18 rabbits received daily injections of 4 ml/kg of 5% PVAc for 1, 2, 4, or 6 weeks; and a sixth group of 5 pregnant rabbits each received a 5 ml/kg-injection of 5% PVAc.

A small amount of the i.v. injected PVAc was excreted in the urine; the remainder was retained in the body. The PVAc injected daily over a long period of time caused enlargement of the spleen, lymph nodes, and liver. The monocyte-macrophage system of the liver, spleen, bone marrow, lymph nodes, adrenal glands, and lungs phagocytosed the injected PVAc, forming foam cells. The cellular storage of PVAc remained unchanged 3 months after treatment. In the treated group of the pregnant rabbits, PVAc was not transferred to the fetus in appreciable amounts.

ANIMAL TOXICOLOGY

Acute Toxicity

PVAc, 25 g/kg as a single dose, was administered orally to rats and mice (strain unspecified) (IARC, 1979). Effects due to oral administration of PVAc included lymphoid infiltration of the liver, depigmented epithelial cells of the renal tubules, and a slight increase in the number of polynucleated cells in the spleen.

Short-term Toxicity

Extracts of a commercial hair spray containing polyvinyl pyrrolidine (PVP)/polyvinyl acetate (PVAc) were dissolved in isotonic saline and injected s.c. in the scapular area of adult mice, rats, and guinea pigs (Gebbers et al., 1979); polymer concentrates were not stated. PVP and PVAc alone in saline were also injected s.c. in the scapular area of mice, rats, and guinea pigs. Control animals received injections of saline. The animals were killed 4, 10, or 30 days after injection and the injection site was biopsied; samples from the liver, spleen, and kidneys were obtained for electron microscopic evaluation. A strong s.c. foreign body reaction with granulomas was seen in the animals injected with hair spray extracts and with PVP/PVAc 4 and 10 days postinjection. No reaction was noted at 30 days. The foreign body reaction consisted of many monocytes, large macrophages, multinucleated giant cells with periodic acid-Schiff (PAS)–positive inclusions, and many foam cells. Lamellar lysosomal inclusions were observed in the macrophages and giant cells. The Kupffer's cells of the liver and macrophages of the spleen contained PAS-positive cytoplasmic inclusions 4 weeks after injection of hair spray extract and PVP/PVAc.

Chronic Toxicity

When PVAc, 250 mg/kg, was administered orally for 12 months to rats and mice, fluctuations in weight, changes in blood composition, changes in liver-to-body weight ratios, and changes in cholinesterase and catalase activities were observed (IARC, 1979). No other details were given.

Dermal Irritation

A dose of 0.1 ml of a solution of 1.25% PVAc in ethanol saline was injected s.c. into the shaved posterior dorsal skin of 24 adult albino rats to determine the irritation potential of the PVAc (Carpenter et al., 1976). Twelve negative vehicle controls and 24 positive controls (carrageenan) were included in the study program. Two rats from the negative control group and four rats from the positive control group and four from the test group were killed on days 3, 7, 14, 21, 28, and 42. The injection sites were removed and preserved for microscopic examination. Tissue samples obtained from the test rats killed on day 3 had a moderate subacute inflammatory infiltrate of lymphocytes and plasma cells. Ulceration, accompanied by edema and tissue destruction, was frequently observed. Tissue samples from the rats killed on day 7 had retained PVAc surrounded by a severe inflammatory response. Ulceration, accompanied by abscesses and necrosis, was present in almost all the rats. In addition to lymphocytes and plasma cells, neutrophils were also present in abundance. The inflammatory response had reduced in severity by day 14, although many plasma cells and lymphocytes were still present. Many areas of granulation tissue were evident, as well as foci of necrosis with ulceration and an accompanying acute response. The tissue samples from the rats killed on day 21 had a moderate inflammatory response, with inflammatory cells and granulation tissue in abundance. By day 28, a minimal inflammatory response was evident, with cicatrization and early maturation of collagen fibrils. By day 42, inflammatory response was minimal, with the epithelium intact and cicatrization of the dermis. The PVAc response was similar to that of the positive control through day 14, at which time the PVAc response was much reduced compared to the positive control. PVAc was considered very irritating when injected s.c., with an initial response similar to that of the positive control except for granuloma formation, which did not occur in the PVAc-treated animals. The adverse irritation reactions to the i.v. injection of PVAc cited in this section are similar to that previously reported as a foreign body reaction by Gebbers et al. (1979) in their short-term toxicity i.v. studies of PVAc using mice, rats, and guinea pigs.

Reproduction and Developmental Toxicity

No studies have reported effects of PVAc on reproduction, teratology, or other developmental toxicity. However, data from pregnant rabbits (Miyasaki, 1975) indicate that PVAc was not transferred to the fetus in appreciable amounts, even when administered by the i.v. route, thus suggesting that no developmental effects could be produced by the usual dermal application of cosmetic ingredients.

GENOTOXICITY

PVAc was tested for mutagenic potential in the Ames test using *Salmonella typhimurium* strains TA92, TA1535, TA100, TA1537, TA94, and TA98, with metabolic activation (Ishidate et al., 1984). PVAc, 98.6% pure and dissolved in ace-

tone, at a maximum dose of 5.0 mg/plate, was not mutagenic under the conditions of the study.

PVAc was also tested for mutagenic potential in the chromosomal aberration test using a Chinese hamster fibroblast cell line (Ishidate et al., 1984). No metabolic activation system was used. The test cells were exposed to three concentrations of the test substance; the maximum concentration was 200 mg/ml. Polyploid cells, as well as cells with chromosomal structural aberrations, were recorded. A result was considered positive if >10% aberrations were found, equivocal if 5.0 to 9.9% aberrations were detected, and negative if there were <4.9% aberrations. The negative controls, consisting of untreated and solvent-treated cells, contained <3.0% aberrations. The maximum incidence of polyploid cells in the treated groups was 2.0%; no chromosomal aberrations were observed at 24 and 48 h. PVAc was negative for mutagenicity under the conditions of the study.

CARCINOGENICITY

In a single inhalation study, 96 rats were exposed 6 h/day, 5 days/week, to vinyl acetate at a concentration of 8,750 mg/m^3 for 1 year and observed until death. There was no evidence that vinyl acetate influenced the incidence of neoplasms (Maltoni, 1976).

Vinyl chloride-vinyl acetate (VC/VA) polymer was tested for strain response differences to s.c. implantation of the polymer in 18 strains of mice (Brand et al., 1977). There was a 90 to 100% incidence of neoplasms in female mice of the CBA/H, CBA/H-T6, BALB/cJ, BALB/cWAT, C57BL/10ScSn strains, in males of the AKR/J strain, and in both sexes of the (C57BL/10ScSnxCBA/H)F_1 strain mice. All other strains had intermediate responses, with incidence of neoplasms in males lower than that in females, with the exception of male AKR mice.

VC/VA powder, equivalent to two films 15 × 22 × 0.2 mm (as in the previous study), was injected s.c. in 30 male and 46 female 6-week-old CBA mice; the mice were observed until death (Brand et al., 1975). One female mouse developed a sarcoma possibly due to the clumping of the powder after administration. No other treatment-related neoplasms were observed. Clayson (1962) concluded that the induction of local sarcomas after the s.c. injection of a substance cannot be regarded as sufficient to state that the substance is a chemical carcinogen.

CLINICAL ASSESSMENT OF SAFETY

Irritation

The available results of occupational exposure to vinyl acetate have been well documented (NIOSH, 1978). Some minor skin and eye irritations to airborne vinyl acetate were noted.

An occlusive skin irritation test (CTFA, 1994) was conducted using 54 female volunteers and an aqueous PVAc solution (50% concentration). Approximately 0.05 ml was placed on a patch test plaster that was applied to the intact forearm area for 24 h. On removal of the plaster, the skin response was immediately scored

on a six-point scale: 0(−), no reaction; 1(+/−), faint or minimal erythema; 2(+), distinct erythema; 3(++), distinct erythema with infiltration, edema, or papules; 4(+++), edema or papules, with vesicles; and 5(++++), crust or necrosis. All 54 subjects had no reaction.

Sensitization

A repeat insult patch test (CTFA, 1994) was conducted using 159 volunteers (26 males and 133 females; aged 16–65 years). Aqueous PVAc emulsions at 50% concentration were used for induction and challenge. Induction was done using ~0.2 ml of the PVAc solution placed onto an occlusive patch and then applied to the back of each subject. Patches were left on for 24 h, removed for 24 h, and a new patch applied after examination of the induction site. This sequence was continued through nine applications and varied only by allowing 48 h between applications of the patch on weekends. Two weeks after the last patch was removed, a challenge patch was applied to a previously unexposed site. All challenge sites were evaluated at 24 and 72 h after application, and subjects were instructed to report any delayed skin reactivity occurring at a later time. Thirteen subjects discontinued the study for reasons unrelated to the conduct of the study. Of the 146 subjects completing the study, none had any skin irritation or allergic contact sensitization at any time.

SUMMARY

PVAc as used in cosmetic products is a latex emulsion known as the homopolymer of ethenyl acetate. It is used in cosmetics as a binder, emulsion stabilizer, and hair fixative at concentrations <25%. It is approved for use in cosmetic products in Japan and as a direct and indirect food additive in the United States.

In animal studies, injected PVAc was stored in the body. Enlargement of the lymph nodes, spleen, and liver was apparent. The irritation potential of a hair spray containing PVAc was evaluated by s.c. injection into adult rats. The test compound produced a severe inflammatory reaction. Although no studies have reported effects of PVAc on reproduction or developmental toxicity, other data indicate that PVAc was not transferred to the fetus in any appreciable amounts, even when administered by the i.v. route. This suggests that no developmental effects could be produced by the usual dermal application of cosmetic ingredients.

PVAc was nonmutagenic in the Ames assay, with and without activation, and in the Chinese hamster fibroblast cell assay. Several carcinogenic implantation studies using mice gave negative results. Inhalation studies of VC/VA using rats did not affect the tumor incidence.

No significant skin or eye irritation due to occupational exposure has been reported. PVAc at a concentration of 50% in a cosmetic product showed no irritation reaction in 54 female volunteers tested with occlusive patches and no irritation or allergic contact sensitization in 146 volunteers in a repeat insult patch test.

DISCUSSION

Available data do not completely identify all possible contaminants that may be found in PVAc. The concentrations of arsenic and heavy metals, however, is sufficiently low such that they present no safety concern. In clinical tests, 50% PVAc aqueous emulsions produced no reactions, suggesting that any unidentified impurities are both nonirritating and nonsensitizing. Neither mutagenicity nor carcinogenicity data suggest any biological activity of any concern for cosmetic use.

CONCLUSION

On the basis of the data presented in this report, the CIR Expert Panel concludes that PVAc is safe as a cosmetic ingredient in the present practice of use.

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SAFETY DATA SHEET

SECTION 1: CHEMICAL PRODUCT and COMPANY IDENTIFICATION

Product Name:	Polyvinyl acetate MW 90,000
Product Code:	P22020
Supplier:	Pfaltz & Bauer, Inc. 172 E. Aurora Street Waterbury, CT 06708 USA
Phone:	203-574-0075
FAX:	203-574-3181
Emergency Phone:	INFOTRAC, US: 1-800-535-5053 INFOTRAC, INTERNATIONAL: +1-352-323-3500

SECTION 2: HAZARDS IDENTIFICATION

Statement of Hazard:	Irritant, Respiratory irritant
Acute Health Hazard:	Irritant to eyes, skin, mucous membranes and respiratory system. May be harmful by ingestion, skin absorption and inhalation.
Chronic Health Hazard:	Not Available
HMIS Rating:	H: 1 F: 0 P: 0
NFPA Rating:	H: 1 F: 0 R: 0

To the best of our knowledge, the toxicological properties of this chemical have not been thoroughly investigated. Use appropriate procedures and precautions to prevent or minimize exposure.

GHS Classification in accordance with 29 CFR 1910 (OSHA HCS):

Acute toxicity, dermal (Category 4), H312
Acute toxicity, inhalation (Category 4), H332
Acute toxicity, oral (Category 4), H302
Serious eye damage/eye irritation (Category 2A), H319
Skin corrosion/irritation (Category 2), H315
Specific target organ toxicity, single exposure; Respiratory tract irritation (Category 3), H335

Pictogram:

Signal Word:	Warning
Hazard Statement(s):	H302 Harmful if swallowed. H312 Harmful in contact with skin. H315 Causes skin irritation. H319 Causes serious eye irritation. H332 Harmful if inhaled. H335 May cause respiratory irritation.
Precautionary Statement(s):	P261 Avoid breathing dust/fume/gas/mist/vapors/spray. P280 Wear protective gloves/protective clothing/eye protection/face protection. P301+P312 IF SWALLOWED: call a POISON CENTER or doctor/physician IF you feel unwell. P302+P352 IF ON SKIN: wash with plenty of soap and water. P304+P340 IF INHALED: Remove victim to fresh air and Keep at rest in a position comfortable for breathing. P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P332+P313 IF SKIN irritation occurs: Get medical advice/attention.

SECTION 3: COMPOSITION/INFORMATION on INGREDIENTS

Chemical Name:	Polyvinyl acetate MW 90,000
CAS Number:	9003-20-7
MDL Number:	MFCD00084457
EINECS Number:	Not Available
Beilstein Registry Number:	Not Available
Molecular Formula:	$[-CH_2CH(O_2CCH_3)-]n$
Molecular Weight:	90000
Content:	As specified in product name.

SECTION 4: FIRST AID MEASURES

Eye Contact:	Flush eyes with large amounts of water for fifteen minutes. Separate eyelids with fingers. If irritation persists, seek medical attention.
Skin Contact:	Wash skin with soap and water. If irritation persists, seek medical attention.
Ingestion:	Do not induce vomiting. Seek medical attention.
Inhalation:	Move to a fresh air environment. Contact a physician if breathing becomes difficult.

SECTION 5: FIRE FIGHTING MEASURES

Flash Point (ºC):	Not Available
Explosion Limits:	Not Available
Auto Ignition Temperature (ºC):	Not Available
Extinguishing Media:	Carbon dioxide, dry chemical powder, alcohol-resistant foam, or water spray
Protective Equipment:	Wear self-contained respirator and fully protective impervious suit.
Specific Hazards:	May emit hazardous fumes under fire conditions.

SECTION 6: ACCIDENTAL RELEASE MEASURES

Personal Protection:	Wear a self-contained breathing apparatus, rubber boots and gloves, and disposable coveralls. Dispose of coveralls after use. Remove from ignition sources if safe to do so. Follow emergency response plan and contact proper authorities if needed. Keep unprotected persons away.
Environmental Protection:	Keep spills out of sewers and bodies of water. Dike and contain the spill with inert material. Absorb on sand, vermiculite or diatomite. Transfer material to a container for disposal or recovery. Ventilate area and wash spill site after material pickup is complete.

SECTION 7: HANDLING and STORAGE

Handling and Storage:	Avoid breathing dust, vapor, mist or gas. Avoid contact with skin and eyes. Avoid prolonged or repeated exposure. Use only in a chemical fume hood. Open and handle container with care. Keep ignition sources away. Store in a tightly closed container in a dry, well-ventilated place.
Sensitivities:	Moisture
Storage Temperature (ºC):	15 to 30

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls: Use product in a well ventilated area or under a fume hood. Use proper lab equipment while handling this product. Keep away from incompatible materials for possible risk of hazardous reaction.

Eye Protection: Wear appropriate protective eyeglass or chemical safety goggles. Make sure that there is an eyewash station in your vicinity.

Skin Protection: Wear impervious gloves and protective clothing.

Respiratory Protection: Use a NIOSH approved respirator when exposure limits are exceeded or if irritation or other symptoms are experienced.

Exposure Limits:

Country	Source	Type	Value
USA	ACGIH	TWA	Not Available
USA	OSHA	STEL	Not Available
USA	OSHA	PEL	Not Available

SECTION 9: PHYSICAL and CHEMICAL PROPERTIES

Appearance: Beads

Odor: Not Available

Odor Threshold: Not Available

Flash Point (ºC): Not Available

Auto Ignition Temperature (ºC): Not Available

UEL % by Volume: Not Available

LEL % by Volume: Not Available

Melting Point (ºC): Not Available

Boiling Point (ºC): Not Available

Evaporation Rate: Not Available

pH Value: Not Available

Density (g/cm³): 1.18

Refractive Index (n^{20}_D):	1.462
Viscosity:	Not Available
Solubility in Water:	Not Available
Solubility in Other:	Soluble in Toluene, Acetone, Chloroform, Alcohol, THF
Vapor Pressure (mmHg):	Not Available
Vapor Density (Air=1):	Not Available

SECTION 10: STABILITY and REACTIVITY

Stability:	Stable under normal temperatures and pressures.
Incompatibility:	Not Available
Reactivity:	Product may react with incompatible materials to release other hazardous substances.
Conditions to Avoid:	Heat, flame, sparks, other ignition sources.
Hazardous Decomposition Products:	Carbon oxides

SECTION 11: TOXICOLOGICAL INFORMATION

RTECS Reference:	Not Available
Target Organs:	Not Available
Toxicity Data:	Not Available
Carcinogenicity:	National Toxicology Program (NTP) listed: Not Available International Agency for Research on Cancer (IARC) listed: Not Available
Potential Symptoms:	Not Available

SECTION 12: ECOLOGICAL INFORMATION

Toxicity:	Not Available

SECTION 13: DISPOSAL CONSIDERATIONS

Contact a licensed professional waste disposal service. Dispose in a manner consistent with federal, state and local environmental regulations.

SECTION 14: TRANSPORT INFORMATION

DOT Shipping Name: Not D.O.T.-Regulated

IMDG Shipping Name: Not Regulated

Marine Pollutant: No

IATA Shipping Name: Not Regulated

SECTION 15: REGULATORY INFORMATION

United States

Toxic Substance Control Act (TSCA) listed: Yes

Superfund Amendments and Reauthorization Act (SARA 302) listed: No

Superfund Amendments and Reauthorization Act (SARA 311/312) listed: No

Superfund Amendments and Reauthorization Act (SARA 313) listed: No

European Union

European Inventory of Existing Chemical Substances (EINECS): Not Available

Canada

Canadian Domestic Substances List (DSL) listed: Yes

Canadian Non-Domestic Substances List (NDSL) listed: No

SECTION 16: OTHER INFORMATION

Date Prepared: 3/9/2021

The information above is presented in good faith. It is believed to be accurate and represents the best information currently available to us. However, we make no warranty with respect to such information and we assume no liability resulting from its use. The user should consider this information as a supplement to other information that may be available and make independent judgement to ensure proper use to protect the health and safety of employees and the environment. Pfaltz and Bauer shall not be held liable for any damage resulting from handling or from contact with the above product.