

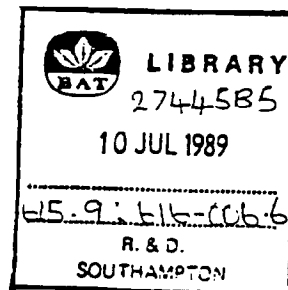
5

Department of Health

Report on Health and Social Subjects

35

Guidelines for the Testing of Chemicals for Mutagenicity



Committee on Mutagenicity of Chemicals in Food,
Consumer Products and the Environment

London
Her Majesty's Stationery Office

400756403

Figure 7.1: Flow diagram for testing strategy for investigating mutagenic properties of a substance*

STAGE 1

Initial Screening

Two tests required (a + b) except where human exposure would be expected to be extensive and/or sustained, and, difficult to avoid, when all three tests are necessary

In Vitro Tests

- (a) Bacterial assay for gene mutation
- (b) Test for clastogenicity in mammalian cells for example metaphase analysis
- (c) Test for gene mutation in mammalian cells (for example the L5178Y TK +/- assay)

Ames

STAGE 3

If risk assessment for germ cell effects is justified (on basis of properties including pharmacokinetics, use and anticipated exposure).

Chromosome damage assay.

STAGE 2

Tests for:

Compounds positive in one or more tests in Stage 1, and
All compounds where high, or moderate, prolonged levels of human exposure are anticipated

In Vivo Tests

- (a) Bone marrow assay for chromosome damage (metaphase analysis or micronucleus test)
Plus, if above negative, and any *in vitro* test positive
- (b) Test(s) to examine whether mutagenicity or evidence of DNA damage can be demonstrated in other organs (eg liver, gut etc)

We have data on this from work we did a number of years ago CSC borderline on +ve -ve.

Quantitative studies need strong justification in view of their complexity, long duration, costs and use of large numbers of animals.

* General guidance only is given in this flow diagram. A compound is expected to produce high or moderate risk. Regulatory Authorities having regard to other relevant information may determine that a flexible approach is adopted. Each case should be considered on its merits on the basis with regard to the selection of tests as well as

400756404