Cytotoxicity, mutagenicity, and tumorigenicity of mainstream smoke from three reference cigarettes machine-smoked to the same yields of total particulate matter per cigarette

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ABSTRACT

The particle phase of mainstream smoke from three types of cigarettes was investigated *in vitro* in the Neutral Red cytotoxicity assay and the *Salmonella typhimurium* Reverse Mutation Assay (Ames Assay) and *in vivo* in the two-stage dermal tumorigenicity assay (Skin Painting Assay) in SENCAR mice. The cigarettes used were the Reference Cigarettes 1R5F, 2R4F, and 2R1F from the University of Kentucky, USA, which, when smoked according to the smoking regimen defined by the International Standards Organization (ISO), produce a yield of approximately 2, 12, and 26 mg total particulate matter (TPM)/cigarette, respectively. All cigarettes were machine smoked according to ISO and then again in such a way that the TPM yields per cigarette equaled the ISO TPM yields of the other two cigarette types.

The TPM from cigarettes with inherently different smoke yields showed similar *in vitro* toxicity and *in vivo* toxicity when, with different smoking regimens, these cigarettes were smoked to the same TPM yield. More intensive smoking conditions were associated with lower *in vitro* and *in vivo* activity per gram of TPM. The strongest decrease, and the tightest correlation, in this regard was observed for dermal tumorigenicity (tumor incidence).