

EVALUATION OF SAFETY OF TOBACCO ADDITIVES

I. Checking by the list

- (1) The list of food additives authorized by the Ministry of Health and Welfare (Japan).
  - (2) FDA / GRAS list or FEMA / GRAS list (U.S.A.).
  - (3) Verordnung Uber Tabakerzeugnisse (Tabakverordnung) (W.G.).
  - (4) Natural Flavouring Substances, Their Sources, and added Artificial Flavouring Substances  
The list of "Council of Europe" 1974.
  - (5) The list of "Hunter's Committee" for Tobacco Additives 1977-9-20 (U.K.)
  - (6) The list of Tobacco Additives, Tobacco Substitutes, authorized by the Government (France).
- A: "Safety" substance.
- B: Substance whose use is restricted ("Restricted").
- C: "Prohibited".
- D: Unknown" ----- "Prohibited" before reinvestigation.

II. Evaluation of Safety of the Results of Biological Tests.

Biological Tests

1. Short-term tests.

A. Tests of additives (themselves).

(1) Acute toxicity tests.

- 1) Acute toxicity tests using cultured mammalian cells.
- 2) Acute oral administration tests using mice.
- 3) Acute oral administration tests using rats.

(2) Genetic toxicity tests.

- 1) Ames' tests.
- 2) Mutagenicity tests using cultured mammalian cells.
- 3) Chromosomal aberration tests using cultured mammalian cells.

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(3) Carcinogenicity tests.

- 1) Morphological transformation test using cultured mammalian cells.

B. Tests of cigarettes with additives (Omissible except for flavor and rice-paper additives).

(1) Acute toxicity tests.

- 1) Acute toxicity tests of smoke condensates using cultured mammalian.
- 2) Acute smoke-inhalation toxicity test using hamsters (or mice).

(2) Genetic toxicity tests.

- 1) Ames' tests of smoke condensates.
- 2) Mutagenicity tests of smoke condensates using cultured mammalian cells.
- 3) Chromosomal aberration tests of smoke condensate using cultured mammalian cells.

(3) Carcinogenicity test.

- 1) Sebaceous gland suppression tests of smoke condensates using mice.

2. Long-term test.

A. Tests of additives (themselves).

- 1) Long-term oral administration toxicity tests using mice (or rats).

B. Tests of cigarette with additives.

- 1) Long-term skin-painting test of smoke condensates using mice.

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