Toxicological profile for

Ethylene-vinyl acetate copolymer

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

Ethene;ethenyl acetate (PubChem)

1.2. Synonyms

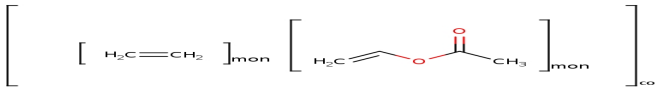
Acetic acid, ethenyl ester, polymer with ethene; Ethylene/VA copolymer; Ethylenevinylacetate copolymer; Ethylene vinyl acetate polymer; Vinyl acetate, ethene polymer; Vinyl acetate, ethylene polymer; Ethylene, polymer with vinyl acetate; Ethylene-vinyl acetate copolymer emulsion; UNII-3H390O24SI; UNII-4OKC630HS6; UNII-8ILA5X28VS; UNII-JK6142KK4O; UNII-L5F16ZG4ZU; UNII-V9BQI51YUL; Vinyl acetate-ethylene copolymer, minimum number average molecular weight (in amu), 69,000; Ethylene vinyl-acetate copolymer (ChemIDplus); Cevilen; Cevilene; Elvax; Elvax 40P; Elvax-40; EVA 260; Sevilene; poly(ethylene-co-vinyl acetate); polyethylene vinyl acetate (PubChem)

1.3. Molecular formula

(C4-H6-O2.C2-H4)x- (ChemIDplus)

1.4. Structural Formula

(ChemIDplus)



1.5. Molecular weight (g/mol)

(114.14)n. The copolymer has a weight averaged molecular weight (Mw) above 6,000 Da, a number averaged molecular weight (Mn) above 2,000 Da, and a molecular mass range of 200 – 10,000 Da (EFSA, 2014)

1.6. CAS registration number

24937-78-8

1.7. Properties

1.7.1. Melting point

(°C): No data available to us at this time.

1.7.2. Boiling point

(°C): No data available to us at this time.

1.7.3. Solubility

Negligible

1.7.4. pKa

No data available to us at this time.

1.7.5. Flashpoint

(°C): 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

(°C): No data available to us at this time.

1.7.8. Decomposition temperature

(°C): Starts decomposing at >230 (EFSA, 2014)

1.7.9. Stability

Stable/Hazardous polymerization will not occur.

1.7.10. Vapor pressure

No data available to us at this time.

1.7.11. log Kow

No data available to us at this time.

2. General information

2.1. Exposure

Migration of Irganox 1010 from ethylene-vinyl acetate films to foods and food-simulating liquids (Abstract). In a series of experiments on the migration of the antioxidant Irganox 1010 from ethylene-vinyl acetate (EVA) films into food-simulating liquids and foods, the antioxidant was found to migrate rapidly from EVA film into n-heptane, 100% ethanol and corn oil. The rate of migration into these media was greater from EVA than from low-density polyethylene (LDPE) under comparable conditions. In contrast, little migration of Irganox 1010 was recorded on exposure of the EVA film to aqueous media, whereas migration from LDPE into such media was relatively high.

As taken from Schwope AD et al. Food Chem Toxicol. 1987, Apr; 25(4):327-30. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/3583159

Ethylene/VA copolymer is used as a binding, emulsion stablising and film forming agent in cosmetics in the EU. As taken from CosIng, undated.

Ethyl vinyl acetate copolymer (CAS RN 24937-78-8) is included on the International Fragrance Association's list of ingredients reported as used in fragrance materials (IFRA).

“Used in orthotics, surfboard and skimboard traction pads, to make artificial flowers, to enhance grip in plastic wraps, improve cold flow of diesel fuel, in HEPA filters, and to make thermoplastic mouthguards and vaginal contraceptives; [REPROTOX] Used for plastic film, laminating, molding, and coating; [Westlake Polymers MSDS] Permitted for use as an inert ingredient in non-food pesticide products [EPA].”

“**Industrial processes with risk of exposure:** Plastic composites manufacturing.”

As taken from Haz-Map (2020), available at https://haz-map.com/

Ethylene/vinyl acetate co-polymer (CAS RN 24937-78-8) is listed as an ingredient (at given concentrations, where specified) in home maintenance (up to 100%), inside the home (10-30%) and personal care products by the CPID.

US Army Military exposure guidelines (MEGs) for Short-Term exposures to chemicals in ambient air:
1 hour Critical Air MEG 2.5E+02 mg/m^3
1 hour Marginal Air MEG 5.0E+01 mg/m^3
1 hr Negligible air MEG 3.0E+01 mg/m^3

As taken from US EPA ACToR database, 2015.

Ethylene/VA copolymer is used as a topical adhesive, binder, dispersing agent, and film former, and ethylene vinyl acetate as a delivery system in non-medicinal natural health products (both CAS RN 24937-78-8) (Health Canada, 2021).

2.2. Combustion products

Polymer degradation and stability

A Purser furnace has been used to investigate the combustion toxicity of ethylene-vinyl acetate copolymer (EVA) with and without fire retardants, under different fire conditions. Steady state flaming combustion has been studied at equivalence ratios Φ varying from 0.5 to 1.5 by driving the materials through the furnace at 750 °C. Yields of CO and CO2 for EVA containing 27% vinyl acetate, and its fire retarded composites, containing fire retardant fillers are presented. The materials contained 30% EVA and 70% hydrated aluminium oxide (ATH), or 65% ATH and 5% zinc hydroxystannate (ZS), or 5% magnesium borate (MgB) or 5% zinc borate (ZB). In each case the same mass of EVA was used in the determination. The yields of CO per g of polymer from the EVA-fire retardant composite samples showed very similar yields of CO under well ventilated conditions to the pure EVA, but generally higher CO yields than the base polymer under the most toxic fuel rich conditions. The exception to this was the sample containing ATH and zinc borate, which did not take up all the available oxygen under fuel rich conditions, and gave a much lower CO yield, corresponding to an eight-fold reduction in the combustion toxicity. Under fuel rich conditions for EVA, 60% of the carbon was lost as volatile organic species other than CO and CO2. For the sample containing zinc borate, this was 50% and for the remaining samples it varied from 20 to 38%. Evidence is presented which indicates that organic material trapped in the solid alumina

residue is oxidised to CO, except in the presence of zinc borate, when it appears to be lost as organic carbon.

As taken from HULL T. Richard et al. Polymer degradation and stability ISSN 0141-3910 CODEN PDSTDW . Congrès, European Conference on Fire Retardant Polymers N°8, Alessandria, ITALIE (06/2001) 2002, vol. 77, n°2 (169 p.) (11 ref.), pp. 235-242

2.3. Ingredient(s) from which it originates

No data available to us at this time.

3. Status in legislation and other official guidance

Ethylene-vinyl acetate appears in the latest synoptic list of monomers/additives for use in food-contact materials. The EU Scientific Committee on Food has not given an ADI figure but stated that polymers with a molecular weight above 1000 daltons are very unlikely to be absorbed from the gastrointestinal tract and thus considered not to present a toxicological risk [from use in food packaging] (Commission 2005).

Poly(ethylene-co-vinyl acetate) (CAS RN 24937-78-8) is included on the US FDA list of Indirect Additives used in Food Contact Substances and is covered under Title 21 of the US Code of Federal Regulations (21 CFR), sections 175.105 (Adhesives), 175.300 (Resinous and polymeric coatings), 176.180 (Components of paper and paperboard in contact with dry food), 177.1200 (Cellophane), 177.1210 (Closures with sealing gaskets for food containers), 177.1350 (Ethylene-vinyl acetate copolymers), 177.1390 (Laminate structures for use at temperatures of 250 °F and above), 178.1005 (Hydrogen peroxide solution) and 179.45 (Packaging materials for use during the irradiation of prepackaged foods).

As taken from FDA, 2022a, 2022b

Copolymer of ethylene and vinyl acetate is listed in the US EPA InertFinder Database (2021) as approved for food and non-food use pesticide products. For food use, it is regulated under Code of Federal Regulations Title 40, Protection of Environment; Part 180, Tolerances and exemptions for pesticide chemical residues in food; Section 180.960 - Polymers; exemptions from the requirement of a tolerance (US EPA, 2021).

“The CEF Panel concluded that the substance ethylene-vinyl acetate copolymer wax does not represent a safety concern for the consumer if the substance is only to be used as an additive up to 2% w/w in polyolefin materials and articles and the migration of low molecular weight oligomeric fraction below 1 000 Da does not exceed 5 mg/kg food.”

As taken from EFSA, 2014.

There is a NONS (Notification of New Substances) dossier on acetic acid, ethenyl ester, copolymer with ethene (F-94; CAS 24937-78-8; EC no. 429-840-1) but, to-date, industry have not submitted a REACH-compliant registration dossier for this chemical (ECHA, 2021).

Acetic acid ethenyl ester, polymer with ethene (poly(ethylene-co-vinyl acetate); CAS RN 24937-78-8; EC no. 607-457-0) is pre-registered under REACH (“envisaged registration deadline 30 November 2010”) (ECHA).

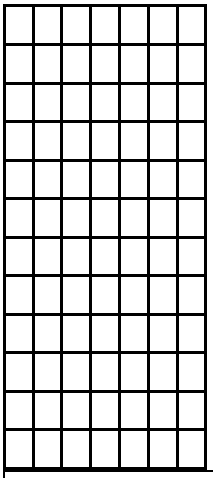
Poly(ethylene-co-vinyl acetate) (CAS RN 24937-78-8; EC no. 607-457-0) is not classified for packaging and labelling under Regulation (EC) No. 1272/2008 (ECHA, 2022).

Ethylene vinyl acetate polymer is listed in the US EPA Toxic Substances Control Act (TSCA) inventory and also in the US EPA 2020 CDR and 2020 CDR Full Exempt lists (Chemical Data Reporting Rule).

The TSCA inventory, and 2020 CDR and 2020 CDR Full Exempt lists are available at https://sor.epa.gov/sor_internet/registry/substreg/searchandretrieve/searchbylist/search.do

Acetic acid ethenyl ester, polymer with ethene (CAS RN 24937-78-8) is included on the New Zealand Inventory of Chemicals and does not have an individual approval but may be used under appropriate group standard (NZ EPA, 2006).

Ethylene-vinyl acetate copolymer (28 or 9% vinyl acetate) and ethylene-vinyl acetate copolymers are included on the US FDA's list of inactive ingredients for approved drug products. They are permitted for use as ingredients in various products, at the following maximum potencies per unit dose and maximum daily exposures:



ETHYLENE-VINYL ACETATE COPOLYMER (28% VINYL ACETATE)	SUBCUTANEOUS	IMPLANT	24937788	8ILA5X28VS
ETHYLENE-VINYL ACETATE COPOLYMER (28% VINYL ACETATE)	VAGINAL	INSERT	24937788	8ILA5X28VS
ETHYLENE-VINYL ACETATE COPOLYMER (28% VINYL ACETATE)	VAGINAL	RING	24937788	8ILA5X28VS
ETHYLENE-VINYL ACETATE COPOLYMER (9% VINYLACETATE)	VAGINAL	INSERT	24937788	4OKC630HS6
ETHYLENE-VINYL ACETATE COPOLYMER (9% VINYLACETATE)	VAGINAL	RING	24937788	4OKC630HS6
ETHYLENE-VINYL ACETATE COPOLYMERS	INTRAUTERINE	SUPPOSITORY, EXTENDED RELEASE	24937788	NA
ETHYLENE-VINYL ACETATE COPOLYMERS	OPHTHALMIC	INSERT, EXTENDED RELEASE	24937788	NA
ETHYLENE-VINYL ACETATE COPOLYMERS	OPHTHALMIC	SOLUTION	24937788	NA
ETHYLENE-VINYL ACETATE COPOLYMERS	SUBCUTANEOUS	IMPLANT	24937788	NA
ETHYLENE-VINYL ACETATE COPOLYMERS	TRANSDERMAL	FILM	24937788	NA
ETHYLENE-VINYL ACETATE COPOLYMERS	TRANSDERMAL	FILM, EXTENDED RELEASE	24937788	NA

As taken from FDA, 2022c

Acetic acid, ethenyl ester, copolymer with ethene (CAS RN 24937-78-8) is a “polymer identified as low concern to human health by application of expert validated rules” and “poses no unreasonable risk to human health based on Tier I assessment under the NICNAS IMAP assessment framework” (AICIS, 2012)

Acetic acid, ethenyl ester, copolymer with ethene (CAS RN 24937-78-8) 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

“In a 120-day oral toxicity study in rats no indication of accumulation was reported. The Panel concludes that no accumulation of ethylene-vinyl acetate copolymer wax in man is anticipated.”

As taken from EFSA, 2014.

4.3. Interactions

No data available to us at this time.

5. Toxicity

5.1. Single dose toxicity

No data available to us at this time.

5.2. Repeated dose toxicity

EVA was implanted subcutaneously in dogs for 1 year. A thin fibrous capsule consisting of fibrous cells with flat nuclei was formed around the substance, and fibroblasts were found sporadically in the internal layer of the capsule. No inflammatory reaction was found (Kojima 1975).

“An oral 120-day rat study on a polymeric additive with a vinyl acetate content of 12-13 % (w/w) and an ethylene content of 87-88 % (w/w) related to the ethylene vinyl acetate copolymer wax under evaluation (vinyl acetate content 6-15% and ethylene content 85-94 %) was performed in 1966. Data were reported on the following parameters: body weights, hematology, urinalysis, serum glutamate pyruvate transaminase levels, liver and kidney weights and histological examinations of 10 inner organs. No substance-related changes were observed in the above parameters in rats fed with a diet containing 50 000 or 100 000 mg/kg bw/day of the test substance compared to control rats (approx. 4 000 or 8 000 mg/kg bw/day), i.e. the NOAEL in this study was considered to be 8 000 mg/kg bw/day (the highest dose tested). Notwithstanding the limited end points of this study these data indicate that ethylene-vinyl acetate copolymer wax has a low sub-chronic toxicity. The

LMWF content of that polymeric additive is not known, but given the similarity between the types of polymer, the content is anticipated to be similar to the LMWF content in the ethylene vinyl acetate copolymer under evaluation (i.e. approximately 10%). Nevertheless considering, conservatively, a LMWF content of only 1% in the polymeric additive used in the 120-day study, for the LMWF of that additive an NOAEL of 80 mg/kg bw/d can be estimated, (assuming that the more heavy fraction is completely non-toxic). The Panel concluded that this NOAEL value would provide a sufficiently large margin of safety of approximately 1000 compared to the exposure to the LMWF from the ethylene vinyl acetate copolymer under evaluation at a maximum migration level of 5 mg/kg food, bearing in mind that uncertainty due to read-across should also be taken into account. This conclusion is in line with supportive data from subchronic studies on oxidised polyethylene waxes evaluated by EFSA (EFSA, 2009). These data included five 90-day rat studies each on different commercial products, with the lowest NOAEL of 500 mg/kg bw/day and a reproduction and developmental toxicity diet rat study (OECD 421) on a LMWF of oxidised polyethylene waxes with a NOAEL of 1 000 mg/kg bw/day or higher."

As taken from EFSA, 2014.

5.3. Reproduction toxicity

Development of a polymeric releasing device for 2'-carbomethoxyphenyl 4-guanidinobenzoate (a proteinase inhibitor): release rate, in vitro antifibrinolytic activity and in utero contraceptive effect (Abstract). A polymeric delivery system consisting of ethylene-vinyl acetate copolymer (EVAc) was developed for 2'-carbomethoxyphenyl 4-guanidinobenzoate (MSGB), a potent inhibitor of the sperm enzyme acrosin. The optimal device consists of copolymer with 40% vinyl acetate by weight (EVAc/40), 65% drug loading and MSGB with a particle size of 250-499 micron. This formulation yields a device that is highly flexible and can be shaped to many forms and sizes. Construction of the device does not alter the properties of MSGB. Well controlled release of MSGB from the device occurs in vitro and in the uteri of rats. The in vitro release rate under "infinite sink" conditions is essentially the same as the in vivo release rate. The contraceptive effect of the MSGB-releasing device was tested in rabbits by placing a blank (control) device in one uterine horn and an MSGB-releasing device in the contralateral horn. In contrast to blank devices, MSGB-releasing devices completely prevent pregnancy, not only by inhibiting fertilization but also by decreasing implantation. MSGB possesses high in vitro antifibrinolytic activity. These results indicate that a very flexible device can be constructed for uterine application which retains its contraceptive effect by release of MSGB. The antifibrinolytic activity of MSGB may further decrease the menorrhagia that can be associated with IUD use.

As taken from Burns JW et al . Contraception. 1988, Sep; 38(3):349-64. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/3168452?dopt=AbstractPlus

5.4. Mutagenicity

"The acetate groups in ethylene-vinyl acetate copolymer wax are expected to be hydrolysed by esterases, similarly to vinyl acetate, and this would leave an ethylene-vinyl alcohol copolymer chain. Neither the copolymer itself nor its hydrolysis product have structural alerts for genotoxicity. Overall, the Panel concluded that the ethylene-vinyl acetate copolymer wax does not raise concern for genotoxicity."

As taken from EFSA, 2014.

5.5. Cytotoxicity

No data available to us at this time.

5.6. Carcinogenicity

No data available to us at this time.

5.7. Irritation/immunotoxicity

EVA was implanted subcutaneously in dogs for 1 year. A thin fibrous capsule consisting of fibrous cells with flat nuclei was formed around the substance, and fibroblasts were found sporadically in the internal layer of the capsule. No inflammatory reaction was found (Kojima 1975).

Elvax 40P (EVX), an ethylene vinyl-acetate copolymer, has been well characterised as an implant material that causes no inflammatory response and is capable of the sustained local release of a wide variety of undenatured macromolecules in vivo (Silberstein & Daniel 1982).

The vaginal immune response following controlled, local administration of a model antigen, ferritin, was determined by using ferritin-releasing ethylene-vinyl acetate copolymer (poly(ethylene-co-vinyl acetate)) vaginal rings to provide long term continuous antigen exposure in mice primed with subcutaneous (SC) or oral ferritin. SC primed mice receiving ferritin-loaded vaginal rings had ferritin-specific IgA in their mucus secretions, while mice receiving blank rings did not. Oral priming with ferritin-loaded polylactic acid (poly(lactic acid)) microspheres also produced significant levels of ferritin-specific IgA in the vaginal secretions, but required the presence of cholera toxin. It was concluded that controlled ferritin delivery to mucosal surfaces, either by oral, biodegradable microspheres or vaginal rings, provided a convenient and reliable method for enhancing vaginal IgA production in mice.

As taken from Wyatt TL et al.Controlled Release; VOL 50 ISS Jan 2 1998, P93-102.

A new method for local delivery of anti-adhesion monoclonal antibodies (MAbs) to an exposed mucosal surface was developed using ethylene-vinyl acetate copolymer (poly(ethylene-co-vinyl acetate) controlled-release devices and their prophylactic potential was evaluated by examining leukocyte adhesion to apical surfaces of T84 cells in the presence of MAbs to leukocyte surface proteins. MAbs against the MAC-1 adhesion receptor inhibited neutrophil attachment to T84 cells by as much as 97%. MAbs against murine leukocyte receptors were produced from several hybridomas and incorporated into the devices. During incubation in sodium chloride (saline) buffer, small polymer discs continuously released active MAbs for 10 days. After insertion into vaginal canals of mice, these polymer disks produced high levels of anti-MAC-1 MAb for several days. It was concluded that MAbs against leukocyte adhesion molecules significantly inhibit the ability of leukocytes to interact with mucosal epithelia in vitro and that these same MAbs can be delivered directly to mucosal surfaces in an active form using polymeric controlled-release devices.

As taken from Parkhurst MR and Saltzman WM. J. Controlled Release; VOL 42 ISS Dec 1996, P273-288.

5.8. All other relevant types of toxicity

Release rates in rats of a macromolecule from an ethylene-vinyl acetate copolymer were shown to be indistinguishable from those of identical implants tested in vitro (Abstract). Ethylene is a low molecular weight hydrocarbon gas with few toxicological properties. In sufficient concentrations ethylene depletes the oxygen level of air and through this mechanism acts as an asphyxiant. No long term toxicological problems have been attributed directly to the gas. Ethylene does not have locally toxic effects (Doull et al 1980). Due to the paucity of information regarding ethylene-vinyl acetate copolymer, the remainder of the toxicological information presented concerns vinyl acetate.

As taken from Brown LR et al. J. Pharm. Sci.; VOL 72 ISS Oct 1983, P1181-1185.

Toxicology of polymers for implant contraceptives for women (Abstract). This article reviews the toxicology of polymers that are used in contraceptive implants. The two main classes of synthetic, nondegradable polymers used in the delivery of female contraceptives are silicone

elastomers (e.g., Silastic) and ethylene co-vinyl acetate (EVA; ELVAX). The controversies surrounding the silicone breast implants have prompted several studies to evaluate the toxicity of silicones. The epidemiologic data obtained thus far have overwhelmingly concluded that no correlation exists between certain chronic symptoms, such as arthritis, in patients and silicone prosthesis. This conclusion has been echoed by the expert panel report by the Institutes of Medicine. Although the IOM report focused on the safety of silicone breast prosthesis, data emerging from the joint reconstruction area also suggests that Silastic is safe for in vivo use. The toxicological studies on EVA are few, and the conclusion thus far is that they elicit no adverse local or systemic response over extended periods in vivo. In conclusion, the prognosis for Silastic and ELVAX as of now is excellent. However, any future implant development using these polymers should place an emphasis on processing parameters to minimize potential small molecule leachants and establish safety as a function of both site and duration of implantation.

As taken from Shastri PV. Contraception. 2002, Jan; 65(1):9-13. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/11861050?dopt=AbstractPlus

PGE2 and angiogenesis (Abstract). The angiogenic capability of PGE2 was tested by implanting pellets of an ethylene vinyl acetate slow release polymer containing PGE2 on the chorioallantoic membrane of 8-day-old chicken embryos. Elvax pellets releasing approximately 0.2, 2.0, or 20 ng/day PGE2 were found to induce neovascular responses. In contrast, pellets releasing 2.0 or 20 ng/day of either PGA2, PGF2, or TXB2 did not appear to be angiogenic when compared with PGE2. These release rates of PGE2 are similar to those reported for a variety of tumors, activated macrophages, inflammatory exudates, and rheumatoid synovia, suggesting that PGE2 may be a key factor in various neovascular reactions. As taken from DM; Auerbach R. Proc Soc Exp Biol Med. 1983, Feb; 172(2):214-8. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/6572402?dopt=AbstractPlus

Effect of PEG6000 on the in vitro and in vivo transdermal permeation of ondansetron hydrochloride from EVA1802 membranes (Abstract). The objective was to evaluate ethylene vinyl acetate (EVA) copolymer membranes with vinyl acetate content of 18% w/w (EVA1802) for transdermal delivery of ondansetron hydrochloride. The EVA1802 membranes containing selected concentrations (0, 5, 10 and 15% w/w) of PEG6000 were prepared, and subjected to in vitro permeation studies from a nerodilol-based drug reservoir. Flux of ondansetron from EVA1802 membranes without PEG6000 was 64.1 +/- 0.6 microg/cm(2.)h, and with 10%w/w of PEG6000 (EVA1802-PEG6000-10) it increased to 194.9 +/- 4.6 microg/cm(2.)h. However, with 15%w/w of PEG6000, EVA1802 membranes produced a burst release of drug which in turn decreased drug flux. The EVA1802-PEG6000-10 membrane was coated with an adhesive emulsion, applied to rat epidermis and subjected to in vitro permeation studies against controls. Flux of ondansetron from transdermal patch across rat epidermis was 111.7 +/- 1.3 microg/cm(2.)h, which is about 1.3 times the required flux. A TTS was fabricated using adhesive-coated EVA1802-PEG6000-10 membrane and other TTS components, and subjected to in vivo delivery in human volunteers against a control. It was concluded from the comparative pharmacokinetic study that TTS of ondansetron, prepared with EVA1802-PEG6000-10 membrane, provided average steady-state plasma concentration on par with multiple-dosed oral tablets, but with a low percent of peak-to-trough fluctuation.

As taken from Krishnaiah YS et al. Pharm Dev Technol. 2009; 14(1):50-61. PubMed, 2010 available at

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=18819031&dopt=AbstractPlus

In vivo biocompatibility of three potential intraperitoneal implants (abstract). The intraperitoneal biocompatibility of PDMS, polyHEMA and pEVA was investigated in rats, rabbits and

rhesus monkeys. No inflammation was evidenced by hematological analyses and measurement of inflammatory markers throughout the experiment and by post-mortem examination of the pelvic cavity. After 3 or 6 months, histological analysis revealed fibrous tissue encapsulating PDMS and PEVA implants in all species and polyHEMA implants in rabbits and monkeys. Calcium deposits were observed inside polyHEMA implants. The intraperitoneal biocompatibility of all 3 polymers makes them suitable for the design of drug delivery systems, which may be of great interest for pathologies confined to the pelvic cavity. As taken from Defrère et al. (2011). Macromol. Biosci. 11(10):1336-45. PubMed, 2012, available at http://www.ncbi.nlm.nih.gov/pubmed/21823236

6. Functional effects on

6.1. Broncho/pulmonary system

No data available to us at this time.

6.2. Cardiovascular system

Ethylene vinylacetate copolymer particles dissolved in polyvinyl alcohol (2,000-mer) solution as an embolic material for vascular anomalies. A preliminary study (Abstract).

We have prepared a new material for embolisation: ethylene vinylacetate copolymer dissolved in polyvinyl alcohol. When in contact with blood, polyvinyl alcohol rapidly becomes a soft gel, which is accompanied by wedging of the ethylene vinylacetate copolymer. We analysed the histopathology of intra-arterial microemboli in rats, after intracarotid injection of this material. We confirmed that it was applicable to embolisation for neurosurgical treatment.

As taken from Kinoshita A et al. Neuroradiology. 1994; 36(1):65-8. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/8108003?dopt=Abstract

Prevention of experimental cerebral vasospasm by intracranial delivery of a nitric oxide donor from a controlled-release polymer: toxicity and efficacy studies in rabbits and rats (Abstract).

BACKGROUND AND PURPOSE: A reduction in the local availability of nitric oxide (NO) may play a role in the etiology of chronic cerebral vasospasm after subarachnoid hemorrhage (SAH). We investigated the toxicity and efficacy of a locally delivered NO donor from a controlled-release polymer in preventing experimental cerebral vasospasm in rats and rabbits, respectively. METHODS: Diethylenetriamine/NO (DETA/NO) was incorporated into controlled release ethylene-vinyl acetate (EVAc) polymers. Twenty-eight rats were used in a dose-escalation toxicity study to establish a maximally tolerated dose of DETA/NO-EVAc polymer. In the efficacy experiment, 20 rabbits were assigned to 4 experimental groups (n=5 per group): sham operation; SAH only; SAH+empty EVAc polymer; and SAH+DETA/NO-EVAc polymer. Treatment was initiated 30 minutes after blood deposition. Basilar artery lumen patency was assessed 72 hours after hemorrhage to evaluate the efficacy of DETA/NO in preventing cerebral vasospasm. RESULTS: In the toxicity study, a dose of 3.4 mg/kg was identified as the LD(20) (dose with 20% mortality during the study period) of this DETA/NO formulation. Brain histology revealed hemorrhage and ischemic changes

at the implantation site associated with high concentrations of DETA/NO. In the efficacy study, treatment with DETA/NO-EVAc polymer resulted in a significant decrease in basilar artery vasospasm compared with no treatment (93.0+/-4.9% versus 71.4+/-11.9%; P=0.035) or compared with treatment with blank EVAc polymer (93.0+/-4.9% versus 73.2+/-6.4%; P=0.003). CONCLUSIONS: Local delivery of DETA/NO prevents vasospasm in the rabbit basilar artery. Local delivery of DETA/NO via polymers is a safe and effective strategy for preventing cerebral vasospasm after SAH in this model.

As taken from Gabikian P; Clatterbuck RE et al. 2002, Nov; 33(11):2681-6. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/12411661?dopt=AbstractPlus

6.3. Nervous system

No data available to us at this time.

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

No data available to us at this time.

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
In vitro genotoxicity	-	JTI Internal Report
In vitro cytotoxicity	-	JTI Internal Report

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 Ethylene Vinyl Acetate Coploymer at 1.886 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)).

When EVA was added to the wrappers of experimental flue-cured tobacco samples, increases in HCN and aldehydes were observed. There was no change in the level of acrolein or formaldehyde (Anon 1986).

9. Heated/vapor emissions toxicity

Aerosol from heated tobacco stick(s) containing Ethylene-Vinyl Acetate Copolymer 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	11.0	Labstat International Inc. (2020a) Labstat International Inc. (2021a)
In vitro genotoxicity	11.0	Labstat International Inc. (2020b) Labstat International Inc. (2021b)
In vitro cytotoxicity	11.0	Labstat International Inc. (2020b) 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, polymer with ethane (CAS RN 24937-78-8) is persistent in the environment.

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

WATER FATE

Evaluation of poly(ethylene-co-vinyl acetate-co-carbon monoxide) and polydimethylsiloxane for equilibrium sampling of polar organic contaminants in water (Abstract). The aim of the present study was to develop a passive absorptive equilibrium sampler that would enable the determination of the concentrations of polar organic compound (POC) in water more efficiently than existing techniques. To this end, a novel plastic material, poly(ethylene-co-vinyl acetate-co-carbon monoxide) (PEVAC), was evaluated and the results were compared with an existing silicone-based passive absorptive equilibrium device. Seven compounds (imidacloprid, carbendazim, metoprolol, atrazin, carbamazepine, diazinon, and chlorpyrifos), a mixture of pharmaceuticals, and pesticides with a logarithmic octanol-water partition coefficient ranging from 0.2 to 4.77 were selected as model substances for the experiments. The results showed that six of the seven selected POCs reached distribution equilibrium within 4 d in the two materials tested. A linear relation with a regression coefficient of more than 0.8906 between the established logarithmic absorbent-water partition coefficient and the calculated logarithmic dissociation partition coefficient of the selected compounds in the two polymers was observed. The correlation between these two coefficients was within one order of magnitude for the compounds that reached equilibrium in the two polymers, which demonstrates that both materials are suitable for mimicking biological uptake of POCs. The PEVAC material showed an enhanced sorption for all selected compounds compared to the silicone material and up to five times higher enrichment for the most polar compound. Fluorescence analysis of the sampler cross-section, following the uptake of fluoranthene, and proof that the sorption was independent of surface area variations demonstrated that the PEVAC polymer possessed absorptive rather than adsorptive enrichment of organic compounds.

As taken from Magnér JA et al. Environ Toxicol Chem. 2009, Sep; 28(9):1874-80. PubMed, 2010 available at http://www.ncbi.nlm.nih.gov/pubmed/19938334?dopt=AbstractPlus

10.2. Aquatic toxicity

The Ecological Categorization Results from the Canadian Domestic Substances List simply state that acetic acid ethenyl ester, polymer with ethane (CAS RN 24937-78-8) is not inherently toxic to aquatic organisms, giving a pivotal value for inherent toxicity of 14 mg/L.

Data accessed May 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, polymer with ethane (CAS RN 24937-78-8) is not bioaccumulative in the environment.

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

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12. Other information

No data available to us at this time.

13. Last audited

May 2022

European Food Safety Authority

EFSA Journal 2014;12(2):3555

SCIENTIFIC OPINION

Scientific Opinion on the safety assessment of the substance ethylene-vinyl acetate copolymer wax, CAS No 24937-78-8 for use in food contact materials[1]

EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

This scientific opinion of the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids deals with the safety assessment of the polymeric additive ethylene-vinyl acetate copolymer wax, CAS No 24937-78-8, FCM substance No 00969 for use as a dispersing agent, lubricant, pigment carrier, and/or a processing aid in the production of plastic materials made from polymers such as polyethylene (PE), polypropylene (PP) or polyethylene terephthalate (PET). Final articles are intended for repeated contact with all types of foodstuffs at any conditions of time and temperature. The copolymer has a weight-averaged molecular weight higher than 6 000 Da and the low molecular weight fraction (LMWF) below 1 000 Da was estimated to be below 10 % w/w The copolymer starts decomposing at temperatures above 230 °C, which is above the maximum process temperature of PE and PP but it is below the maximum process temperature of PET. The Panel considered that in the absence of information on possible thermal decomposition products, the use of the substance in PET should be excluded. The specific migration of the LMFW from polyolefins was conservatively estimated to be up to approximately 5.8 mg/kg food. There is no evidence of genotoxicity of ethylene-vinyl acetate copolymer wax. A 120 day oral toxicity study in rats showed no indication of accumulation. Therefore, the CEF Panel concluded that the substance ethylene-vinyl acetate copolymer wax does not raise a safety concern for the consumer if it is used as additive up to 2 % in polyolefins and the migration of low molecular weight oligomeric fraction below 1 000 Da does not exceed 5 mg/kg food.

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KEY WORDS

ethylene-vinyl acetate copolymer wax, CAS No 24937-78-8, FCM substance No 00969, food contact materials, safety assessment, evaluation

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[1] On request from the Bundesamt für Verbraucherschultz und Lebensmittelsicherheit, Germany, Question No EFSA-Q-2013-00282, adopted on 18 December 2013.

[2] Panel members: Ulla Beckman Sundh, Mona-Lise Binderup, Claudia Bolognesi, Leon Brimer, Laurence Castle, Alessandro Di Domenico, Karl-Heinz Engel, Roland Franz, Nathalie Gontard, Rainer Gürtler, Trine Husøy, Klaus-Dieter Jany, Martine Kolf-Clauw, Catherine Leclercq (until July 2013), Jean-Claude Lhuguenot (until November 2012), Wim Mennes, Maria Rosaria Milana, Iona Pratt, Kettil Svensson, Maria de Fátima Tavares Poças, Fidel Toldrá and Detlef Wölfle. One member of the Panel did not participate in the discussion on the subject referred to above because of potential conflicts of interest identified in accordance with the EFSA policy on declarations of interests. Correspondence: cef@efsa.europa.eu

[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Food contact materials: Mona-Lise Binderup, Laurence Castle, Riccardo Crebelli, Alessandro Di Domenico, Roland Franz, Nathalie Gontard, Ragna Hetland Bogen, Martine Kolf-Clauw, Eugenia Lampi, Maria Rosaria Milana, Maria de Fátima Tavares Poças, Philippe Saillard, Kettil Svensson and Detlef Wölfle for the preparatory work on this scientific opinion.

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SUMMARY

Within the general task of evaluating substances intended for use in materials in contact with food according to the Regulation (EC) No 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with foodstuffs, the CEF Panel received a request from the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, for safety assessment of the substance ethylene-vinyl acetate copolymer wax following a corresponding application from the applicant BASF SE, Germany.

The safety assessment of ethylene-vinyl acetate copolymer wax with CAS No 24937-78-8 and the FCM substance No 00969 was requested for use as additive in polymers such as polyethylene (PE), polypropylene (PP), or polyethylene terephthalate (PET) at a maximum use level of 2 % (w/w) in plastics. Final articles are intended for repeated contact with all types of foodstuffs at any condition of time and temperature.

The substance has not been evaluated by the SCF or AFC/CEF Panels. However, the comonomers, ethylene (85-94 %) with FCM substance No 00125 and vinyl acetate (6-15 %) with FCM substance No 00231, used to manufacture the copolymer are authorised as monomers for food contact materials with a specific migration limit (SML) of 12 mg/kg for vinyl acetate and no SML for ethylene.

The copolymer has a weight-averaged molecular weight higher than 6 000 Da and the low molecular weight fraction (LMWF) below 1 000 Da was estimated to be below 10 % w/w. The copolymer starts decomposing at temperatures above 230 °C, which is above the maximum process temperature of polyethylene and polypropylene but it is below the maximum process temperature of PET. The Panel considered that in the absence of information on possible thermal decomposition products, the use of the substance in PET should be excluded. Specific migration of the LMWF was estimated for extruded films of low density polyethylene (LDPE) containing copolymer wax (ethylene-vinyl acetate copolymer with a maximum content of 20 % of vinyl acetate). Tests were performed as time-dependent migration experiments using food simulants such as 95 % ethanol and olive oil. Migration of the LMWF from a worst-case polymer (i.e. LDPE) containing the highest intended concentration of the copolymer additive (i.e. 2%) was conservatively estimated to be up to approximately 5.8 mg/kg.

The substance is a polymeric additive without any structural alert for genotoxicity and it is manufactured using authorised monomers. In a 120-day oral toxicity study in rats no indication of accumulation was reported. The Panel concludes that no accumulation of ethylene-vinyl acetate copolymer wax in man is anticipated.

The CEF Panel concluded that the substance ethylene-vinyl acetate copolymer wax does not represent a safety concern for the consumer if the substance is only to be used as an additive up to 2 % w/w in polyolefin materials and articles and the migration of low molecular weight oligomeric fraction below 1 000 Da does not exceed 5 mg/kg food.

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BACKGROUND AS PROVIDED BY THE LEGISLATION

Before a substance is authorised to be used in food contact materials and is included in a positive list EFSA´s opinion on its safety is required. This procedure has been established in Articles 8 and 9 of the Regulation (EC) No 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food[4].

According to this procedure the industry submits applications to the Member States competent Authorities which in their turn transmit the applications to the EFSA for their evaluation. The application is supported by a technical dossier submitted by the industry following the SCF guidelines for the "presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation" (EC, 2001).

In this case, EFSA received an application from Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, requesting the evaluation of the additive ethylene-vinyl acetate copolymer wax with the CAS No 24937-78-8 and the FCM substance No 00969.

TERMS OF REFERENCE AS PROVIDED BY THE LEGISLATION

EFSA is required to carry out assessment on the risks originating from the migration into food of the additive ethylene-vinyl acetate copolymer wax, intended to be used as an additive in plastic materials (PE, PP and PET) for food contact articles and to deliver a scientific opinion according to Regulation (EC) No 1935/2004 the European Parliament and of the Council on materials and articles intended to come into contact with food.

[4] Commission Regulation (EC) No 1935/2004 of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC. OJ C 117, 30.4.2004, p. 1.

ASSESSMENT

1. Introduction

The European Food Safety Authority was asked by the Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Germany, to evaluate the safety of ethylene-vinyl acetate copolymer wax with CAS No 24937-78-8 and FCM substance No 00969. The request has been included in the EFSA's register of received questions under number EFSA-Q-2013-00282. The dossier was submitted by the applicant, BASF SE, Germany.

2. General information

According to the applicant, the substance ethylene-vinyl acetate copolymer wax is a polymeric additive intended to be used as a dispersing agent, lubricant, pigment carrier, and/or processing aid, in the production of plastic materials made from polymers such as polyethylene (PE), polypropylene (PP) or polyethylene terephthalate (PET). The additive is intended to be used up to a maximum level of 2 % w/w in plastics for the food contact article. Final articles are intended for repeated contact with all types of foodstuffs under any conditions of time and temperature.

The substance has not been evaluated previously by the SCF or the AFC/CEF Panels. However, the co-monomers, ethylene (85-94 %) with FCM substance number 00125 and vinyl acetate (6-15 %) with FCM substance number 00231, used to manufacture the copolymer are authorised as monomers for food contact materials[5] with a specific migration limit (SML) of 12 mg/kg food for vinyl acetate and no SML for ethylene.

3. Data available in the dossier used for this evaluation

The studies submitted for evaluation followed the SCF guidelines for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation (EC, 2001).

Non-toxicity data:

- Data on identity
- Data on physical and chemical properties
- Data on intended use and authorisation
- Data on migration of the substance
- Data on residual content of the substance
- Data on oligomers
- Data on identification, quantification and migration of a reaction product

Toxicity data:

- Bacterial gene mutation test on oxidised polyethylene waxes
- *In vitro* mammalian cell gene mutation test on oxidised polyethylene waxes
- *In vitro* mammalian chromosome aberration test on oxidised polyethylene waxes
- 120-day oral toxicity study in rats
- 90-day oral toxicity rat studies on oxidised polyethylene waxes

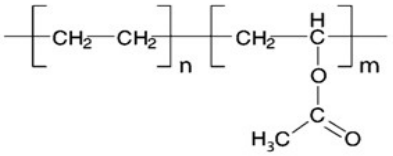
[5] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. Text with EEA relevance. OJ L 12, 15.1.20121, p. 1-89.

4. Evaluation

4.1. Non-toxicological data

Chemical formulae: $[C_2H_4]_n[C_4H_6O_2]_m$

Chemical structure:



The copolymer has a weight averaged molecular weight (Mw) above 6 000 Da, a number averaged molecular weight (Mn) above 2 000 Da, and a molecular mass range of 200 - 10 000 Da. The copolymer is insoluble in water and in *n*-octanol. The Log Po/w was not provided. The low molecular weight fraction below 1 000 Da (LMWF) is estimated to be below 10 % w/w in the copolymer, therefore below 0.2 % (2000 mg/kg) in final articles.

The purity is higher than 99.98 %. Residual ethylene and vinyl acetate monomers in the copolymer are estimated to be no more than 50 and 150 mg/kg respectively. Ethylene monomer residues are unlikely to be present in the final article due to the chemical's volatility and the high temperatures and degassing steps used in manufacturing of the copolymer. The amount of vinyl acetate potentially migrating into food was calculated to be at least two orders of magnitude below the SML of 12 mg/kg.

The copolymer starts decomposing at temperatures above 230 °C, which is above the maximum process temperature of polyethylene and polypropylene but below the maximum process temperature of PET. Therefore, thermal decomposition of the copolymer may occur during the manufacture of PET materials and articles containing the additive. The possible degradation products were not addressed by the applicant. The Panel considered that in the absence of information on possible thermal decomposition products, the use of the substance in PET should be excluded. Specific migration of the LMWF was estimated for extruded films of low density polyethylene (LDPE) containing the copolymer (maximum content of 20 % of vinyl acetate). Tests were performed as time-dependent migration experiments using food simulants such as 95 % ethanol and olive oil. By using analysis of the simulants by gas chromatography and by gel permeation chromatography, along with migration modelling calculations, migration of the LMWF from a worst-case polymer (i.e. LDPE) containing the highest intended concentration of the copolymer (i.e. 2 %) was conservatively estimated to be up to approximately 5.8 mg/kg. Approximately 90 % of the migrated amount consisted of oligomers with a molecular weight below 500 Da and the remaining 10 % was in the range of 500 to 1 000 Da.

4.2. Toxicological data

The substance is a polymeric additive manufactured using the monomers ethylene and vinyl acetate, evaluated by the SCF in 1999 (SCF, 1999) and authorised with no SML and with a SML of 12 mg/kg food, respectively.

Ethylene is considered non-genotoxic and of low toxicological potential (HSBD, 2006).

A risk characterization of vinyl acetate was performed in the context of Council Regulation (EEC) No 793/93[6] on the evaluation and control of existing substances (EU-RAR, 2008). According to the EU-RAR, vinyl acetate is rapidly hydrolysed by carboxylesterases to acetic acid and vinyl alcohol, which quickly rearranges to acetaldehyde. At high concentrations of vinyl acetate the detoxifying activity of

[6] Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances. OJ L 84, 5.4.1993, p. 1.

aldehyde dehydrogenases is overwhelmed, and non-physiological high intracellular concentrations of acetaldehyde are produced. Acetaldehyde is a metabolic intermediate with low background concentrations, with genotoxic and carcinogenic effects limited to non-physiologically high concentrations. Genotoxicity data on vinyl acetate are in line with the hypothesis that vinyl acetate genotoxicity is mediated by acetaldehyde: similarly to acetaldehyde, vinyl acetate is genotoxic *in vitro*, with a threshold nonlinear dose-response (Budinsky et al., 2013), and non-genotoxic *in vivo* when evaluated at non-lethal doses (Albertini, 2013). The EU-RAR concluded that genotoxicity of vinyl acetate is based on a threshold mode of action, and it is limited to toxic doses (EU-RAR, 2008).

Long-term inhalation or oral administration of vinyl acetate to experimental animals produced tumors at the primary site of exposure. According to the EU-RAR, carcinogenicity of vinyl acetate is based on a secondary mechanism, due to the intracellular accumulation of acetaldehyde at high concentrations of vinyl acetate which results in increased cell proliferation and possibly DNA damage. Thus vinyl acetate is considered a high dose, threshold carcinogen (EU-RAR, 2008).

The Panel agreed with the conclusions of the EU-RAR and considered the low amounts of vinyl acetate possibly migrating into food to be of no toxicological concern.

The acetate groups in ethylene-vinyl acetate copolymer wax are expected to be hydrolysed by esterases, similarly to vinyl acetate, and this would leave an ethylene-vinyl alcohol copolymer chain. Neither the copolymer itself nor its hydrolysis product have structural alerts for genotoxicity. Overall, the Panel concluded that the ethylene-vinyl acetate copolymer wax does not raise concern for genotoxicity.

An oral 120-day rat study on a polymeric additive with a vinyl acetate content of 12-13 % (w/w) and an ethylene content of 87-88 % (w/w) related to the ethylene vinyl acetate copolymer wax under evaluation (vinyl acetate content 6-15% and ethylene content 85-94 %) was performed in 1966. Data were reported on the following parameters: body weights, hematology, urinalysis, serum glutamate pyruvate transaminase levels, liver and kidney weights and histological examinations of 10 inner organs. No substance-related changes were observed in the above parameters in rats fed with a diet containing 50 000 or 100 000 mg/kg bw/day of the test substance compared to control rats (approx. 4 000 or 8 000 mg/kg bw/day), i.e. the NOAEL in this study was considered to be 8 000 mg/kg bw/day (the highest dose tested). Notwithstanding the limited end points of this study these data indicate that ethylene-vinyl acetate copolymer wax has a low sub-chronic toxicity. The LMWF content of that polymeric additive is not known, but given the similarity between the types of polymer, the content is anticipated to be similar to the LMWF content in the ethylene vinyl acetate copolymer under evaluation (i.e. approximately 10%). Nevertheless considering, conservatively, a LMWF content of only 1% in the polymeric additive used in the 120-day study, for the LMWF of that additive an NOAEL of 80 mg/kg bw/d can be estimated, (assuming that the more heavy fraction is completely non-toxic). The Panel concluded that this NOAEL value would provide a sufficiently large margin of safety of approximately 1000 compared to the exposure to the LMWF from the ethylene vinyl acetate copolymer under evaluation at a maximum migration level of 5 mg/kg food, bearing in mind that uncertainty due to read-across should also be taken into account. This conclusion is in line with supportive data from subchronic studies on oxidised polyethylene waxes evaluated by EFSA (EFSA, 2009). These data included five 90-day rat studies each on different commercial products, with the lowest NOAEL of 500 mg/kg bw/day and a reproduction and developmental toxicity diet rat study (OECD 421) on a LMWF of oxidised polyethylene waxes with a NOAEL of 1 000 mg/kg bw/day or higher.

In the absence of data on potential accumulation and taking account of the likely hydrolysis of the substance to an ethylene-vinyl alcohol copolymer chain, the Panel considered as supporting evidence results from the studies on oxidised polyethylene waxes, which have a very low solubility in water and octanol, similar to ethylene-vinyl acetate copolymer wax. The results of these studies do not indicate an accumulation potential of oxidised polyethylene waxes, i.e. no precipitation was observed in

sensitive tissues such as liver or lymph nodes (EFSA, 2009). Therefore, the Panel concluded that similarly no accumulation of ethylene-vinyl acetate copolymer wax in man is anticipated.

CONCLUSIONS

Having considered the above-mentioned data, the CEF Panel concluded that the substance ethylene-vinyl acetate copolymer wax does not raise a safety concern for the consumer if the substance is used as additive up to 2 % w/w in only polyolefin materials and articles and the migration of low molecular weight oligomeric fraction below 1 000 Da does not exceed 5 mg/kg food.

DOCUMENTATION PROVIDED TO EFSA

1. Ethylene Vinyl Acetate, Copolymer Wax/eg A-C, Luwax. February 2013. Submitted by BASF SE.

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GLOSSARY AND ABBREVIATIONS

AFC	Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
CAS	Chemical Abstracts Service
CEF	Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
Da	Dalton
EC	European Commission
EEC	European Economic Community
EFSA	European Food Safety Authority
EU	European Union
EU-RAR	European Union Risk Assessment Report
FCM	Food Contact Materials
LDPE	Low Density Polyethylene
LMWF	Low Molecular Weight Fraction
Mn	Averaged Molecular Weight
Mw	Molcular Wight
NOAEL	No Observed Adverse Effect Level
OECD	Organisation of Economic Co-operation and Development
SCF	Scientific Committee on Food
SML	Specific Migration Limit
PE	Polyethylene
PET	Polyethylene Terephthalate
Po/w	Octanol/Water partition coefficient
PP	Polypropylene

SAFETY DATA SHEET

according to Regulation (EC) No. 1907/2006

Version 6.4
Revision Date 07.09.2021
Print Date 01.12.2021
GENERIC EU MSDS - NO COUNTRY SPECIFIC DATA - NO OEL DATA

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifiers

Product name	:	Poly(ethylene-co-vinyl acetate)
Product Number	:	340502
Brand	:	Aldrich
REACH No.	:	A registration number is not available for this substance as the substance or its uses are exempted from registration, the annual tonnage does not require a registration or the registration is envisaged for a later registration deadline.
CAS-No.	:	24937-78-8

1.2 Relevant identified uses of the substance or mixture and uses advised against

Identified uses	:	Laboratory chemicals, Manufacture of substances

1.3 Details of the supplier of the safety data sheet

Company	:	Merck Life Science Sp.z.o.o. Szelągowska 30 PL-61-626 POZNAN
Telephone	:	+48 61 8290-100
Fax	:	+48 61 8290-120
E-mail address	:	TechnicalService@merckgroup.com

1.4 Emergency telephone

Emergency Phone #	:	+(48)-223988029 (CHEMTREC) 998 (Straz pozarna)

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Not a hazardous substance or mixture according to Regulation (EC) No 1272/2008.

2.2 Label elements

Not a hazardous substance or mixture.

2.3 Other hazards

This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

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SECTION 3: Composition/information on ingredients

3.1 Substances

Formula : C6H10O2
CAS-No. : 24937-78-8

No components need to be disclosed according to the applicable regulations.

SECTION 4: First aid measures

4.1 Description of first-aid measures

If inhaled
If breathed in, move person into fresh air. If not breathing, give artificial respiration.

In case of skin contact
Wash off with soap and plenty of water.

In case of eye contact
Flush eyes with water as a precaution.

If swallowed
Never give anything by mouth to an unconscious person. Rinse mouth with water.

4.2 Most important symptoms and effects, both acute and delayed

The most important known symptoms and effects are described in the labelling (see section 2.2) and/or in section 11

4.3 Indication of any immediate medical attention and special treatment needed

No data available

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media
Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.

5.2 Special hazards arising from the substance or mixture

Carbon oxides

5.3 Advice for firefighters

Wear self-contained breathing apparatus for firefighting if necessary.

5.4 Further information

No data available

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Avoid dust formation. Avoid breathing vapors, mist or gas.
For personal protection see section 8.

6.2 Environmental precautions

No special environmental precautions required.

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6.3 Methods and materials for containment and cleaning up
Sweep up and shovel. Keep in suitable, closed containers for disposal.

6.4 Reference to other sections
For disposal see section 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling

Advice on protection against fire and explosion
Provide appropriate exhaust ventilation at places where dust is formed.

Hygiene measures
General industrial hygiene practice.
For precautions see section 2.2.

7.2 Conditions for safe storage, including any incompatibilities

Storage conditions
Store in cool place. Keep container tightly closed in a dry and well-ventilated place.

Storage class
Storage class (TRGS 510): 13: Non Combustible Solids

7.3 Specific end use(s)
Apart from the uses mentioned in section 1.2 no other specific uses are stipulated

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Ingredients with workplace control parameters

8.2 Exposure controls

Personal protective equipment

Eye/face protection
Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN 166(EU).

Skin protection
Handle with gloves. Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good laboratory practices. Wash and dry hands.

The selected protective gloves have to satisfy the specifications of Regulation (EU) 2016/425 and the standard EN 374 derived from it.

Body Protection
Choose body protection in relation to its type, to the concentration and amount of dangerous substances, and to the specific work-place., The type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

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Respiratory protection
Respiratory protection is not required. Where protection from nuisance levels of dusts are desired, use type N95 (US) or type P1 (EN 143) dust masks. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU).

Control of environmental exposure
No special environmental precautions required.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

a)	Appearance	Form: Beads
b)	Odor	No data available
c)	Odor Threshold	No data available
d)	pH	No data available
e)	Melting point/freezing point	75 °C
f)	Initial boiling point and boiling range	No data available
g)	Flash point	No data available
h)	Evaporation rate	No data available
i)	Flammability (solid, gas)	No data available
j)	Upper/lower flammability or explosive limits	No data available
k)	Vapor pressure	No data available
l)	Vapor density	No data available
m)	Density	0,941 g/cm3
	Relative density	No data available
n)	Water solubility	No data available
o)	Partition coefficient: n-octanol/water	No data available
p)	Autoignition temperature	340 °C
q)	Decomposition temperature	No data available
r)	Viscosity	Viscosity, kinematic: No data available Viscosity, dynamic: No data available
s)	Explosive properties	No data available
t)	Oxidizing properties	No data available

9.2 Other safety information
No data available

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SECTION 10: Stability and reactivity

10.1 Reactivity
No data available

10.2 Chemical stability
Stable under recommended storage conditions.

10.3 Possibility of hazardous reactions
No data available

10.4 Conditions to avoid
No data available

10.5 Incompatible materials
Strong oxidizing agents, Strong acids

10.6 Hazardous decomposition products
In the event of fire: see section 5

SECTION 11: Toxicological information

11.1 Information on toxicological effects

Acute toxicity
Oral: No data available
Inhalation: No data available
Dermal: No data available

Skin corrosion/irritation
No data available

Serious eye damage/eye irritation
No data available

Respiratory or skin sensitization
No data available

Germ cell mutagenicity
No data available

Carcinogenicity
No data available

Reproductive toxicity
No data available

Specific target organ toxicity - single exposure
No data available

Specific target organ toxicity - repeated exposure
No data available

Aspiration hazard
No data available

11.2 Additional Information

To the best of our knowledge, the chemical, physical, and toxicological properties have not been thoroughly investigated.

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SECTION 12: Ecological information

12.1 Toxicity
No data available

12.2 Persistence and degradability
No data available

12.3 Bioaccumulative potential
No data available

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment
This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product
Offer surplus and non-recyclable solutions to a licensed disposal company.

Contaminated packaging
Dispose of as unused product.

SECTION 14: Transport information

14.1 UN number

ADR/RID: -	IMDG: -	IATA: -

14.2 UN proper shipping name

ADR/RID:	Not dangerous goods
IMDG:	Not dangerous goods
IATA:	Not dangerous goods

14.3 Transport hazard class(es)

ADR/RID: -	IMDG: -	IATA: -

14.4 Packaging group

ADR/RID: -	IMDG: -	IATA: -

14.5 Environmental hazards

ADR/RID: no	IMDG Marine pollutant: no	IATA: no

14.6 Special precautions for user

Further information
Not classified as dangerous in the meaning of transport regulations.

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SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

This material safety data sheet complies with the requirements of Regulation (EC) No. 1907/2006.

15.2 Chemical Safety Assessment

For this product a chemical safety assessment was not carried out

SECTION 16: Other information

Further information

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