POLYVINYL ALCOHOL

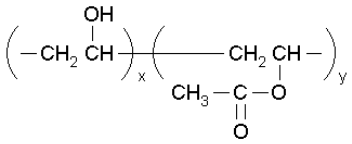
SYNONYMS

Ethanol homopolymer, Alcotex 17F-H, Alcotex 88/05, Alcotex 88/10, Alcotex 99/10, Alkotex, Alvyl, Aracet APV, CCRIS 8526, Cipoviol W 72, Covol, Covol 971, EP 160, Elvanol, Elvanol 50-42, Elvanol 51-05G, Elvanol 5105, Elvanol 52-22, Elvanol 52-22G, Elvanol 522-22, Elvanol 70-05, Elvanol 71-30, Elvanol 73125G, Elvanol 90-50, Elvanol T 25, Enbra OV, Ethenol, homopolymer, FH 1500, GH 20, GL 02, GL 03, GLO 5, GM 14, Galvatol 1-60, Gelvatol, Gelvatol 1-30, Gelvatol 1-60, Gelvatol 1-90, Gelvatol 20-30, Gelvatol 2060, Gelvatol 2090, Gelvatol 3-91, Gohsenol, Gohsenol AH 22, Gohsenol GH, Gohsenol GH 17, Gohsenol GH 20, Gohsenol GH 23, Gohsenol GL 03, Gohsenol GL 05, Gohsenol GL 08, Gohsenol GM 14, Gohsenol GM 14L, Gohsenol GM 94, Gohsenol KH 17, Gohsenol MG 14, Gohsenol N 300, Gohsenol NH 05, Gohsenol NH 17, Gohsenol NH 18, Gohsenol NH 20, Gohsenol NH 26, Gohsenol NK 114, Gohsenol NL 05, Gohsenol NM 114, Gohsenol NM 14, Gosenol KH-17, Gtohsenol GL 05, HSDB 1038, Kuralon VP, Kurare 217, Kurare PVA 205, Kurare Poval 120, Kurare poval 1700, Kurate poval 120, Lamephil OJ, Lamicel, Lemol, Lemol 12-88, Lemol 16-98, Lemol 24-98, Lemol 30-98, Lemol 5-88, Lemol 5-98, Lemol 51-98, Lemol 60-98, Lemol 75-98, Lemol GF-60, Liquifilm Forte, Liquifilm Tears, M 13/20, Mowiol, Mowiol 26-88, Mowiol 4-88, Mowiol N 30-88, Mowiol N 50-98, Mowiol N 50/88, Mowiol N 70-98, NH 18, NM 11, NM 14, NSC 108129, PVA, PVA (VAN), PVA 008, PVAL 45/02, PVAL 55/12, PVS 4, Partially hydrolysed polyvinyl alcohol, Poly(1-hydroxyethylene), Polydesis, Polyethenol, Polysizer 173, Polyvinol, Polyvinyl alcohol, Polyvinyl alcohol 18/11, Polyviol, Polyviol M 13/140, Polyviol MO 5/140, Polyviol W 25/140, Polyviol W 28/20, Polyviol W 40/140, Poval, Poval 117, Poval 120, Poval 1700, Poval 203, Poval 205, Poval 205S, Poval 217, Poval 217S, Poval 420, Poval C 17, Resistoflex, Rhodoviol, Rhodoviol 16/200, Rhodoviol 4-125P, Rhodoviol 4/125, Rhodoviol R 16/20, Sloviol R, Solvar, Sumitex H 10, UNII-532B59J990, Vibatex S, Vinacol DT, Vinacol MH, Vinalak, Vinarol, Vinarol DT, Vinarol ST, Vinarole, Vinavilol 2-98, Vinyl alcohol polymer.

CHEMICAL FORMULA

C_2H_4O

CHEMICAL STRUCTURE



IDENTIFIER DETAILS

CAS Number	:	9002-89-5
CoE Number	:	-
FEMA	:	-
EINECS Number	:	209-183-3
E Number	:	-

CLP CLASSIFICATION

Ingredient CLP Classification: No

Endpoint	Classification	Category
Acute Oral Toxicity	-	-
Acute Dermal Toxicity	-	-
Acute Inhalation Toxicity	-	-
Skin Corrosive/irritant	-	-
Eye Damage/Irritation	-	-
Respiratory Sensitisation	-	-
Skin Sensitisation	-	-
Mutagenicity/Genotoxicity	-	-
Carcinogenicity	-	-
Reproductive Toxicity	-	-
Specific Target Organ Toxicity	-	-
Aspiration Toxicity	-	-

SPECIFICATIONS

Melting Point: 228°C
Boiling point: -

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
50mg/kg bw	JECFA	2004	-

FDA Status:

Section Number	Comments
177.1670	Polyvinyl Film
177.1200	Cellophane
175.105	Adhesives
a)175.300 & b) 175.320	a) Resinous and polymeric coatings, b) Resinous and polymeric coatings for polyolefin films.
a)176.170 & b) 176.180	a) Components of paper and paperboard in contact with a) aqueous and fatty foods, b) dry food

HUMAN EXPOSURE

Reported Uses: Polyvinyl alcohol (PVA) is used in cosmetics as a binder, film former, and viscosity-increasing agent. It is used at various concentrations up to 25% of the formulation in 1994 according to the FDA [concentrations are no longer reported. PVA is also used by the plastic industry for various applications and in pharmaceutical products as a viscosity increasing agent as well as a lubricant in ophthalmic solutions. It is also used for several clinical applications and has been investigated as a potential carrier molecule for internal tumour investigations [Nair, 1998].

TOXICITY DATA

In Vivo Toxicity Status

The critical evaluation of PVAs reported that PVA was of low oral toxicity, poorly absorbed by the gastro-intestinal tract, did not accumulate in the body after oral administration, was not mutagenic or clastogenic and had a reported NOAEL of 5000 mg/kg bw/day in a 90-day dietary study and in a two-generation reproduction study (which was the highest dose tested). The authors concluded that 'the existing information on PVA supports its safe use as a coating agent for pharmaceutical and dietary supplement products' [DeMerlis *et al*., 2003].

Species	Test Type	Route	Reported Dosage
Rat	LD_{50}	Oral	>21.5g/kg
Mouse	LD_{50}	Oral	>10g/kg
Dog	LD_{50}	Oral	>20g/kg

[Nair, 1998]

Species	Test Type	Route	Reported Dosage	Effect
Guinea Pig	LD_{50}	Oral	18750mg/kg	BEHAVIORAL: Muscle weakness GASTROINTESTINAL: "Hypermotility, diarrhea" LIVER: Other changes
Mouse	LD_{50}	Oral	14270mg/kg	BEHAVIORAL: Muscle weakness GASTROINTESTINAL: "Hypermotility, diarrhea" LIVER: Other changes
Mouse	LD_{50}	Oral	14700mg/kg	BEHAVIORAL: Altered sleep time (including change in righting reflex) BEHAVIORAL: Somnolence (general depressed activity) BEHAVIORAL: Muscle weakness
Rat	LD_{50}	Oral	>20,000mg/kg	BEHAVIORAL: Altered sleep time (including change in righting reflex) BEHAVIORAL: Somnolence (general depressed activity) BEHAVIORAL: Muscle weakness
Rat	LD_{50}	Oral	23,854mg/kg	BEHAVIORAL: Muscle weakness GASTROINTESTINAL:

				"Hypermotility, diarrhea" LIVER: Other changes

[ToxNet, 2010]

Three male rabbits received 10-25 injections of 5% PVA solution through the marginal vein of the external ear over a five-day period. The only difference was that the most severe and extensive lesions were found in the lungs, spleen and testes (the subcutaneous route did not produce lesions in the lung, but did in the liver and kidney) [Nair, 1998].

When injected into the anterior chamber of one globe in each of 12 rabbits, PVA did not produce any significant changes compared with controls. Intraocular pressure measurement, slit-lamp examinations and whole-eye examinations were all carried out regularly for 6 months [Nair, 1998].

In an experiment investigating absorption, six adult Charles River albino rats were dosed by intubation 100 mg/day PVA for 7 days. This acclimation period was followed by administration of radioactive PVA [same dose] in a 5% solution. Half the group received this every day for 5 days and the other half for 10 days. Urine and feces were examined daily for radioactivity and at the end of the experiment the animals were sacrificed and the liver, brain, kidneys, and samples of body fat were examined. The experiment was repeated using 4 mongrel dogs with the only other difference being the use of a higher dose of 2g PVA. There was no sign of overt toxicity and weight gain was normal. No treatment related lesions were noted at necropsy. No radioactivity was detected in the urine although some was noted in the feces. Absorption was dependent upon molecular weight of polyvinyl alcohol and ranged between 0.6-1.29 ppm in the brain, 0.52-1.35 ppm in the kidneys and 1.21-6.91 ppm in the liver [Nair, 1998].

A standard textbook states that high toxicity is dependent upon water solubility rather than molecular weight [Gosselin, 1976].

In a short-term parenteral toxicity study, 12 albino rats were administered 20 injections over four weeks, containing a 5% PVA solution. Six animals were sacrificed at the end of dosing and the remainder 2 weeks later (one died during dosing). Pathologic alterations were more severe in the animals killed 2 weeks after dosing. A ‘substantial amount’ of PVA was found at the site if injection which produced necrosis and granulomatous inflammatory tissue. Little PVA was found in the lymph nodes, but it was found concentrated in the kidneys. It was also found in the lumen of blood vessels of several organs. The authors note that vascular occlusion occurred in the lungs of some of the rats and these capillaries had swollen endothelial cells. The spleens were moderately enlarged, dark red in colour and firm. In all of the rats, an isolated number of Kupffer cells in the liver were swollen. Other organs examined (no exact details given) were considered to be grossly normal but contained small groups of foam cells. Occasionally, swollen macrophages and multinucleated giant cells were noted (no discussion of these results is given) [Nair, 1998].

Three of four Beagle dogs (one untreated control) were administered (daily) 20 ml polyvinyl alcohol solution (47 mg in solution) via silastic cannula in the right external jugular vein. After one week, a decrease in packed cell volume (in blood) was noted. This decrease continued to the end of the study when it was 64% of the initial value. There was no change in body weight, feed consumption, gastrointestinal function or blood urea nitrogen. The study was terminated at week 3 following the onset of dose-related central nervous system depression (CNS). This was indicated by bilateral depression of the extensor postural thrust, hopping, front limb placing and rear limb reflexes. Serum protein, potassium, sodium, and phosphorous levels were all reduced. Hematologic assays found monocytosis, immature neutrophilia, polymorphonuclear leukocyte toxicity, decreased hemoglobin, and a reduced erythrocyte count. Slight anisocytosis and many large platelets were also observed. No gross lesions were found but foam cells were identified in glomeruli. Although no significant renal damage occurred, the authors infer that this would have been observed if the duration of the experiment had not been cut short by the adverse CNS effects [Nair, 1998].

In a study investigating hypertension, groups of Sprague-Dawley rats received 1ml of 5% PVA solution either by subcutaneous or intraperitoneal injection for 28 days (presumably one dose per day). Twenty-eight days after the final dose, half the animals were dosed with 0.1 mg *d*-aldosterone-21 acetate in sesame oil for the next 7 days (presumably once per day). Over the duration of the experiment 7 animals died, one of which had developed severe peripheral edema and ascites. All other animals were sacrificed, organs and tissues were microscopically examined. At necropsy, the liver, kidneys, spleen and heart of polyvinyl alcohol treated animals weighed significantly higher than those of control animals and the kidney & hearts of intraperitoneally treated animals were higher still. Adrenal glands were significantly smaller in polyvinyl alcohol treated animals. Histopathological changes included dilated hepatic sinusoids, multinucleate giant cells in the liver (only in *i.p.* treated animals) and deposits of polyvinyl alcohol in the spleen and kidneys as well as intense macrophage and giant-cell proliferation (greater in *i.p.* treated animals). Arterial changes around the above organs were noted and consisted of hypertrophy, inflammation, and necrosis. About half of the rats treated with PVA also demonstrated polyarteritis nodosa of the pancreas. Foam cells were also noted in the hearts of *i.p.* treated animals. None of the lesions could be specifically attributed to aldosterone treatment [Nair, 1998].

In a short study investigating polymerisation, groups of 12 Hiltzman rats received daily subcutaneous injections of 1 ml of 5% PVA (various molecular weights), in physiological saline, for 29 days. They also had access (*ad libitum*) to drinking water containing 1 % sodium chloride. Following sacrifice, some accumulation was noted in various organs, the extent of which was dependent upon the molecular weight of the polyvinyl alcohol the group had been exposed too. Hypertension (denoted as systolic pressure greater than 150 mmHg) was also dependent upon molecular weight [increase molecular weight = increase hypertension]. The heart, kidneys, liver and spleen sizes were also enlarged with the same correlation as above. Of the three molecular sizes investigated, the medium size polyvinyl alcohol (133,000) was the only

one to produce polydipsia. In this case, marked renal damage was noted as well as widespread cardiovascular lesions. The authors point out that this group consumed on average, more of the salt solution than the other groups of rats. It was concluded that the size of the molecule was responsible for the toxic effects and lesion development, and not the chemical structure of PVA [Nair, 1998].

Intravaginal exposure to polyvinyl alcohol in $B6C3F_1$ mice, or New Zealand white rabbits, produced little more than irritation and enlargement of uterine horns [mice only] at dose levels of 25 % w/w, over a 30-day period (mice only, limited details given regarding rabbit dose) [Nair, 1998].

Kelly *et al*., (2003) reported a study in which the potential systemic and neurotoxicity of PVA was assessed when administered to Sprague-Dawley rats in the diet for a period of 90-days at 2000, 3500 and 5000 mg/kg/day (clinical observations, ophthalmology, body weight, food consumption, haematology, coagulation, clinical chemistry, urinalysis, motor activity and functional observational evaluation in addition to gross and microscopic pathology indicated that the no-observed-adverse-effect level (NOAEL) was 5000 mg/kg/day. PVA was also shown to be non-mutagenic in the Ames and lymphoma assay, as well as the mouse micronucleus test [Kelly *et al*., 2003].

PVA has been used as a scientific tool to produce various animal models of kidney and liver conditions. For example, subchronic intraportal injections of 4.8g PVA (large molecular weight) into mongrel dogs produced hepatic cirrhosis within 6 months. Smaller dose (0.8g) were still able to produce the same condition but 22 months of dosing was required [Nair, 1998].

Carcinogenicity and Mutagenicity

In a 2 year study, $B6C3F_1$ mice gave no evidence of carcinogenic activity of polyvinyl alcohol following intravaginal administration of 25% PVA in deionized water, according to an NTP report [NTP, 1996].

In a micronucleus test, groups of six $SLC\text{-}BDF_1$ mice received intraperitoneal injections of 156, 311, or 622 mg/kg of PVA mixed with polyoxethylenenonylether or PVA alone (only at 622 mg/kg). Following sacrifice 24 hours post dosing, a slight increase in micronuclei of the bone marrow was noted in the high mixed dose group. All other doses, including the high dose of polyvinyl alcohol alone, did not significantly induce micronuclei in the bone marrow, of the any of the test animals. The authors concluded that the mixture was non-mutagenic (the authors were concerned with the mixture, and not with PVA itself). The authors state that PVA is capable of acting as a spindle poison (no details are given to substantiate this claim) [Nair, 1998].

IARC have cited several studies whereby some test animals (mainly rats) developed tumours as a result of subcutaneous implants of PVA sponges. Tumours developed at site of implantation. However, IARC also make reference to animal data whereby PVA powder in rats did not result in local

sarcomas. They concluded that human & animal data was insufficient and require further studies to be carried out in order to classify its carcinogenic potential (categorised in Group 3) [Nair, 1998; IARC, 1996 and 1999].

In a study investigating the cancer inhibitory effect of a copper complex, PVA was used as both a vehicle and one control, the other control substance being saline. Groups of 20 female SJL/J mice (highly susceptible to type B reticulum cell sarcoma (RCS)) received weekly/biweekly subcutaneous injections of 0.1 ml of a copper complex in polyvinyl alcohol (1.4%), or 0.1 ml of one of the control substances [group of 10 mice for polyvinyl alcohol]. Dosing continued for 6 or 12 weeks. The group receiving PVA alone had the same incidence of RCS as the saline controls [Nair, 1998].

Dermal Toxicity

In a dermal irritation test with groups of Kb1: JW rabbits, 0.3 ml of 10% polyvinyl alcohol was applied to the clipped back for 24 hours. Immediately after patch removal, the Primary Irritation Index (PII) was 0.2 out of 8 (Draize scoring system). Twenty-four hours later erythema was noted in 3 out of 4 rabbits whose skin was abraded prior to application of the patch. No reactions were observed at 72 hours [Nair, 1998].

Neat PVA applied to the skin of nine rabbits (occluded patch) failed to demonstrate any signs of irritation up to 24 hours after patch removal. In a similar study with 6 rabbits, irritation was described as minimal, with 3 animals maintaining a score of 1 out of 8 for 24 hours [Nair, 1998].

In a short case report, a 42-year old woman suffered an edematous, scaley and pruritic eruption of the eyelids following use of a contact lens wetting solution containing PVA. These eye lesions returned following challenge with the same solution. Eyelids returned to normal following discontinuation of use of the fluid and symptoms did not return during the 6 month follow up period (No comment is made as to which of the many ingredients present in the fluid was responsible for the irritation) [Yorav *et al*., 1987].

Patches containing 13% PVA were applied to the backs of 12 volunteers for 23 hours/day for 21 consecutive days. The total irritation score for all 12 subjects was 10 out of a possible 756 (no details regarding scoring system are given) [Nair, 1998].

In a modified sensitisation study, three 0.1 ml intradermal injections of 10% PVA in distilled water were injected into 5 Hartley albino guinea pigs. Following challenge 3 weeks later, no reactions were observed [Nair, 1998].

In an insult patch test, one hundred volunteers were exposed to a peel-off facial mask containing 13% PVA for 24 hours, 3 times a week, for 3 weeks. Two weeks later, they were challenged with a 24-hour patch. Three volunteers suffered one reaction during induction, described as “barely perceptible – minimal faint (light pink) uniform or spotty erythema”. No other reactions were observed in any of the volunteers, up to 48 hours post challenge. Another

challenge study failed to demonstrate any significant dermal irritation when 104 volunteers were exposed to 5% PVA (no other details given) [Nair, 1998].

Neat PVA applied to the shaved skin of 20 albino mice (1.0 ml/kg/day, 5 days/wk for 5 wk) revealed no difference in body weights or physical appearance compared to control groups. However, the average hematocrit and red blood cell values were significantly lower compared to controls. At necropsy, no changes were found that could be attributed to PVA [Nair, 1998].

PVA was described as “relatively well tolerated” in 3 rabbits receiving 2 ml of 10 % W/W of the test substance on the right & left flanks. Application was daily, 5 days per week for 6 weeks, and any excess was removed. Evaluation of skin thickness/dryness and histopathological analysis was carried out (no other details given regarding the outcome of these analysis) [Guillot *et al*., 1992].

In a 13-week dermal study, 10 female albino rats received 5 weekly applications of a peel-off facial mask containing 13% PVA to shaved dorsal skin. Each application lasted for 15 minutes. The skin irritation was said to have “stabilised” (no other details given). Blood samples from weeks 6 and 13 revealed no differences in hematologic or serum chemistry parameters. No significant toxic effects were noted at necropsy (no other details given) [Nair, 1998].

Reproductive and Developmental Studies

The Cosmetic Ingredient Review (CIR) Expert Panel in assessing the safety of PVA concluded that the bulk of animal data supported the theory that PVA was safe at higher concentrations than those tested in clinical trails. The Panel holds the position that PVA does not present a reproductive, or developmental toxicity risk, and is safe as used in cosmetics [Nair, 1998].

In an epidemiological study investigating the effect of parental occupation on the risk of reproductive complications, the PVA industry was associated with a 1.5 fold increase in premature birth. Data was collected by means of questionnaires to parents and medical staff and compared with birth and death certificates [Savitz *et al*., 1989].

A recent reproductive toxicity study in which male and female Sprague-Dawley rats (26/sex/group) were administered 0, 2000, 3500 and 5000 mg/kg/day for two generations, and gonadal function, of the F(1) and F(2) offspring, estrous cycle, mating behaviour, conception, gestation, parturition, lactation weaning, and growth development were monitored, (parents treated 70-days prior to mating, during, throughout gestation and lactation, until sacrifice).Revealed unformed stools in animals exposed to 3500 and 5000 mg/kg/dy in P(0) and F(1) parental animals (attributed to high levels of PVA, which was subsequently excreted in the stools). The authors concluded that ‘PVA had no effect on P(0), F(1) male or female reproductive performance or pup survival, growth, organ weights, and macroscopic or microscopic observations at doses of 2000, 3500, and 5000 mg/kg/day’. The reported no-

observed-effect level was 5000 mg/kg/day for both parents and offspring in this study [Rodwell *et al*., 2003].

Inhalation Toxicity

In a study investigating the toxicity of fire effluents from a variety of textiles and upholstery materials, a polyvinyl alcohol – polyvinyl chloride (PVA-PVC) textile was pyrolised and Wistar rats exposed to the various products. The PVA-PVC was heated either to 500°C or to 700°C. The vapours and combustion gases produced were cooled and diluted with air in a mixing chamber, before being passed over the test animals for 30 minutes, at a speed of 400 l/h. The ratio of the mass sample to the total air volume was 18 mg/l. Of the toxic gases measured, CO levels were 4000ppm in the airflow at 700°C, compared with 1800ppm at 500°C. HCN was not detected at the lower temperature and was considered less than 5ppm at 700°C. HCL (produced due to the presence of PVC) was detected at 630ppm at 700°C, and 2070ppm at the lower pyrolysis temperature. In the rats, carboxy haemoglobin (COHb) levels were recorded from blood taken from the tips of tails of those that survived, and from the heart of those that died during the experiment. Of those that survived (19 rats), COHb in the blood ranged from 20-26%. The COHb level of the only fatality was 64% (not considered by the authors to be very high) and occurred in the 700°C pyrolysis test. Contrary to all other materials tested, PVA-PVC test animals did not demonstrate any sign of a slow down in weight gain during the observation period, but following autopsy lung lesions were most marked in these animals. The authors concluded that no general conclusions could be made regarding the relationship between chemical composition and animal toxicity of airborne combustion products [Kallonen *et al*., 1985].

Other Relevant Studies

In 3 male Fischer 344 rats, no radioactivity was detected in any tissues 48 hours after a single oral dose of 0.01 mg/kg bw of radioactive (C^{14}) PVA. In another group of 3 male F344 rats, radioactivity was detected corresponding to 0.05 % of total polyvinyl alcohol administered over the 10 consecutive doses that they had received (0.01 mg/kg bw radioactive (C^{14}) polyvinyl alcohol per dose). Virtually all the PVA was excreted via the faeces [Nair, 1998].

Following a single tail injection of 0.1 mg/ml/kg C^{14} PVA in female rats, 17% of the dose was retained in the liver after 24 hours, 64% was excreted in the urine and 3% in the feces. Three days later only 12% was found in the liver, 5% in the feces and 64% in the urine. After 10 days, 4% was found in the liver, 13% in the feces and none in the urine (the authors make no comment as to the interpretation of these results) [Nair, 1998].

A similar experiment investigating the intravaginal route of administration showed that the absorption was greater via this route compared with oral routes. No signs of toxicity were seen. The test animals were rats and they were dosed 3mg/kg C^{14} PVA per day for 10 days [Nair, 1998].

When PVA is administered by subcutaneous injection, it is almost exclusively localised to the glomerular mesangium of the kidneys (no other test details given) [Nair, 1998].

PVA has been used in various immunological investigations as a scientific tool because it is known not to effect the immune response system including phagocytosis [Nair, 1998].

Behavioural data

No data identified

***In Vitro* Toxicity Status**

Carcinogenicity and Mutagenicity

In an Ames study, PVA was considered overall to be negative using *S.typhimurium* strains TA100, TA98, and TA1537, with or without a metabolic activation system. Concentrations used were up to 1000 μg/plate. The authors point out that although the TA98 plates, with metabolic activation, showed a small increase in the number of revertants, the increase was less than twice the spontaneous rate and they did not consider the result to be meaningful [Nair, 1998].

PVA has been used in the *in vitro* chromosome aberration study as a negative control using Chinese hamster V-79 cells (dose of 0.03 mg/ml). (Inferring that polyvinyl alcohol does not produce chromosome aberrations in the above cell line) [Nair, 1998].

PVA scored 0.7-0.8 out of 4 (0=No damage, 4=>50% damage) when applied to freshly excised rabbit corneas (no other relevant details given) [Nair, 1998].

Additional information concerning the *in vitro* mutagenicity of this material may be found in “An Interim report on data originating from Imperial Tobacco Limited’s Genotoxicity testing programme September 2003” or “An updated report on data originating from Imperial Tobacco Limited’s external Genotoxicity testing programme – Round 2 August 2007”.

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