Pigment Red 172

Ingredient synonym names

FD&C Red No. 3-aluminum lake
11150 Dispersed Pink
Acid Red 51:1
Ariabel Rose 300504
C.I. 45430:1
C.I. Acid Red 51:1
C.I. Food Red 14:1
C.I. Pigment Red 172
Certolake erythrosine
Erythrosine-aluminum lake
Food Red 14:1
Food Red No. 3-aluminum lake
Japan Food Red No. 3 aluminum lake
Japan Red 3 aluminum Lake

IDENTIFIER DETAILS

Ingredient chemical structure

CAS Number	FEMA Number	Additive Number
12227-78-0	-	-

Ingredient EC Number	FL Number	CoE Number
235-440-4	-	-

Chemical formula C20H8I4O5.2/3Al

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

Pigment Red 172

0	0	0

SPECIFICATIONS

Melting Point	Unavailable	Boiling Point	Unavailable

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg)	0.1 mg/kg (EFSA, 2011)
Acceptable Daily Intake (ADI) comments	-
FDA Status	CFR21 74 - LISTING OF COLOR ADDITIVES SUBJECT TO CERTIFICATION 74.303- FD&C Red No. 3. 74.1303 - FD&C Red No. 3. 81 - GENERAL SPECIFICATIONS AND GENERAL RESTRICTIONS FOR PROVISIONAL COLOR ADDITIVES FOR USE IN FOODS, DRUGS, AND COSMETICS 81.10 - Termination of provisional listings of color additives. 81.30 - Cancellation of certificates. 176 - INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS 176.170 - Components of paper and paperboard in contact with aqueous and fatty foods.

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

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

The literature contains no data to suggest that pigment red 172 occurs in nature.

References - Ingredient Natural Occurence

No data identified

Ingredient Reported Uses

It is used as a food colouring, in printing inks, as a biological stain, a dental plaque disclosing agent and a radiopaque medium. Erythrosine is commonly used in sweets such as some candies and popsicles, and even more widely used in cake-decorating gels. It is also used to colour pistachio shells. As a food additive, it has the E number E127. In Europe erythrosine is exclusively authorised for use in cocktail, candied Bigarreaux cherries (94/36/EC).

References - Ingredient Reported Uses

No data identified

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

No data identified

In Vivo Carcinogenicity/Mutagenicity

The Scientific Panel on Food Additives and Nutrient Sources added to Food has re-evaluated the safety of Erythrosine (E 127) when used as a food colouring substance. The Panel considered the weight-of-evidence still showed that the tumorigenic effects of Erythrosine in the thyroid gland of rats are secondary to its effects on thyroid function and not related to any genotoxic activity. Erythrosine-induced rodent thyroid tumours may be considered of limited relevance to humans; an approach which is consistent with previous evaluation of Erythrosine [EFSA, 2011].

In a study conducted by Borzelleca et al., (1987) Charles River CD-1 mice were fed FD & C Red No. 3 in the diet at levels of 0.3, 1.0 and 3.0% in a long-term toxicity/carcinogenicity study. Each group consisted of 60 males and 60 females. Two concurrent control groups each of 60 males and 60 females received the basal diet. Maximum exposure was 24 months. The no-adverse-effect levels established in this study were 3.0% (an average intake of 4759 mg/kg/day) for male mice and 1.0% (1834 mg/kg/day) for female mice.

FD&C Red No.3 (erythrosine) has been used as a dye in foods, drugs and cosmetics since its approval by the US Department of Agriculture in 1907. In 1977 the Certified Color Manufacturers' Association (CCMA) initiated studies on FD&C Red No.3 including chronic toxicity and carcinogenicity studies in rats and mice. Data from the CCMA chronic studies revealed an increased incidence of thyroid follicular cell hyperplasia and adenomas in male rats that received 4% FD&C Red No.3 in the diet (2464 mg/kg/day) during life-time (30 months) following in utero exposure (Lin et al., 1986).

References - In Vivo Carcinogenicity/Mutagenicity

Borzelleca JF, Hallagan JB. (1987). Lifetime toxicity/carcinogenicity study of FD & C Red No. 3 (erythrosine) in mice. Food Chem Toxicol. Oct;25(10):735-7.

EFSA (2011). http://www.efsa.europa.eu/en/efsajournal/pub/1854.htm. Last accessed 26th March 2012

Dermal Toxicity

No data identified.

References - Dermal Toxicity

No data identified.

Reproductive/ Developmental Toxicity

In a study conducted by Borzelleca et al., (1987) FD & C Red No. 3 was fed to Charles River CD rats as a dietary mixture in two long-term toxicity/carcinogenicity studies. The studies consisted of an in utero and an F1 phase. In the former, the compound was administered to five groups of the F0 generation rats (60 of each sex/group) at levels of 0.0, 0.0, 0.1, 0.5 or 1.0% ('original study') and 0.0 or 4.0% ('high-dose study'). The concurrent control groups received the basal diet. After random selection of the F1 animals, the long-term phase was initiated using the same dietary levels and 70 rats of each sex/group, including the three control groups. Rats were exposed for a maximum of 30 months. No compound-related effects were noted in the in utero phase. Mean body weights of the

female F1 rats on 4.0% FD & C Red No. 3 (3029 mg/kg/body weight/day) were significantly lower than those of controls (P less than 0.01) throughout the study. Food consumption increased in all treated groups in a dose related manner. There were no significant effects on the haematology, serum chemistry and urinalysis and no compound-related effects on survival. In male rats receiving 4.0% FD & C Red No. 3 (2464 mg/kg/day) thyroid weights were increased, with a mean weight of 92 mg compared to 44 mg for controls, and statistically significant increases in the incidence of thyroid follicular cell hypertrophy, hyperplasia and adenomas were recorded. A numerically increased incidence of thyroid follicular adenomas in female rats given 0.5, 1.0 or 4.0% FD & C Red No. 3 was not statistically significant. The no-observed-adverse-effect levels established in these studies were 0.5% (251 mg/kg/day) for male rats and 1.0% (641 mg/kg/day) for females.

References - Reproductive/ Developmental Toxicity

Borzelleca JF, Capen CC, Hallagan JB. (1987). Lifetime toxicity/carcinogenicity study of FD & C Red No. 3 (erythrosine) in rats. Food Chem Toxicol. Oct;25(10):723-33.

Inhalation Toxicity

No data identified.

References - Inhalation Toxicity

No data identified.

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 Scientific Panel on Food Additives and Nutrient Sources added to Food has re-evaluated the safety of Erythrosine (E 127) when used as a food colouring substance. Erythrosine (E 127) is a xanthene-dye which has been previously evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1990 and the EU Scientific Committee for Food (SCF) in 1989. Both committees have established an Acceptable Daily Intake (ADI) of 0-0.1 mg/kg bw/day. Erythrosine is exclusively authorised for use in cocktail and candied cherries, and Bigarreaux cherries (94/36/EC). The Panel considered the weight-of-evidence still showed that the tumorigenic

effects of Erythrosine in the thyroid gland of rats are secondary to its effects on thyroid function and not related to any genotoxic activity. Erythrosine-induced rodent thyroid tumours may be considered of limited relevance to humans; an approach which is consistent with previous evaluation of Erythrosine. The Panel considered Erythrosine has a minimal effect in humans at a clinical oral dose of 200 mg daily over 14 days, while a dose of 60 mg daily was without effect (Gardner et al., 1987). The current ADI adopted by the JECFA and the SCF is based on this study. The Panel concurred with their identification of this as the critical study. The 60 mg dose was taken to be the equivalent of 1 mg/kg bw/day. By applying a safety factor of 10 to allow for the small number of subjects used in the study and its relatively short duration, an ADI of 0-0.1 mg/kg bw per day was derived. The Panel concludes that the present database does not provide a basis to revise the ADI of 0.1 mg/kg bw/day. The Panel concluded that at the current levels of use intake estimates for adults on average is 0.0031 mg/kg bw/day and 0.01 mg/kg bw/day at the 95th percentile, and consequently are below the ADI of 0.1 mg/kg bw/day. The Panel considered there would be no safety concerns at current levels of exposure including other sources of exposure (EFSA, 2011).

Approximately equal numbers of male and female Mongolian gerbils, Meriones unguleulatus, were given erythrosine (FD & C Red No. 3) by diet and by oral intubation. In the dietary study, four groups evenly divided by sex were treated for 105 weeks at levels of 0, 1, 2 or 4%. In the intubation study, four groups were intubated by stomach tube twice weekly for 97 weeks with an aqueous solution at levels of 0, 200, 70 or 900 mg/kg. Clinical effects of dietary administration were depression of loss of weight, ranging from mild in groups fed 1% to marked in groups fed 4%. The dietary study also shoed that dose-related changes occure in the thyroid of animals fed the 1-4% diets. These changes were characterized by the enlargement, with increased storage of colloid, of a majority of the follicles, associated with less prominent but consistent foci of very small follicles (microfollicles) and, in a few animals, focal hyperplasia and intralumina and interstitial leucocytic infiltration. Although intubation, a definite effect similar to that in the dietary study was not found. Evaluation of the primarily of epitheloid cells surrounded by lymphocytes. Although special diagnostic procedures, including stains for micr-organisms, failed to identify the cause, a microbial aetiology was suspected, as this is most common for this type of lesion. In both studies, there was more granulomatosis in the controls than in the treated animals, but in the intubation study there was no evidence of a relation to dose, [Collins et al., 1976].

References - In Vivo - Other Relevant Studies

Collins et al., (1976). Effects of chronic oral administration of erythrosine in the Mongolian gerbil. Food. Cosmet. Toxicol. 14: 233-248.

EFSA (2011). http://www.efsa.europa.eu/en/efsajournal/pub/1854.htm. Last accessed 26th March 2012.

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

In a report by Lin et al., 1986, results of published studies on the mutagenicity of FD&C Red No.3 are critically reviewed. Additional mutagenicity tests including Ames Salmonella/microsome assay, L5178Y TK+/- mouse lymphoma assay, mouse micronucleus test and mitotic recombination assay with yeast Saccharomyces cerevisiae strain D5 are described. These test results together with the literature review indicate that FD&C Red No.3 can be considered non-mutagenic across several genetic endpoints including gene mutation, chromosome aberrations, primary DNA damage and cell transformation. The results of the genotoxicity assessment generally exclude FD&C Red No.3 as a genotoxic initiator and suggest that some other mechanism is responsible for the increase in tumors (Lin et al., 1986).

References - In Vitro Carcinogenicity/Mutagenicity

Lin GH, Brusick DJ. (1986). Mutagenicity studies on FD&C red No.3. Mutagenesis. 1986 Jul;1(4):253-9.

In Vitro - Other Relevant Studies

No data identified.

References - In Vitro - Other Relevant Studies

No data identified.

Emissions and Associated Toxicity Data

No data identified.

References - Emissions and Associated Toxicity Data

No data identified.