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Risk assessment of peak exposure to genotoxic carcinogens: a pragmatic approach

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Abstract

Short-term exposures to relatively high concentrations or doses are a regular cause of concern. Since carcinogenicity is often of great personal and social relevance the question arises whether short-term exposure (1–10 days) to a carcinogenic substance may contribute to tumour development and, if so, whether this contribution to the cancer risk can be quantified.

The present object was to explore the possibility of a pragmatic estimation of the cancer risk of peak exposure to a genotoxic carcinogen relative to the cancer risk of the same cumulative dose of this carcinogen distributed over lifetime. A report published by the Health Council of The Netherlands served as point of departure. Published data strongly suggests that short-term or single exposure can indeed give rise to tumour formation in animal experiments.

The application of a dose-rate correction factor (DRCF), defined as a factor by which the tumour incidence caused by a specific dose of a chemical carcinogen at low-dose rates is multiplied to derive the tumour incidence at high-dose rates, appears to be a feasible approach. Theoretical models calculated maximum values for the DRCF of up to seven for a young child acutely exposed to an initiator or first-stage carcinogen. A maximum value of 8.3 was calculated from animal experiments.

A decision tree is presented which allows the pragmatic assessment of the carcinogenic risk following short-term exposure to genotoxic carcinogens. It is recommended to validate this decision tree with model-substances.

Author Keywords: Genotoxic carcinogen; Carcinogenic risk; Short-term exposure; Dose-rate correction factor

Article Outline