



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

FEB 3 1986

MEMORANDUM

SUBJECT: METAM-SODIUM
Request to Specify Mutagenicity Testing
Battery

Caswell 780
EPA #039003

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1-31-86

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J.E.H. 2/3/86
16/10/85 2/3/86

Registrant: Stauffer Chemical Company, on behalf of the Metam-Sodium Task Force (letter: J.R. Solga, Chairman to G. Werdig, dated October 16, 1985).

Action Requested: Specify a battery of mutagenicity tests, as requested by Hazard Evaluation Division/ Science Integration Staff (HED/SIS) (Data Call-In coversheet, dated October 21, 1985).

TB Recommendations: Data from the following mutagenicity tests would satisfy preliminary "first tier" requirements for the "alternative approach" indicated in the Task Force letter:

A. For Gene Mutation

1. Salmonella typhimurium/Microsome (Ames) Test, employing the standard Ames tester strains (TA 1535, TA 1537, TA 1538, TA 98, TA 100) for evidence of base-pair (BP) and/or frame-shift mutation, and TA 92 for cross-linkage. If positive results are obtained, no further gene-mutation studies would be required at this time; the test substance would be considered a mutagen. If Ames testing is negative, an in vitro assay in mammalian cells would be required, employing any one of the following standard assay systems:
2. Mouse lymphoma (L5178Y)/Thymidine kinase (TK); or Chinese hamster ovary (CHO)/Hypoxanthine guanine phosphoribosyl transferase (HGPRT); or Chinese hamster lung (V79)/HGPRT (or ouabain).

Alternatively (and if available), testing for sex-linked recessive lethals in Drosophila melanogaster would be acceptable for the gene mutation requirement.

B. For Chromosome Aberrations

1. A cytogenetic assay for (structural) chromosome damage, performed either in vitro or in vivo. The in vitro cytogenetic assay may be conducted in any established mammalian cell line (e.g., L5178Y, CHO, V79); or in primary cell cultures, (animal or human), e.g., lymphocytes cultured in vitro. If positive results for (structural) chromosome damage are obtained, no further cytogenetic assays would be required at this time; the test substance would be considered a clastogen (=chromosome-breaker).

If the in vivo approach is selected, any one of the following are acceptable:

Rodent bone-marrow cytogenetics, assessing either sister-chromatid exchanges (SCE), or structural plus numerical chromosome aberrations. Alternatively, a micronucleus test (MT) in rodent polychromatic erythrocytes (PCE) may be performed.

C. For DNA Damage/Repair. Any two of the following assays for detecting effects on DNA damaging, and/or repair mechanisms are acceptable in a preliminary screening battery:

1. Bacterial differential toxicity, employing repair-deficient and repair-competent sister strains of Bacillus subtilis, or Escherichia coli, or S. typhimurium (the last, less commonly used).

OR: SCE assayed in vitro in mammalian cell lines (e.g., CHO, WI-38), or in primary cultures (e.g., human lymphocytes).

OR: Unscheduled DNA synthesis (UDS) in established human cell lines (e.g., HeLa, WI-38), or in primary cultures (e.g., human skin fibroblasts, rodent hepatocytes).

In addition, the following type of short-term (in vitro) assay has been submitted as part of a preliminary screen (not presently required by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Guidelines): Any one of the in vitro mammalian cell transformation systems, such as mouse BALB-3T3, or C3H-10T 1/2, or Syrian hamster BHK-21, among others.