Cellulose acetate

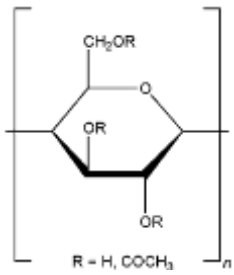
Ingredient synonym names

A 432-130B;
Acetate cotton;
Acetate ester of cellulose;
Acetic acid, cellulose ester;
Acetose;
Acetyl 35;
Acetylcellulose;
Allogel;
Ampacet C/A;
Bioden;
Ca (cellulose acetate);
Cellidor;
Cellidor A;
Cellit K 700;
Cellit L 700;
Cellulose 2,5-acetate;
Cellulose acetate;
Cellulose monoacetate;
Cellulose, 2,5-diacetate;
Cellulose, acetate;
Cellulose, diacetate;
Cellulose, triacetate;
Crellate;
DP 02;
DP 06;
E 376-40;
E 383-40;
E 394-30;
E 394-40;
E 394-45;
E 394-60;
E 398-10;
E-400-25;
Eastman 298-10;
Etrol OEM;
HSDB 964;
Monoacetylcellulose;
Nicollembal;
Nixon C/A;
PP 612;
PP 613;
PP 628;
Plastacele;
Stripmix;
Strux;
Tenite I;
UNII-3J2P07GVB6;
Vladipor;
t-Cellit;

Cellulose acetate

IDENTIFIER DETAILS

Ingredient chemical structure



CAS Number	FEMA Number	Additive Number	Ingredient EC Number
9004-35-7	-	-	-

CAS Additional Number	FL Number	CoE Number
103288-81-9 109321-21-3 120300-14-3 125807-44-5 155860-40-5 50806-92-3 58318-12-0 58517-46-7 66419-14-5 70992-66-4 71812-17-4 81210-20-0 81210-21-1 87582-55-6	-	-

Chemical formula (C8H13O6)n

Ingredient CLP Classification

Ingredient REACH Registration Number

-

Acute Oral Toxicity	Eye Damage/Irritation	Carcinogenity
0	0	0
Acute Dermal Toxicity	**Respiratory Sensitisation**	**Reproductive Toxicity**
0	0	0
Acute Inhalation Toxicity	**Skin Sensitisation**	**Aspiration Toxicity**
0	0	0
Skin Corrosive/Irritant	**Mutagenicity/ Genotoxicity**	**Specific Target Organ Toxicity**
0	0	0

SPECIFICATIONS

Cellulose acetate

Melting Point	260°C	Boiling Point	Decomposes upon further heating.

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg)	-
Acceptable Daily Intake (ADI) comments	In 2018 The EFSA ANS Panel concluded that there was no need for a numerical ADI and that there would be no safety concern at the reported uses and use levels for the unmodified and modified celluloses. The Panel considered an indicative total exposure of around 660–900 mg/kg bw per day for microcrystalline, powdered and modified celluloses.
FDA Status	CFR21: 175: Indirect food additives: adhesives and components of coatings 175.105: Adhesives 175.230: Hot-melt strippable food coatings. 175.300: Resinous and polymeric coatings. 177: Indirect food additives: polymers 177.1200: Cellophane 182: Substances generally recognised as safe 182.90: Substances migrating to food from paper and paperboard products.

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

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

Cellulose acetate was first prepared in 1865, and is the acetate ester of cellulose. Although the starting material cellulose occurs in nature cellulose acetate does not.

References - Ingredient Natural Occurence

-

Ingredient Reported Uses

Wide range of clothes, cigarette filters, ink reservoirs for fibre tip pens, disposable nappies, surgical products and playing cards.

References - Ingredient Reported Uses

-

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

The following data is related to cellulose.

LD50 >3160mg/kg - Rat (oral)
LD50 >5000mg/kg - Rat (oral)
LD50 >3169mg/kg - Rat (intraperitoneal)
LD50 >5.3mg/litre - Rat (inhalation)
LD50 >2000mg/kg - Rat (dermal)

JECFA (1998). 49th meeting on the safety evaluation of certain food additives and contaminants; 55 – 78.

In Vivo Carcinogenicity/Mutagenicity

The following data is related to cellulose.

JECFA (1998) reported that various cellulose preparations have been tested for genotoxicity in several different assay systems. Poor solubility / pre-absorption of the test material were commonly quoted as a problem in carrying out the tests. Overall, JECFA (1998) reported that there was no evidence that microcrystalline cellulose is genotoxic. Results for genotoxicity assays are summarised below (test system - test cells - concentration - results) [JECFA, 1998]:
In vivo mammalian micronucleus assa y- Bone marrow polychromatic erythrocytes of ICR mice -5000 mg / kg bw (oral)- Negative
In vivo mammalian micronucleus assay -B one marrow polychromatic erythrocytes of CD-1 [ICR] mice- 5000 mg/ kg bw (oral) -Negative

In 2018 the EFSA ANS Panel concluded that their structural, physicochemical and biological similarities, allows for read-across between all the celluloses. despite the limitations of some of the studies, the available data do not indicate a genotoxic concern for microcrystalline cellulose, methyl cellulose and carboxy methyl cellulose, and by read-across, of the other modified and unmodified celluloses [EFSA ANS, 2018].

References - In Vivo Carcinogenicity/Mutagenicity

JECFA (1998). 49th meeting on the safety evaluation of certain food additives and contaminants; 55 – 78.

EFSA ANS. Re-evaluation of celluloses E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 466, E 468 and E 469 as food additives. EFSA Journal 2018, 16(1)5047.

Dermal Toxicity

The following data is related to cellulose:
The application of 50 mg CellulonTM, (a cellulose fibre produced by the bacterial fermentation of employing a strain of Acetobacter acetic sub species xylinium most closely represents microcrystalline and powdered cellulose) in to the eyes of six rabbits was reported to be mildly irritating after 1 hour but the redness had subsided 24 hours after application. A 500 mg sample of CellulonTM applied to the shaved skin of six rabbits was reported to be well tolerated with no dermal effects [HCN, 2002].

References - Dermal Toxicity

HCN (2002), Health council of the Netherlands. Committee on the Updating of Occupational Exposure Limits.

Cellulose, Health based reassessment of Administrative Occupational exposure Limits. The Hague. (http://www.gr.nl./Pdf.php?ID=254).

Reproductive/ Developmental Toxicity

The following data is related to cellulose:

Groups of 25 presumed pregnant Charles River Sprague-Dawley CD rats were administered 0 [control], 25,000 or 50,000 mg/kg Avicel [a proprietary microcrystalline cellulose] in the diet ad libitum on days 6 to 15 of gestation [equivalent to 2.2 and 4.6 g/kg bw/day respectively]. The authors reported no evidence of reproductive toxicity, including teratogenicity, in any of the test animals. Under the conditions of the study, the maternal and foetal NOEL was > 50,000 mg / kg diet [equivalent to 4.6 g/kg bw/day] [JECFA, 1998].

Concerning reproductive and developmental toxicity, data are available for microcrystalline cellulose, methyl cellulose, hydroxypropyl cellulose and sodium carboxy methyl, cellulose. The substances were tested in mice, rats, hamsters and/or rabbits with oral dosing via gavage. Adverse effects on reproductive performance or developmental effects were not observed with modified and unmodified celluloses at doses greater than 1,000 mg/kg bw by gavage (often the highest dose tested). Specific toxicity data were not always available for all the celluloses for all endpoints. In general, the most complete data sets were available for microcrystalline cellulose and sodium carboxy methyl cellulose. Given the similarities in their structure, relevant physicochemical, metabolic and toxicological properties, the EFSA ANS Panel considered it possible to read-across between all the celluloses [EFSA ANS, 2018].

References - Reproductive/ Developmental Toxicity

JECFA (1998). 49th meeting on the safety evaluation of certain food additives and contaminants; 55 – 78.

EFSA ANS. Re-evaluation of celluloses E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 466, E 468 and E 469 as food additives. EFSA Journal 2018, 16(1)5047.

Inhalation Toxicity

The following data is related to cellulose acetate.

Aerodynamic diameter is a major determinant of particle and fibre deposition and toxicity in the respiratory tract. To characterize cellulose acetate fibres released from the filter end of cigarettes puffed under conditions approximating smoking, Collazo et al., (2002) designed multistage impactors to determine the aerodynamic diameters of large fibres with circumscribed diameters between 20 and 35 microm and aspect ratios ranging from subfibre ratios up to 40. This range of diameters encompasses all of the cellulose acetate fibre sizes that are commercially manufactured. When commercially available cigarettes with filters made from acetate fibres in this circumscribed diameter range were puffed directly into the impactor, on average 10 fibres/cigarette were released and their aerodynamic diameters were determined. In our studies, we found that the aerodynamic diameters of the cellulose acetate fibres were always greater than 23 microm. Using standard lung deposition models, we concluded that the fibres are nonrespirable with a very low probability of penetration to the distal lung. The authors conclude their findings demonstrate release of only a small number of these large fibres with an extremely low likelihood of reaching the distal lung indicate that these fibres are not a risk for human lung disease, [Collazo et al., 2002].

The following data is related to cellulose.
Groups of male Crl: CDBr rats were exposed to nose only to cellulose fibres for 6 hours/day 5days/week for 2 weeks, at target concentrations of 300 and 575 fibres per ml (with a median fibre length of 10-13 of the rat were then evaluated on Days 1, 10, and at 1 and 3 months after exposure by bronchoalveolar lavage. There was reported to be a moderate to slow clearance of cellulose fibres, with a transient pulmonary inflammatory response

which was reported to have returned to control levels within 10 days post exposure [HCN, 2002].

Groups of Wistar rats were exposed via whole body inhalation to 0 (n=3) or 1000 (n=6) fibres/ml, 7 hours a day for 1,or 3,or 8,or 14 days of exposure during a 3-week period. The majority of fibres were within the respirable size range with the mean concentration 73.mg/m3. Inhalation was reported to be associated with an inflammatory response that peaked on the first day of exposure and declined with subsequent exposures. The in vitro production of the pro inflammatory cytokine tumour necrosis factor by lavaged alveolar macrophages had markedly declined by Day 14 of exposure. The authors concluded that the inflammatory response in the lungs was less than that of crocidolite, and decreased over the 14-day exposure period [HCN, 2002].

Intratracheal administration of 7.5 mg/kg (approximately 3 mg/g lung tissue) twice weekly for six weeks was reported caused pulmonary toxicity in hamsters (n=4). The histological findings included significant numbers of granulomata and increased areas intra alveolar septa. The authors concluded that the accumulation of particles and toxicity might be due to an overload of the lungs capacity to remove insoluble foreign material and the intrinsic toxicity of cellulose. The committee concluded that it was unlikely that the threshold limit value (TLV) currently set for nuisance dusts of 5 mg/m3 respirable fraction was likely to reach the intra tracheal level of 7.5 mg/kg, and that exposure by the intra tracheal route was more toxic than that via inhalation exposure. The committee also concluded that the current toxicological information was insufficient to recommend a health based exposure level [HCN, 2002].

In a study conducted by Adamis et al., (1997) male Sprague Dawley rats were intratracheally administered 15 mg of cellulose, quartz or saline. Rats were then serially sacrificed 1-30 days after a single exposure. Peritoneal macrophages were also incubated both in the presence and absence of cellulose. On the first day after exposure cellulose treatment resulted in an inflammatory response with leukocyte migration. One week after exposure there was reported to be oedema with cell infiltration in the alveoli and interstitium. Multinuclear foreign body cells were found to contain phagocytosed cellulose. At one month after exposure there was reported to be widening of the alveolar septa, fibrosis of the alveoli and bronchi. Exposure to quartz reported to have lead to more extensive inflammatory response and marked fibrosis occurred. There was no lactate dehydrogenase (LDH) release from cellulose fibre exposed peritoneal macrophages. The authors concluded that cellulose dust was cytotoxic in the lungs when tested in vivo.

Tatrai et al., [1996] examined the pulmonary toxicity of cellulose. Sprague-Dawley-rats were given single intratracheal doses of 15 milligrams respirable cellulose and the lungs were examined morphologically after 6 and 12 months. The immune response to cellulose was also assessed at 1, 7, and 14 days after exposure, by examination of blood and bronchoalveolar lavage samples. Granulomatous inflammation was identified in the pulmonary interstitium of cellulose treated animals after 6 months. This was associated with damaged elastic fibres, decreased numbers of alveolar type-I pneumocytes and increased numbers of type-II pneumocytes. These changes were more pronounced after 12 months. Electron microscopy identified hypertrophic type-II cells, cytoplasmic lamellar inclusions in intermediate cells, thickened endothelial basement membranes, accumulation of collagen fibres in alveoli and capillary walls, and the presence of interstitial fibroblasts in alveolar walls. No alterations in serum immunoglobulin levels were seen. IgA was increased significantly in alveolar fluid 2 weeks after exposure. The authors conclude that these results underscore the importance of in vivo testing of cellulose as an asbestos substitute, and the urgency of developing a hygienic standard for cellulose use [Tatrai et al., 1996]. In additional studies intratracheal administration of 15 mg of respirable germ free pine dust or cellulose were reported to cause identical changes inn the lungs of rats after one month, fibrosing alveobronchiolitis. As the severity of the histological findings between the two studies were not stated then, a direct comparison was not possible. A fibre free extract of the wood dust, however, was not reported to cause any histological changes of the lung [HCN, 2002].

A single Intratracheal dose of respirable cinnamon dust, cinnamon dust extract or cellulose were administered to rats that were sequentially examined 1 and 7 days, and 1 month after exposure. Histopathological examination revealed the formation of alveobronchiolitis at the end of the first and seventh days with fibrotic changes by the

end of the fist month for both respirable cinnamon and cellulose. Ads the extract of cinnamon dust caused no histological changes the authors concluded that it was the cellulose content of the cinnamon dust that caused the histological changes [Tatrai et al., 1995].

References - Inhalation Toxicity

Adamis et al., (1997). In vitro and in vivo assessment of the pulmonary toxicity of cellulose. J. Appl. Tox. 17: 137-141.

Collazo H, Crow WA, Gardner L, Phillips BL, Dyer WM Jr, Marple VA, Utell MJ. (2002). Aerodynamic diameter measurement of cellulose acetate fibers from cigarette filters: what is the potential for human exposure? Inhal. Toxicol. 14(3):247-62.

HCN (2002), Health council of the Netherlands. Committee on the Updating of Occupational Exposure Limits. Cellulose, Health based reassessment of Administrative Occupational exposure Limits. The Hague. (http://www.gr.nl./Pdf.php?ID=254).

Tatrai et al., (1996). In vivo pulmonary toxicity of cellulose in rats. Journal of Applied Toxicology 16 (2), 129 – 135.

Tatrai et al., (1995). The pulmonary toxicity of cinnamon dust in rats. Indian Journal of Medical Research. 102: 287-292.

Cardiac Toxicity

No data identified.

References - Cardiac Toxicity

No data identified.

Addictive Data

No data identified

References - Addictive Data

No data identified

Behavioral data

No data identified.

References - Behavioral data

No data identified.

In Vivo - Other Relevant Studies

The following data is related to cellulose acetate:
Lucas et al., (2000) reported the results of an investigation into the cause of conjunctivitis, hearing loss, diminished vision, and headaches in seven patients 7-24 h after haemodialysis treatment. Eleven-year-old dialysis modules were identified as a common link between these patients. Degradation of the cellulose acetate (CA) material was identified as the cause of this incident. Degradation products were characterized from retrieved CA

dialysis membranes. A series of synthesized CA degradation products was tested in vitro to assess toxicity. Based on the toxicity of the material preparations to the cells, animal tests were performed on selected CA degradation extracts and compared to extracts from actual dialysis membranes. Rabbits were IV-injected with extracts from a 13-year-old dialyzer, synthesized model compounds, and compared to controls. Ophthamological evaluation of the rabbits showed eye injury (iritis/ciliary flush) when the animals were treated with the old dialyzer or synthesized model compounds. Isolation and characterization of a toxic fraction from both of these extracts strongly indicated that oxidative stress at some point in the storage or manufacture of CA dialyzers created degradation products that reproduced some of the patient symptoms identified at Hospital A.

In a study conducted by Thomas et al., (1991), cellulose acetate was administered by way of a dietary admixture to Sprague-Dawley rats (20/sex/group) at dose levels of 0, 500, 2500 and 5000 mg/kg body weight/day for 94-96 days. Physical observations, body weight and food consumption measurements were made before testing and throughout the study. Ophthalmoscopic examinations were conducted on all animals before testing and just prior to study termination. Haematology, clinical chemistry and urinalysis were performed at 1.5 and 3 months on 10 animals/sex/group. After 3 months of treatment the animals were killed, terminal body weights and organ weights were measured and ratios calculated. Histopathological examination of tissues from the control and high-dose groups was conducted. The authors concluded that the evaluation of physical observations, ophthalmology, body weight, food consumption, haematology, clinical chemistry, organ-to-body-weight ratios, gross pathology and histopathology revealed no evidence of an adverse effect related to treatment with cellulose acetate.

The following data is related to cellulose:
Le Leu et al., (2009) compared control and cellulose based diets with a variety of high amylose maize starches (HAMS) diets in a 4-week study in Sprague-Dawley rats (n=12/group). The cellulose based diet showed similar outcomes to the control diet with respect to final body weight, caecal pH was comparable between cellulose diet and control diet, as was cell turnover and apoptotic index. Distal colon crypt atrophy was increased in control diet fed rats than in all other diets. Faecal output was found to be increased compared to control, with slightly increased caecal contents and slightly lower caecal weight compared to control. Levels of short chain fatty acids, a marker of fermentation, in the faeces and caecal contents were slightly decreased in the cellulose diet compared to the control diet [Le Leu et al., 2009].

There was reported to be little data for epidemiological evidence of disease in workers although there are expected to be high levels of exposure in the work place. Epidemiological evidence although sparse, there is reported to be little evidence of disease even though there are high exposure levels in the work place. Exposures to hardwood associated dust has apparently been linked with the development of sinusoidal cancer, however soft woods were reported to be significantly less potent in their effects indicating that cellulose was not the causative agent. There exists a general lack of data on the pulmonary toxicity of inhaled cellulose. In summary the few in vitro and in vivo studies tat have been conducted suggest that respirable microcrystalline cellulose may be biopersistent in the lung and may produce pulmonary inflammation [Warheit et al., 2001].

Groups of five male weanling Sprague-Dawley rats received 0 - 20 % cellulose in their diet over a period of 17 days. Absorption of magnesium and zinc were significantly lower in the higher dose groups [10 - 20 %]. Histopathology of the gastrointestinal tract revealed mitotic activity and an increase in neutrophils in crypt epithelial cells, particularly of the duodenum and jejunum [JECFA, 1998].

Four rats were fed 14C-labelled microcrystalline cellulose at 10 or 20% of their diet. Faecal recoveries account for between 96 – 104% with no radioactivity appearing in the urine [JECFA 1998].

Rats, pigs and dogs have been used to study the persorption of microcrystalline cellulose. Animals were starved for 12 hours prior to administration of 0.5, 140 and 200 g of the test compound. Particles were found in the venous blood of all animals 1 - 2 hours after administration with the largest particle sizes being found in the blood of rats [JECFA 1998].

One human subject was fed 150g of microcrystalline cellulose daily for 15 days prior to receiving 14C-labelled cellulose. There was reported to be no excretion in either the respired air or urine, with all the activity (98.9 +/- 3 %) being found excreted in the faeces within 2 days [JECFA 1998].

Randomly bred rats of both sexes were divided into groups that received a control diet or a control diet plus 330 mg/kg microcrystalline cellulose for a period of 6 months. Six rats from each groups were killed, their organs examined, and tissues taken for histopathology. No effects of the treatment were observed [JECFA, 1998].

Groups of Crl:CD rats [20/sex per group] were administered 0 [control] 25,000 or 50,000 mg/kg bw Avicel [a proprietary microcrystalline cellulose] in the diet for 90 days. A few test animals were reported to present with chromodacryorrhea [a flow of blood-stained tears] and chromorhinorrhea [a blood-stained nasal discharge], but the authors state that this was not considered to be biologically significant. The authors reported no adverse effects for body weight, organ weights, or clinical chemistry for the test animals. Histopathological examination of 34 organs or tissues also provided no evidence of toxicity of microcrystalline cellulose. The authors noted that the NOEL exceeded 50,000 mg/kg diet [JECFA, 1998].

Avicel (which contained 85% microcrystalline cellulose and 15% calcium alginate) was administered at 0 or 45000 mg/kg in a high fibre diet in male Wistar rats, along with 1, 2-dimethyl hydrazine dihydrochloride (25 mg/kg subcutaneously once weekly for 16 weeks). There was reported to be a reduction in the numbers of animals bearing colon tumours and a significant reduction in the numbers of tumours/rat in the high fibre group. Tumours of the ear canal and small bowel there was no significant difference between any of the treatment groups [JECFA 1998].

Groups of Sprague Dawley rats (20 rats/dose/sex) were administered by oral gavage extra fine microcrystalline cellulose (particle size 6 □m) at 0, 500, 2500 or 5000 mg/kg/day as a 25% suspension in water for 90 consecutive days. The only treatment related sign was reported to be pale faeces, however this was considered to be of no toxicological importance. There were no toxicological findings found, with no microcrystalline particles detected in any organ or tissue including gut associated lymphoid tissue, liver, lung, spleen and the brain. In the 5000 mg/kg/ group there was reported to be no histopathological findings reported in any the 36 tissues examined, with no macroscopic or microscopic changes due to microemboli or granulomatous inflammatory lesions [JECFA 1998].

Three groups of 50 male and 50 female rats received either: 30% ordinary cellulose, dry microcrystalline cellulose, or microcrystalline cellulose gel in their diet for 72 weeks. Male rats receiving the gel had higher liver and kidney weights compared with controls. Gross and histopathology showed some dystrophic calcification of renal tubules in females; all other organs were reported as unremarkable. Tumour incidence did not differ between the groups [JECFA, 1998].

Intravenous drug abuse of tablets has lead to the detection of microcrystalline deposits in various tissues of 21 fatality cases. In some cases there was reported to be an associated granulomatous lesion [JECFA 1998].

References - In Vivo - Other Relevant Studies

JECFA (1998). 49th meeting on the safety evaluation of certain food additives and contaminants; 55 – 78.

Le Leu et al., (2009) Effect of high amylose maize starches on colonic fermentation and apoptotic response to DNA-damage in the colon of rats. Nutrition & Metabolism. 6:11.

Lucas A. D., Kalson J. A., Hutter J. C., Wallis R. R., (2000). Identifying toxic degradation products in cellulose acetate dialyzers. Journal of biomedical materials research. 53 (5):449-456

Thomas, WC, McGrath, LF, Baarson, KA, Auletta, CS, Daly, IW, McConnell, RF, (1991). Subchronic oral

toxicity of cellulose acetate in rats. Food Chem Toxicol. 29(7): 453-8

Warheit et al., (2001) Man made respirable sized organic fibers: what do we know about their toxicological profiles? Industrial Health. 39: 119-125.

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

The following data is related to cellulose.

Additional information concerning the in vitro mutagenicity and genotoxicity 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".

JECFA (1998) reported that various cellulose preparations have been tested for genotoxicity in several different assay systems. Poor solubility / pre-absorption of the test material were commonly quoted as a problem in carrying out the tests. Overall, JECFA (1998) reported that there was no evidence that microcrystalline cellulose is genotoxic. Results for genotoxicity assays are summarised below (test system - test cells - concentration - results) [JECFA, 1998]:
Reverse mutation - Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA153 - 8 50 – 5000 μg / plate - Negative
Reverse mutation - Escherichia coli WP2uvrA - 10 – 5000 μg / plate - Negative
Forward mutation - Mouse lymphoma L5178Y cells, TK locus - 100 – 1000 μg / ml - Negative
UDS with confirmatory assay - Rat liver primary cell cultures - 10 – 1000 μg / ml - Negative

References - In Vitro Carcinogenicity/Mutagenicity

Internal Document. An Interim report on data originating from Imperial Tobacco Limited's Genotoxicity testing programme September 2003
Internal Document - An updated report on data originating from Imperial Tobacco Limited's external Genotoxicity testing programme – Round 2 August 2007

JECFA (1998). 49th meeting on the safety evaluation of certain food additives and contaminants; 55 – 78.

In Vitro - Other Relevant Studies

The following data is related to cellulose acetate:

In an experiment conducted by Agyei-Aye K et al., (2004) the release of cellulose acetate fibres, charcoal, and other particles from cigarettes with charcoal and activated charcoal/resin filters was investigated. For the first time in such studies, efforts were made to identify the particles that were eluted using other analytical techniques in addition to light microscopy. Other corrective measures were also implemented. During the studies it was found that trimming of larger filters to fit smaller filter housings introduced cellulose acetate-like particles from the fibres of the filter material. Special, custom made-to-fit filters were used instead. Tools such as forceps that were used to retrieve filters from their housings were also found to introduce fragments onto the filters. It is believed that introduction of such debris may have accounted for the very large number of cellulose acetate and charcoal particles that had been reported in the literature. Use of computerized particle-counting microscopes appeared to result in excessive number of particles. This could be because the filter or smoke pads used for such work do not have the flat and level surfaces ideal for computerized particle-counting microscopes. At the high magnifications that the pads were viewed for particles, constant focusing of the microscope would be essential. It was also found

that determination of total particles by using extrapolation of particle count by grid population usually gave extremely high particle counts compared to the actual number of particles present. This could be because particle distributions during smoking are not uniform. Lastly, a less complex estimation of the thickness of the particles was adopted. This and the use of a simple mathematical conversion coupled with the Cox equation were utilized to assess the aerodynamic diameters of the particles. The authors concluded that their findings demonstrated that compared to numbers quoted in the literature, only a small amount of charcoal, cellulose acetate shards and other particles are released. It was also shown that those particles would have a low likelihood of reaching the lung, [Agyei-Aye et al., 2004].

In a study conducted by Dang et al., (1997) some commercial degradable plastics were tested in a cell culture screen including; a plasticized cellulose acetate, an aliphatic polyester (Bionolle), polyhydroxybutyrate-co-hydroxyvalerate (Biopol), and polycaprolactone (TONE polymer). Cell culture medium with serum was used as extraction medium. Methods for the determination of morphology and viability of cells cultured in the extract were investigated. Phase-contrast light microscopy of cells, enhanced by neutral red staining, provides high-contrast images for qualitative evaluation of cell morphology and lysis. Compared to the determination of protein using the Bradford method and of neutral red uptake, the determination of dehydrogenase activity using 3-[4,5-dimethylthia-zol-2-yl]-2,5-diephenyl-tetrazolium bromide (MTT) is more sensitive and accurate. The relative MTT activity of cells cultured in fresh extracts indicate that TONE polymer (all shapes) and Bionolle (test bars and films) are comparable to materials currently used in the food industry (polyethylene terephthalate, atactic and isotactic polystyrene) with no toxic effects on cells.

References - In Vitro - Other Relevant Studies

Agyei-Aye K, Appleton S, Rogers RA, Taylor CR. (2004). Assessment of the elution of charcoal, cellulose acetate, and other particles from cigarettes with charcoal and activated charcoal/resin filters. Inhal. Toxicol. 16(9):615-35.

Dang, F. Birchler and E. Wintermantel. (1997). Toxicity screening of biodegradable polymers. II. Evaluation of cell culture test with medium extract. Journal of Polymers and the Environment. 5 (1): 1566-2543.

Emissions and Associated Toxicity Data

The following data relates to Cellulose:
Baker et al., [2004] examined the effects of the addition of 482 tobacco ingredients upon the biological activity and chemistry of mainstream smoke. The ingredients, essentially different groups of flavourings and casings, were added in different combinations to reference cigarettes. The addition of cellulose fibre at 28,400 ppm was determined not to have affected the mutagenicity of the total particulate matter (TPM) of the smoke in either the Ames, in vitro micronucleus assay or the neutral red assay when compared with that of the control cigarettes [Baker et al., 2004].

It has been suggested that a large number of free radicals are generated by the burning of cellulose, and that radicals produced in the gas phase are metastable, but decompose in solution [Lachocki et al., 1988]. The authors suggest that these free radicals could cause lung damage and question the role of free radicals in emphysema and carcinogenesis [Lachocki et al., 1988].

Kuroda et al., (1985) reported on the mutagenicity of cellulose pyrolysates against a number of Salmonella typhimurium strains [Kuroda et al., 1985]. The authors found that pyrolysed cellulose, 400 µg per plate, [at 500-800 degrees C] led to the production of material [PAH's] that was mutagenic against TA97 in the presence of an S9 fraction. It had a positive mutagenic effect in strains TA98 and TA100 also, but there were less His+ revertants [Kuroda et al., 1985].

References - Emissions and Associated Toxicity Data

Baker RR, et al., (2004) An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. Food Chem. Toxicol. 42 Suppl: S53-83

Kuroda et al. (1985). Mutagenicity of pyrolyzates of natural substances towards Salmonella typhimurium TA97. Agric. Biol. Chem., 49, 1893

Lachocki et al. (1988). Persistent free radicals in the smoke of common household materials: Biological and clinical implications. Envir. Res., 45, 127.