

Meeting date:

9 &10 November
2006Open Gov.
Status:

Fully Open

Secretary's Report for 8th Meeting, 9 & 10 November 2006

A. Progress on minuted actions arising during the 7th Meeting, 20th June 2006

Min. Ref.	Action	Status
2.21	HSE to provide definitions for TD50 and T ₂₅ and to further analyse the application of cut-off values in the identification of high potency carcinogens.	Provided below
2.22	HSE to consider further what potency rank(s) to assign the established human carcinogens.	See below
4.12	Working group evaluating the effectiveness of WELs and COSHH Essentials to produce a paper outlining the group's proposal for the November 2006 WATCH meeting.	Update to be provided at the November 2006 meeting.
4.18	HSE to assemble an appropriate package of documentation on "new and emerging issues" to facilitate decisions on how best to arrive at clear conclusions at the November 2006 meeting of WATCH.	Papers : WATCH/2006/9,10,11 to be presented at the November 2006 meeting

2.21 Definitions for TD50 and T25

- taken from the EU Commission document, "Guidelines for setting specific concentration limits for carcinogens in Annex I of Directive 67/548/EEC, Inclusion of potency considerations"

TD50

In an attempt to measure tumorigenic potency from experimental data Sawyer devised the TD50 concept, which was defined as a daily dose rate required to halve the probability of remaining tumourless at the end of a standard life-span (Sawyer et al., 1984). It is based upon two important assumptions: that there is linearity between dose and the hazard to tumour onset and that tumour onset times are observable. The measurement is complicated by premature deaths due to causes other than tumorigenesis and the inability to observe of the time of tumour onset. The latter facts leads to an assumption that if an animal dies and is found to have a tumour, then the time of death was the time of tumour onset. Consequently, the measure of tumour incidence is confounded with mortality and biased TD50 estimates can be derived (Portier and Hoel, 1987). If, on the other hand, tumours do not significantly alter survival, then TD50 values become related to the rate-of-death-with-tumour, rather than the tumour incidence rate (Meier et al., 1993). This undermines the objective of the carcinogenicity study, which is to evaluate tumour incidence (McKnight and Crowley, 1984). The list of carcinogens for which a TD50 was determined has been extended substantially due to the use of this concept by Ames, Gold and co-workers (Peto et al, 1984; Gold et al., 1984; and many later publications by Gold and co-workers).

T25

The T25 estimate of potency (Dybing et al., 1997), which is quite similar to the TDx method, is defined as the daily dose in mg per kg bodyweight) inducing an increased (above background) tumour incidence of 25 % upon lifetime exposure. The T25 method could be viewed as a normalised TDx method, where the tumour response has been set to 25%. The use of T25 values for potency ranking has several advantages in comparison to the TD50 and TI methods. Firstly, it does not require complex computations after establishment of a significant increase in tumour incidence. Also, T25 values are much more likely to be within the range of the experimental data and the use of data from the lowest dose giving a significant response, should in most instances reduce the problem of non-neoplastic mortality to an acceptable degree. Finally, the data profile needed for calculating a T25 value is less exhaustive, e.g. time to tumour data are not needed. Although the T25 method only takes into consideration one single dose-response point, the results using the T25 methods are in excellent agreement with the modelled results using the linear multistage (LMS) method (US EPA, 1986) and the LED10 methods (US EPA, 1996) (Dybing et al., 1997; Sanner et al., 2001).

2.22 Potency ranking for human carcinogens

Following the discussion about potency at the 7th meeting of WATCH in June 2006, HSE has revised the lists of carcinogens such that:

- human carcinogens are listed as a single group, with no further sub-division; and
- the remaining carcinogens are divided according to published T25 and/or TD50 values, with $T25 \leq 1$ mg/kg/day or $TD50 \leq 2$ mg/kg/day signifying a potential for high potency. These revised lists are presented in the table below.

Human carcinogens within the scope of the DRP chemical carcinogens programme.

CARCINOGEN(S)	Human carcinogen classification	Main tumour site(s) after occupational exposure	Estimates of risk published by other organisations/individuals	
			EPA ^a or WHO ^b unit risk estimates per $\mu\text{g}/\text{m}^3$ lifetime exposure	Estimates of risk from other sources
4-Aminobiphenyl and its salts	EU/IARC	Bladder	-	-
Arsenic and compounds including gallium arsenide	EU/IARC	Skin, Lung	4.5×10^{-3} ^a 1.5×10^{-3} ^b	10^{-2} - 10^{-3} ^c
Auramine and its manufacture	IARC	Bladder	-	-
Benzene	EU/IARC	Leukaemia	$2.2-7.8 \times 10^{-6}$ ^a $4.4-7.5 \times 10^{-6}$ ^b	9.2×10^{-6} ^c
Benzidine and its salts	EU/IARC	Bladder	6.7×10^{-2} ^a	-
Beryllium and compounds	IARC	Lung	2.4×10^{-3} ^a	-
Bis(chloromethyl)ether	EU/IARC	Lung	0.062 ^a	-
Butadiene	EU	Lympho-haemopoietic	4.0×10^{-6} ^a	4.4×10^{-6} ^d
Cadmium and compounds	IARC	Lung	$4.2-4.4 \times 10^{-3}$ ^a	12×10^{-3} ^e

Chlorodimethyl ether	EU/IARC	Lung	*	-
Chromium VI compounds	IARC	Lung	$1.1-13 \times 10^{-2}$ ^b (geometric mean 4.2×10^{-2})	-
Coal - soots, tar, pitch and tar fumes	IARC	Skin (coal tar), oesophagus (soots)	6.2×10^{-4} ^a (coke oven emissions)	
Erionite	EU/IARC	Mesothelioma	-	-
Ethylene oxide	IARC	Leukaemia	1.0×10^{-4} ^a	$0.86-1.3 \times 10^{-5}$ ^f 4.2×10^{-5} ^g
Ferrous foundry particulate	IARC	Lung	-	-
Formaldehyde	IARC	Nasal	1.3×10^{-5} ^a	-
2-Naphthylamine	EU/IARC	Bladder	-	-
Nickel oxides, sulphide, subsulphide and carbonate	EU/IARC	Lung, nasal cavity and sinuses	-	2.4×10^{-4} (oxide) ^h
Nickel chloride and sulphate	EU/IARC	Lung, nasal cavity and sinuses	-	7.0×10^{-4} ^h
Rubber process dust and fumes	EU/IARC	Bladder, stomach, lung	-	-
Sulphuric acid mist	EU/IARC	Larynx, lung	-	-
Vinyl chloride	EU/IARC	Liver	8.8×10^{-6} ^a	
Wood dust (hard and soft)	IARC	Nasal cavities and paranasal sinuses	-	-

^a EPA, ^b WHO, ^c Wahrendorf and Becher 1990, ^d Roller and Nies, 1999, ^e LAI, 1992, ^f OSHA 1983, ^g Denk and Filsher 1990, ^h Roller 1998, * a unit risk value has not been calculated for CDME but the EPA consider that it is likely to be higher than that for BCME.

B. Updates on other activities

Nothing to report.