

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)

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)

* General guidance only is given in this flow diagram. Decisions regarding, for example, whether a specific compound is expected to produce high or moderate, but prolonged, exposure would normally be taken by Regulatory Authorities having regard to other relevant data, and on a case-by case basis.