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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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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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JEH 2/3/86
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 abberrations. *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.