

DRAFT EH64 ENTRY FOR CHLOROBENZENE

8-hour TWA:	1 ppm
15-minute STEL:	3 ppm
Notation:	Skin

IDENTITY AND PROPERTIES

CAS No:	108-90-7
EC No:	203-628-5
Empirical formula:	C ₆ H ₅ Cl
Synonyms:	Benzene chloride, chlorobenzol, monochlorobenzene, MCB, phenyl chloride
Vapour pressure:	1.14 kPa at 20°C
Melting point:	-44.9°C
Boiling point:	131.6°C
MWt:	112.56
Conversion factor:	1 ppm = 4.68 mg.m ⁻³ (20°C, 101 kPa)

Chlorobenzene is a colourless liquid with a mild aromatic odour. It has a vapour density 3.88 times that of air and is explosive in the range 1.3 - 7.1% in air. The odour threshold is about 0.21 ppm (0.98 mg.m⁻³).

CLASSIFICATION AND LABELLING

Chlorobenzene is classified in the Approved Supply List. This list is taken directly from Annex I to the Dangerous Substances Directive (67/548/EEC). Annex I is a list of dangerous substances for which harmonised classification and labelling have been agreed at a Community level in accordance with the procedure laid down in the Directive. Information on the classification and labelling assigned to this substance and any specific concentration limits that may be applicable can be found at: <http://ecb.jrc.it/classification-labelling/>. More information about the current UK Chemicals (Hazard Information for Packaging and Supply) Regulations can be found at: <http://www.hse.gov.uk/chip/index.htm>.

OCCURRENCE AND USE

Chlorobenzene is not manufactured in the UK and is only used as a process solvent or chemical intermediate and as a laboratory reagent. Approximately 20 companies use

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chlorobenzene as a process solvent or chemical intermediate. The numbers exposed during its use in the chemical industry is estimated to be between 100 and 300. The numbers exposed during its use as a laboratory reagent could be more, however, such workers are likely to have very infrequent exposures.

EXPOSURE

Of 38 reported personal air sampling results from a user of chlorobenzene, one was at 3 ppm 8-hour TWA, the others all below 1 ppm. Earlier results at one chemical site were up to 6 ppm 8-hour TWA, with 83% of results less than 1 ppm 8-hour TWA. At another site the highest personal air sampling result was 0.2 ppm 8-hour TWA. The highest exposure data received was from a company who used chlorobenzene until the end of 1998 as a chemical intermediate. Exposures were up to 329 ppm for the duration of the task (1 to 2 hours) and 59 ppm when time weighted over the 8 hour shift. Peak exposure concentrations would have been higher than these values.

Exposure data modelled with the Estimation and Assessment of Substance Exposure (EASE) model gave predictions for short-term exposures of 4.6 to 6.7 ppm 15-min TWA for sampling, 1.3 to 50 ppm 15-min TWA for tanker unloading, and 1 to 100 ppm 15-min TWA for vessel charging. These are likely to be overestimates and actual exposures in such operations will be dependent on the nature of the controls in place. The above short-term exposure compares reasonably well with the full shift exposure. For example, 3.5 ppm 8-hour TWA for a worker exposed during tanker unloading (30 minutes) and quality control sampling (2 periods of 15 minutes). Occupational exposure during repackaging of chlorobenzene and laboratory use are thought to be generally lower than the above values.

It is therefore concluded that exposure is generally below 50 ppm 8-hour TWA and in most cases below 10 ppm 8-hour TWA. It is further concluded that the data demonstrates that it is likely that control to less than 5 ppm 8-hour TWA is reasonably practicable. Although exposures of higher than this have been obtained it was not felt that these represented the majority of exposures and what it is reasonably practicable to achieve. Indeed the most recent data that HSE holds suggests that most results are below 1 ppm.

There is little information about short-term exposures. Short term exposures of up to 100 ppm 15-min TWA were modelled using EASE. However, the higher values represented only modest standards of control being in operation. If realistic but more stringent controls are incorporated, the model predicts exposures below 10 ppm.

Dermal exposure can occur during the use of chlorobenzene, where operators come into contact with surfaces contaminated from splashing or condensed vapour, or as a result of direct contact onto the skin. During its use in chemical plants, where it is used in generally closed systems, dermal exposure is only likely during activities such as sampling and the uncoupling of pipes. A range of 0 to 0.1 mg.cm⁻².day⁻¹ was predicted using EASE assuming that there may be at most incidental (i.e. one significant) contact in a shift. However, on most days no such accidental contacts will occur and exposure will be towards the bottom of this range.

ATMOSPHERE MEASUREMENT

Indicating colourimetric tubes for short-term measurements of chlorobenzene in air are commercially available and capable of detecting 0.5 ppm. Other chlorinated hydrocarbons can interfere with different sensitivities. Real-time instruments with infra-red or photo-acoustic detection that can detect less than 1 ppm are also available. Personal exposure to vapour in air can be measured by pumped sampling on charcoal tubes (solvent desorption method NIOSH 1003)¹ or Tenax (thermal desorption method MDHS 72)² and analysis by gas chromatography. Earlier NIOSH data published as method S133³ suggests that the carbon tube method, with carbon disulphide and coconut shell charcoal, may not meet the >75% desorption efficiency criterion below 5 ppm at the maximum sample volume of 40 litres. This factor is sensitive to the type of carbon and the addition of solvent modifiers. Synthetic carbons perform better than coconut shell charcoal with respect to desorption efficiency.

OSHA have indicated a preference for 1% dimethylformamide in carbon disulphide⁴. With respect to other factors, solvent desorption methods would generally comply with EN 482⁵ on overall uncertainty and with EN 1076⁶ on environmental effects above 5 ppm. The pumped thermal desorption method MDHS 72 has a detection limit of <0.02 ppm for a 10 litre sample. MDHS 72 has been partially validated for chlorobenzene and is likely to comply with EN 482 and EN 1076 for both long-term and short-term sampling at <1 ppm where desorption efficiency was >97%. Diffusive sampling is feasible on carbon-type badge devices with solvent desorption (MDHS 88)⁷. However, uptake rates are generally lower than pumped flow-rates and the desorption efficiency criterion of >75% may not be met below 15 ppm for 8 hours. Carbon-type diffusive badges are unlikely to be suitable for 15 minute sampling below 25 ppm. Users must verify the solvent desorption efficiency of chlorobenzene with their chosen collection medium, otherwise their procedure may not comply with EN 1076 or EN 838⁸ at low concentrations. Thermal desorption diffusive tube samplers are feasible (MDHS 80)⁹ and have adequate sensitivity for the measurement of <0.1 ppm for 8-hr sampling and of <3 ppm for 15 minute sampling.

BIOLOGICAL MONITORING

Biological monitoring may be a useful aid to the assessment of occupational exposure to chlorobenzene. There are no data to relate metabolite concentrations to health effects but there are data to show a good correlation between levels of 4-chlorocatechol in urine samples collected at the end of shift and inhaled chlorobenzene. After exposure to chlorobenzene at 1 ppm for 8 hours, the urine concentration of 4-chlorocatechol would be around 5 mmol.mol⁻¹ creatinine (6.4 mg.g⁻¹). Elimination of 4-chlorocatechol in urine is biphasic with half-lives of 2.2 and 17.3 hours.

There are several methods for the determination of 4-chlorocatechol in urine^{10,11,12,13}. All are based on hydrolysis of glucuronide and sulphate conjugates of 4-chlorocatechol and HPLC with UV detection. The most recent and well validated method is that of Heinrich-Ramm. This method was developed and evaluated to support the DFG biological monitoring programme.

Briefly: the method hydrolyses 5ml of urine, containing 3-ethylphenol internal standard, in 25% HCl at 90°C for 2 hours and after cooling extracts the chlorocatechol into diethyl ether. The ether extract is transferred to a clean vial and the ether removed under nitrogen. The residue is redissolved in HPLC mobile phase and injected into a C₁₈ column at 34 °C. Detection is at 205 nm. The method is linear from 0.5 mg.l⁻¹ to 50 mg.l⁻¹ with a detection limit of 0.1 mg.l⁻¹ and a coefficient of variation for within-day imprecision of 2.3% and a day to day imprecision of 4.9%. No interfering peaks have been found in chromatograms at levels greater than 0.5 mg.l⁻¹ from people not occupationally exposed to chlorobenzene.

TOXICOKINETICS¹⁴

Few data on the toxicokinetics of chlorobenzene in humans are available. The data which are available relate to metabolism and excretion. The available animal data largely relate to the inhalation and oral routes of exposure. There are no data regarding the dermal route of exposure.

Human and animal studies show that chlorobenzene is absorbed to a substantial extent via the oral and inhalation routes, but do not allow quantification of absorption via these routes. From the physico-chemical properties of chlorobenzene and by analogy with other chlorobenzenes it is predicted that chlorobenzene will be readily absorbed via the dermal route.

Following absorption, chlorobenzene is distributed throughout the body, principally to the fat, liver, lungs and kidneys. Given the lipid solubility of chlorobenzene it is likely to accumulate in body fat, although this may depend on the extent of metabolism.

Comparative *in vitro* studies suggest qualitatively similar metabolic profiles in rats, mice, rabbits, guinea-pigs and humans. *In vitro* data also indicate that human liver microsomes are twice as efficient as mouse liver microsomes in metabolising chlorobenzene and also that

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human liver microsomes have a greater affinity for chlorobenzene than mouse liver microsomes.

In vitro and *in vivo* human and animal data indicate that chlorobenzene is initially oxidised by the microsomal cytochrome P450 system to a reactive arene oxide, which has the potential to bind with rat and mouse liver, kidney and lung DNA, RNA and proteins.

The arene oxide is subsequently converted either via non-enzymic reactions to 3 and 4 isomers of chlorophenol or via enzymic activity to a glutathione (GSH) conjugate or to dihydrodiol derivatives. The GSH conjugates are either eliminated unchanged in the faeces or are transformed to more water soluble products and are excreted in the urine as 4-chlorophenylmercapturic acid. The dihydrodiol derivatives are converted principally to 4-chlorocatechol and to a lesser extent to 3-chlorocatechol which are also excreted in the urine. Animal and human studies have shown that excretion of chlorobenzene and/or its metabolites in the urine is rapid (within 24 hours). In instances of high exposure concentrations, both inhalatory and orally, unchanged chlorobenzene has also been detected in expired air, the proportion of chlorobenzene exhaled increasing with increasing exposure concentration, indicating saturation of metabolism.

HEALTH EFFECTS¹⁴

Animal studies

Chlorobenzene is of moderate acute toxicity in rats and mice following single inhalation exposures of chlorobenzene vapour, with 6-hour LC₅₀ values of around 2780 ppm and 1840 ppm in rats and mice respectively. Chlorobenzene is of low acute toxicity following single oral exposure in rats, rabbits and guinea-pigs, with LD₅₀ values of >2250 mg.kg⁻¹. The mouse however appears to be slightly more sensitive following single oral exposures, with LD₅₀ values in the range 1400 - 2300 mg.kg⁻¹. Chlorobenzene is of low acute toxicity in the rabbit following single dermal exposures with LD₅₀ values of >2000 and >7500 mg.kg⁻¹ being identified.

Signs of acute toxicity in animals exposed to chlorobenzene via all routes include hyperaemia of the mucous membranes, increased salivation and lacrimation and evidence of disturbance of the central nervous system. Pathological findings of hypertrophy and necrosis of the liver and of the proximal tubules of the kidneys are reported. In all acute exposure studies, death generally occurred as a result of respiratory failure.

Limited animal data indicate that direct contact with liquid chlorobenzene is irritating to the skin but only mildly irritating to the eyes. No useful data are available regarding the potential of chlorobenzene to cause irritation to the respiratory tract. However, given the skin/eye irritancy it is possible that chlorobenzene could cause respiratory tract irritation.

Chlorobenzene did not induce skin sensitisation in a guinea-pig maximisation study. There are no data regarding the potential of chlorobenzene to cause respiratory tract sensitisation.

With respect to repeated dose toxicity, animal data indicate that the liver, kidneys and possibly the haematopoietic tissues are the target organs of chlorobenzene toxicity.

Inhalation studies demonstrate that in rats no effects on the liver occurred following chlorobenzene exposures of up to 75 ppm for 24 weeks^{15,16}. At 250 ppm for 24 weeks and at 150 and 450 ppm for ~22 weeks liver weights were increased by 13 to 36% compared with controls with evidence of minimal to moderate hepatocellular hypertrophy in males at 150 and 450 ppm for ~22 weeks but not in animals at 250 ppm for 24 weeks^{15,16}. In dogs no adverse liver effects were observed following exposures to 165 or 300 ppm for 90 days. Decreased liver weights (magnitude not reported) and vacuolisation of the hepatocytes were reported following exposures to 440 ppm for 90 days. No adverse liver effects were reported in rabbits at exposures of up to 250 ppm for 24 weeks.

Data from 90-day and 2-year oral gavage studies in both rats and mice suggest that the liver changes induced are similar to those following inhalation exposure but also indicate a

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sensitive marker for chlorobenzene-induced liver changes is elevated levels of urinary porphyrin^{17,18}. No adverse liver effects, including changes in porphyrin levels were observed in either species at doses of 60, 125 or 250 mg.kg⁻¹.day⁻¹ for 90 days. At 500 and 750 mg.kg⁻¹.day⁻¹ for 90 days increased liver weights (up to ~100%), increased urinary porphyrin levels and centrilobular hepatocellular degeneration were observed in rats (all mice in these test groups had died). No evidence of liver damage was reported in rats in a 2-year study at doses up to 120 mg.kg⁻¹.day⁻¹ (the highest dose tested) or in mice at 60 mg.kg⁻¹.day⁻¹. In male mice and only at 120 mg.kg⁻¹ bw.day⁻¹ an increased incidence of neoplastic nodules in the liver was observed. No evidence of liver toxicity in dogs was reported to occur in animals administered 27 mg.kg⁻¹ bw.day⁻¹ for 13 weeks. Hepatotoxicity (nature and severity not reported) was reported in dogs administered 54 and 273 mg.kg⁻¹.day⁻¹ for 90 days.

Although data from a 2-year oral study in mice clearly indicate a NOAEL for liver effects of 60 mg.kg⁻¹ bw.day⁻¹ hepatotoxicity (not specified) was reported in dogs at 54 mg.kg⁻¹.day⁻¹ for 90 days. Overall therefore, it is not possible to identify a clear NOAEL for the liver effects resulting from chlorobenzene exposure.

Kidney damage was observed in male rats (increased incidence of tubular and interstitial kidney lesions and proximal tubule degeneration, regeneration & necrosis) and in the dog (cytoplasmic vacuolisation of the epithelium of the collecting tubules or unspecified histopathological changes) following both inhalation and oral exposures, and in the mouse following oral exposure (proximal tubule degeneration, regeneration & necrosis). However in each species the kidney effects were only manifest at exposure concentrations or doses equal to or greater than those inducing liver damage. No evidence of kidney damage was reported in the available rabbit inhalation study.

Animal data also indicate that haematological changes occur in rats, mice, rabbits and dogs following inhalation exposures to chlorobenzene, and in rats, mice and dogs following oral exposures. The inhalation data suggest that the mouse is the more sensitive species with respect to the development of haematological changes.

Data from the available repeated rat inhalation study show no haematological changes following exposure to 75 ppm for 11 or 24 weeks (the 11 week time-point being an interim sacrifice in the 24 week study). Haematological changes were observed in the same study in animals at 250 ppm both at 11 and 24 weeks; changes reported were in PMNs, platelets, white blood cell, reticulocyte and monocyte numbers. In the two available rat oral studies (a 90-day and a 2-year study) in which haematological analysis was conducted (no interim analyses were conducted in either study), no haematological changes were reported at dose levels of 60, 120 (the top-dose tested) mg.kg⁻¹.day⁻¹ for 2 years or at 60, 125 or 250 mg.kg⁻¹.day⁻¹ for 90 days. An increased mortality rate in animals administered 500 mg.kg⁻¹.day⁻¹ for 90 days limited the extent of haematological analyses conducted, consequently no adverse findings in standard haematological parameters were reported. However at necropsy an increased incidence of myeloid depletions in bone marrow were observed in these animals. In animals administered 750 mg.kg⁻¹.day⁻¹ for 90 days, (the increased mortality rate did not limit haematological analyses in this group) reduced white blood cell and reticulocyte counts and lymphoid and/or myeloid depletions in thymus, spleen and bone marrow were reported.

In the repeated inhalation study in mice, haematological effects (changes in white blood cell, lymphocyte, monocyte and neutrophil numbers) were observed at exposures of 21 ppm for 3 months and at 550 ppm for 3 weeks¹⁹. As these were the only concentrations and time points investigated a no effect level cannot be identified for haematological changes in the mouse exposed via inhalation. No changes in standard haematological parameters were reported in the animals at doses of up to 250 mg.kg⁻¹.day⁻¹ for 90 days, or up to 120 mg.kg⁻¹.day⁻¹ for 2 years (the top-dose tested). However, blood analysis was only conducted at the end of the dosing period in both of these studies. In the 90-day study, animal deaths prevented blood analysis at the higher doses (500 and 750 mg.kg⁻¹.day⁻¹). However, at necropsy evidence of mild to moderate myeloid depletions of the bone marrow and minimal to moderate lymphoid necrosis or depletion of the thymus were observed in animal at 250, 500 and 750 mg.kg⁻¹.day⁻¹ for 90 days.

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In the repeated inhalation study in rabbits haematological changes (changes in PMNs, platelets, white blood cell, reticulocyte and monocyte numbers) were observed following exposure to 75 and 250 ppm, the only concentrations tested. No oral rabbit studies are available.

In the available repeated inhalation exposure studies in dogs, haematological analysis was only conducted in the 90-day study. In this study, no treatment-related haematological changes were reported at 165 or 330 ppm. At 440 ppm, reduced leukocyte counts (not quantified) were reported, as well as evidence of aplastic bone marrow at necropsy. No findings were reported in animals at lower exposure concentrations. In the repeat oral study in dogs no effects on haematopoietic tissues were reported at doses of $27 \text{ mg.kg}^{-1} \text{ bw.day}^{-1}$ for 90 days. An increased number of immature leukocytes was observed at $54 \text{ mg.kg}^{-1} \text{ bw.day}^{-1}$, and histopathological changes in the haematopoietic tissues (nature and severity of response not reported) were observed in animals administered $273 \text{ mg.kg}^{-1} \text{ bw.day}^{-1}$.

Taking all of the available data together there are some indications that chlorobenzene may produce changes in haematological parameters. However, there is clearly significant variation in the observations made and uncertainty remains over whether or not the changes are chance findings or indicative of a real treatment-related effect. Furthermore, if the findings are considered to be related to treatment, then there is uncertainty in the identification of a NOAEL.

In terms of genotoxicity, negative results have been reported in bacterial studies and in studies in mammalian cells *in vitro* with respect to chromosome aberrations, SCE and UDS at non-cytotoxic concentrations¹⁴. However, a clear and dose-related positive result has been reported in an *in vitro* gene mutation assay in mouse lymphocytes, in the presence of metabolic activation.

There are no reliable data from mutagenicity studies conducted *in vivo* according to validated test methods. Overall, in light of the positive *in vitro* data and the fact that chlorobenzene has not been adequately tested *in vivo*, uncertainties remain with respect to the *in vivo* genotoxic potential of chlorobenzene.

Oral (gavage) carcinogenicity studies with chlorobenzene did not induce an increased incidence in any tumour type in rats of either sex at doses of up to $120 \text{ mg.kg}^{-1} \text{ .day}^{-1}$ or in mice of either sex at doses of up to $60 \text{ mg.kg}^{-1} \text{ .day}^{-1}$.¹⁸ Although survival rates in top-dosed animals were slightly reduced compared with controls, no clinical signs of toxicity, changes in body weights or gross treatment-related lesions were observed. Therefore it is uncertain whether the top-doses tested were actual maximum tolerated doses (MTDs) and therefore whether the studies were in fact adequate for the determination of carcinogenic potential.

No carcinogenicity studies via the inhalation or dermal routes are available.

No evidence for effects on fertility or reproductive performance were observed in a two generation study in which rats were exposed to up to 450 ppm chlorobenzene vapour²⁰. No adverse histopathological findings in the reproductive organs were observed in males at up to 150 ppm or in females at up to 450 ppm. An increased incidence (severity not reported) of degeneration of the testicular germinal epithelium in males exposed to 450 ppm was noted at necropsy. Despite these lesions there were no adverse effects on the fertility or reproductive performance of these animals. No adverse histological findings were observed in the gonads of rats or rabbits, following repeated inhalation exposures of up to 250 ppm (1138 mg.m^{-3}) for 24 weeks.

Bilateral atrophy of the seminiferous epithelium was noted in dogs exposed to 273 ppm ($\sim 1500 \text{ mg.m}^{-3}$) chlorobenzene vapour for 90 days.

No adverse histological findings were observed in the gonads of rats or mice following repeated oral dosing of up to $750 \text{ mg.kg}^{-1} \text{ .day}^{-1}$ for 90 days or $120 \text{ mg.kg}^{-1} \text{ .day}^{-1}$ and $60 \text{ mg.kg}^{-1} \text{ .day}^{-1}$ for 2 years, respectively, or in dogs following administration of up to $273 \text{ mg.kg}^{-1} \text{ .day}^{-1}$ for 90 days.

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No evidence of any chlorobenzene treatment-related developmental effects have been observed in rats, mice or rabbits, at doses up to 590 ppm on days 5-16/18 of gestation, this being the highest concentration tested. Evidence of some degree of maternal toxicity (reduced food consumption and body weight gain and increased liver weights) was observed at 590 ppm (2685 mg.m⁻³) in all species tested.

Overall, it is concluded that chlorobenzene is not a reproductive toxicant.

Human data

The only information available on the effects of chlorobenzene in humans derive from isolated case reports of poisoning, occupational exposure studies or one volunteer study. No data on the actual levels of exposure are reported in any of the case reports, and interpretation of the occupational exposure studies is confounded by exposure to mixtures of other substances. In a human volunteer study, some individuals self-reported sensations of disagreeable odour and drowsiness (4/4), a heavy feeling in the head and/or headache (3/4), a throbbing pain in the eyes (2/4) and a sore throat (1/4) during exposure to 60 ppm chlorobenzene of an unspecified purity for 3-hours in the morning, followed by a 4-hour exposure period in the afternoon, with a 1-hour interval in between¹³.

BASIS FOR SETTING THE LIMIT

There are no reliable human data available on which to base an occupational exposure limit for chlorobenzene. The evidence from a range of animal species indicates that the liver and bone marrow are the key target organs of chlorobenzene toxicity in experimental animals. From the information available, the relevance of the animal data on these effects to human health is uncertain. Given that they might be relevant, it is not possible to identify a clear NOAEL for the liver effects of chlorobenzene in animals.

In relation to the haematological effects observed with chlorobenzene, the pattern of information suggests that the mouse may be more sensitive to these effects than other experimental species. However, haematological investigations have not been systematically carried out in all studies, and there is significant variability in the results available from different studies. This leads to uncertainty as to whether or not the reported changes in individual studies represent reliable toxicological observations or chance findings. However, it is perhaps significant that chlorobenzene is structurally similar to benzene, which is metabolised in a similar manner to chlorobenzene, both molecules undergoing initial ring hydroxylation. Therefore, the well-documented haematological effects of benzene add weight to the concern for haematological changes with chlorobenzene. From the information available for chlorobenzene, it is not possible to identify a clear NOAEL for haematological changes across the experimental species examined; changes were reported in mice following repeated exposure to 21 ppm, the lowest airborne concentration tested.

In light of the positive *in vitro* genotoxicity data and the inadequate *in vivo* testing of chlorobenzene there are uncertainties regarding the *in vivo* mutagenic potential of chlorobenzene.

In the only available carcinogenicity study, no increase in the incidence of any tumour type was observed in rats or mice. However, as it is uncertain whether the top doses tested were maximum tolerated doses (MTDs), the adequacy of this study and therefore of the negative result is questionable. Therefore in the absence of any other relevant data, there remain uncertainties with respect to the carcinogenic potential of chlorobenzene.

Exposure data demonstrate that control to less than 5 ppm (8-hour TWA) is reasonably practicable, and that most results are below 1 ppm. Although higher exposure results have been obtained, these are not typical and exceed what it is reasonably practicable to achieve. The available toxicological data do not identify clear positive evidence for serious effects on human health at 1 ppm or 5 ppm; rather, the position is one of uncertainty.

On this basis, the Workplace Exposure Limits (WELs) have been based on the levels of exposure that is reasonably practicable for all sectors of industry to achieve. Taking into

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account the above information and the Indicative Occupational Exposure Limit Values (IOELVs) for chlorobenzene listed in the 1st Consolidated IOELV Directive (2000/39/EC), ACTS considered that values of 1 ppm (8-hour-TWA) and 3 ppm (STEL) are appropriate. It was not necessary to amend the WELs to take account of the revised IOELVs for monochlorobenzene listed in the 2nd Consolidated IOELV Directive (2006/15/EC).

Based on the predicted high level of dermal absorption, it is concluded that a 'Skin' notation is required. There is no evidence to support a 'Sen' notation. The carcinogenicity data do not warrant a 'Carc' notation.

Although no biological monitoring guidance value has been set, the methods and relationships set out in the biological monitoring section above may be useful in monitoring exposure.

HISTORY

1984 – 1988: Recommended Limit (RL) of 75 ppm (8-hr TWA).

1989 – 2000: The RL was withdrawn and following a WATCH/ACTS review an Occupational Exposure Standard (OES) of 50 ppm (8-hr TWA) was introduced.

2000: The OES was withdrawn owing to uncertainties about the thresholds for haematological effects and uncertainties about whether or not chlorobenzene possessed genotoxic or carcinogenic potential. CHAN 16 was issued pending the establishment of a Maximum Exposure Limit (MEL).

2002 – 2005: The CHAN was withdrawn and to implement the 1st Consolidated IOELV Directive, MELs of 1 ppm (8-hr TWA), 3 ppm (STEL, 15-minute reference period) with a 'Sk' notation were established.

2005 – present: The MELs were translated into WELs of 1 ppm (8-hr TWA), 3 ppm (15-minute reference period) with a 'Sk' notation. It was not necessary to amend these WELs to implement the revised IOELVs listed in the 2nd Consolidated IOELV Directive.

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