P114 Genotoxicity studies of 2,6-dinitrotoluene (2,6-DNT)

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Abstract: 2,6-DNT is a known rat liver carcinogen, and the metabolic activation of intestinal microflora is involved in the appearance of its genotoxicity. The potential genotoxicity of 2,6-DNT was evaluated using the bacterial reverse mutation test (Ames test), *in vitro* chromosomal aberration test (*in vitro* CH), young rat liver micronucleus test (LMNT), and peripheral blood micronucleus test (PBMNT). 2,6-DNT showed a moderate mutagenic potential in the Ames test, was slightly positive in the *in vitro* CH test, and was negative in the PBMNT. Conversely, 2,6-DNT was clearly positive in the LMNT. In addition, it has been reported that 2,6-DNT was positive in the *in vivo/in vitro* unscheduled DNA synthesis (UDS) test. These results suggest that selection of a test system that takes into consideration the target organ is important for *in vivo* genotoxicity assessment of chemicals.

2,6-ジニトロトルエン(2,6-DNT)の遺伝毒性試験

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P115 Can the Micronucleus Assay be Integrated into the General Toxicity Evaluation?

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Micronucleus assays are performed mostly with a single or double dose treatment. However, if the micronucleus assays with a repeated dose treatment of two weeks or longer can be performed in rats, not only can the labor and number of the animals be reduced, but toxicokinetic and other diverse information regarding general toxicity can be obtained simultaneously with information regarding the genetic toxicity from the same animals, which is of great benefit for the comprehensive safety evaluation of chemicals.
We have carried out micronucleus assays in rats with a four-week repeated treatment as the 13th Collaborative Study of the CSGMT. This study was conducted to compare the sensitivity of the assay between the short-term and long-term treatments of the same chemicals and to evaluate the possibility of conducting a concurrent micronucleus assay with the general toxicology assays using same animals. Recently, there has been discussion about revising the ICH guideline S2, and the integration of the micronucleus assays into the general toxicity evaluation has become much more important. Although the results of this study have been introduced at the 27th JEMS, we evaluated anew the possibility of conducting a micronucleus assays as a part of the general toxicity evaluation introducing the latest findings and data.

小核試験の一般毒性試験への組み込みは可能か？

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