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Fate of [^{14}C]Vinyl Chloride following Inhalation Exposure in Rats¹

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Fate of [^{14}C]Vinyl Chloride Following Inhalation Exposure in Rats. WATANABE, P. G., MCGOWAN, G. R., MADRID, E. O., AND GEHRING, P. J. (1976). *Toxicol. Appl. Pharmacol.* 37, 49-59. Inhalation exposure to vinyl chloride (VC) has been shown to be carcinogenic in rats and man. It is important in assessing the toxicological potential of inhaled VC to understand the disposition of VC in the body. Therefore, the objective of the present study was to determine the fate of inhaled [^{14}C]VC at different exposure concentrations in rats. Male rats were exposed to 10 or 1000 ppm [^{14}C]VC for 6 hr and the routes and rates of elimination of ^{14}C activity were followed for 72 hr after termination of exposure. Following exposure to 10 ppm of VC, urinary ^{14}C activity and expired VC comprised 68 and 2%, respectively, of the recovered radioactivity. After exposure to 1000 ppm of VC, the proportion of the radioactivity in the urine decreased while that expired as VC increased representing 56 and 12%, respectively. The pattern of pulmonary elimination of VC per se was described by similar apparent first-order kinetics following 10 or 1000 ppm with respective half-lives of 20.4 and 22.4 min. The elimination of ^{14}C activity in the urine occurred in accordance with a two-exponential equation; the half-lives for the initial phase of excretion were 4.6 and 4.1 hr following 10 and 1000 ppm, respectively. The percent of the recovered ^{14}C activity remaining in the carcass after 72 hr was 14 and 15% at the respective low and high exposure level. VC per se was not found in tissues. The urinary ^{14}C activity was separated by high pressure liquid chromatography into three major metabolites corresponding to *N*-acetyl-S-(2-hydroxyethyl)cysteine, thiodiglycolic acid, and a third unidentified metabolite. The proportions of the urinary metabolites were not markedly influenced by the exposure magnitude. The fate of inhaled [^{14}C]VC was shown to be dose-dependent; this is consistent with previous studies on the fate of VC following ingestion as well as inhalation.

Inhalation exposure to vinyl chloride (VC) has been shown to be carcinogenic in rats (Maltoni and Lefemine, 1974) and in man (Creech and Johnson, 1974; Tabershaw and Cooper, 1974). Preliminary studies on the fate of inhaled VC (Hefner *et al.*, 1975) indicated that VC was metabolized in part to polar products which were excreted in the urine. By using kinetic parameters and inhibitors of drug metabolism it was shown that the fate of VC was dependent on the magnitude of exposure. Also, the data led to

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CIS 75-1929 Order of 20 November 1974 to supplement the list of processes requiring special medical supervision (Arrêté du 20 novembre 1974 complétant la liste des travaux nécessitant une surveillance médicale spéciale). *Journal officiel de la République française*, Paris, France, 30 Nov. 1974, Vol. 106 No.280, p.11979 (In French)

The item "processes for the polymerisation of vinyl chloride" is added to the list of processes requiring special medical supervision in the schedule appended to the Order of 22 June 1970. (03967)

CIS 75-1930 A recommended standard: An identification system for occupationally hazardous materials. HEW Publication No. (NIOSH) 75-126. National Institute for Occupational Safety and Health, Post Office Building, Cincinnati, Ohio 45202, USA, 1974. 63p. 30 ref. (In English)

Recommendations following the guidelines laid down in the Occupational Safety and Health Act 1970, designed for the rapid determination of hazard from exposure to materials found in the workplace. Sections are devoted to the scope, objective, basis and components of the recommended identification system for labelling hazardous materials, and the use of posters, labels (lettering, colours, etc.) and safety data sheets. A glossary of terms, tables of suggested label wording (health hazards, fire hazards, reactivity and explosive hazards, first aid, waste disposal), etc. are appended. (03968)

CIS 75-1931 Behavioral toxicology - Early detection of occupational hazards. HEW Publication No. (NIOSH) 74-126. National Institute for Occupational Safety and Health, Post Office Building, Cincinnati, Ohio 45202, Superintendent of Documents, Government Printing Office, Washington, D.C. 20402, USA, 1974. 507p. illus. 464 ref. Price: US-\$7.45. (In English)

Sections of the 1970 OSH Act emphasise the need to include behavioural factors in examining problems of occupational safety and health, and to develop new methods in handling these problems. This book records the proceedings of the Behavioural Toxicity Workshop held in Cincinnati on 24-29 June 1973. After an introductory session (behavioural toxicology in the development of threshold limit values, research programmes, etc.), the various sessions deal with the following themes: worker exposure to solvents (anaesthetics, carbon disulfide, trichloroethylene, methylene chloride, carbon monoxide); pesticides; metals (mercury, lead and other polyvalent cations, methyl mercury); toxic gases, irritants, odours, alcohol and effects of drug reactions; demonstrations (controlled environment chamber, test batteries, etc.); overview (development of behavioural toxicology in the USA, use of conditioned reflex methods in Soviet research, etc.). (03971)

CIS 75-1932 Carcinogenicity of vinyl chloride - literature survey (Action cancérigène du chlorure de vinyle - Revue bibliographique). Cangueneux A., Morel C. *Cahiers de notes documentaires - Sécurité et hygiène du travail*, Paris, France, 2nd quarter 1975, No.79, Note No.956-79-75, p.201-206. 93 ref. (In French)

Brief survey of the historical background to present-day knowledge and awareness of the toxicity of vinyl chloride monomer (VCM), the carcinogenicity of which has been demonstrated by animal experiments and observed cases of workers engaged in cleaning out polymerisation autoclaves, the first of which date from Jan. 1974. From comparison of VCM with more highly carcinogenic substances, a safe TLV would fall between 25 and 10ppm. (03992)

CIS 75-1933 Hazardous chemical reactions - 29. Lithium (Réactions chimiques dangereuses - 29. Lithium). Leleu J. *Cahiers de notes documentaires - Sécurité et hygiène du travail*, Paris, France, 2nd quarter 1975, No.79, Note No.961-79-75, p.263-264. (In French)

Enumeration and description of the possible reactions between lithium and 13 substances (organic and inorganic). The references used are quoted for each reaction. (03997)

CIS 75-1934 Hazardous chemical reactions - 30. Sodium and sodium-potassium alloys (Réactions chimiques dangereuses - 30. Sodium et alliages sodium-potassium). Leleu J. *Cahiers de notes documentaires - Sécurité et hygiène du travail*, Paris, France, 2nd quarter 1975, No.79, Note No.962-79-75, p.265-270. (In French)

Enumeration and description of the possible reactions of sodium and sodium-potassium alloys with 80 substances or groups of substances (organic and inorganic). The references used are quoted for each reaction. (03998)

CIS 75-1935 Chlorine (Klor) Veiledning nr.7, Directorate of Labour Inspection (Direktoratet for arbeidstilsynet), Postboks 8103, Oslo-Dep., Norway, Sep. 1974. 7p. Gratis. (In Norwegian)

Directives for the safe handling, transport and storage of chlorine: chemical and physical properties; toxic effects; personal protective equipment; first aid; advice on safe working methods with chlorine; testing of respirators; safety measures for road transport and storage of chlorine; directives for water chlorination facilities; cleaning and maintenance of storage and working

CIS 75-1936 Cleaning with trichloroethylene (Rensarbaid med trikloretylen) Veiledning nr.9, Directorate of Labour Inspection (Direktoratet for arbeidstilsynet), Postboks 8103, Oslo-Dep., Norway, Sep. 1974. 3p. Gratis. (In Norwegian)

Regulations issued under the Workers Protection Act of 1956 laying down rules for the use of trichloroethylene: properties; toxic effects; fire hazards; enclosure of cleaning plant; mechanical ventilation; skin protection; gas freeing of cleaning plant before repairs, maintenance or inspection; fire prevention. (04015)

CIS 75-1937 Methylenebis(2-chloroaniline)(MBOCA): A new chemical carcinogen (Méthylène-bis-o-chloroaniline (MBOCA): un nouveau cancerogène chimique). Bertazzi P.A. *Medicina del lavoro*, Milano, Italy, Mar.-Apr. 1975, Vol.66, No.2, p.61-84. 15 ref. (In Italian)

Methylenebis(2-chloroaniline) is used as a catalyst in the polyaddition of polyurethanes. This article refers to various investigations which have demonstrated the toxicity and carcinogenicity (particularly involving the liver) of this substance, and its tendency to be absorbed by the skin. Its carcinogenicity is confirmed not only by animal experiments but also by tumours observed in workers exposed to this substance in the chemical industry. Recommended safety measures: replacement of methylenebis(2-chloroaniline) by a harmless or less toxic substance; safety engineering and industrial hygiene; wearing of respirators and protective clothing; medical supervision. (04016)

CIS 75-1938 A charcoal sampling method and a gas chromatographic analytical procedure for carbon disulfide. McCammon C.S., Quinn P.M., Kupe R.E. *American Industrial Hygiene Association Journal*, Akron, USA, Aug. 1975, Vol.36, No.8, p.618-625. illus. 8 ref. (In English)

A test method for sampling and analysing samples for carbon disulfide (CS₂) is described. CS₂ was adsorbed on charcoal tubes, eluted with benzene, and determined with a gas chromatograph equipped with a sulfur flame photometric detector. The sensitivity of the method was 1µg. The tubes were also tested for breakthrough volumes, sample stability, and the effect of air transport and temperature changes. (04045)

CIS 75-1939 Absorption, distribution and excretion of terephthalic acid and dimethyl terephthalate. Moffitt A.E., Clary J.J., Lewis T.R., Blenck M.D., Farrow V.B. *American Industrial Hygiene Association Journal*, Akron, USA, Aug. 1975, Vol.36, No.8, p.633-641. 15 ref. (In English)

Structural formulae and physical and chemical properties of terephthalic acid (TA) and dimethyl terephthalate (DMT). Radiotracer studies in rabbits and rats using C-14-labelled TA and DMT showed: (1) rapid absorption and excretion of TA and DMT without evidence of tissue accumulation on single or repeated oral and intratracheal administration; (2) no skin irritation after single or repeated dermal application, and no significant skin absorption of TA; (3) recovery of 11-13% of the (single or repeated) cutaneous doses from urine and faeces within 10 days; (4) no significant absorption of TA after ocular instillation; (5) 33% excretion of a single ocular dose of DMT, with no evidence of tissue accumulation or eye damage. TA and DMT thus appeared to be rapidly absorbed and excreted without significant accumulation in the tissues. (04047)

CIS 75-1940 Free silica SiO₂. Analytical guides. American Industrial Hygiene Association, Akron. *American Industrial Hygiene Association Journal*, Akron, USA, Aug. 1975, Vol.36, No.8, p.642-645. 13 ref. (In English)

Principle, method of collection, interferences, special reagents and equipment, range, sensitivity and accuracy are detailed for the X-ray diffraction, infrared spectroscopy, and colorimetric methods for determining free silica with brief comments. (04048)

CIS 75-1941 Measurement of liver-cadmium concentrations in patients and industrial workers by neutron-activation analysis. Harvey T.C., McLellan J.S., Thomas B.J., Frenlin J.H. *The Lancet*, London, United Kingdom, 7 June 1975, Vol.1, No.7919, p.1269-1272. illus. 37 ref. (In English)

Description of a new, rapid, non-surgical technique for measuring tissue cadmium concentrations in the liver, in which the specific changes produced by irradiation with neutrons are analysed. Studies in 4 men with known or suspected poisoning showed very high liver cadmium levels of 35-200µg (non-exposed subjects <1.0ppm), and these are compared with urine cadmium concentrations in a table (there was little correlation). The radiation dose used in clinical studies was 0.1-1.0rem and the detection limit of cadmium was 1.0ppm. Short literature review of pathology of cadmium poisoning. Further studies are planned. (04049)

CIS 75-1942 The minimal oral toxicity level for mevinphos in man. Rider J.A., Furek E.J., Swader J.L. *Toxicology and Applied Pharmacology*, New York, USA, Apr. 1975, Vol.32, No.1, p.97-100. illus. 4 ref. (In English)

To determine the safe exposure level for organophosphate insecticide, mevinphos (2-ethylhexyl 1-methylphenyl dimethyl phosphorothioate) was fed to man volunteers for 30 days. The depression of cholinesterase activity

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