P144 Issues on the Application of the GHS Classification Criteria for Germ Cell Mutagens

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The United Nations published the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) in 2003, 2005 and 2007. The GHS requests the classification of chemicals on 10 health hazard endpoints that include germ cell mutagenicity. The classification system provides for three categories (1A, 1B and 2) of germ cell mutagens to accommodate the weight of evidence available. The criteria of these categories are also provided. Classification is made on the basis of well conducted, sufficiently validated tests. Evaluation of the test results should be done using expert judgement and all the available evidence should be weighted for classification. Several issues, however, were identified during the course of the Japanese GHS classification project and other exercises on the application of the GHS classification criteria. These include 1) lack of understanding about GHS classification criteria, 2) shortage of information collection, 3) insufficient review of the information, 4) discrepancy of expert judgement, and 5) difficulty of weighting evidence from limited information. Examples, e.g., acrylonitrile, ethanol, sodium chlorite, will be presented. Genetic toxicologists as classifier should consider 1) definition of GHS criteria, 2) detailed review of several authoritative documents including original articles, if necessary, 3) hazard based classification, not for risk assessment, and 4) data reliability. Harmonization or consensus of "weight of evidence" is also needed.

生殖細胞変異原のGHS分類基準適用における問題点

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P146 Assessment the toxicity of the organic extracts in the Yangtze River and Jialing River surface water in Chongqing Area (China) using *in vitro* bioassay

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To investigate potential toxicity of the organic pollutants in the river water of Chongqing area, organic pollutants were extracted from Yangtze River and Jialing River surface water at August 2004 and January 2005. The Ames tests showed that the sample from Jialing River at January 2005 with strain TA97, TA98, and TA100 and the sample from Yangtze River at January 2005 with strain TA 98 had positive mutagenic activity at the present or absent of exogenous microsomal activation system (S9). After exposed to the extracts, the proliferation of H4IIE cell decreased according to the exposure time and dose. The ethoxy-resorufin-O-deethylase (EROD) tests showed that the toxic equivalencties (TEQ) of each sample were among 0.9-13.3×10-4(pg 2,3,7,8-TCDD/L river water). Incubation of the H4IIE cells with the organic extracts caused a time-dependent induction of cytochrome P450 1A1 (CYP1A1) mRNA expression as detected by reverse transcriptase - polymerase chain reaction (RT-PCR). All the samples showed a positive binding of organic extracts to AhR and activating of xenobiotic response element (XRE) as determined by electrophoretic mobility shift assay (EMSA). These *in vitro* investigations indicated that organic extracts from Yangtze River and Jialing River had mutagenic potential and could induce H4IIE cells CYP1A1 express and inhibit H4IIE cells proliferation.

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