**Table 15 (contd)**

| Country or region | Concentration (ppm) [mg/m$^3$] | Interpretation | Carcinogen classification |
|---|---|---|---|
| United Kingdom (OES) | 25 | TWA | Sk |
| | 50 | STEL | Sk |
| USA | | | |
| ACGIH (TLV) | 20 | TWA | A3[b] |
| NIOSH (REL) | 5 | TWA | Sk |
| OSHA (PEL) | 50 | TWA | Sk |

From Arbejdstilsynet (2002); Health & Safety Executive (2002); Työsuojelusäädöksiä (2002); Deutsche Forschungsgemeinschaft (2003); Suva (2003); ACGIH Worldwide (2004); European Union (2004); INRS (2005)
MAC/MAK, maximum allowable concentration; OES, occupational exposure standard; PEL, permissible exposure limit; REL, recommended exposure limit; STEL, short-term exposure limit; TLV, threshold limit value; TWA, full-shift time-weighted average
[a] Sk, skin notation
[b] A3, confirmed animal carcinogen with unknown relevance to humans

# 3. Studies of Cancer in Experimental Animals

## 3.1 Inhalation

### 3.1.1 *Mouse*

Groups of 50 male and 50 female B6C3 $F_1$ mice, 7–8 weeks of age, were exposed to 2-butoxyethanol (> 99% pure) vapour by whole-body exposure at concentrations of 0, 62.5, 125 or 250 ppm [0, 302, 604 or 1208 mg/m$^3$] for 6 h per day on 5 days per week for 104 weeks. Complete necropsies were performed on all mice, at which time all organs and tissues were examined for macroscopic lesions and all major tissues were examined microscopically. Survival of male mice exposed to 125 or 250 ppm was significantly lower (by pair-wise comparison) than that of the control group (39/50 controls, 39/50 low-dose, 27/50 mid-dose ($p = 0.021$) and 26/50 high-dose ($p = 0.015$)). In females, survival was not affected (29/50 controls, 31/50 low-dose, 33/50 mid-dose and 36/50 high-dose). The body weights in control and treated animals were comparable except in high-dose female mice in which a 17% decrease in body weight was observed. In males, the incidences of haemangiosarcoma of the liver were: 0/50 (control), 1/50 (low-dose), 2/49 (mid-dose) and 4/49 (high-dose). The incidence in high-dose males (250 ppm) was significantly increased ($p = 0.046$, Poly-3 test) relative to controls and the trend test was positive ($p = 0.014$, Poly-3 test); this incidence exceeded the range in the historical control values (0–4%). Two of the four mice treated with 250 ppm that had liver haemangiosarcomas also had

haemangiosarcomas in either the bone marrow and heart or bone marrow and spleen; it was not possible to determine whether these were primary or metastatic tumours. One liver haemangiosarcoma developed in a low-dose female mouse. In female mice, dose-related increases in the incidence of forestomach squamous-cell papilloma were observed (0/50 control, 1/50 low-dose, 2/50 mid-dose and 5/50 high-dose). There was a single forestomach squamous-cell carcinoma in the high-dose group only. The combined incidence of forestomach squamous-cell papillomas and carcinoma was significantly increased ($p = 0.034$, Poly-3 test) in the high-dose group (250 ppm) and the trend was positive ($p = 0.002$; Poly-3 test); the incidence exceeded the range (0–3%) in historical controls. In males, the incidences of forestomach squamous-cell papillomas were 1/50 control, 1/50 low-dose, 2/49 mid-dose and 2/49 high-dose animals. One squamous-cell carcinoma developed in the mid-dose group. The incidence in treated males was not significantly different from that in controls. Accompanying these neoplasms in females and, to a lesser extent, in males were exposure-related increases in the incidences of ulcer and epithelial hyperplasia of the forestomach. In addition, there was a possible exposure-related increase in the incidence of hepatocellular carcinoma in high-dose males (control, 10/50; low-dose, 11/50; mid-dose, 16/49; and high-dose, 21/49; $p \leq 0.01$, Poly-3 test) (National Toxicology Program, 2000).

### 3.1.2 *Rat*

Groups of 50 male and 50 female Fischer 344/N rats, 7–8 weeks of age, were exposed to 2-butoxyethanol (> 99% pure) vapour by whole-body exposure at concentrations of 0, 31.2, 62.5 or 125 ppm [0, 151, 302 or 604 mg/m$^3$] for 6 h per day on 5 days per week for 104 weeks. Complete necropsies were performed on all rats, at which time all organs and tissues were examined for macroscopic lesions and all major tissues were examined microscopically. No exposure-related adverse effects on survival were observed. The survival rates in males were 19/50 (control), 11/50 (low-dose), 21/50 (mid-dose) and 24/50 (high-dose), and those in females were 29/50 (control), 27/50 (low-dose), 23/50 (mid-dose) and 21/50 (high-dose). No exposure-related increases in the incidence of tumours was found in males. In females, the incidences of benign pheochromocytomas in the adrenal medulla were 3/50 (control), 4/50 (low-dose), 1/49 (mid-dose) and 7/49 (high-dose). In addition, one malignant pheochromocytoma developed in the high-dose (125-ppm) group. The combined incidence of benign and malignant tumours in females had a positive trend ($p = 0.044$, Poly-3 test); however, the incidence in females exposed to 125-ppm was not significantly increased relative to that in concurrent controls, but slightly exceeded the range for historical controls (2–13%) from 2-year inhalation studies. Overall, the slight increase in incidences of pheochromocytomas was considered to be an equivocal finding and could not be attributed with certainty to exposure to 2-butoxyethanol (National Toxicology Program, 2000).