## MATE

## **1. Production and Use**

### **1.1 Introduction**

Mate is native to the area of South America between 18° and 25° S latitude and from the Atlantic Ocean to the Paraguay River. This area takes in a portion of southern Brazil and Paraguay, Uruguay and northern Argentina. The plant was used to make a beverage by the indigenous populations of the area long before the first Spanish colonists arrived early in the sixteenth century. Jesuit priests who arrived in the middle of the century gradually took over control of most of the producing areas and began cultivation of selected varieties to ensure supply. Virtually all of Argentinian and Brazilian production is now cultivated, while much of Paraguayan production is derived from wild plants (Graham, 1984).

#### **1.2 Production processes**

## (a) Botany and culture

Mate ('Yerba mate', 'Jesuits' tea', 'Paraguayan tea', 'yerba') is prepared from the leaves of *Ilex paraguariensis* St. Hil, a member of the Aquifoliaceae (holly) family, which is native to Paraguay and Argentina. The tree can grow to 12-16 m in the wild but is usually cultivated as a shrub 3-6 m tall with numerous stems. The leaves are dark-green, 15-20 cm long and short-stalked with an acuminate tip and finely dentated edges. It has small white flowers, which grow in forked clusters in the axils of the leaves, and violet-black berries, each of which contains four to eight seeds (Graham, 1984; Vázquez & Moyna, 1986).

Mate is propagated by seed; the seedlings are transplanted to a shaded nursery where they remain for 9-12 months, and are finally transferred to the plantation when they reach a height of 30-80 cm. During the first year, the plant must be protected against wind and low temperatures. Plantations consist of 800-1000 trees per hectare pruned to a height of 3-6 m to facilitate harvesting. Harvesting, which can start in the fourth or fifth year, is annual and takes place from May to October; it consists of cutting off smaller leafy branches with a knife. A good plantation yields 20-25 kg fresh leaves per tree (Graham, 1984).

(b) Processing

Information obtained from Graham (1984).

(i) *Traditional* 

The trees are cleared of vines and smaller branches are cut off. These leaf-bearing branches are 'toasted' momentarily over an open fire to reduce the moisture content, but avoiding 'blackening'; this process is known as *supeco*. They are dried further by heating for 12-24 h on a platform of poles suspended over an open fire. An alternative procedure involves the use of a dome-shaped structure (*barbaqua*), over which the toasted branches are spread; hot air is conducted through a tunnel from a fire some distance away. This procedure avoids direct deposition of smoke on the leaf and requires 5-15 h.

Threshing separates leaf from bark and twigs. Further grading by sifting is carried out, and the product is packed in 30-60-kg bags and aged. Additional grading and blending is practised to provide greater uniformity.

(ii) Modern

The toasting step is now frequently carried out by passing the branches through a perforated rotating metal cylinder in an inclined position over an open fire for a very short time. The cylinders used are about 2-2.5 m in diameter and 4 m in length. This process is known as *sepecadora*.

The *barbaqua* step may be carried out in a specially constructed room with a frame above the floor to contain the leaves, which are dried with hot air conducted from a fire. Leaf temperatures reach 80-100°C. Some caffeine is lost at the higher temperature.

Further grinding and sifting are carried out, and many different grades of mate are made available. Ageing, which is extremely important to produce a palatable beverage, may take place over 6-18 months.

#### 1.3 Production, trade and consumption

Production of all types of mate is concentrated in Argentina (Misiones, Corrientes; 172 000 tonnes in 1987), Brazil (Parana, Santa Catarina, Rio Grande do Sul; 80 000-120 000 tonnes per year) and Paraguay (60 000 tonnes per year) (Graham, 1984).

To prepare the mate, ground leaves are poured into a gourd to three-quarters of its internal volume, with the gourd's hole tilted about  $30^{\circ}$  from the vertical. The

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gourd is then held upright and warm water (60-80°C) is poured on the depressed side of the surface of the mate. The wet mate swells within 3-5 min, and a metal straw with a filtering head (known as a *bombilla*) is introduced to the bottom of the gourd. This step eliminates the possibility that the consumer will suck up powdered mate. Small volumes of hot water (90-95°C) are then poured onto the mate around the *bombilla*, and the consumer sips through the *bombilla* until the sound of air rushing in makes a typical chirping noise. This operation is repeated (and the gourd circulates around a group of drinkers if there are more than one) until the flavour diminishes. The *bombilla* is then removed and inserted into a different place in the mate ('turning the mate round'). Once the drink has lost its taste, the *cebadura* (the charge of yerba used and the operation of adding water) is finished (Vázquez & Moyna, 1986).

Mate is consumed mainly in Argentina, Bolivia, Brazil, Chile, Ecuador, Paraguay and Uruguay, usually as a hot beverage. To a much lesser extent, it is drunk in Germany as a cold beverage. It is also drunk chilled in Paraguay and southwestern Brazil, with milk or water and sugar. Burnt sugar, lemon or lime juice are sometimes added instead of milk; 20% of mate is drunk in this manner in Brazil. Consumption of mate in Argentina is increasing and was 162 329 tonnes in 1987 (equivalent to 5.14 kg *per caput*). Uruguay imports 18 000-24 000 tonnes per year, with an average annual consumption of 6-8 kg per person (Vázquez & Moyna, 1986).

Table 1 gives data on production, trade and consumption of mate in South America in 1977.

Country	Production	Exports	Waste	Consumption	Consumption per caput (kg/year)
Paraguay	20	1	2	17	6.2
Uruguay	18	0	0	18	6.2
Argentina	143	4	0	139	5.4
Brazil	100	23	5	72	0.6
Chile	0	0	0	4	0.3
Total	281	28	7	250	

Table 1.	Mate production,	trade and	consumption	(in thousands
	s) in 1977 <i>a</i>		-	

"From Gilbert (1984)

In Argentina, the commercial product must be free from extraneous matter, well preserved and must contain less than 11% moisture, 9% total ash, 1.5% ash in

10% hydrochloric acid and 15% fibre and more than 0.6% caffeine and 25% aqueous extract (Ministerio de Agricultura y Ganadería, 1971).

## 2. Chemical Composition

Two early accounts were given of the composition of the beverage mate, especially as consumed in several South American countries (Hauschild, 1935; Hegnauer, 1964). More recent estimates of its composition have been compiled by Graham (1984) and by Belitz and Grosch (1986), although these are brief and contain negligible reference to volatile components. Clifford and Ramirez-Martinez (1990) determined the caffeine and chlorogenic acid contents of a number of commercial packets of mate.

#### 2.1 Nonvolatile compounds

#### (a) Caffeine and other purines

Graham (1984) stated that the caffeine content of the mate leaf was 0.9-2.2%, depending on the age of the leaf; whilst Belitz and Grosch (1986) stated that, while one-third of the total dry matter is solubilized with hot water, only half of the available caffeine is released, to give 19-28 mg/100 g of solution (brew). Côrtes (1953) measured 25 mg per 120-ml cup. These figures are reasonably consistent.

Dried mate leaves were analysed for methylxanthines by high-performance liquid chromatography, and caffeine was found at 0.56%, theobromine at 0.03% and theophylline at 0.02% (Vázquez & Moyna, 1986).

Stavric *et al.* (1988) analysed two samples of mate leaves (purchased in Ottawa, Canada) for extractable methylxanthines. After steeping 1 g of loose leaves for 2 min in 44 ml water, they found 7 mg (157  $\mu$ g/ml) caffeine and 2 mg (45.7  $\mu$ g/ml) theobromine. When the steeping time was increased to 5 min, the extractable caffeine and theobromine contents were 9 and 3 mg, respectively.

Clifford and Ramirez-Martinez (1990) recently examined five commercial samples of two types of mate leaf of South American origin, purchased in the UK and the Federal Republic of Germany, using high-performance liquid chromatography, and reported caffeine at 0.89-1.73% and theobromine at 0.45-0.88%, with very small quantities of other unidentified purine alkaloid-like components. Theophylline was not detected in these samples. Quantities were also assessed per cup, after following the instructions for use given on the packet, which were not necessarily South American practices; the amount of caffeine per cup was 12-33 mg and that of theobromine, 6-17 mg.

#### (b) Chlorogenic acids

Chlorogenic acids are a family of mono- and di-acyl quinic acids. Quinic acid is 1L-1(OH),3,4/5-tetrahydroxycyclohexane carboxylic acid. The common acylating residues are caffeic acid (3,4-dihydroxycinnamic acid), ferulic acid (3-methoxy-4-hydroxycinnamic acid) and para-coumaric acid (4-hydroxycinnamic acid), thus producing caffeoylquinic acids, dicaffeoylquinic acids, feruloylquinic acids, para-coumaroylquinic acids and caffeoylferuloylquinic acids. Two samples of mate leaf that yielded brown extracts contained 1.11-1.27% caffeoylquinic acids, 0.39-0.42% feruloylquinic acids, 0.62-1.12% dicaffeoylquinic acids and 2.88-2.89% total chlorogenic acids; levels of 4.53-4.71%, 0, 4.03-4.56% and 9.16-9.76%, respectively, were found in three samples yielding greenish extracts (Clifford & Ramirez-Martinez, 1990). The authors could not define which processes or species were responsible. They also analysed the brews and found that those made with the first two samples contained 16-41 mg caffeoylquinic acids and 1.8-9.5 mg dicaffeoylquinic acids per cup; the last three contained 107-133 mg caffeoylquinic acids and 36-44 mg per cup dicaffeoylquinic acids.

## (c) Other components

Some other components are listed in Table 2.

Component	Amount		
Sucrose	3.33 (% dry wt of leaf)		
Raffinose	0.44 (% dry wt of leaf)		
Glucose	0.27 (% dry wt of leaf)		
Fructose	0.16 (% dry wt of leaf)		
Trigonelline	0.50 (% dry wt of leaf)		
Choline	15 μg/g		
Thiamine	1 μg/g		
Riboflavin	Trace		
Ascorbic acid	20 μg/g		
Folic acid	16 μg/g		
Total extractable ash	5.99 (% dry wt of leaf)		

Table 2. Components of mate other than caffeine and other purines and chlorogenic  $acids^a$ 

"From Graham (1984)

Some 60 species of plants occur in some samples of mate along with *I. paraguariensis* (Graham, 1984).

Aglycones of the family Aquifoliaceae that have been identified in mate are rutin (quercetin-3-O-rutinoside), quercetin-3-O-glucoside and kaempferol-3-O-

rutinoside. Triterpenes can also be found. The main component is ursolic acid (Ohem & Hölzl, 1988).

## 2.2 Volatile compounds

No data were available.

## 2.3 Contaminants

Ruschenburg (1985) reported the presence of relatively large quantities (24-461  $\mu$ g/kg) of benzo[*a*]pyrene in eight commercial samples of mate leaf bought in the Federal Republic of Germany, but only 0.02-0.12  $\mu$ g/l in the beverage (made from 15 g mate leaf and 1 l of water).

## **3. Biological Data Relevant to the Evaluation of** Carcinogenic Risk to Humans

## 3.1 Carcinogenicity studies in animals

No data were available to the Working Group.

## 3.2 Other relevant data

(a) Experimental systems

No data were available to the Working Group.

- (b) Humans
  - (i) Absorption, distribution, metabolism and excretion

No relevant data were available to the Working Group.

(ii) Toxic effects

A brief report on mate drinking in Uruguay suggested that some of its pharmacological effects were probably due to its caffeine content (Pronczuk *et al.*, 1987; see also the monograph on caffeine, p. 299).

An endoscopic survey was carried out in southern Brazil by Muñoz et al. (1987) to investigate the presence of lesions of the oesophagus presumed to be precancerous (chronic oesophagitis, atrophy and dysplasia) in relation to mate

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drinking. A total of 120 male unskilled workers were interviewed at their work places on mate intake, alcohol drinking and smoking habits. Of these, 36 were non-mate drinkers or drank mate less than once a week, and they were matched to 36 daily drinkers of similar age, smoking and alcohol drinking habits. Of the 72 subjects selected, 60 (83%) agreed to undergo an endoscopy of the oesophagus during which biopsy samples were taken. The samples were examined independently by two pathologists, who agreed on 57 out the 60. There was virtually no difference in the endoscopic findings in the oesophagi of drinkers and nondrinkers of mate. The presence of histopathological oesophagitis, however — which had been defined *a priori* as the most valid outcome — was 2.2 times more frequent (p < 0.05) among drinkers in an unmatched analysis. A matched analysis showed that this ratio was [3.3].

(iii) *Effects on reproduction and prenatal toxicity* No data were available to the Working Group.

(iv) Genetic and related effects

No data were available to the Working Group.

# 3.3 Case reports and epidemiological studies of cancer in humans

(a) Descriptive epidemiology and cohort studies

No data were available to the Working Group.

(b) Case-control studies

The studies are summarized in Table 3, at the end of this section.

(i) Oesophagus

Vassallo et al. (1985) studied 226 incident cases (185 male, 41 female) of histopathologically confirmed squamous-cell carcinoma of the oesophagus treated at the Oncology Institute of Montevideo, Uruguay, between 1979 and 1984. A total of 469 unmatched controls (386 men, 83 women) with cancers at other sites were obtained from the same institute; these constituted mainly cancers of the skin (24%), colon or rectum (14%) and prostate (11%). Information on sociodemographic variables and on consumption of tobacco, alcohol and mate was obtained during the routine interviews to which patients were submitted prior to diagnostic evaluation. Men who drank more than one litre of mate per day were five times more likely to develop oesophageal cancer than nondrinkers of mate, after adjustment for age, tobacco and alcohol intake. For women, the corresponding age-adjusted relative risk (RR) was 34.6. For men and women together, a clear dose-response relationship was observed. The joint effects of mate and tobacco and of mate and alcohol appeared to be multiplicative. [The Working Group noted that the issue of information bias, reflecting the assumption among health professions that mate drinking is involved in the etiology of oesophageal cancer, was not adequately addressed.]

Victora et al. (1987) studied all cases of oesophageal cancer treated in 11 main hospitals and radiotherapy units in the two largest cities in a southern Brazilian state in 1985-86. Of 190 patients with histologically confirmed squamous-cell carcinoma, 171 (90%) were included in the study (135 male, 36 female). For each case, two sex-, age- and hospital-matched controls were selected, who did not include patients with diseases of the upper gastrointestinal tract or with conditions associated with use of tobacco or alcohol. Cases and controls were interviewed about intake of mate, other hot beverages, alcohol and a number of foodstuffs, as well as on smoking and socioeconomic status. A matched analysis was carried out. Relative to controls, cases had lower socioeconomic status, were more likely to smoke, to drink alcohol and to eat meat, and were less likely to eat fruit. In the crude matched analysis, daily mate drinkers were 1.9 times more likely to have oesophageal cancer than nondaily drinkers (p = 0.006). Dose-response trends with daily intake and with duration of the habit were observed. After adjustment for alcohol consumption, smoking, place of residence and meat and fruit intake, the RR associated with daily drinking of mate was reduced to 1.5 (nonsignificant; one-tailed test). Cases were no more likely than controls to report drinking mate hot or very hot. [The Working Group noted that no data were available to assess whether the range of temperatures was wide enough to permit an informative analysis.]

De Stefani et al. (1990) carried out a case-control study in Uruguay on 261 oesophageal cancer patients (199 male, 62 female) at the four main hospitals in Of 268 patients with histologically confirmed Montevideo in 1985-88. squamous-cell carcinoma of the oesophagus, seven (3%) could not be interviewed. For each case, two controls matched by age, sex and hospital were selected, who did not have a diagnosis of tobacco- or alcohol-related disease; the most common diagnoses among controls were hernia (15%) and diseases of the eye (14%) and gall-bladder (11%). An unconditional analysis was carried out; RRs were adjusted for age, sex, region, alcohol, duration of smoking and type of tobacco. Mate was drunk by 98% of cases and 91% of controls. There was a strong dose-response relationship between the daily amount of mate drunk and the risk of oesophageal cancer; this effect was observed in men and in women. There was also a significant association with the duration of the habit, but the dose-response curve was not as clear as for the daily amount drunk. The authors reported no consistent association between the reported temperature at which mate was drunk and the risk for cancer. [The Working Group noted that the dose-effect relationships within temperature strata (very hot, hot, warm) were evaluated, but the effect of temperature per se was not reported.]

## (ii) Mouth and pharynx

In the case-control study by Franco *et al.* (1989), described in detail on p. 164, a dose-response relationship for oral cancer was observed in a crude matched analysis for daily drinkers of mate in three Brazilian cities; they had a nonsignificant two-fold increase in risk over that in nondrinkers of mate. After adjustment for smoking and alcohol, mate drinking was associated with a nonsignificant RR of 1.6, and no dose-response effect was seen.

In another case-control study from Uruguay, the association between mate drinking and cancer of the oral cavity and pharynx was investigated. A total of 108 male cases of squamous-cell carcinoma of the oral cavity (excluding lip and salivary glands) and of the pharynx admitted to a university hospital in 1985-86 were included; 286 controls from the same hospital with diagnoses other than diseases related to smoking and alcohol consumption were selected. Interviews were carried out by social workers who were unaware of the diagnosis of the patients. A dose-response association between daily intake of mate and risk for oropharyngeal cancer was observed (crude RR, 1.0, 2.8 and 7.8 for < 11 per day, 1-1.991 per day and >2 1 per day). This trend was still present after adjustment for confounding variables (age, smoking and alcohol intake) (De Stefani *et al.*, 1988). [The Working Group noted that no attempt was made to compare the temperature at which mate was drunk by cases and controls.]

#### (iii) Larynx

A case-control study in Montevideo, Uruguay, included 107 histologically confirmed male incident cases of squamous-cell carcinoma of the larynx diagnosed at one hospital and 290 controls selected from the same hospital between June 1985 and May 1986. A questionnaire eliciting information on tobacco, alcohol, diet and mate drinking was administered by three trained interviewers. Controls were patients who had diseases other than those associated with tobacco and alcohol consumption. A significantly increased risk was found for mate drinking *versus* no drinking of mate (RR, 3.4; 95% confidence interval, 1.8-6.6), and there was a significant dose-response relationship after adjustment for age, tobacco and alcohol (De Stefani *et al.*, 1987).

#### (iv) Bladder

A case-control study of 99 male cases of histologically confirmed bladder cancer and two groups each of 99 controls (one hospital, one neighbourhood) identified between March 1983 and December 1985 in La Plata, Argentina, included information on mate, besides coffee and tea drinking. The participation rate was 97% of cases and 96% of controls. Although a significant positive trend with dose was observed for coffee (see p. 127), no such association was found for mate (see Table 3) (Iscovich *et al.*, 1987). [The Working Group noted that no adjustment was made for coffee consumption.]

## 4. Summary of Data Reported and Evaluation

#### 4.1 Exposure data

Mate, an aqueous infusion prepared from dried leaves of *Ilex paraguariensis*, is consumed mainly in Argentina, Bolivia, Brazil, Chile, Ecuador, Paraguay and Uruguay. It is usually drunk very hot following repeated addition of almost boiling water to the infusion; in Paraguay and southwestern Brazil, however, it is also drunk cold. Among numerous constituents, caffeine, theobromine and a number of chlorogenic acids have been identified in mate.

#### 4.2 Experimental carcinogenicity data

No data were available to the Working Group.

#### 4.3 Human carcinogenicity data

Three case-control studies in South America have investigated the association between mate drinking and oesophageal cancer. Two studies from Uruguay reported an increased risk among drinkers and dose-response relationships, even after adjustment for confounding variables, including alcohol consumption and smoking. Heavy drinkers of mate were approximately ten times more likely to develop cancer than people who did not drink mate. Another study in southern Brazil showed a nonsignificant increase in risk for oesophageal cancer among daily drinkers of mate after adjustment for confounding variables; however, intake levels were lower than in the previous studies, and no attempt was made to assess a possible dose-response relationship.

The role of mate in oral cancer was the subject of another case-control investigation in Brazil. The crude analysis showed a dose-response effect with the frequency of mate drinking, but this effect was no longer present after adjustment for smoking and alcohol consumption. After such adjustment, mate drinkers were 1.6 times more likely to have oral cancer than nondrinkers of mate — a nonsignificant difference. A case-control study from Uruguay reported a dose-response association between mate drinking and oropharyngeal cancer, which remained after adjustment for age, alcohol and smoking.

Reference, location	Site	Subjects (cases, controls)	Mate consumption	Relative risk (95% CI)	Comments
Vassallo <i>et al.</i> (1985) Uruguay	Oesophagus	Men (185, 386)	None 0.01-0.49 l/day 0.50-0.99 l/day ≥ 1 l/day	1.0 1.1 (0.2–5.0) 3.1 (1.2–7.8) 4.8 (1.9–12.1)	p < 0.001; adjusted for age, tobacco and alcohol consumption
		Women (41, 83)	None 0.01–0.49 l/day 0.50–0.99 l/day ≥ 1 l/day	1.0 2.1 (0.1–31.7) 12.5 (2.0–80.1) 34.6 (4.9–246.5)	p < 0.001; adjusted for age
Victora <i>et al.</i> (1987) Brazil	Oesophagus	Men and women (171, 342)	Less than daily Daily	1.0 1.5 (0.9–2.5)	Nonsignificant; adjusted for alcohol, smoking, residence, fruit and meat intake; 90% confidence interval
De Stefani <i>et al.</i> (1990) Uruguay	Oesophagus	Men and women (261, 522)	None 0.01-0.49 l/day 0.50-1.49 l/day 1.50-2.49 l/day ≥ 2.50 l/day	1.0 2.5 (0.8–8.4) 3.6 (1.3–9.9) 6.1 (2.1–17.3) 12.2 (3.8–39.6)	Adjusted for age, sex, region, alcohol and smoking
Franco <i>et al.</i> (1989) Brazil	Mouth	Men and women (232, 464)	< 1 cup/month 1-30 cups/month > 30 cups/month	1.0 1.6 (0.8–3.3) 1.6 (0.8–3.3)	Nonsignificant; adjusted for alcohol and smoking
De Stefani <i>et al.</i> (1988) Uruguay	Oral cavity and pharynx	Men (108, 286)	< 1 l/day 1.0−1.99 l/day ≥2 l/day	1.0 2.5 (1.1–5.7) 5.2 (2.1–13.1)	p < 0.001; adjusted for age, smoking and alcohol

Table 3. Summary of results of case-control studies on cancer and mate consumption

Reference, location	Site	Subjects (cases, controls)	Mate consumption	Relative risk (95% CI)	Comments
De Stefani <i>et al.</i> (1987) Uruguay	Larynx	Men (107, 290)	0.0-0.49 l/day 0.5-0.99 l/day 1.0-1.49 l/day ≥1.5 l/day	1.0 3.2 (0.9-10.3) 2.6 (0.8-8.2) 4.9 (1.7-14.3)	p < 0.001; adjusted for age, tobacco and alcohol
Iscovich <i>et al.</i> (1987) Argentina	Bladder	Men (99, 198)	None <10 drinks/day 10−19 drinks/day ≥20 drinks per day	1.0 2.0 0.9 0.8	Trend not significant; adjusted for age and smoking

# Table 3 (contd)

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One study from Uruguay reported a three-fold increased risk for laryngeal cancer among mate drinkers, with a significant dose-response relationship after adjustment for age, tobacco and alcohol.

The results of a case-control study of bladder cancer in Argentina showed no evidence of trend in risk with increasing consumption of mate.

Overall, the case-control studies on mate drinking and cancer of the upper gastrointestinal tract suggest a strong association, whereas no such association was seen in one study of bladder cancer. These findings would be compatible with an effect of mate drinking due either to the composition of the beverage or to the temperature at which it is consumed or both, since all of these studies were conducted in populations that consume hot mate. No data were available on populations that drink cold mate. Some issues must be resolved before a conclusive result is obtained: (i) Awareness of the possibility that mate drinking may increase the risk for cancer of the upper gastrointestinal tract may have led to increased reporting of mate drinking for cancer cases as compared to controls. (ii) The results require confirmation by other groups of investigators. (iii) The possibility of residual confounding by alcohol drinking and tobacco smoking cannot be excluded entirely, although this was adjusted for in all of the studies.

## 4.4 Other relevant data

An endoscopic survey from southern Brazil showed that daily drinkers of hot mate had a prevalence of histologically confirmed oesophagitis which was three times higher than that of nondrinkers of mate.

#### 4.5 Evaluation<sup>1</sup>

There is *limited evidence* for the carcinogenicity of hot mate drinking in humans. No data were available on the drinking of cold mate.

There are no data on the carcinogenicity of mate in experimental animals.

#### **Overall evaluation**

Mate is not classifiable as to its carcinogenicity to humans (Group 3). Hot mate drinking is probably carcinogenic to humans (Group 2A).

<sup>&</sup>lt;sup>1</sup>For description of the italicized terms, see Preamble, pp. 27-31.

## 5. References

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