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BIOLOGICALLY BASED DOSE-RESPONSE (BBDR) MODELING USING BIOMARKERS FOR CANCEER RISK ASSESSMENT

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Abstract Biologically Based Dose-Response (BBDR) models were developed using biomarkers for cancer risk assessment.

To establish the relationship among biomarkers, exposure dose and tumor response, biomarkers in the lung, liver, stomach or blood were measured after a single or continuous administration of selected carcinogen (; BaP) in mice or rats.

In the case of quantitative biomarker, the equation of relationships among the quantitative biomarkers, exposure dose and tumor response also obtained from animal experiments and 2-yr bioassay data and produced a mathematical three-dimensional equation. The three-dimensional equation of relationships among the quantitative biomarkers, exposure dose and tumor response was able to predict a cancer risk in animals and it could be extrapolated to human case when appropriate safety factor was employed. For human monitoring, quantitative biomarker was obtained and measured in blood of 50 heavy tobacco smokers and 50 non-smokers. Then, a methodology for cancer risk assessment modeling was investigated using the mathematical formulas and biomarkers of DNA, protein or lipid-adduct (e.g., TG adduct) obtained from blood sample in humans.

These issues also include qualitative biomarkers. We demonstrated and concluded that the contents of protein carbonyl and level of 4-HNE could be used as qualitative biomarker to estimate the oxidative damage, which reflects exposure to mixture chemicals or carcinogens.

These results indicate that the more accurate and convincing methodology for cancer risk assessment was developed in this achievement and could be applied to estimate the human exposure to carcinogens and risk assessment.

keyword : Cancer risk assessment, Carcinogen, Biomarker, BaP, CCl4