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FEASIBILITY OF USING BACTERIAL STRAINS (MUTAGENESIS) TO TEST FOR ENVIRONMENTAL CARCINOGENS



**Environmental Research Laboratory
Office of Research and Development
U.S. Environmental Protection Agency
Gulf Breeze, Florida 32561**

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FEASIBILITY OF USING BACTERIAL STRAINS (MUTAGENESIS)
TO TEST FOR ENVIRONMENTAL CARCINOGENS

by

John E. Evans
Department of Biology
University of Houston
Houston, Texas 77004

Grant No. R-804586

Project Officer

Al W. Bourquin
Environmental Research Laboratory
Gulf Breeze, Florida 32561

ENVIRONMENTAL RESEARCH LABORATORY
OFFICE OF RESEARCH AND DEVELOPMENT
U.S. ENVIRONMENTAL PROTECTION AGENCY
GULF BREEZE, FLORIDA 32561

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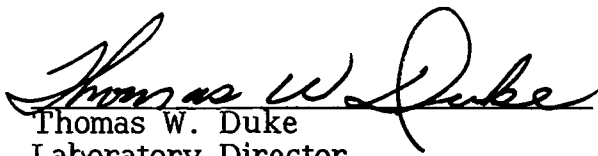
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FOREWORD

The protection of our estuarine and coastal areas from damage caused by toxic organic pollutants requires that regulations restricting the introduction of these compounds into the environment be formulated on a sound scientific basis. Accurate information describing dose-response relationships for organisms and ecosystems under varying conditions is required. The Environmental Research Laboratory, Gulf Breeze, contributes to this information through research programs aimed at determining:

- the effects of toxic organic pollutants on individual species and communities of organisms;
- the effects of toxic organics on ecosystem processes and components;
- the significance of chemical carcinogens in the estuarine and marine environments.

A great deal of information has been published concerning the presence of carcinogens in the environment. This report compiles and evaluates reports dealing with mutagenesis testing techniques and their use in screening for chemical carcinogens.


Thomas W. Duke
Laboratory Director
Environmental Research Laboratory
Gulf Breeze, FL 32561

ABSTRACT

A rapidly growing store of data is available relative to the potential mutagenicity and carcinogenicity of new products or chemical substances manufactured for commerce in recent years. Literature regarding mixtures, such as chemical wastes, however, is scarce and hard to find.

A literature review was undertaken to assess feasibility of using bacteria as screening agents to detect environmental carcinogens. Mutagenicity data were included in the study because growing experimental evidence indicates that most chemical carcinogens are mutagens, and many mutagens may be carcinogens.

This investigation found that bacterial mutagenesis can be used to initiate a series of studies designed to screen for potential mutagens and carcinogens in mixed chemical wastes.

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SECTION 1

INTRODUCTION

We can no longer treat environmental mutagenicity and/or carcinogenicity as an irrelevance (Bridges, 1972).

Prevention of disease is one of the most powerful motivations for improving the environment; and among the growing roster of environmental diseases, one is beginning to emerge as predominant: cancer (Commoner, 1975).

The purpose of this study was to assess from the literature the feasibility of using bacterial mutants in a screening test for carcinogens in mixed chemical wastes, sometimes associated with the occurrence of cancer in man, e.g., petrochemical effluents (IARC MONOGRAPHS, X:12, 1976).

The rationale for including mutagenicity data in the study is based on the growing volume of experimental evidence indicating that most chemical carcinogens are mutagens, and many mutagens may be carcinogens. But, whatever the exact correlation between carcinogenicity and mutagenicity may be, the connection is of highly practical significance in that mutagenicity testing procedures are used and have a demonstrated predictive value for chemically induced carcinogenicity (IARC MONOGRAPHS, XI:21, 1976; Ames, 1974; Ames, 1972).

SECTION 2

CONCLUSIONS

LITERATURE REVIEW

An urgency attached to the comparatively new and growing field of chemical and genetic toxicology renders duplication of research a waste and a hazard. A real need exists for literature relative to chemical mutagenicity and carcinogenicity to be readily available in a concise and systematic format in publications devoted to that area of study (Wassom, 1973; Wassom and Malling, 1976).

The Environmental Mutagenicity Information Center, formed in 1969, reports that literature in this field is found in approximately 2000 different periodicals and publications. In its on-going attempt to collect, store, and provide information by improved methods, the Center gained the services of the Oak Ridge National Laboratory's Computer Center "Name Match" program (Wassom et al., 1976; Sobels et al., 1976).

Among the journals devoted primarily to mutagenicity and carcinogenicity is MUTATION RESEARCH, ENVIRONMENTAL MUTAGENICITY AND RELATED SUBJECTS, REVIEWS IN GENETIC TOXICOLOGY, and GENETIC TOXICITY AND TESTING. Varied related information, providing insight into the numerous methods and analyses available for use in detecting and enumerating environmental mutagens, is presented in the four volumes of CHEMICAL MUTAGENS: PRINCIPLES AND METHODS FOR THEIR DETECTION. The International Agency for Research on Cancer (IARC), Lyon, France, reports its findings regarding the properties and potential carcinogenicity of specific chemical substances in IARC MONOGRAPHS.

Microbiol Mutagenicity Assay Systems

Epidemiological studies document man's increasing exposure to mutagens and potential carcinogens. Analyses contribute this increase to pollution from chemicals, chemical by-products, and naturally occurring substances in the environment. The genetic hazards associated with this building environmental crisis require a re-thinking of the old and development of new attitudes and methods for detection and assessment (Legator, Zimmering, and Connor, 1976; SCAND. REV., 1976).

The framework for testing and evaluation of chemical mutagens and/or potential carcinogens is guided by three general principles:

- 1) No chemical mutagen and/or carcinogen shall be used or released in the environment if a satisfactory substitute exists.
- 2) The extent of screening procedures should be related to the degree to which man is likely to be exposed.
- 3) Mutagens and/or carcinogenic substances may be used with appropriate safety measures if the benefits are judged to outweigh the hazards. (Adapted from Bridges, 1974)

A variety of assay systems has been developed for detecting chemical mutagens and/or carcinogens, but few have been validated. Table 1 is a partial listing of microbiol assay systems (Miller and Miller, 1971).

TABLE 1. MICROBIOL ASSAY SYSTEM
FOR MUTAGENS AND/OR CARCINOGENS^a

Test System	Reference
<u>Salmonella typhimurium</u> (Ames)	Ames, Lee and Durston. PROC. NAT. ACAD. SCI., <u>70</u> , 782-786, 1973.
<u>Salmonella typhimurium</u> (host-mediated)	Legator and Malling. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECTION, <u>2</u> , 569-589, 1971.
<u>E. coli</u> (Bridges)	Bridges. LAB. PRACT., <u>21</u> , 413-419, 1972.
<u>E. coli</u> (T4 bacteriophage)	Hartman, et al., SCIENCE <u>172</u> , 1058-1060, 1971.
<u>E. coli</u> (prophage induction)	Goldschmidt, Miller and Matney, MICROB. GENET. BULL., <u>41</u> , 3-4, 1976.
<u>B. subtilis</u> (transforming DNA)	Freese and Strack. PROC. NAT. ACAD. USA, <u>48</u> , 1796-1803, 1962.
<u>B. subtilis</u> (inhibition)	Kada. MUTAT. RES., <u>38</u> , 34, 1976.
<u>B. subtilis</u> (spores)	MacGregor and Sacks. MUTAT. RES., <u>38</u> , 271-286, 1976.
<u>Klebsiella pneumoniae</u>	Kramers, Knaap and Voogd. MUTAT. RES., <u>31</u> , 65-68, 1975.

TABLE 1. MICROBIOL ASSAY SYSTEMS (cont.)

Test System	Reference
<u>Citobacter freundii</u>	Kramers, Knaap and Voogd. MUTAT. RES., <u>31</u> , 65-68, 1975.
<u>Dictyostelium discoideum</u>	Liwerant and Pereira Da Silva. MUTAT. RES., <u>33</u> , 135-146, 1975.
<u>Streptomyces coelicolor</u>	Carere, et al., MUTAT. RES., <u>38</u> , 136, 1976.
<u>Saccharomyces cerevisiae</u>	Parry. LAB PRACT., <u>21</u> , 417-419, 1972.
<u>Saccharomyces cerevisiae</u>	Chambers. SCIENCE, <u>83</u> , s13, 1976.
<u>Saccharomyces pombe</u>	Loprieno. MUTAT. RES., <u>29</u> , 237, 1975.
<u>Aspergillus nidulans</u>	Käfer, Marshall and Cohen. MUTAT. RES., <u>38</u> , 141, 146, 1976.
<u>Neurospora crassa</u>	de Serres. CHEM. MUTAGENS. PRIN. METHODS THEIR DETECTION, <u>2</u> , 311, 342, 1971.
<u>Drosophila</u>	Zimmering. ANN. N.Y. ACAD. SCI., <u>269</u> , 26-33, 1975.

^aDrosophila is included because it is sensitive and inexpensive.

A comparison of various types of genetic lesions induced by mutagens and/or carcinogens and detected by various assay procedures is presented in Table 2 (Legator, Zimmering, and Connor, 1976).

TABLE 2. GENETIC LESIONS DETECTED BY VARIOUS TEST SYSTEMS

Systems	Mutations		Chromosomal aberrations				Induced recombination	Test systems for detecting metabolites
	Forward and/or reverse	Specific loci (multiple)	Dominant lethal	Translocation	Deletions and duplications	Nondisjunction		
Microbial								
a. Procaryote								
1. <u>S. typhimurium</u>	X							X
2. <u>E. coli</u>	X							X
b. Fungal								
1. <u>Neurospora</u>	X				X			X
2. <u>Aspergillus</u>	X	X				X	X	
3. <u>Yeast</u>	X	X	X			X	X	X
Plant								
a. <u>Vicia</u>				X	X	X		
b. <u>Tradescantia</u>	X			X	X	X		
Insects								
a. <u>Drosophila</u>	X	X	X	X	X	X	X	X
b. <u>Habrobracon</u>	X	X	X				X	
c. <u>Bombyx</u>	X	X						
In vitro mammalian cell systems								
a. Chinese hamster	X			X	X	X		X
b. Mouse lymphoma	X			X	X	X		X
In vivo mammalian systems								
a. Mouse		X	X	X	X	X		
b. Rat			X	X	X	X		
Man			X	X	X			

^a From Legator, Zimmering and Connor, 1976.

Table 3 (McCann et al., from Bridges, 1976) is of particular interest with respect to the relationship between carcinogenicity and mutagenicity. Eighty-seven and seven-tenths percent of all carcinogens were detected as positive in the Salmonella system. Using E. coli, Rosenkranz showed 85% of the carcinogens tested to be positive (Rosenkranz, 1976).

TABLE 3. CORRELATION OF ANIMAL CARCINOGENICITY AND BACTERIAL MUTAGENICITY
WITH AND WITHOUT METABOLIC ACTIVATION^a

Group of compounds	Carcinogens detected as bacterial mutagens	Non-carcinogens not mutagenic to bacteria	Compounds of uncertain carcinogenicity detected as mutagens
Aromatic amines, etc.	23/25	10/12	5/7
Alkyl halides, etc.	17/20	1/3	1/1
Polycyclic aromatics	26/27	7/9	1/1
Esters, epoxides, carbamates, etc.	13/18	5/9	0/1
Nitro aromatics and heterocycles	28/28	1/4	0/2
Miscellaneous organics	1/6	13/13	0/1
Nitrosamines	20/21	2/2	1/1
Fungal toxins and antibiotics	8/9	5/5	-
Mixtures (cigarette smoke condensate)	1/1	-	-
Miscellaneous heterocycles	1/4	7/7	-
Miscellaneous nitrogen compounds	7/9	2/4	-
Azo dyes and diazo compounds	11/11	2/3	3/3
Common laboratory biochemicals	-	46/46	-
Total	157/178	101/117	11/17

^a McCann et al., from Bridges, 1976.

Purchase et al. (1976) evaluated six short-term carcinogenicity tests. Their results are presented in Tables 4 and 5. They "clearly establish that the Ames test and the cell transformation assay are both able to detect a high percentage of a wide range of carcinogens."

TABLE 4. RESPONSE IN THE SIX SHORT-TERM TESTS TO EIGHT
CARCINOGENIC AND NON-CARCINOGENIC PAIRS^a

Test compound	Ames test	Cell trans- formation	Rabin's test	Subcu- taneous implants	Sebaceous gland suppression	Tetra- zolum reduction	Animal carcino- genicity
4-Nitroquinoline-N-oxide	+	+	+	+	+	+	+
3-Methyl-4-nitroquinoline-N-oxide	-	-	-	-	-	-	-
Benzidine	+	+	+	-	+	-	+
3,3',5,5'-Tetramethylbenzidine	-	-	+	-	-	-	-
2-Acetylaminofluorene	+	+	+	-	-	-	+
4-Acetylaminofluorene	-	-	+	b	b	b	-
9,10-Dimethylantracene	+	+	-	+	+	+	+
Anthracene	-	-	+	-	-	-	-
Dimethylcarbamoyl chloride	+	+	-	+	+	-	+
Dimethylformamide	-	-	-	-	-	-	-
1-Fluoro-2,4-dinitrobenzene	+	+	-	+	+	-	+
1,3-Dinitrobenzene	-	-	-	-	+	-	-
β-Naphthylamine	+	-	+	-	+	+	+
α-Naphthylamine	-	-	-	-	-	-	-
Nitrosofolic acid	+	+	+	-	-	-	+
Diphenylnitrosamine	-	-	+	-	+	+	-
Number of pairs correctly identified	8	7	2	4	5	3	

^a From Purchase et al., 1976.

^b Not tested

TABLE 5. PERCENTAGE OF ACCURATE PREDICTIONS FOR 58
CARCINOGENS AND 62 NON-CARCINOGENS
IN SIX SHORT-TESTS^a

CARCINOGENS		Per Cent
1	Ames test	91
2	Cell transformation	91
3	Rubin's test	71
4	Subcutaneous implants	37
5	Sebaceous gland suppression	67
6	Tetrazolium reduction	40
NON-CARCINOGENS		
1	Ames test	93
2	Cell transformation	97
3	Rubin's test	71
4	Subcutaneous implants	95
5	Sebaceous gland suppression	64
6	Tetrazolium reduction	73

^a From Purchase et al., 1976.

One method of environmental screening for mutagens and/or carcinogens involves the use of different bacterial strains to detect specific changes in the DNA. The assessment of mutagenic and/or carcinogenic activity by bacterial mutagenesis may be carried out in one of three ways or combinations thereof: a) without activation by liver homogenates, b) by activation with liver homogenates, and c) in a host-mediated assay. Such tests as a and b are relatively quick, easy, and inexpensive methods to indicate whether an agent is a mutagen and/or potential carcinogen.

Green, Muriel, and Bridges (1976) found a modified Luria-Delbrück fluctuation test of value when an increase in sensitivity is required to detect mutagens and/or potential carcinogens.

It appears that no bacterial system by itself will be an ideal test for any one substance, but that one system may complement another, e.g., Ames test (*Salmonella*) and Bridges (*E. coli*). Further, the testing proce-

dures may be expanded. For example, in the three-tier approach to mutagenicity and/or carcinogenicity screening, a substance shown in initial testing to be positive or negative is further evaluated in other assay systems on a quantitative basis related to its potential risk to man; in other words, a hazard or benefit assessment (Bridges, 1974).

Microbiol Mutagenicity Assay Systems for Mixed Chemical Wastes

Currently, most mutagenic and/or carcinogenic test systems have been used to assay selected chemicals and/or groups of pure chemicals for their potential hazardous effects (McCann et al., 1975; McCann and Ames, 1976; and Epstein and Legator, 1971). Attention to assessment of mixed chemical wastes is overdue (Clive, 1977). It appears to be a new problem area that has been slow to develop (de Serres, 1977).

Table 6 lists some types of complex mixtures that were screened for mutagenic and/or carcinogenic substances.

TABLE 6. POTENTIAL MUTAGENS AND/OR
CARCINOGENS IN COMPLEX MIXTURES

Nature of Mixture	References
Atmospheric Mutagens	Fishbein, L. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., <u>4</u> , 219-319, 1976. Newell, G., 1977. Personal communication. Brusick, D., 1977. Personal communication. Butterworth, B. E., 1977. Personal communication.
Food Additives	Shahin, M. M. and R. C. von Borstel. MUTAT. RES., <u>38</u> , 215-374, 1976.
Natural Substances	Clark, A. M. MUTAT. RES., <u>32</u> , 361-374, 1976. Clark, C. H. MUTAT. RES., <u>31</u> , 63-64, 1975.
Oil Spills	Payne, J. F. SCIENCE, <u>196</u> : 10, 1977.

TABLE 6. (Cont.)

Nature of Mixture	References
Marine Environment	Parry, J. M., D. J. Tweats and M. A. J. Al-Mossawi. NATURE, <u>364</u> : 538-540, 1976.
Products of Synthetic Fuels (EDC tar)	Rao, T. K., et al. Eighth Annual Meeting Environ. Mutagen Soc., 47-48, 1977. Rubin, I. B., et al. ENVIRON. RES., <u>12</u> , 358-365, 1976. Epler, J. L. Proc. Symp. Management of Residuals from Synthetic Fuels Production, 1976. Epler, J. L. Eighth Annual Meeting Environ. Mutagen Soc., 47, 1977. Commoner, B., 1977. Personal communication. Vithayathil, A., 1977. Personal communication.
*Mixed Chemical Wastes (effluents)	Terraso, M., 1977. Personal communication. Commoner, B. In IDENTIFICATION AND ANALYSIS OF ORGANIC POLLUTANTS IN WATER. Edited by L. H. Keith. Ann Arbor: Ann Arbor Science, 1977. Vithayathil, A., 1977. Personal communication. Commoner, B., Chem. Congress paper, 1975.
Cigarette Smoke Condensates	Kier, L. D., E. Yamasaki and B. N. Ames. PROC. NAT. ACAD. SCI. USA, <u>71</u> , 4159-4163, 1974.

*The prime interest of this study

TABLE 6. (Cont.)

Nature of Mixture	References
	Hutton, J.J., and C. Hackney. CANCER RES., <u>35</u> , 2461-2468, 1975.
	Bock, F. G., A. P. Swain and R.L. Stedman. J. NAT. CANCER INST., <u>49</u> , 477-483, 1972.
	Kubota, H., W. H. Griest, and M. R. Guerin. Paper at the 9th Conf. Trace Substances in Environ. Health, 1975.
	Wynder, E.L. and D. Hoffman. BR. J. CANCER <u>24</u> , 574-587, 1970.
	Wynder, E. L. and G. Wright CANCER, <u>10</u> , 255-271, 1957.
Urine and Blood	Legator, M. S., T. H. Connor and M. Stoeckel. SCIENCE, <u>188</u> , 1118-1119, 1975.
	Legator, M.S., T. Connor and M. Stoeckel. ANN. N.Y. ACAD. SCI., <u>269</u> , 16-20, 1975.
	Legator, M. S., M. Stoeckel and T. Connor. MUTAT. RES., <u>26</u> , 456, 1974.
Urine	Durstun, W. E., and B. N. Ames. PROC. NAT. ACAD. SCI. USA, <u>71</u> , 737-741, 1974.
Soot	Commoner, B., 1977. Personal communication.
	Tilly, W. G., 1977. Personal communication.
Tar Sands	von Borstel, R. C., 1977. Personal communication.

TABLE 6. (Cont.)

Nature of Mixture	References
Vinyl Chloride Industry Waste Products	Rannug, U., and C. Ramel. <i>MUTAT. RES.</i> , <u>38</u> , 113, 1976.
Hair Dyes	Mohn, G. R., and F. J. de Serres. <i>MUTAT. RES.</i> , <u>38</u> , 116-117, 1976. Shafer, N., and R.W. Shafter. <i>N. Y. ST. J. MED.</i> , <u>76</u> , 394-396, 1976. Ames, B. N., H. O. Kammen and E. Yamasaki. <i>PROC. NAT. ACAD. SCI. USA</i> , <u>72</u> , 2423-2427, 1975.
Flame Retardants	Prival, M.J., et al. <i>SCIENCE</i> , <u>195</u> , 76-78, 1977. Blum, A., and B. N. Ames. <i>SCIENCE</i> <u>195</u> , 17-23, 1977.
Waters	McCann, J. See Appendix A.

In the Ames test system (Ames et al., 1973), three factors limit the detection of chemical mutagens: 1) the concentration of the mutagen and/or potential carcinogen is too low compared to the amount of inert material in the mixed waste, 2) the mixed waste contains toxic agents that kill the genetic indicator organism and prevent the growth of mutant colonies, and 3) the mixture contains a concentration of histidine which interferes with the scoring of histidine revertants when *Salmonella typhimurium* strains are used (Bartsch, 1977). The second and third limitations can be overcome by appropriate fractionation procedures and the first, partially by concentration methods. The results presented in Table 6 have taken these points into account in most cases, e.g., fractionation (Epler, 1976 in Rubin et al., 1976).

In this connection, Clark (1977) raises two questions: 1) Do synergistic or antagonistic reactions complicate the situation in testing mixed wastes? 2) Do detoxification processes occur in mixed chemical wastes? To these a third might be added: Do conversion processes occur in mixed wastes, e.g., conversion of non-carcinogens to carcinogens?

In dealing with mixtures, Parry (1977) reports the liquid fluctuation test to be of greater value than the plate assay, but recommends a microbiol screen consisting of both a plate assay using *Salmonella* and a liquid fluctuation test in *E. coli*.

Marquardt and Siebert (1977) emphasize the importance of a basic philosophy in prescreening for carcinogenicity. They suggest:

- 1) It has not been possible to develop a single method that will give full information about the genetic activity of a substance.
- 2) It has not been possible to develop a battery of mutagenicity tests that can be used in every single case schematically.
- 3) It is important to test both dimensions of mutational events:
 - a) The chromosomal-level induction of chromosome aberrations.
 - b) The molecular-level induction of definite types of molecular mutations.

Table 7 lists considerations to study design for the screening of mixed chemical wastes.

TABLE 7. SOME CONSIDERATIONS IN CHOOSING A STUDY DESIGN TO EVALUATE POTENTIAL MUTAGENS AND/OR CARCINOGENS IN MIXED CHEMICAL WASTES

-
- | | |
|----|--|
| 1. | Establish a basic research philosophy for prescreening for mutagens and/or carcinogens, e.g., standardization. (Marquardt and Siebert, 1977) |
| 2. | Is the prescreening concerned with a fractionated or unfractionated mixed waste? e.g., protocol to be used. (Tilly, 1977; Clark, 1977) |
| 3. | Determine the toxicity and/or solubility of the substance, e.g., kind of test to be used. |
| 4. | Is a specific mutagen known to be present or is the test being carried out as a screening assay without prior suspicion as to the nature of the substance? e.g., kind of test to be used. (Clark, 1977) |
| 5. | Consider the pharmacokinetics of the substance. (Marquardt and Siebert, 1977). |
| 6. | Is screening to be limited to the Ames test or is it to be extended with complimentary test, fluctuation tests, tier analysis. e.g., in the case of negatives and false positives. (Parry, 1977; Bridges, 1977; Green, Muriel and Bridges, 1976) |
| 7. | Arrange for disposal of hazardous materials: TAKE ADEQUATE SAFETY MEASURES. (Tarr, 1977; Matney, 1977). |
-

PREDICTIVE VALUE OF SHORT TERM MUTAGENICITY/CARCINOGENICITY TESTING

At least five distinct considerations must be taken into account in evaluating the potential hazard of a substance: 1) Is the substance mutagenic and/or carcinogenic? 2) Is the agent likely to be mutagenic and/or carcinogenic to man? 3) What dose of the mutagen and/or carcinogen is being received, or will likely be received at a risk to the population or individual? 4) What is the risk of exposure to the substance? 5) What is the acceptable risk? (Bridges 1971)

Answers to these questions cannot be obtained by short term testing alone. The recognition of problems relative to short term testing led Bridges (1974) to propose a tier system of testing (de Serres, 1976a).

On the other hand, it has been reported recently that short-term testing has a high predictive value in assaying for mammalian carcinogens. Purchase (1976) states that the Ames test and a cell transformation assay are both sufficiently sensitive to carcinogenicity.

The predictive value of short-term tests, including assays in microbiol systems, had been discussed widely (Legator and Zimmering, 1975; Dean, 1976; McCann et al., 1975; McCann and Ames, 1976; Sobels, 1976; Rochkov et al., 1976; Bartsch, 1976; Purchase, 1976; Matter, 1976; de Serres, 1976b; Bridges, 1976a, b).

SUMMARY

This study has noted the debate and salesmanship active in the growing field of genetic toxicology. However, the growing awareness and world-wide concern over this problem are refreshing.

Increased research aimed at improvements and conveniences for man, not least of which are new energy sources, is proliferating new substances that enter the environment in the form of marketable products or disposable wastes. A rapidly growing store of data is available relative to the potential mutagenicity and/or carcinogenicity of given products or substances, but literature dealing with work on mixtures, such as chemical wastes, is difficult to find.

Testing of mixed chemical wastes should focus on: 1) a long-range objective--to establish a screen sufficiently sensitive (toward 100%) to detect potential mutagens and/or carcinogens; 2) a short-range objective--to design an inexpensive tool that can be used to reduce pollution, even as little as 20% (Terraso).

Intensive study should be undertaken concerning numerous potentially hazardous mixtures being released in the environment in voluminous quantities each day from untold numbers of known and unknown sources.

This monumental task could begin with experimentation using the Ames test, which has been validated as relatively easy, quick and an inexpensive method.

It is difficult to select a specific mutagenicity test appropriate for pre-screening pure substances. Choosing an assay system for mixed substances is involved. Particular data regarding a test gives it greater relevance than another in a given situation, i.e., those systems which a) permit the identification of the nature of induced genetic changes and b) demonstrate that the change is transmitted to subsequent generations. Mutagenicity testing using organisms that are well understood genetically, e.g., Escherichia coli, Salmonella typhimurium, Saccharomyces and Drosophila, meet the requirements outlined here. (IARC MONOGRAPHS XI: 22, 1976).

This study has found it feasible to use bacterial mutagenesis to initiate a series of studies designed to screen for potential mutagens and/or carcinogens in mixed chemical wastes.

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APPENDIX A

PARTIAL LIST OF PERSONS CONCERNED WITH THE MONITORING OF WATERS - AMES TESTING

(Prepared by Dr. Joyce McCann)

People Interested in Mutagenicity of Water Resources (Rivers, Lakes, Drinking Water, Waste Water etc.)

<u>Person</u>	<u>Area of Interest</u>
Argardy, Dr. Franklin Vice President, URS Corp. 155 Bovet Road San Mateo, CA 94402	Consulting firm on pollution
Asketh, Dr. Phoebe Environmental Research and Technology, Inc. 696 Virginia Road Concord, MA 01742	Detection of mutagens in air and water environments
Butler, Dr. Janis Analytical & Research Chemists and Biologists Wilson Laboratories 631 East Crawford P. O. Box 28 Salina, KA 67401	Drinking water analyses; industrial waste
Chriswell, Dr. Colin D. Assistant Chemist II 316 Metallurgy Ames Laboratory, Department of Energy Iowa State University Ames, IA 50011	Analysis of water concentrates using GC mass spectrophoto- meter

Clowes, Dr. Royston C.
Department of Biology
The University of Texas at Dallas
Box 688
Richardson, TX 75080

Efficiency of local water
purification and mutagenic
effects of chloramine
treatment

Fordham, Dr. W. D.
Associate Professor of Chemistry
Farleigh Dickinson University
Teaneck-Hackensack Campus
Teaneck, NJ 07666

Detection and isolation of
carcinogens from Hackensack
River

Gough, Dr. Michael
Assistant Professor
Department of Microbiology
School of Basic Health Sciences
Health Sciences Center
State University of New York
Stony Brook, NY 11794

Analysis of storm water
runoffs, sewage

Grabow, Dr. Wilhelm O. K.
National Institute for Water
Research
Council for Scientific and
Industrial Research
P. O. Box 395
Pretoria 0001, South Africa

Water analysis

Kelly, Mr. Thomas J. Jr.
59 Tyler Street
Hyde Park, MA 02136

Fresh water testing; frog
mutations

Kool, Dr. H.
Rifksinstitut voor Drinkwater-
voorziening
Parkweg 13
Den Hague, The Netherlands

Detection and isolation of
carcinogens in drinking
water

McCormick, Dr. Neil G.
Research Microbiologist
Biotechnology Group
Food Sciences Laboratory
Department of the Army
U.S. Army Natick Research and
Development Command
Natick, MA 01760

Biodegrade nitroaromatics
from H₂O discharges

Moore, Dr. Richard L.
Faculty of Medicine
Division of Pathology
The University of Calgary
2920 24 Avenue N.W.
Calgary, Canada T2N 1N4

Water quality study -- rivers
in Alberta, Canada

Ogg, Dr. James E.
College of Veterinary Medicine
and Biomedical Sciences
Department of Microbiology
Colorado State University
Fort Collins, CO 80523

Mutagenic chemicals in waste
water

Pelon, Dr. William
Department of Tropical Medicine
and Medical Parasitology
Louisiana State University Medical Center
1542 Tulane Avenue
New Orleans, LA 70112

Detection of carcinogens in
water samples

Poppel, Mr. David
Graduate Research Assistant
Department of Botany
The University of Massachusetts
Amherst, MA 01002

Detection of mutagens in
river water

Roberts, Ms. Lesley Joyce
Research Assistant
Indiana Public Interest Research
Group of Bloomington, Inc.
703 East 7th
Bloomington, IN 47401

Water quality in regional
water resources

Solse, Dr. Mark
Assistant Professor of Environ-
mental Microbiology
Department of Environmental
Sciences and Engineering
The School of Public Health
The University of North Carolina
Chapel Hill, NC

Detection of mutagens/
carcinogens in water and
wastewater

Stang, Mr. William J.
Chief, Microbiology Section
Environmental Protection Agency
Office of Enforcement
National Enforcement Investigations
Center
Building 53, Box 25227
Denver Federal Center
Denver, CO 80225

Mutagens/carcinogens in
water

Starkey, Mr. Roland J. Jr.
Graduate Student
Ecology Laboratory
Room 308, Disque Hall
Department of Biological Sciences
Drexel University
Philadelphia, PA 19104

Occurrence of mutagenic
agents in the aquatic
environment

Stewart, Mr. Ken
c/o Dr. Leah Koditschek
Department of Microbiology
Montclair State College
State of New Jersey
Upper Montclair, NJ 07043

Tardiff, Dr. Robert G.
Executive Director
Board on Toxicology and Environ-
mental Health Hazards
National Academy of Sciences/
National Research Council
2101 Constitution Avenue, N.W.
Washington, D.C. 20418

Wilson, Dr. John E.
School of Public Health and
Community Medicine
Department of Environmental
Health, SC-34
University of Washington
Seattle, WA 98195

Recovery and viability of E.
coli in polluted estuarine
sediment. Assay for muta-
genic activity with Salmonella/
Microsome test

Mutagenic activity of drinking
water concentrates

Water analysis

APPENDIX B

PARTIAL LIST OF PERSONS CONCERNED WITH ENVIRONMENTAL MONITORING

(Prepared by Dr. William R. Lower)

<u>Laboratory</u>	<u>Area of Interest</u>
Abrahamson, Dr. S. Department of Zoology University of Wisconsin Madison, WI 53706	Drosophila, mutagenesis testing
Bartling, Mr. G. Cancer Research Center P. O. Box 1268 Columbia, MO 65201	Salmonella: environmental
Bishop, Dr. Jack Division of Mutagenesis National Center for Toxicological Research Mail Code 8 Jefferson, AK 72079	Development and validation of mutagenesis protocols-proving animal dose and response data
DeMarini, Dr. D. M. Department of Biological Sciences Illinois State University Normal, IL 69761	Water of lakes and cigarette smoke. Lower eucaryotes as test systems.
Epler, Dr. James L. Unit Leader, Biology Division Oak Ridge National Laboratory Oak Ridge, TN 37830	Microbial system, Drosophila, mammalian cells
Evans, Dr. John E. Department of Biology University of Houston Houston, TX 77004	Ames testing of mixed chemical wastes

Fevers, Mr. Ritchie
Division of Mutagenesis
National Center for Toxicological
Research
Mail Code 8
Jefferson, AK 72079

Flessel, Dr. Peter
Environmental Biochemistry Group
Air and Industrial Hygiene
Laboratory
California State Department of
Health
2151 Berkeley Way
Berkeley, CA 94704

Franklin, Dr. Ralph
Soil Scientist
Environmental Programs
Division of Biomedical and Environ-
mental Research
Department of Energy
Washington, DC 20545

Gentile, Dr. J. M.
Department of Biological Sciences
Hope College
Holland, MI 49423

Grant, Dr. William F.
Genetics Laboratory
MacDonald Campus of McGill
University
Ste. Anne de Belleone
Quebec, Canada HOA ICO

Hardigree, Dr. Alice
Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, TN 37830

Hooper, Dr. Kim
Department of Biochemistry
University of California
Berkeley, CA 94704

Johnson, Dr. F. M.
Chemistry and Life Sciences
Division
Research Triangle Institute
Research Triangle Park, NC 27709

Ames assay, air and industrial
samples, heavy metal muta-
genesis

Changes in ecological para-
meters, particularly in energy
facilities or fuel cycles

Plant vs. animal activation
studies; mutagenesis of
naturally occurring microbial
populations

Cytogenetics of pesticides

Water, pesticides, mutagenic
and carcinogenic potency:
Salmonella system

Bioassay-environmental
analysis

Laimer, Dr. F. W.
Biology Division
Oak Ridge National Laboratory
Oak Ridge, TN 37830

Lower, Dr. William R.
Environmental Trace Substances
Research Center
University of Missouri, Columbia
Columbia, MO 65201

Ma, Dr. Te-Hsiu
Department of Biological Science
Western Illinois University
Macomb, IL 61455

Nauman, Dr. Charles H.
Biology Department
Brookhaven National Laboratory
Upton, NY 11973

Pelroy, Dr. Richard
Battell North West
Richland, WA 99352

Plewa, Dr. Michael J.
100 Environmental Research
Laboratory
Institute for Environmental
Studies
University of Illinois
Urbana, IL 61801

Rao, Dr. T. K.
Biology Division
Oak Ridge National Laboratory
P. O. Box Y
Oak Ridge, TN 37830

Rogers, Dr. Sam
Chemistry Department
Montana State University
Bozeman, MT 59715

Sandhu, Dr. Shahbeg
Research Biologist
Health Effects Research Laboratory
Protection Agency
Research Triangle Park, NC 27711

Gene mutation and mitotic
recombination assays with
yeast applications to moni-
toring synthetic fuel
technologies

Environmental monitoring,
heavy metal mutagenesis
Tradescantia, corn, soy-
bean, Peromyscus, domestic
animals, Drosophila

Tradescantia, chromosome
damage, air and water
pollutants

Tradescantia, chemical
mutagen/physical mutagen
somatic, mutation induction

Plant activation, Zea maize
wx locus assay, pesticide
evaluation

Salmonella typhimurium, E.
coli, energy related -
environmental effluents

Chemistry of rafter dust,
Tradescantia, microbial
systems

Cellular toxicity, mutagenesis
and cellular neoplastic trans-
formation (oncogenesis)

Schairer, Dr. Lloyd A.
Biology Department
Brookhaven National Laboratory
Upton, NY 11973

Tradescantia test system in
the lab as well as in the
mobile monitoring vehicle -
field testing

Schmidt-Collerus, Dr. Josef
Denver Research Institute
University of Denver
Denver, CO 80200

Stebbins, Dr. James H.
Health Division MS881
Los Alamos National Laboratory
Los Alamos, NM 87454

Human population studies

Sumner, Dr. Darrell
CIBA-GEIGY Corporation
Greensboro, NC 27420

Pesticide metabolism

Tomkins, Dr. Darrell J.
Department of Pediatrics
McMaster University Medical Center
Hamilton, Ontario Canada L8S 4J9

Human and plant populations

Vyse, Dr. E. R.
Department of Biology
Montana State University
Bozeman, MT 59715

Drosophila - air monitoring,
pesticide testing

Warren, Dr. G. R.
Chemistry Department
Montana State University
Bozeman, MT 59715

Microbial systems

Zimmering, Dr. Sam
Division of Biological and
Medical Sciences
Brown University
Providence, RI 02912

Mutagenicity testing of envi-
ronmental compounds in Dro-
sophila and improvement of
techniques for mutagenicity
testing in Drosophila

APPENDIX C

PARTIAL LIST OF PERSONS CONCERNED WITH SCREENING MIXED CHEMICAL WASTES FOR MUTAGENIC OR CARCINOGENIC ACTIVITY

(Prepared by Dr. John E. Evans)

<u>Person</u>	<u>Area of Interest</u>
Bridges, Professor Bryn A. Director, MRC Cell Mutation Unit University of Sussex Falmer, Brighton BN1 9QG England	Mixtures
Brusick, Dr. David Director, Department of Genetics Litton Bionetics 5516 Nicholson Lane Kensington, MD 20795	Air samples
Chrisp, Dr. C. E. Radiobiology Laboratory University of California Davis, CA 95616	Coal ash
Clark, Professor A. M. Department of Biology The Flinders University of South Australia Bedford Park, South Australia 5042	Mixed wastes
Epler, Dr. James L. Unit Leader, Biology Division Oak Ridge National Laboratory Oak Ridge, TN 37830	Energy systems

Lower, Professor William R. Group Leader, Environmental Trace Substances Research Center University of Missouri Route 3 Columbia, MO 65201	Air samples
Ma, Professor Te-Hsiu Department of Biological Sciences Western Illinois University Macomb, IL 61455	Gaseous pollutants Water solutions
Parry, Professor James M. Department of Genetics University College of Swansea Singleton Park Swansea SA2 8PP, U.K.	Hydro-carbon mixtures
Terraso, Dr. Michael F. Laboratory Director Harris County Pollution Control Department 107 North Munger Box 6031 Pasadena, TX 77506	Mixed chemical wastes
Thilly, Professor William G. Department of Nutrition and Food Science Rm E18-664 Cambridge, MA 02139	Mixed chemical wastes
Tokiwa, Professor Hiroshi Fukuoka Environmental Research Center, 39 Mukaeda Dazaifu-machi, Chikushi-gun Fukuoka, 818-01, Japan	Air samples
Urwin, Dr. Colin Huntingdon Research Centre Huntingdon, Cambs., U.K.	Cutting oils
Venitt, Dr. S. Division of Chemical Carcinogenesis Institute of Cancer Research Pollards Wood Research Station Nightengales Lane Chalfont St. Giles, Bucks, HP8 4SP, U.K.	Food color mixtures

Vithayathil, Dr. Antony J.
Project Coordinator
Center for the Biology of Natural
Systems
Washington University
Box 1126
St. Louis, MO 63130

Mixed chemical wastes
Air samples

von Borstel, Professor R. C.
Department of Genetics
The University of Alberta
Edmonton, Canada T6G 2E9

Tar sands
Mixed chemical wastes

APPENDIX D

SELECTED REFERENCES CONCERNED WITH MUTAGENESIS AS A SCREENING TOOL

(Prepared by Dr. John E. Evans)

MICROBIOL ASSAY SYSTEMS FOR ENVIRONMENTAL CARCINOGENS AND/OR MUTAGENS

Agnet, Y., J. L. Dorange and P. Dupuy

Mutagenicity of Peracetic Acid on Salmonella typhimurium. MUTAT. RES.,
XXXVIII: 119, 1976.

An abstract

Mutagenicity testing by procedure of Ames (Salmonella)

Alper, M. D., and B. N. Ames

Positive Selection of Mutants With Deletions of Gal- chl Region of the
Salmonella Chromosome as a Screening Procedure for Mutagens That
Cause Deletions. J. BACT., CXXI: 259-266, 1975. 32 refs.

This paper presents a positive selection procedure for mutants with long
deletions in the gal region of the chromosomes of Salmonella typhimurium
and Escherichia coli. The technique is of value in the screening of
mutagens for their ability to generate long deletions in the bacterial
deoxyribonucleic acid.

Ames, B. N.

A Bacterial System for Detecting Mutagens and Carcinogens. ENVIRON.
SCI.: AN INTERDISCIPLINARY MONOGRAPH SERIES, 57-66, 1972.
12 refs.

Characteristics of the Ames Mutagenicity Test are discussed, e.g.,
simplicity, sensitivity, comprehensiveness and strain characteristics.
Mutagenicity testing procedure is given.

Ames, B. N.

A Combined Bacterial and Liver Test System for Detection and Classification of Carcinogens as Mutagens. GENETICS, LXXVIII: 91-95, 1974. 8 refs.

A general discussion paper dealing with a system for detection of mutagens and carcinogens. They postulate that carcinogens cause cancer by somatic mutation and suggest that this combined detection system is a simple procedure for detecting carcinogens.

Mutagenicity testing by procedure of Ames.

Ames, B. N., H. O. Kamman and E. Yamasaki

Hair Dyes are Mutagenic: Identification of a Variety of Mutagenic Ingredients. PROC. NAT. ACAD. SCI. USA, LXXII: 2423-2427, 1975. 36 refs.

Hair dying chemicals are carcinogens or mutagens as shown by the S. typhimurium tester strains.

Ames, B. N., F. D. Lee and W. E. Durston.

An Improved Bacterial Test System for the Detection and Classification of Mutagens and Carcinogens. PROC. NAT. ACAD. SCI. USA, LXX: 782-786, 1973. 18 refs.

An improved S. typhimurium tester strain deficient in lipopolysaccharide, known as deep rough, has been constructed for detection of carcinogens as mutagens.

The techniques for using the strains for detecting mutagens are shown to be extremely sensitive and convenient. The specificity of frameshift mutagenesis is clarified. A test is described, comparing mutagenic killing in deep rough strains with and without DNA excision repair, and a test using forward mutagenesis in a deep rough strain lacking excision repair.

Ames, B. N., J. McCann and E. Yamasaki.

Methods for Detecting Carcinogens and Mutagens With the Salmonella/mammalian-microsome Mutagenicity Test. MUTAT. RES., XXXI: 347-364, 1975. 29 refs.

Various facets of the Salmonella/mammalian microsome mutagenicity test are described and discussed, including the standard plate test, the use and storage of the bacterial tester strains, preparation and use of the liver homogenates (S-9), and the methods of inducing the rats for elevated microsomal enzyme activity. Application and interpretation of results is discussed.

Mutagenicity testing by procedure of Ames (Salmonella).

Ames, B. N., P. Sims and P. L. Grover.

Epoxides of Carcinogenic Polycyclic Hydrocarbons are Frameshift Mutagens. SCIENCE, CLXXVI: 47-49, 1972. 20 refs.

K-region epoxides of the carcinogens benz[a]anthracene, dibenz[a,h]-anthracene, and 7-methylbenz[a]anthracene are mutagenic in strains of *S. typhimurium* designed to detect frameshift mutagens. Parent hydrocarbons, K-region diols and phenols and some other epoxides are inactive as mutagens in these tests. Polycyclic hydrocarbon epoxides, and other presumed proximal carcinogens, are discussed as examples of intercalating agents with reactive side chains. It has been shown previously that intercalating agents with reactive side chains are potent frameshift mutagens.

Mutagenicity testing by procedure of Ames.

Ames, B. N., and H. J. Whitfield, Jr.

Frameshift Mutagenesis in Salmonella. COLD SPRING HARBOR SYMPOSIA, XXXI: 221-225, 1966. 17 refs.

A basic discussion of frameshift mutation in Salmonella is presented, describing ICR mutagens, a group of new acridine-like compounds which are powerful mutagens in bacteria. Evidence is presented, suggesting that these compounds add and/or delete nucleotides from DNA.

Mutagenicity testing by procedure of Ames.

Ames, B. N., and C. Yanofsky

The Detection of Chemical Mutagens With Enteric Bacteria. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., I: 267-282, 1971. 19 refs.

Any test system for mutagens should be calibrated against the known mutagens to determine the ease and sensitivity of the test in detecting these compounds before trying new substances. We believe bacteria are the system of choice for mass screening of new compounds on the basis of simplicity, sensitivity, economy, and range of compounds detected. Characteristics of the bacterial mutagenicity test are described.

Mutagenicity testing by the procedure of Ames.

Ames, B. N., et al.

Carcinogens as Frameshift Mutagens: Metabolites and Derivatives of 2-acetyl-amino Fluorene and Other Aromatic Amine Carcinogens. PROC. NAT. ACAD. SCI. USA, LXIX: 3128-3132, 1972. 66 refs.

Certain metabolites of carcinogenic substances, 2-acetyl-aminofluorene, nitro and derivatives of 5 other aromatic amines are frameshift mutagens. It is suggested that carcinogens are carcinogenic as a result of a reactive intercalation into DNA. The utility of a set of bacterial strains for detecting carcinogens as mutagens is shown.

Mutagenicity screening by procedure of Ames.

Ames, B. N., et al.

Carcinogens are Mutagens: A Simple Test System Combining Liver Homogenates for Activation and Bacteria for Detection. PROC. NAT. ACAD. SCI. USA, LXX: 2281-2285, 1973. 23 refs.

Carcinogens and mutagens cause cancer by somatic mutation. Eighteen carcinogens are shown to be activated by liver homogenates, forming potent frameshift mutations in S. typhimurium. We believe that these carcinogens have in common a ring system sufficiently planar for a stacking interaction with DNA base pairs and a part of the molecule capable of being metabolized to a reactive group: these structural features are discussed in terms of the theory of frameshift mutagenesis. We propose that these carcinogens, and many others that are mutagens, cause cancer by somatic mutation. A simple, inexpensive and extremely sensitive test for detection of carcinogens as mutagens is described. It consists of the use of a rat or human liver homogenate for carcinogen activation and a set of Salmonella histidine mutants for mutagen detection. The homogenate, bacteria and a TPHN-generating system are all incubated together on a petri plate. With the most active compounds, as little as a nanogram can be detected.

Mutagenicity testing by procedure of Ames (Salmonella).

Andrews, A. W., E. S. Zawistowski and C. R. Valentine.

A Comparison of the Mutagenic Properties of Vinyl Chloride and Methyl Chloride. MUTAT. RES., XL: 273-276, 1976. 9 refs.

A screening program for environmental gases using the Ames assay has shown that vinyl chloride and methyl chloride are highly mutagenic.

Mutagenicity testing by procedure of Ames.

Anton, D. N. and L. V. Orce.

Envelope Mutation Promoting Autolysis in S. typhimurium. MOLEC. GEN. GENET., CXLIV: 97-105, 1976.

Two strains independently isolated in S. typhimurium display abnormal autolytic activity when nutrient broth becomes alkaline. They also show increased sensitivity to deoxycholate, EDTA, and sodium dodecyl sulfate. Response to acridine orange remains normal. In both strains a single stable mutation is responsible for all the changes.

Mutagenicity testing by procedure of Ames.

Bamford, D., et al.

Mutagenicity and Toxicity of Amitrole. III. Microbial Tests. MUTAT. RES., XL: 197-202, 1976. 15 refs.

Amitrole inhibits bacterial growth both in E. coli and S. typhimurium at a concentration of 0.5% in minimal medium.

Mutagenicity was tested by differential growth comparisons on E. coli strains defective in DNA polymerase I and a revertant. Known mutagens were used as positive controls.

Mutagenicity testing by procedure of Ames.

Bardodej, Z.

Metabolic Studies and the Evaluation of Genetic Risk from the Viewpoint of Industrial Toxicology. MUTAT. RES., XLI: 7-14, 1976. 43 refs.

The paper is concerned with important industrial chemicals, e.g., solvents, and monomers used in the production of plastics, which have been found to be more dangerous than had been suspected. Some of them are mutagens and carcinogens. Mutagenicity testing by procedures of Ames and using *Drosophila* is mentioned.

Bartsch, H., A. Camus and C. Malaveille.

Comparative Mutagenicity of N-nitrosamines in a Semi-Solid and in a Liquid Incubation System in the Presence of Rat or Human Tissue Fractions. MUTAT. RES., XXXVII: 149-162, 1976.

The rat liver microsome-mediated mutagenicities of a series of N-nitroso-dialkylamines and heterocyclic N-nitrosamines were determined in a liquid incubation system using S. typhimurium TA1530. The influence on mutation frequency of the concentration of co-factors for mixed-function oxidase and composition and molarity of the buffer was investigated, using N-nitrosomorpholine as substrate. The mutagenicity of the N-nitroso compounds in the liquid incubation system under optimal reaction conditions at equimolar concentration was compared quantitatively with that obtained in a soft-agar incorporation assay.

The plate incorporation assay is more effective in detecting chemicals whose metabolic conversion into mutagens occurs at a low rate. Incorporation of liver microsomal enzymes in a soft-agar layer prolongs their viability for up to several hours.

Mutagenicity testing by procedure of Ames (Salmonella)

Bartsch, H., and R. Montesano.

Mutagenic and Carcinogenic Effects of Vinyl Chloride. MUTAT. RES., XXXII: 93-114, 1975. 100 refs.

The available data concerning the biological hazards of VCM show that this compound is toxic, mutagenic and carcinogenic in man, as well as in animals.

The mutagenic action of VCM in microbial systems has been demonstrated. Mutagenicity testing by procedure of Ames.

Bartsch, H., et al.

Tissue-Mediated Mutagenicity of Vinylidene Chloride and 2-Chlorobutadiene in S. typhimurium. NATURE, CCLV: 641-643, 1975. 20 refs.

We have examined the mutagenicity of VDC and 2-chlorobutadiene in S. typhimurium strains, using a tissue-mediated assay which has been found effective in detecting the mutagenicity of various carcinogens, such as nitrosamines, vinyl chloride and many others.
Mutagenicity testing by the procedure of Ames.

Benditt, E. P.

The Origin of Atherosclerosis. SCI. AM., CCXXXVI: 74-85, 1977. 5 refs.

The monoclonal hypothesis, which holds that the proliferating cells of an atherosclerotic plaque all stem from one mutated cell, suggests new lines of research on the causes of coronary disease.

Mutagenicity testing by procedure of Ames (Salmonella)

Blum, A., and B. N. Ames

Flame-Retardant Additives as Possible Cancer Hazards. SCIENCE, CXCIV: 17-23, 1977. 53 refs.

The flame retardant in children's pajamas is a mutagen.

Mutagenicity testing by procedure of Ames.

Braun, R., and J. Schöneich

The Influence of Ethanol and Carbon Tetrachloride on the Mutagenic Effectivity of Cyclophosphamide in the Host-Mediated Assay with S. typhimurium. MUTAT. RES., XXXI: 191-194, 1975. 10 refs.

Synergistic effects of the type described here are of interest with respect to chemical mutagenesis in man. A modern trend in medicine is the simultaneous administration to patients of two and more drugs. Furthermore, patients may obtain and use drugs from irregular sources in addition to those prescribed or may abuse drugs during therapeutic treatments. In the cases described here uncontrolled potentiation of mutagenic effects might be possible and should be taken into consideration.

Mutagenicity testing by procedure of Ames.

Brem, H., A. B. Stein and H. S. Rosenkranz

The Mutagenicity and DNA-Modifying Effect of Haloalkanes. CANCER RES., XXXIV: 2576-2579, 9 refs.

A series of haloalkanes, some of them widely used in industry and in the home, are shown to be mutagenic for S. typhimurium and preferentially to inhibit the growth of DNA polymerase-deficient E. coli. It was found that the relative activities of the test substances differed when examined in these systems and that one of the agents was active in the pol A₁-system only. In view of these results it is suggested that both assays be used in routine screening of environmental agents.

Mutagenicity testing by procedure of Ames and DNA polymerase-deficient E. coli.

Bridges, B. A.

Simple Bacterial Systems for Detecting Mutagenic Agents. LAB. PRACT., XXI: 413-419, 1972. 8 refs.

Bacteria may be used to detect specific types of mutational damage. Most mutagens, however, are not very specific and a more useful system is one that responds to a wide variety of mutagenic agents. Detailed descriptions are given of techniques that can be used with the bacterium E. coli WP2 which mutates from tryptophan requirement to independence. A number of strains deficient in repair functions are available which give useful information about the type of DNA damage and the mechanism of mutagenesis with a particular agent.

Mutagenicity testing - E. coli.

Bridges, B. A., R. E. Dennis and R. J. Munson

Differential Induction and Repair of Ultraviolet Damage Leading to True Reversions and External Suppressor Mutations of an Ochre Codon in E. coli B/r WP2. GENETICS, LVII: 897-908, 1967. 28 refs.

Evidence is presented that a number of E. coli strains have chain-terminating codons at their auxotrophic loci. They may mutate to prototrophy either by true reversion at the chain-terminating codon or by mutation at suppressor loci. The two types of prototroph may be distinguished by the ability of the latter to support growth of T4 phage also carrying chain-terminating mutations. In E. coli B/r WP2 Try-, which appears to have an ochre codon, both types of mutation arise spontaneously.

Mutagenicity testing - E. coli.

Bridges, B. A., R. E. Dennis and R. J. Munson.

Mutation in E. coli B/r WP2 Try- by Reversion or Suppression of a Chain-Terminating Codon. MUTAT. RES., IV: 502-504, 1967. 17 refs.

We conclude from our results that E. coli B/r WP2 carries a chain-terminating mutation, possibly an ochre (UAA codon), at one of its tryptophan loci. Bacteria may mutate to prototrophy either by a presumed true reversion at this locus or by an external ochre suppressor mutation.

Mutagenicity testing - E. coli.

Bridges, B. A., J. Law and R. J. Munson.

Mutagenesis in E. coli. II. Evidence for a Common Pathway for Mutagenesis by Ultraviolet Light, Ionizing Radiation and Thymine Deprivation. MOLEC. GEN GENETICS, CIII: 266-273, 1968. 27 refs.

Both thymine starvation and gamma radiation, like ultraviolet light, produce base change mutations to prototrophy in E. coli and EXr+ phenotype is involved in the mutation process. DNA strand breakage is a direct or indirect consequence of all three treatments suggesting that the filling of gaps in DNA by a process involving the EXr gene product may be a common step in mutagenesis.

Mutagenicity testing - E. coli.

Bridges, B. A., and R. P. Mottershead.

Mutagenic DNA Repair in E. coli. MOLEC. GEN. GENET., CXLIV: 53-58, 1976. 28 refs.

The POLC temperature-sensitive DNA polymerase III mutation from E. coli BT1026 has been transduced into E. coli WP2 and WP2 UVRA. In excision-deficient CM741 UV-induced Trp+ mutations progressively lost their photoreversibility during post-irradiation incubation at 34°. Immediately after transfer to 43°, however, there was no further loss of reversibility although post-replication strand joining still occurred and uptake of 3H-thymidine into DNA continued for 20 to 30 min. In excision-proficient CM731, UV lesions capable of leading to Str. mutations disappeared during post-irradiation incubation at restrictive temperature and there was no increase in the number remaining after exposure to photoreversing light. In contrast, at permissive temperature, pre-mutational lesions were not lost and became progressively converted into non-photoreversible mutations. It is concluded that a function of the POLC gene is necessary for error-prone repair to occur and that this function is defective at 43° in the enzyme specified by the POLC allele from BT1026. This function seems not to be essential for most post-replication or excision repair or for normal DNA replication and may be particularly involved in the insertion of incorrect bases during error-prone repair.

Mutagenesis testing E. coli.

Bridges, B. A., R. P. Mottershead and C. Collella.

Induction of Forward Mutations to Colicin E₂ Resistance in Repair Deficient Strains of E. coli: Experiments with Ultraviolet Light and Captan. MUTAT. RES., XXI: 303-313, 1973. 8 refs.

The present experiments confirm the previous observation made with spot-test technique that captan produces excisable DNA damage in bacteria that leads to the formation of mutations via a pathway dependent upon the EXRA+ gene.

Mutagenicity testing - E. coli.

Bridges, B. A., and R. J. Munson.

Mutagenesis in E. coli: Evidence for the Mechanism of Base Change Mutation by Ultraviolet Radiation in a Strain Deficient in Excision-repair. PROC. ROY. SOC. B., CLXXI: 213-226, 1968. 23 refs.

The mutagenic action of UV radiation has been studied upon E. coli WP 2 Try HCR growing exponentially at 37°C. Although this strain is unable to excise pyrimidine dimers from its DNA, it showed no detectable reduction in growth rate after exposure to a dose of UV calculated to produce several dozen pyrimidine dimers per chromosome. As judged by photoreversibility of mutations to prototrophy, dimers at mutable sites may persist for up to about 4 generation times after UV and may give rise to mutations with a low probability in each replication cycle during this period. The slow disappearance of dimers takes place whether or not DNA replication is inhibited and indirect evidence suggests that excision-repair may not be involved. Mutations are established only when DNA replication is taking place and are not expressible on unsupplemented medium until approximately one generation time after being established. Mutagenicity testing - E. coli.

Bridges, B. A., et al.

Mutagenicity of Dichlorvos and Methyl Methane-Sulphonate for E. coli WP 2 and Some Derivatives Deficient in DNA Repair. MUTAT. RES., XIX: 295-303, 1973. 26 refs.

The mutagenic and lethal action of methyl methanesulphonate and dichlorvos has been studied on E. coli WP 2 and some derivatives deficient in DNA repair genes. The EXRA⁺ and RECA⁺ alleles were necessary for significant mutagenesis by either compound, and the UVRA gene affected neither the lethal nor mutagenic responses. Increased sensitivity to both compounds was shown by the EXRA and VRAEXRA strains and in a more pronounced way by the UVRA POLA, RECA and UVRAEXRAPOLA strains. Bacteria deficient at the POLA locus were 2 and 3 times more mutable by DDVP and MMS respectively. Single strand breaks were detectable by alkaline sucrose gradient centrifugation after both MMS and DDVP treatment of POLA bacteria.

Mutagenicity testing in E. coli.

Bridges, B. A., et al.

Repair-Deficient Bacterial Strains Suitable for Mutagenicity Screening: Tests With the Fungicide Captan. CHEM.-BIOL. INTERACT., X: 77-84, 1972. 19 refs.

A spot test with selected repair-deficient strains of E. coli is described which not only provides a sensitive assay for the mutagenic activity of chemicals, but also gives useful information about the characteristics of the mutagenic process. The production of this volatile mutagen is greater at alkaline pH. The excisable DNA damage produced by the mutagen does not depend on EXRA⁺ and RecA⁺ repair functions for its mutagenicity.

Mutagenicity testing by E. coli.

Brock, R. D.

Differential Mutation of the B-galactosidase Gene of E. coli. MUTAT. RES., XI: 181-186, 1972. 11 refs.

A range of mutagenic agents has been tested using the B-galactosidase locus of E. coli. Treatment with alkylating agents diethyl sulphate, ethyl methanesulphonate and N-methyl-N'-nitro-N-nitrosoguanidine induced a higher frequency of mutation when applied to the active gene than when applied to the inactive gene. X-Rays and base analogues 5-bromodeoxyuridine and 2-aminopurine had the same mutagenic efficiency for both active and inactive genes.

Mutagenicity testing - E. coli.

Brown, J. P., and R. J. Brown.

Mutagenesis by 9,10-anthraquinone Derivatives and Related Compounds in S. typhimurium. MUTAT. RES., XL: 203-224, 1976. 51 refs.

Ninety 9,10-anthraquinone derivatives and related anthracene derivatives were screened for mutagenicity with 5 S. typhimurium tester strains with and without mammalian microsomal activation. About 35% of the compounds tested are considered to be mutagenic. Three patterns of mutagenesis were apparent.

Mutagenicity testing - Procedure of Ames.

Carere, A., et al.

Mutational Studies With Some Pesticides in Streptomyces coelicolor and Salmonella typhimurium. MUTAT. RES., XXXVIII: 136, 1976.

An abstract

Mutagenicity testing by procedure of Ames (Salmonella) and in Streptomyces coelicolor.

Carere, A., et al.

Point Mutations Induced by Pharmaceutical Drugs. MUTAT. RES., XXIX: 235, 1975.

To rapidly test the mutagenic activity of pharmaceutical drugs, two genetic systems have been set up in the filamentous bacterium Streptomyces coelicolor.

An abstract.

Mutagenicity testing - S. coelicolor.

Chambers, C., and S. K. Dutta.

Mutagenic Tests of Chlordane on Different Microbial Tester Strains. SCIENCE, LXXXIII: s13, 1976.

Three different microbial tester strains of Saccharomyces cerevisiae D₃, D₄ and D₅ to measure mitotic recombination and mitotic gene conversion

events; and three tester strains of S. typhimurium strains TA1535, TA100 and TA1538 for detecting base-pair substitution and frameshifts were used to test the potential mutagenic effects of chlordane, a chlorinated cyclodiene.
Mutagenicity testing by the procedure of Ames (Salmonella) and in S. cerevisiae.

Combes, R. D.

Inability of Genetic Systems of B. subtilis to Detect a Mutagenic Effect of Low Frequency Ultrasound. J. APPL. BACT., XXXIX: 219-226, 1975. 21 refs.

Possible mutagenic effects of low frequency ultrasound have been assessed with genetic systems of B. subtilis. Ultrasound was unable to cause a detectable increase in the spontaneous frequency of back-mutation irrespective of the degree of killing. Similar treatments were incapable of producing mutagenic lesions that could be detected by the system of transformation after in vitro treatment of DNA. Transforming activity and molecular weight could be reduced without a corresponding decline in linkage between two contiguous markers. It is concluded that mutagenic effects of ultrasound could not be detected by these genetic systems.

Mutagenicity assay in B. subtilis.

Commoner, B.

Chemical Carcinogens in the Environment. Paper presented at the First Chemical Congress of the North American Continent, Mexico City, Mexico, December 1, 1975. 8 refs.

A paper on environmental carcinogens, e.g., petrochemical effluents and air pollutants.

Mutagenicity testing by procedure of Ames (Salmonella).

Commoner, B., A. J. Vithayathil and J. I. Henry.

Detection of Metabolic Carcinogen-fed Rats by Means of Bacterial Mutagenesis. NATURE, CCXLIX: 850-852, 1974. 9 refs.

Thus, metabolic intermediates of AAF and DAB can be detected in the urine of rats fed on diets that contain these carcinogens by means of tests based on mutagenicity towards a strain of S. typhimurium, while the urine of rats on normal diets yields no significant response in these tests.
Mutagenicity testing by procedure of Ames.

Connor, T. H., et al.

The Contribution of Metronidazole and Two Metabolites to the Mutagenic Activity Detected in Urine of Treated Humans and Mice. CANCER RES., XXXVII: 629-633, 1977. 12 refs.

The urine of two patients receiving therapeutic doses of the trichomonacide, metronidazole, was analyzed for mutagenic activity using the histidine auxotroph TA1535 of S. typhimurium. The activity detected in the urine was significantly higher than could be accounted for by the presence of the administered drug. Chromatographic analysis of the urine indicated the presence of the metabolite, which, when tested in vitro with AT1535 was found to be ten times more active than metronidazole. An additional urinary metabolite was found to be inactive when similarly tested. The in vitro mutagenic activity of metronidazole and the two metabolites were unchanged by the addition of phenobarbital-or Arclor-induced rat liver homogenate to the test system. Metronidazole and the hydroxymethyl metabolite reverted S. typhimurium TA100 but not TA1537, TA1538 or TA98, and the acetic acid metabolite failed to revert any of the tester strains. Findings using mice indicate the production of metabolites from the parent compound by the liver of the intact animal which could not be determined by use of the standard in vitro liver homogenate system. Mutagenicity testing by procedure of Ames.

Corran, J.

The Induction of Supersuppressor Mutants of B. subtilis by Ethyl Methanesulphonate and the Posttreatment Modification of Mutation Yield. MOLEC. GEN. GENETICS, CIII: 42-57, 1968. 24 refs.

Supersuppressor mutants have been induced in a strain of B. subtilis with the chemical mutagen ethyl methanesulphonate. The yield of mutants recovered is dependent on the degree of supplementation of the selective plating medium with minute quantities of either nutrient broth or the previously required growth supplements. The optimal quantities of these media additives have been established and the superiority of nutrient broth described. This "broth effect" has been shown to be due to components of the nutrient broth other than the previously required growth substances.

Mutagenicity tested in B. subtilis.

Couch, D. B. and M. A. Friedman.

Interactive Mutagenicity of Sodium Nitrite, Dimethylamine, Methylurea and Ethylurea. MUTAT. RES., XXXI: 109-114, 1975. 20 refs.

Groups of mice were treated per os with sodium nitrite either alone or in combination with nitrosatable amino compounds and tested in the host-mediated assay. When mice were treated with sodium nitrite in combination with dimethylamine a small but significant increase in mutant frequency was observed. Ethylurea or methylurea in combination with sodium nitrite induced 10- or 850-fold increases in MF, respectively. The response to methylurea was dose-dependent with a 6- and 30-fold increase in MF at 5.4 and 11.5 mg/kg NaNO_2 and a 6-fold increase at 108 mg/kg methylurea. That this response reflected gastric nitrosation was shown by the disappearance of the response if NaNO_2 administration preceded methylurea treatment by 10 min. High MF's were observed if NaNO_2 was administered 10 or 20 min. after methylurea.

Mutagenicity testing by procedure of Ames.

Czygan, P., et al.

Microsomal Metabolism of Dimethylnitrosamine and the Cytochrome P-450 Dependency of Its Activation to a Mutagen. *CANCER RES.*, XXXIII: 2983-2986, 1973. 17 refs.

Oxidative demethylation of the secondary carcinogen dimethylnitrosamine by the isolated mouse liver microsomes and the activation of DMN to a bacterial mutagen showed similar kinetics. The rates of demethylation and DMN activation increased following induction of the cytochrome P-450 mixed-function oxidase system by polychlorinated biphenyls. Both the oxidative demethylation and the activation of DMN to a mutagen were inhibited by carbon monoxide, and the inhibition was maximally reduced by monochromatic light at 450 nm. These observations indicate that both microsomal metabolism and activation of DMN to a mutagen are cytochrome P-450 dependent.

Mutagenicity testing - procedure of Ames.

DeLuca, J. G., et al.

Comparative Mutagenicity of ICR-191 to *S. typhimurium* and Diploid Human Lymphoblast. *MUTAT. RES.*, XLVI: 11-18, 1977. 16 refs.

Concentration-dependent mutagenicity of ICR-191 has been measured in *S. typhimurium* strain TA98 and in a diploid human cell line. In both cell systems, approximately equigenerational exposure produced mutation linearly related to concentration in the lower range of ICR-191 concentrations tested. Saturation behavior was observed in the human cell assay but not in the bacterial assay. However, a 25-fold greater concentration of ICR-191 was required to induce a significant rise in the mutant fraction in the *S. typhimurium* assay than in the human cell assay. These differences may be linked to the differences in the biochemical events required for mutation or in the time of exposure to ICR-191.

Mutagenicity testing by procedure of Ames (Salmonella).

Durstun, W. E., and B. N. Ames

A Simple Method for the Detection of Mutagens in Urine: Studies With the Carcinogen 2-acetylaminofluorene. *PROC. NAT. ACAD. SCI., USA*, LXXI: 737-741, 1974. 25 refs.

The addition of commercial β -glucuronidase to the petri plates along with the urine, liver homogenate and bacteria allows detection of metabolites that are excreted in urine as β -glucuronide conjugates. By this method mutagenic activity is readily demonstrated with urine of rats administered as little as 200 ug of the carcinogen. In this case the major urinary metabolite that is detected appears to be a glucuronide conjugate.

Ellenberger, J., and G. Mohn.

More about Intravascular Mutagenicity Testing. MUTAT. RES., XXIX: 235, 1975.

The usefulness of the multi-purpose strain E. coli K-12 GalR^S₁₈/arg₅₆/nad₁₁₃ has been investigated. A comparison of the retention by the liver between a deep rough strain of S. typhimurium is made.

An abstract.

Mutagenicity testing - E. coli and S. typhimurium.

Epler, J. L.

Comparative Mutagenesis. Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee. 11 refs.

The major goal of this mutagenesis research group is to provide a means of testing the mutagenicity of those compounds produced by various existing or proposed methods of energy generation.

To approach the problems of testing large numbers of compounds, we set up a form of the "tier system" utilizing Salmonella, E. coli, yeast, human leukocytes, mammalian cells and Drosophila.

Mutagenicity testing by the procedure of Ames (Salmonella), in E. coli, in Drosophila and in tissue culture.

Epler, J. L., et al.

Feasibility of Application of Mutagenicity Testing to Aqueous Environmental Effluents. EIGHTH ANNUAL MEETING ENVIRON. MUTAGEN SOC. Colorado Spring, Colorado, 1977, p. 47.

An abstract.

The Salmonella test system developed by Ames was applied as a prescreen for ascertaining the biohazard of complex environmental aqueous effluents.

Mutagenicity testing by procedure of Ames (Salmonella)

Fahrig, R.

Development of Host-Mediated Mutagenicity Tests-Yeast Systems. II. Recovery of Yeast Cells out of Testes, Liver, Lung and Peritoneum of Rats. MUTAT. RES., XXXI: 381-394, 1975. 8 refs.

All studies in the host-mediated assay using yeast cells have been performed with the diploid yeast strains D-3 and D-4 of S. cerevisiae, suited for the observation of mitotic recombination and gene conversion. Results underline the importance of the problem of organ-specific activity of mutagens for the host-mediated assay in particular and mutagenicity testing in general.

Mutagenicity testing in a yeast system (host mediated).

Ficsor, G., et al.

An Organ-Specific Host-Mediated Microbial Assay for Detecting Chemical Mutagens in Vivo: Demonstration of Mutagenic Action in Rat Testes Following Streptozotocin Treatment. MUTAT. RES., XIII: 283-287, 1971. 8 refs.

A method is described in which tester bacteria enclosed in diffusion bags are implanted in the testes or in the peritoneal cavities of rats subsequently injected with the chemical mutagen, streptozotocin. Three hours after streptozotocin treatment, the bacteria are recovered and plated on appropriate media to determine the frequency of induced mutations. The MF among bacteria obtained from both the testes and peritoneal cavities of streptozotocin-treated rats was manifold greater than among bacteria obtained from control animals.

Mutagenicity testing by procedure of Ames--host mediated.

Frantz, C. N., and H. V. Malling

The Quantitative Microsomal Mutagenesis Assay Method. MUTAT. RES., XXXI: 365-380, 1975. 18 refs.

Mammals can convert some non-mutagenic compounds to highly mutagenic metabolites. Such promutagens will not be detected by mutagenicity screening techniques which use microorganisms to detect genetic damage unless mammalian metabolism is first allowed to act on the chemicals. Also, the active mutagen metabolites may be short-lived, such as alkylating agents which combine with many common chemical groups, so that the organism must be in close spatial and temporal contact with the metabolism of the promutagen in order to detect mutagenic activity.

Mutagenicity testing -- procedure of Ames.

Frease, E., and H. B. Strack

Induction of Mutations in Transforming DNA by Hydroxylamine. PROC. NAT. ACAD. USA, XLVIII: 1796-1803, 1962. 23 refs.

This paper reports that the mutagenic reactivity of DNA bases is greatly increased when the strands are partially or completely separated. Prototroph transforming DNA of B. subtilis was treated with HA. The recipients were tryptophan-dependent bacteria that cannot grow on indole. They were plated on a medium containing indole and other nutrients required for mutant isolation, except tryptophan.

Mutagenicity testing -- B. subtilis transforming DNA.

Garner, R. C., E. C. Miller and J. A. Miller.

Liver Microsomal Metabolism of Aflatoxin B₁ to a Reactive Derivative Toxic to S. typhimurium TA1530. CANCER RES., XXXII: 2058-2066, 1972. 45 refs.

On the basis of the data presented, it is tentatively suggested that the derivative that is toxic to S. typhimurium TA1530 and the one that reacts with nucleic acids are identical. The possible relationship of this derivative to the hepatocarcinogenicity of aflatoxin B₁ is discussed. Mutagenicity testing by procedure of Ames.

Garner, R. C., A. L. Walpole and F. L. Rose.

Testing of Some Benzidine Analogues for Microsomal Activation to Bacterial Mutagens. CANCER LETTERS, 1: 39-42, 1975. 13 refs.

Analogues of benzidine were assayed for mutagenic activity towards S. typhimurium TA1538 in the presence and absence of a liver enzyme preparation. Purified 3,3'-dichloro-benzidine and the technical grade material had some direct mutagenic activity, but this was increased over 50-fold by addition of a liver mixed function oxidase preparation. In the presence of the liver preparation, 3,3'-dichlorobenzidine was approximately 10 times more active than benzidine, while 3,3',5,5'-tetrafluorobenzidine was of approximately equipotency. On the other hand, 3,3',5,5'-tetramethylbenzidine had no mutagenic activity alone or in conjunction with a liver preparation; 3,3'-Dianisidine had slight mutagenic activity in the presence of liver but none in its absence.

Mutagenicity testing by procedure of Ames.

Goldschmidt, E. P., R. Miller and S. T. Matney

Induction of Prophage in a Lysogen of a Deep Rough Strain of E. coli: A Possible Method for Detecting Carcinogens. MICROB. GENET. BULL., XLI: 3-4, 1976.

A brief note on a possible method for detecting carcinogens.

Mutagenicity testing and prophage induction.

Goldschmidt, E. P., et al.

Isolation of Deep Rough Mutants of E. coli Suitable for Testing Carcinogens for Mutagenesis. MICROB. GENET. BULL., XXXIX: 19-20, 1975.

A brief note on a method used to isolate deep rough mutants of E. coli.

Mutagenicity testing in E. coli.

Grant, E. L., et al.

Mutagenicity and Putative Carcinogenicity Tests of Several Polycyclic Aromatic Compounds Associated With Impurities of the Insecticide Methoxychlor. MUTAT. RES., XL: 225-228, 1976. 7 refs.

Several polycyclic hydrocarbons, which are associated as impurities in commercial samples of the insecticide methoxychlor, have been tested in the Ames mutagenicity test with strains of S. typhimurium, TA1535, TA1537, TA1538 and TA98. Activation by liver microsomes induced with either phenobarbital or Aroclor was examined. The only active compound

was 3,6,11,14-tetra-methoxydibenzo (g,p)chrysene, mutagenic to strain TA98.
Mutagenicity testing by procedure of Ames.

Green, M. H. L., and W. J. Muriel.

Mutagen Testing Using TRP+ Reversion in E. coli. MUTAT. RES., XXXVIII: 3-32, 1976. 25 refs.

A detailed paper discussing four ways of performing mutational screening tests, using E. coli strain WP2: spot tests, treat and plate tests, simplified fluctuation test and use of a liver microsomal fraction. The merits, defects and pitfalls of the system are described. The E. coli system is to be regarded as complimentary to the S. typhimurium test system.

Mutagenicity testing in E. coli.

Green, M. H. L., and W. J. Muriel.

Use of Repair-Deficient E. coli Strains and Liver Microsomes to Characterize Mutagenesis by Dimethylnitrosamine. CHEM.-BIOL. INTERACT., XI: 63-65, 1975. 10 refs.

DMN mutagenesis using suitable E. coli strains was examined. It was confirmed that DMN is not mutagenic when incubated with liver microsomes in soft agar, although it is mutagenic using the Malling system of incubation with microsomes in liquid and bubbling air through the mixture. This aeration did not seem helpful and the method described was adapted.

Mutagenicity testing in E. coli.

Green, M. H. L., W. J. Muriel and B. A. Bridges

Use of a Simplified Fluctuation Test to Detect Low Levels of Mutagens. MUTAT. RES., XXXVIII: 33-42, 1976. 10 refs.

As a mutagen screening procedure a modification of the Luria and Delbrück fluctuation test was used in which the individual tubes are scored by eye for the presence or absence of a mutation.

The test is simple and extremely sensitive, detecting concentrations of mutagens up to 100-fold lower than conventional tests.

Measuring mutation to tryptophan independence in E. coli strain WP2 it was found that methyl methanesulphonate, mitomycin C, dichlorvos and K_2CrO_4 are all positively mutagenic in the test, whereas $NiCl_2$ is negative. Chronic exposure to low levels of mutagens using this method appears to induce more mutations than might be predicted.

Mutagenicity testing in E. coli.

Green, M. H. L., et al.

Mutagenic DNA Repair in E. coli. V. Mutation Frequency Decline and Error-Free Post-Replication Repair in an Excision-Proficient Strain. MUTAT. RES., XLII: 33-44, 1977. 36 refs.

Mutation frequency decline is an irreversible loss of newly-induced suppressor mutations occurring in excision-proficient E. coli during a short period of incubation in minimal medium before plating on broth or Casamino acids-enriched selective agar.

Mutagenicity testing-- E. coli.

Guerin, M. R., and J. L. Epler.

Determining Emission Measurements Needs for an Emerging Industry-Advanced Fossil Fuels Utilization. (Paper presented at the First Conference on Determining Fugitive Emissions Measurements Needs, Hartford, Connecticut, May 17, 1976). 25 refs.

The paper presents one approach to establishing reliable methods and generating data of value in prioritizing environmental and health studies. Measurements needs are identified through an experimental assessment of existing methods.

Mutagenicity testing by procedure of Ames (Salmonella)

Hardigree, A. A., and J. L. Epler

Mutagenicity of Plant Flavonols in Microbial Systems. EIGHTH ANNUAL MEETING ENVIRON. MUTAGEN SOC. Colorado Springs, Colorado, 1977, p. 48.

An abstract.

Extraction techniques yielding partially purified preparations of flavonols from natural products are being carried out and coupled to bioassays for mutagenic activity(s) present in the crude materials.

Mutagenicity testing by procedure of Ames (Salmonella)

Hartman, P. E., et al.

Hycanthone: A Frameshift Mutagen. SCIENCE, CLXXII: 1058-1060, 1971. 22 refs.

Rapid spot-test screening of antischistosomal agents reveals that hycanthone is a potent frameshift mutagen while the closely related compound, miracil D, is nonmutagenic in Salmonella. Both hycanthone and miracil D are frameshift mutagens for T4 bacteriophage during growth in E. coli.

Mutagenicity testing in Salmonella, T4 bacteriophage - E. coli.

Hauser, R., and B. E. Matter.

Localization of E. coli K-12 in Livers of Mice Used for an Intra-Anguineous Host-Mediated Assay. MUTAT. RES., XLVI: 45-48, 1977. 7 refs.

The intrasanguineous host-mediated assay is a considerable improvement of the technique devised for combination of mammalian metabolism and micro-organisms for mutagenicity testing. After intravenous injection of E. coli K-12 into rats and mice, sufficient numbers of bacteria are recoverable from the liver within a period of 180 min to be screened for mutation induction. Since the liver is the main organ carrying out drug-metabolism, this method turned out to be more sensitive compared to the intraperitoneal host-mediated assay, i.e., some mutagenic compounds are already detectable at relatively low dose-levels.

Mutagenicity testing -- E. coli.

Herbold, B., and W. Buselmaier.

Comparative Investigations With Different Bacterial Strains. MUTAT. RES., XXXVIII: 118, 1976.

An abstract.

Mutagenicity testing by the procedure of Ames (Salmonella)

Herbold, B., and W. Buselmaier

Induction of Point Mutations by Different Chemical Mechanisms in the Liver Microsomal Assay. MUTAT. RES., XL: 73-84, 1976. 10 refs.

A selection of chemical agents with different mechanisms of chemical mutability was tested with the liver microsomal assay, using different S. typhimurium tester strains. The tested agents were all well-known mutagens and divided as alkylating agents, anti-metabolites, acridines and those that form radicals in the cell. All of the mutagens except amethopterin gave positive results, showing that this system is very sensitive.

In comparing the strains and mutagens a correlation was noted between the diameter of the molecule and the permeability of the bacterial cell membrane.

Mutagenicity testing by procedure of Ames (Salmonella).

Hince, T. A., and S. Neale

Physiological Modification of Alkylating-Agent Induced Mutagenesis. I. Effect of Growth Rate and Repair Capacity on Nitrosomethyl-Urea-Induced Mutation of E. coli. MUTAT. RES., XLVI: 1-10, 1977. 41 refs.

The effects of repair capacity and growth rate on the induction of mutations by N-methyl-N-nitrosourea was investigated using the trpE reversion system of E. coli WP2 and some repair-deficient derivatives isogenic for this gene. In all these strains reducing the growth rate prior to MNUA-

treatment caused a reduction in the mutational response, however major differences were observed between strains.
Mutagenicity testing in E. coli.

Hong, J.-S. and B. N. Ames

Localized Mutagenesis of Any Specific Small Region of the Bacterial Chromosome. PROC. NAT. ACAD. SCI. USA, LXVIII: 3158-3162, 1971. 29 refs.

A method called localized mutagenesis is described for the isolation of temperature-sensitive and other types of mutations in any specific small region of the bacterial chromosome. The principle of this method is to mutate the transducing DNA rather than the bacterial DNA. One can select for the introduction of this mutated DNA into any particular region of the bacterial chromosome by transducing an auxotrophic marker in that region to prototrophy, thereby introducing new mutations in the neighborhood. This method has been used to isolate many different temperature-sensitive mutations in genes of unknown function in particular regions of the chromosome. Since the method is very simple, it can be used to saturate any region of the map with mutations in essential genes, or for various types of genetic manipulations. Although hydroxylamine-mutagenized phage P22 and S. typhimurium have been used, the method should be applicable to other mutagens and bacteria and transducing phage.

Hutton, J. J. and C. Hackney.

Metabolism of Cigarette Smoke Condensates by Human and Rat Homogenates to Form Mutagens Detectable by S. typhimurium TA1538. CANCER RES., XXV: 2461-2466, 1975. 19 refs.

Nineteen fractions of whole condensate of smoke from the University of Kentucky Reference Cigarette IRI were tested for mutagenicity in vitro using a bacterial indicator system.

Mutagenicity testing -- procedure of Ames.

Imray, F. P. and D. G. Macphee.

Spontaneous and Induced Mutability or Frameshift Strains of S. typhimurium carrying UvrB and PolA Mutations. MUTAT. RES., XXXIV: 35-42, 1976. 18 refs.

Three strains of S. typhimurium carrying frameshift mutations affecting the histidine genes showed increased sensitivity to mutagenesis by ICR-191 if they were made deficient in excision repair by deleting the UVRB gene. One frameshift strain also showed increased sensitivity to mutagenesis by ICR-191 when it carried either of two different polA alleles, whereas the hisD3052 and hisC207 frameshifts reduced sensitivity to mutagenesis in the presence of these alleles. Studies of spontaneous back mutation to prototrophy revealed significant mutator effects of the polA1 mutation on reversion of the hisD3052 frameshift and of the polA3 mutation on rever-

sion of the hisD3076 frameshift. Other smaller mutator effects of the polA alleles on reversion of the his may also be present.
Mutagenicity testing -- procedure of Ames.

Ishidate, M., Jr., K. Yoshikawa and M. Nakadate.

Studies on Screening Methods for Carcinogens in Vitro: Comparative Studies on Chromosomal Aberration and Bacterial Mutation Induced by N-acylated N-nitroso Compounds. MUTAT. RES., XXXVIII: 339-340, 1976.

A comparative study of N-acylated N-nitroso compounds, using the mammalian cytogenetic assay, the rec assay with B. subtilis and the point mutation assay in E. coli and/or S. typhimurium.

Ishizawa, M. and H. Endo.

Mutagenesis of Bacteriophage T₄ by a Carcinogen, 4-nitroquinoline 1-oxide. MUTAT. RES., XII: 1-8, 1971. 34 refs.

The mutagenic behavior of 4-nitroquinoline I-oxide was investigated in bacteriophage T₄. It was mutagenic for intracellular but not for extracellular phages. Mutations induced in the rII region of T₄ by treatment of intracellular phages with the carcinogen were classified. More than half the mutants were of the transition type revertible with the base analogues, but nearly all failed to respond to hydroxylamine mutagenesis. None of the induced mutants was capable of reverting with the carcinogen or proflavine.

Mutagenicity testing -- T₄ bacteriophage.

Isono, K., and J. Yourno

Chemical Carcinogens as Frameshift Mutagens: Salmonella DNA Sequence Sensitive to Mutagenesis by Polycyclic Carcinogens. PROC. NAT. ACAD. SCI. USA, LXXI: 1612-1617, 1974. 23 refs.

Other investigators have shown that several polycyclic carcinogens are frameshift mutagens in Salmonella. Mutagenic potency of these compounds is assessed by ability to induce reversion of histidine-requiring frameshift mutants to prototrophy.

Mutagenicity testing -- procedure of Ames.

Kada, T.

Rec Assay with Cold Incubation With and Without Metabolic Reactivation in Vitro. MUTAT. RES., XXXVIII: 34, 1976.

Improvement in the sensitivity by the above procedures with cold incubation allowed us to carry out the rec assay in combination with activation with rat liver homogenate in vitro.

Mutagenicity in B. subtilis.

Käfer, E., P. Marshall and G. Cohen.

Well-Marked Strains of *Aspergillus* for Tests of Environmental Mutagens: Identification of Induced Mitotic Recombination and Mutation. *MUTAT. RES.*, XXXVIII: 141-146, 1976. 17 refs.

Induction of mitotic recombination in diploids of *A. nidulans* is used as an indicator of mutagenic effects, and the induced segregants are identified either as mitotic crossovers or as products resulting from chromosomal segregation. However, for these last systems, better strains are available which can facilitate identification of the various types of induced segregants and help elucidate the effects of the environmental mutagen. Mutagenicity procedures -- *Aspergillus*.

Kappas, A., et al.

Benomyl -- A Novel Type of Base Analogue Mutagen? *MUTAT. RES.*, XL: 379-382, 1976. 16 refs.

It is believed that the action of benomyl may be understood if it is seen as a novel type of mutagen needing to be incorporated into DNA but once incorporated, seen by the cell as a non-pairing purine with a large alkyl or aryl group attached.

Mutagenicity testing by the procedure of Ames (Salmonella) and in *E. coli*.

Kee, S. G., and J. E. Haber.

Cell Cycle-Dependent Induction of Mutations Along a Yeast Chromosome. *PROC. NAT. ACAD. SCI. USA*, LXII: 1179-1183, 1975. 20 refs.

The relation between DNA replication and the action of the mutagen N-methyl-N'-nitro-N-nitrosoguanidine has been studied in *S. cerevisiae*. The frequencies of reversion to prototrophy of six autotrophic markers located along one arm of chromosome VII were examined as a function of the vegetative cell cycle. Exponentially growing cells were treated with nitrosoguanidine and then separated by zonal rotor centrifugation into fractions equivalent to stages in the cell cycle. The frequency of reversion of five of the six markers is greatest during the period of DNA replication. Each marker has a single point of maximum reversion, approximately 10-fold greater than the frequency observed at other points in the cell cycle. For any one marker the effect of nitrosoguanidine is restricted to an interval shorter than the period of DNA replication. The two markers most distant from each other, *ade5* and *leu1*, both have their highest reversion frequency early during DNA replication. The results indicate that nitrosoguanidine acts primarily during DNA replication and that different markers appear to be affected at different intervals during the DNA biosynthetic period.

Mutagenicity testing in yeasts.

Kier, L. D., E. Yamasaki and B. N. Ames.

Detection of Mutagenic Activity in Cigarette Smoke Condensates. PROC. NAT. ACAD. SCI. USA, LXXI: 4159-4163, 1974. 23 refs.

The S. typhimurium microsomal test system for mutagenic activity was used to detect the presence of mutagenic compounds in the smoke condensates of several types of cigarettes. The condensates were shown to contain compounds which could cause frameshift mutations when activated by microsomal enzymes. Most of the activity of the whole condensate was in basic fractions and in a weakly acidic fraction.

Mutagenicity testing -- procedure of Ames.

Kondo, S., et al.

Base-Change Mutagenesis and Prophage Induction in Strains of E. coli With Different DNA Repair Capacities. GENETICS, LXVI: 187-217, 1970. 58 refs.

The method adopted in these experiments to probe mutagenesis was to compare mutation frequencies with various agents in E. coli strains possessing different radiosensitivities due to different DNA repair capacities.

Mutagenicity testing by phage induction in E. coli.

Kramers, P. G. N.

The Mutagenicity of Saccharin. MUTAT. RES., XXXII: 81-92, 1975. 46 refs.

Seventeen different reports are available dealing with the mutagenic effects of saccharin. Many are incomplete. Mainly tested as its sodium salt, saccharin has been found to be weakly mutagenic in Salmonella at very high doses, in Drosophila at moderate doses, and in mice at moderate to high doses. The compound is a weak chromosome breaker in onion root tips and in Chinese hamster cells. For most of these, and for other test systems as well, a number of doubtful or negative results have also been reported. Altogether the evidence for chromosome-breaking properties is stronger than for the induction of point mutations.

Contradictions might be related to the occurrence of impurities.

Mutagenicity testing in Salmonella (Ames test), Drosophila and mice.

Kramers, P. G. N., A. G. A. C. Knaap and C. E. Voogd.

Lack of Mutagenicity of Chlormequat Chloride in Drosophila and in Bacteria. MUTAT. RES., XXXI: 65-68, 1975. 11 refs.

Based on these data and on the suspicion that CCC, since it is a quaternary ammonium compound, could have alkylating properties, it was considered worthwhile to test the compound for mutagenicity.

Mutagenicity testing in Drosophila, Klebsiella pneumoniae and Citrobacter freundii.

Legator, M. S., T. H. Connor and M. Stoeckel

Detection of Mutagenic Activity of Metronidazole and Niridazole in Body Fluids of Humans and Mice. SCIENCE, CLXXXVIII: 1118-1119, 1975. 6 refs.

After humans were treated at therapeutic doses with the trichomonacide metronidazole and the antischistosomal agent niridazole, mutagenic activity was demonstrable in their urines when tested with the histidine auxotroph of Salmonella typhimurium. Both compounds were active in the host-mediated assay in mice, and evidence of activity was found in the blood and urine of mice treated with niridazole but not with metronidazole. Mutagenicity testing by procedure of Ames (Salmonella).

Legator, M. S., T. Connor and M. Stoeckel

The Detection of Mutagenic Substances in the Urine and Blood of Man. ANN. N. Y. ACAD. SCI., CCLXIX: 16-20, 1975. 10 refs.

This report describes the analysis of body fluids of individuals exposed to selected drugs, and it is anticipated that this technique combined with cytogenetic and repair studies will greatly extend our ability to detect mutagenic agents in the human population.

Mutagenicity testing by procedure of Ames (Salmonella).

Legator, M. S., and H. V. Malling.

The Host-Mediated Assay, a Practical Procedure for Evaluating Potential Mutagenic Agents in Mammals. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., II: 569-589, 1971. 35 refs.

In this assay, the mammal, during treatment with a potential chemical mutagen, is injected with an indicator microorganism in which mutation frequencies can be measured. After a sufficient time period, the microorganisms are withdrawn from the animal and the induction of mutants determined. The comparison between the mutagenic action of the compound (a) on the microorganism directly and (b) in the host-mediated assay indicated whether (1) the host can detoxify the compound or (2) mutagenic products can be formed as a result of host metabolism.

Mutagenicity testing by procedure of Ames (Salmonella) and a heterokaryon of Neurospora crassa.

Legator, M. S., M. Stoeckel and T. Connor

Techniques for Isolating Mutagenic Substances From Urine and Blood of Treated Mammals Using Histidine Auxotrophs of S. typhimurium as the Indicator Organisms. MUTAT. RES., XXVI: 456, 1974.

An abstract

Mutagenicity testing by procedure of Ames (Salmonella)

Legator, M. S., S. Zimmering and T. H. Connor

The Use of Indirect Indicator Systems to Detect Mutagenic Activity in Human Subjects and Experimental Animals. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., IV: 171-191, 1976. 22 refs.

A discussion of host-mediated assay relative to other mutagenicity screens. Mutagenicity testing by procedure of Ames (Salmonella).

Legator, M. S., et al.

Mutagenic Effects of Captan. ANN. N. Y. ACAD. SCI., CLX: 344-351, 1969. 15 refs.

Captan has proved fungicidal against a wide variety of plant and animal pathogens. This fungicide and its related compounds are widely used as agricultural sprays, seed treatments and as protectants in paints, plastics, leather, and fabrics. A low toxicity has been reported in laboratory and farm animals. Although Captan has been in wide use for over decade, comparatively little is known about the genetic effect of this compound. The present study has undertaken to determine possible mutagenic effects of Captan. The mutagenic activity was evaluated in bacteria, in a heteroploid human embryonic lung cell line and in a cell line derived from the kidney of the rat-kangaroo.

Mutagenicity testing in E. coli, cell line, L-132.

Longnecker, D. S., et al.

Trial of a Bacterial Screening System for Rapid Detection of Mutagens and Carcinogens. CANCER RES., XXXIV: 1658-1663, 1974. 7 refs.

A bacterial test system for detection of mutagens and carcinogens based on a DNA polymerase-deficient mutant strain of E. coli was applied to the study of several newly synthesized nitrosamines and other compounds. Mutagenicity testing in E. coli.

Loprieno, N., et al.

The Use of Yeast Systems in Environmental Mutagenesis. MUTAT. RES., XXIX: 237, 1975.

Two alkylating monofunctional agents were used to induce genetic effects such as gene conversions and gene recombinations in diploid strains of S. cerevisiae and S. pombe and gene mutation in a haploid strain of S. pombe.

Mutagenicity testing in yeast.

McCalla, D. R., and D. Voutsinos

On The Mutagenicity of Nitrofurans. MUTAT. RES., XXVI: 3-16, 1974. 36 refs.

Twenty-two nitrofurans were tested for ability to induce revertants of *E. coli* WP2 and its *uvrA*-derivative from *tryp*- to *tryp*+. All proved to be mutagenic while two furan analogues proved to be inactive. Test strains containing *exrA*- or *recA*- genes were not induced to mutate, suggesting that mutants arise in the other strains during repair of damage to DNA by the "error-prone" repair system.

Two mutant strains isolated from WP2 *uvrA*- on the basis of resistance to nitrofurazone were not mutated by nitrofurazone or N-(4-(5-nitro-2-furyl)-2-thiazolyl) formamide indicating that the ultimate mutagens are likely to be a reduction product rather than the nitrofurans *per se*.

Several of the nitrofurans cause induction of prophage leading to mass lysis in *E. coli* T44 (2) λ , a strain which is known to be very sensitive to heat and certain chemicals.

Mutagenicity testing in *E. coli*.

McCalla, D. R., D. Voutsinos and P. L. Olive.

Mutagen Screening With Bacteria: Nitridazole and Nitrofurans. *MUTAT. RES.*, XXXI: 31-37, 1975. 21 refs.

The mutagenic activity of nitrofurans derivatives and of nitridazole is easily demonstrated by spot tests using *E. coli* WP2 and its *uvrA* derivative but not by spot tests using the *S. typhimurium* strains developed by Ames. Quantitative tests show that *S. typhimurium* TA1538 is weakly induced to revert by nitridazole. However, the maximum yield of revertants is well below that obtained with *E. coli* WP2 *uvrA*. None of the Salmonella strains respond to the three nitrofurans tested even in quantitative tests. Those strains contain the reductase required for metabolic activation of the nitrofurans and treatment of a *uvr*+ Salmonella strain with nitridazole or with nitrofurazone causes single-strand breaks in DNA.

Mutagenicity testing by procedure of Ames (Salmonella) and in *E. coli*.

McCann, J.

Mutagenesis, Carcinogenesis and the Salmonella Test. *CHEM. TECHNOL.*, (November): 682-687, 1976. 11 refs.

A talk presented by Dr. McCann in which she discusses the Salmonella test, how and why it works in testing environmental chemicals and modifications of the test itself.

Mutagenicity testing by procedure of Ames (Salmonella).

McCann, J. and B. N. Ames.

A Simple Method for Detecting Environmental Carcinogens as Mutagens. *ANN. N. Y. ACAD. SCI.*, CCLXXI: 5-13, 1976. 29 refs.

The development of this test system, recent improvements in the test, and evidence indicating that the test is reliable and efficient for the detection of carcinogens as mutagens are summarized in this brief review.

McCann, J. and B. N. Ames.

Detection of Carcinogens as Mutagens in the Salmonella/Microsome Test: Assay of 300 chemicals: Discussion. PROC. NAT. ACAD. SCI. USA, LXXIII: 950-954, 1976. 71 refs.

About 300 carcinogens and non-carcinogens of a wide variety of chemical types have been tested for mutagenicity in the simple Salmonella/microsome test. The test uses bacteria as sensitive indicators of DNA damage, and mammalian liver extracts for metabolic conversion of carcinogens to their active mutagenic forms. There is a high correlation between carcinogenicity and mutagenicity: 90% (157/175) of the carcinogens were mutagenic in the test, including almost all of the known human carcinogens that were tested. Carcinogens negative in the test and apparent false positives are discussed.

There is evidence that chemical carcinogens and radiation, likely to initiate most human cancer and genetic defects, do so by damage to DNA.

Mutagenicity testing by procedure of Ames (Salmonella).

McCann, J. and B. N. Ames.

Discussion Paper: The Detection of Mutagenic Metabolites of Carcinogens in Urine With the Salmonella/Microsome Test. ANN. N. Y. ACAD. SCI., CCLXIX: 21-25, 1975. 20 refs.

It is recommended that the Salmonella/microsome in vitro test be used for the immediate screening of industrial chemicals, food additives, drugs and other chemicals to which humans are exposed until more extensive animal tests are conducted.

Mutagenicity testing by procedure of Ames (Salmonella).

McCann, J. and B. N. Ames.

The Salmonella/Microsome Mutagenicity Test: Predictive Value for Animal Carcinogenicity. To appear in ORIGINS OF HUMAN CANCER, Proceedings of the Conference, Cold Spring Harbor Laboratory, New York, 1976. 62 refs.

A discussion of the Ames Mutagenicity Test (Salmonella) relative to carcinogenicity.

McCann, J., et al.

Detection of Carcinogens as Mutagens: Bacterial Tester Strains With R Factor Plasmids. PROC. NAT. ACAD. SCI. USA, LXXII: 979-983, 1975. 31 refs.

This paper extends the utility of the previously described method by introducing two new bacterial strains which can detect many carcinogens not detected before or with less sensitivity. The new strains TA100 and TA98 contain an R factor plasmid. The R factor increases mutagenesis with certain mutagens, but not others. Mutagens that become more effective work through an error-prone recombinational repair.

Mutagenicity testing by the procedure of Ames.

McCann, J., et al.

Detection of Carcinogens as Mutagens in the Salmonella/Microsome Test: Assay of 300 Chemicals. PROC. NAT. ACAD. SCI. USA, LXXII: 5135-5139, 1975. 72 refs.

About 300 carcinogens and non-carcinogens of a wide variety of chemical types have been tested for mutagenicity in the simple Salmonella/microsome test. The test uses bacteria as sensitive indicators for DNA damage, and mammalian liver extracts for metabolic conversion of carcinogens to their active mutagenic forms. Quantitative mutagenicity data from linear dose-response curves are presented. There is a high correlation between carcinogenicity and mutagenicity.

Mutagenicity testing by procedure of Ames (Salmonella).

McCann, J., et al.

Mutagenicity of Chloroacetaldehyde, a Possible Metabolic Product of 1,2-dichloroethane (Ethylene Dichloride), Chloroethanol (Ethylene Chlorohydrin), Vinyl Chloride, and Cyclophosphamide. PROC. NAT. ACAD. SCI. USA, LXXII: 3190-3193, 1975. 60 refs.

Chloroacetaldehyde is mutagenic in the previously described bacterial test system and is of interest because it is a possible metabolite in mammals of the large volume industrial chemicals, 1,2-dichloroethane and vinyl chloride and of the antineoplastic agent cyclophosphamide. Chloroacetaldehyde reverts a new Salmonella bacterial tester strain TA100. Chloroacetaldehyde is shown to be hundreds of times more effective in reversion of TA100 than is chloroethanol, a known metabolic precursor of chloroacetaldehyde and a possible metabolite of dichloroethane and vinyl chloride, or than vinyl chloride, which is itself mutagenic for TA100. Chloroethanol is shown to be activated by rat liver homogenates to a more highly mutagenic form with reversion properties similar to chloroacetaldehyde.

Mutagenicity testing by procedure of Ames (Salmonella).

McCuen, R. W., G. Stohrer and F. M. Sirotnak.

Mutagenicity of Derivatives of the Oncogenic Purine N-Oxides. CANCER RES., XXIV: 378-384, 1974. 42 refs.

Acetoxy esters of purine N-oxides inactivate and induce mutations in *B. subtilis*-transforming DNA. The esters were the chemical models available for the sulfate esters believed to be formed in vivo. There is a reasonable correlation between the mutagenicity of various acetoxy esters and the oncogenicity of the parent N-oxide derivatives. The acetoxy esters of 3-hydroxyxanthine and 3-hydroxy-1-methylguanine were the most potent mutagens. The acetoxy ester of 7-hydroxyxanthine was also a strong mutagen. Most of the 3-acetoxyxanthine-induced mutations spontaneously reverted to wild type. It was concluded that mutation induction in transforming DNA by the acetoxy esters of purine N-oxides occurs by both transition and transversion base-pair substitution.

Mutagenicity testing in *B. subtilis* (transforming DNA).

MacGregor, J. T., and L. E. Sacks.

The Sporulation of B. subtilis as the Basis of a Multi-gene Mutagen Screening Test. MUTAT. RES., XXXVIII: 271-286, 1976. 60 refs.

The sporulation system of B. subtilis provides the basis for detection of a wide variety of mutagens.

The effectiveness of the test, relative to other test systems, remains to be determined.

Mutagenicity testing in a sporulating system (B. subtilis).

MacPhee, D. G.

Salmonella typhimurium his G46 (R-Utrecht): Possible Use in Screening Mutagens and Carcinogens. APPL. MICROBIOL., XXVI: 1004-1005, 1973. 3 refs.

S. typhimurium LT2 his G46 becomes a more sensitive strain for assaying mutagens and carcinogens when it carries the resistance transfer factor R-Utrecht.

Mutagenicity testing by procedure of Ames (Salmonella).

Maher, V. M., et al.

Mutations and Decreases in Density of Transforming DNA Produced by Derivatives of the Carcinogens 2-acetyl-aminofluorene and N-methyl-4-aminoazobenzene. MOL. PHARMACOL., IV: 411-426, 1968. 50 refs.

The observations in this paper, while suggestive of a role for mutation in carcinogenesis by AAF and MAB, also emphasize the problems inherent in the interpretation of such data on the mutagenic activity of chemical carcinogens. Reactive compounds, such as the alkylating agents and the esters studied above, react not only with DNA, but also with RNA, protein and probably other constituents. Hence, the ability of a carcinogen to induce mutations, even in a system that avoids metabolism of the agent, cannot provide proof that a mutational mechanism is involved in the carcinogenic process it induces. Nevertheless, assays for mutagenesis in nonmetabolizing systems appear to be useful tools in searches for the ultimate biologically reactive forms of chemical carcinogens.

Mutagenicity testing in B. subtilis (transforming DNA).

Malaveille, C., et al.

Comparative Mutagenicity Studies With S. typhimurium of Dimethylnitrosamine (DMN) and Diethylnitrosamine (DEN), After Metabolic Activation With Liver and Lung Microsomes. MUTAT. RES., XXXIX: 238, 1975.

An abstract on mutagenicity

Mutagenicity testing by procedure of Ames (Salmonella).

Malling, H. V.

Dimethylnitrosamine: Formation of Mutagenic Compounds by Interaction With Mouse Liver Microsomes. MUTAT., RES., XIII: 425-429, 1971. 20 refs.

Dimethylnitrosamine (DMN) is a potent carcinogen in several rodents. The carcinogenicity of the compound appears to be organ- and species-specific and depends on the route of administration.

Mutagenicity testing by procedure of Ames (Salmonella).

Meadows, M. G., S.-K. Quah and R. C. von Borstel.

Mutagenic Action of Hycanthone and IA-4 on Yeast. J. PHARMACOL. EXP. THER., CLXXXVII: 444-450, 1972. 22 refs.

Two antischistosomal compounds, hycanthone and IA-4, were tested for their mutagenicity in the yeast S. cerevisiae. The test system included measurement of survival of the yeast and reversion of the mutants his1-7, hom3-10 and lys1-1. Reversion of the mutant his1-7 indicates that mutagenicity is by base substitution, reversion of hom3-10 suggests that mutagenicity is by base additions or deletions, and reversion of lys1-1 may be by forward mutation to supersuppression (probably due to base substitution, base addition or base deletion) or by reversion of the super-suppressible locus itself (believed to be by base substitution). Hycanthone at pH 5.9 and 7.0 depresses survival and reverts all three markers in our test system. IA-4 at pH 5.9 is not mutagenic in our experiments, although it does depress survival slightly.

Mutagenicity testing in yeasts.

Milvy, P., and A. J. Garro.

Mutagenic Activity of Styrene Oxide (1,2-epoxyethyl-benzene), a Presumed Styrene Metabolite. MUTAT. RES., XL: 15-18, 1976. 12 refs.

Styrene, in contrast to vinyl chloride which is mutagenic per se for S. typhimurium, did not exhibit mutagenic activity. Inhaled styrene vapor is however rapidly metabolized. Earlier toxicological studies in man indicated that the metabolism of styrene did not appear to be harmful and its current threshold limit value (TLV) is 100 ppm, 8 h time weighted average (Federal Register 39 [1974] 23543). However, considering the correlation between mutagenic and carcinogenic activities which are now emerging, and the established carcinogenic activity in man of the related monomer vinyl chloride, for which a TLV of 1 ppm recently has been set, we suggest that inhaled styrene vapor may be activated to a potentially carcinogenic compound and that exposure at the currently acceptable levels of styrene may pose a health threat to workers.

Mutagenicity testing by procedure of Ames (Salmonella).

Mohn, G. R., and F. J. De Serres.

On The Mutagenic Activity of Some Hair Dyes. MUTAT. RES., XXXVIII: 116-117, 1976.

An abstract.

Mutagenicity testing by procedure of Ames (Salmonella) and in E. coli.

Mohn G., et al.

Mutagenicity Studies in Microorganisms in Vitro, with Extracts of Mammalian Organs, and With the Host-Mediated-Assay. MUTAT. RES., XXIX: 221-233, 1975. 20 refs.

The paper is restricted to a few points of practical importance concerning differential DNA repair, plate tests versus liquid tests, new developments of the host-mediated assay, and interactions between mutagenic chemicals.

Monti-Bragadin, C., M. Tamaro and E. Banfi.

Mutagenic Activity of Platinum and Ruthenium Complexes. CHEM.-BIOL. INTERACT., XI: 469-472, 1975. 7 refs.

cis-Dichlorodiammineplatinum(II) (cis-PtCl₂(NH₃)₂) and dichlorotetrakis(dimethylsulfoxide) ruthenium(II) (RuCl₂ (DMSO)₄) have been tested as mutagens for strains of S. typhimurium carrying the his G46 missense mutation. Their activity, which has been compared with the activity of mitomycin C, depends on the presence in the test bacteria of the pKM101 plasmid and is affected by the function of the excision repair system. It seems that each drug interacts with DNA by a different mechanism.

Mutagenicity testing by procedure of Ames (Salmonella).

Murayama, I.

Mutation by Mitomycins in the Ultraviolet Light-Sensitive Mutant of E. coli. MUTAT. RES., XVIII: 117-119, 1973. 16 refs.

This paper presents evidence that monofunctional mitomycins induced mutation in UV-sensitive strains with much higher frequency than that in wild-type bacteria, while MRC did not induce mutation in these Uvr-strains.

Mutagenicity testing in E. coli.

Nakajima, T., and S. Iwahara.

Mutagenicity of Dimethylnitrosamine in the Metabolic Process by Rat Liver Microsomes. MUTAT. RES., XVIII: 121-127, 1973. 10 refs.

The mutagenicity of dimethylnitrosamine for bacteria was investigated by means of the metabolic activation process of the compound with rat liver microsomes.

Three strains of streptomycin (SM)-dependent E. coli having tetracycline (TC)-resistance factor (Sd- E. coli (TC) were derived for this study.

The reverse mutation in these strains from SM dependence to non-dependence was used as the marker for mutagenicity. The drug resistance factor (R factor) which was transferred to these strains was used in order to get around the bacterial contamination throughout the experiments. The study of the mutagenicity of DMN metabolites has been made by incubating DMN with rat liver microsomes and cofactor system in the presence of indicator bacterial cells.

The reverse mutation was markedly induced for all of three strains in the complete incubation mixture but it was not observed when the cofactor system was omitted or the liver microsomal suspension was replaced by the kidney cell sap. When the indicator bacterial cells were added to the mixture in which DMN was previously incubated with the microsomes and cofactor system, the mutagenicity was extremely decreased.

Mutagenicity testing in E. coli.

Neale, S.

Mutagenicity of Nitrosamides and Nitrosamidines in Microorganisms and Plants. MUTAT. RES., XXXII: 229-266, 1976. 232 refs.

Nitrosamides, nitrosamidines and nitrosamines, which comprise one of the most potent groups of carcinogens known, are also highly mutagenic. Non-mammalian systems, with the exception of *Drosophila*, generally lack the metabolic activity required to convert compounds such as the nitrosamines to active mutagens or carcinogens; the mutagenic action of those nitroso compounds which require metabolic activation has been reviewed separately in this series by Montesano and Bartsch who discussed in detail the role of nitroso compounds in carcinogenesis. Nitrosamides and nitrosamidines elicit exceptionally high mutagenic responses in non-mammalian systems.

Nelson, W. H., et al.

Thermal Effects on Genetic Events in Microbial Tester Strains. SCIENCE, LXXXIII: 54, 1976.

It is apparent that these microbial tester strains are ideal to distinguish between heat versus microwave induced biological change.

An abstract.

Mutagenicity testing in E. coli and S. typhimurium.

Nishioka, H.

Mutagenic Activities of Metal Compounds in Bacteria. MUTAT. RES., XXXI: 185-189, 1975. 11 refs.

Fifty-Six metal compounds were tested by the rec assay. Compounds showing positive results in the assay such as potassium dichromate, ammonium molybdate and sodium arsenite were then examined as to their capacities to induce reversions in E. coli Trp- strains possessing different DNA repair pathways.

Mutagenicity testing in E. coli and B. subtilis.

Oesch, F.

Differential Control of Rat Microsomal "Aryl Hydrocarbon" Monooxygenase and Epoxide Hydratase. J. BIOL. CHEM., CCLI: 79-87, 1976. 70 refs.

In this paper is reported the following:

1. There are striking similarities in the postnatal control of epoxide hydratase and monooxygenase in rats with respect to both endogenous and exogenous factors. This could be taken to indicate that the two microsomal systems, epoxide hydratase and a rate-limiting entity of the multicomponent monooxygenase, are under common biosynthetic control, and a selective induction might be intrinsically impossible.
2. Dissociation of epoxide hydratase and monooxygenase induction was achieved by transplacental treatment of fetal rat liver with some, but not all, inducers.
3. Biological relevance of selective induction was assessed by monitoring the ability of corresponding liver preparations to lead to altered accumulation of benzo[a]pyrene metabolites mutagenic for S. typhimurium TA1537.

Mutagenicity testing by procedure of Ames (Salmonella).

Parry, J. M.

Mitotic Recombination in Yeast as a Test of Genetic Damage. LAB. PHACT., XXI: 417-419, 1972. 16 refs.

In the presence of mutagenic agents, heteroallelic diploid cultures of the yeast Saccharomyces cerevisiae produce prototrophic recombinants by a process of mitotic gene conversion. This process is characterized by a lack of specificity with regard to the mode of action of the mutagen. Thus mitotic gene conversion provides a convenient technique for the detection of possible mutagenic activity, using a eukaryotic organism. A simple technique suitable for the detection of the genetic activity of environmental chemicals is described.

Mutagenicity testing in yeast.

Parry, J. M., D. J. Tweats and M. A. J. Al-Mossawi.

Monitoring the Marine Environment for Mutagens. NATURE, CCCLXIV: 538-540, 1976. 17 refs.

Our assay detects mutagens in the tissue of the mussel Mytilus edulis in areas of obvious industrial pollution.

Mutagenicity testing by procedure of Ames (Salmonella) and in E. coli.

Payne, J. F.

Oil Spills: Effects of Petroleum on Marine Organisms. SCIENCE, CXCVI: 10, 1977.

Mutagenicity testing by procedure of Ames (Salmonella).

Prival, M. J. et al.

Tris (2,3-Dibromopropyl) Phosphate: Mutagenicity of a Widely Used Flame Retardant. SCIENCE, CXCV: 76-78, 1977. 15 refs.

Tris (2,3-dibromopropyl) phosphate, a widely used flame-retardant additive for textiles, is mutagenic to histidine-requiring strains of *S. typhimurium*. Extracts of fabrics treated with this compound are also capable of inducing mutations in these bacterial strains.

Mutagenicity testing by procedure of Ames (Salmonella).

Rannug, U., R. Göthe and C. A. Wachtmeister.

The Mutagenicity of Chloroethylene Oxide, Chloroacetaldehyde, 2-chloroethanol and Chloroacetic Acid, Conceivable Metabolites of Vinyl Chloride. CHEM.-BIOL. INTERACT., XII: 251-263, 1976. 28 refs.

The ability of four conceivable metabolites to cause base-pair substitution directly in *S. typhimurium* TA1535 has been compared. The main comparison was performed at initial concentrations from 0.1 to 1.5 mM. In this region, however, a mutagenic effect was observed only with chloroethylene oxide and chloroacetaldehyde, the former being approximately 20 times more effective than the aldehyde when compared on a molar basis. 2-chloroethanol and chloroacetic acid were studied also at higher concentration, and a weak mutagenic response was found with 1M 2-chloroethanol solution. With chloroacetic acid no enhancement of the mutation frequency could be detected.

Chloroethylene oxide was found to be approximately 450 times more effective as a mutagen than chloroacetaldehyde when the comparison is based on exposure doses. Similarly, chloroethylene oxide was 10,000-15,000 times more effective as a mutagen than ethylene oxide, used as a positive control.

Mutagenicity testing by procedure of Ames (Salmonella).

Rannug, U., and C. Ramel.

The Mutagenicity of Waste Products from the Vinyl Chloride Industries. MUTAT. RES., XXXVIII: 113, 1976.

An abstract.

Mutagenicity testing by procedure of Ames (Salmonella).

Rao, T. K., et al.

Correlation of Mutagenic Activity of Energy Related Effluents With Organic Constituents. EIGHTH ANNUAL MEETING ENVIRON. MUTAGEN SOC. Colorado Springs, Colorado, 1977, pp. 47-48.

An abstract.

We have applied the short-term testing to crude products and effluents from the synthetic fuel technologies. Class fractionation and column chromatography of the test materials and the coupled bioassays can be used to identify the most active fractions.

Mutagenicity testing by procedure of Ames (Salmonella).

Rasmussen, R. E., and I. Y. Wang.

Dependence of Specific Metabolism of Benzo[a]pyrene on the Inducer of Hydroxylase Activity. *CANCER RES.*, XXXIV: 2290-2295, 1974. 24 refs.

The data presented here indicate that PB and polycyclic hydrocarbons induced mixed-function oxidases in rat liver which had different specificities toward BP. The observed differences in the mutagenic activity of BP when metabolized by PB- or 3-MC-induced enzymes were in part due to differences in the induced level of epoxide hydrazase. It cannot be ruled out that other metabolites of BP may also be responsible for some of its mutagenic and carcinogenic effects, but our results strongly favor the long-held idea that the K region is probably involved. Mutagenicity testing by procedure of Ames (Salmonella).

Rosenkranz, H. S., Jr., W. T. Speck and J. E. Stambaugh.

Mutagenicity of Metronidazole: Structure-Activity Relationships. *MUTAT. RES.*, XXXVIII: 203-206, 1976. 14 refs.

Recent reports of the mutagenicity of metronidazole for bacterial species have caused concern regarding the safety of this widely used antiprotozoan and antibacterial agent. Because it might be possible to synthesize derivatives of metronidazole devoid of genetic activity yet still retaining chemotherapeutic effectiveness, it was thought of interest to examine the mutagenic activity of several simple derivatives of metronidazole.

Mutagenicity testing by procedure of Ames (Salmonella).

Rubin, I. B., et al.

Fractionation of Synthetic Crude Oils from Coal for Biological Testing. *ENVIRON. RES.*, XII: 358-365, 1976. 18 refs.

A separation procedure that has been used extensively for the reproducible fractionation of cigarette smoke condensate for carcinogenic properties has been applied to coal liquefaction products. Two types of product oils, one a light oil and the other a heavy tar, have been processed successfully by this procedure. Mutagenicity of the major fractions of the light oil product was tested by microbiological techniques using several strains of *S. typhimurium*, and some mutagenic effect was shown by four of the fractions. The possible carcinogenicity and mutagenicity of the individual fractions are discussed in relation to the reported effects of corresponding cigarette smoke condensate fractions.

Mutagenicity testing by procedure of Ames (Salmonella).

Ryttman, H., and G. Zetterberg.

Induction of Mitotic Recombination With N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) in *Saccharomyces cerevisiae*. A Comparison Between Treatment in Vitro and in the Host-Mediated Assay. *MUTAT. RES.*, XXXIV: 201-216, 1976. 29 refs.

Two methods, treatment in vitro and the host-mediated assay method, were compared in their ability to demonstrate the induction by MNNG of mitotic recombination in a diploid strain of S. cerevisiae. MNNG had a strong activity in vitro but not in the host-mediated assay at the concentrations tested. When the genetic effects of MNNG have been tested in different test systems, sometimes negative, sometimes positive results have been obtained. The relevance of different tests for risk evaluation is discussed, and it is concluded from the data on MNNG that tests on whole mammals may sometimes give false negative results because the cells tested are in parts of the body less accessible to the mutagen. Increasing doses of MNNG by treatment in vitro gave decreasing frequencies of mitotic recombination, indicating damage to the recombinational system in the cells. Dose-response relationships for recombination and mutation are discussed.

Mutagenicity testing in S. cerevisiae.

Seiler, J. P.

Toxicology and Genetic Effects of Benzimidazole Compounds. MUTAT. RES., XXXII: 151-168, 1975. 90 refs.

Benzimidazoles have been tested for mutagenicity in a variety of test systems. The first investigations were made with microorganisms and only lately have mammals been used to assess mutagenic activity for these compounds. The mutation of E. coli to streptomycin resistance has been used to reveal the weak mutagenic properties of benzimidazole. With the S. typhimurium strains of Ames, it was found that benzimidazole acts as a base-substituting agent.

A discussion of the toxicity of benzimidazole compounds.

Shahin, M. M.

The Non-Mutagenicity and -recombinogenicity of Vinyl Chloride in the Absence of Metabolic Activation. MUTAT. RES., XL: 269-272, 1976. 7 refs.

In view of the fact that most carcinogens are also mutagens, it appears desirable to determine whether or not the carcinogen vinyl chloride is capable of interfering with the genetic material. We have tested the ability of this compound to induce reversion and mitotic recombination in the yeast S. cerevisiae.

Mutagenicity testing in Saccharomyces cerevisiae.

Shahin, M. M., and R. C. von Borstel.

Genetic Activity of the Antimicrobial Food Additives Af-2 and H-193 in Saccharomyces cerevisiae. MUTAT. RES., XXXVIII: 215-224, 1976. 27 refs.

The genetic activity of the antimicrobial food additives AF-2 and H-193 has been investigated in S. cerevisiae. The strains chosen for the studies were D5 for the induction of mitotic recombinational events and XV185-14C

for the induction of reversion of the mutants. When three concentrations of AF-2 were used in the reversion system of strain XV185-14C, there was an increase in the frequency of hom⁺ and his⁺ revertants as a function of incubation time, while the lysine mutant exhibited a very low frequency of induced reversion. When AF-2 and H-193 were compared at the same concentration and exposure time, AF-2 exhibited a higher genetic activity in both systems than H-193. However, H-193 was genetically more active in inducing revertants than AF-2, when the comparison was made at the same survival level. Cells of both haploid and diploid strains were found to be more sensitive to inactivation by AF-2 than by H-193. The haploid strain was more sensitive to both compounds than the diploid strain.

Mutagenicity testing in S. cerevisiae.

Shahin, M. M., and R. C. von Borstel

Mutagenic and Lethal Effects of α -Benzene Hexachloride, Dibutyl Phthalate and Trichloroethylene in Saccharomyces cerevisiae. To be published in MUTAT. RES.

S. cerevisiae strain XV185-14C for reversion studies was used to investigate the genetic activity of α -benzene hexachloride dibutyl phthalate and trichloroethylene. The results indicate that none of the three compounds was genetically active when yeast cells were treated in phosphate buffer (pH 7.0) in the absence of metabolic conversion. However, in the presence of the 9000 g supernatant of mice liver homogenate, NADP, glucose-6-phosphate, phosphate buffer (pH7.4), MgCl₂ KCl, the components which were used for the metabolic conversion, trichloroethylene proved to be a powerful mutagen. It increases the frequency of homoserine, histidine and lysine revertants over those of the control levels. Trichloroethylene appears to induce frameshift as well as base substitution mutations.

Mutagenicity testing in yeasts.

Sharma, C. B. S. R., and R. K. Sahu.

Cytogenetic Hazards from Agricultural Chemicals. I. A Preliminary Study on the Responses of Root Meristems to Exotoxin from B. thuringiensis a Constituent of a Microbial Insecticide, Thuricide. MUTAT. RES., XLVI: 19-26, 1977. 46 refs.

It is reported for the first time that the exotoxin, thuringiensin A, from Bacillus thuringiensis, a component of the insecticide thuricide, inhibits spindle and cytokinesis and induces micronuclei, chromocentric nuclei and minor deviations in spindle biprophases and bimetaphases. Spindle seems to have been inhibited even in bimetaphase. Microtubular systems and chromosomes are implicated as the primary targets. Most effects resemble those of caffeine, colchicine, aminopyrin, chloral hydrate and vinblastine to different extents, and are therefore suggestive of the anti-neoplastic and mutagenic potentialities of the exotoxin. The extensive use of thuricide on crop plants in view of its mutagenic potential, may be hazardous. The results also suggest that the exotoxin may be used as a

pretesting agent in chromosome analysis and as a candidate-tagging tool for synchronization and cell cycle analysis, besides its probable utility in studies on cancer cells.

Shirasu, Y., et al.

Mutagenicity Screening of Pesticides in the Microbial System. MUTAT. RES., XL: 19-30, 1976. 24 refs.

A survey on the mutation induction capacity was made in the microbial system on 166 pesticides, including 57 fungicides, 63 herbicides and 46 insecticides. The screening methods consisted of the rec-assay procedure, a sensitivity test utilizing H17 Rec+ and M45 Rec- strains of B. subtilis, as well as the reversion assays on plates utilizing auxotrophic strains of E. coli (WP2) and S. typhimurium. Chemicals inducing reversions were detected only among those showing positive effects in the rec-assay but not among negative samples. In addition to Captafol, Captan, Dexon and NBT of which mutagenicities have been previously reported, Dichlorvos, Flopet, 2-hydrazinoethanol (HEH), 5-nitro-1-naphthanitrile (NNN) and Vamidothion were found to be mutagens in our systems.

Mutagenicity testing by procedure of Ames -- Salmonella, B. subtilis and in E. coli.

Siebert, D.

A New Method for Testing Genetically Active Metabolites. Urinary Assay With Cyclophosphamide (Endoxan, Cytoxan) and Saccharomyces cerevisiae. MUTAT. RES., XVII: 307-314, 1973.

Cyclophosphamide (Endoxan, Cytoxan), a cytostatic substance, was tested for its genetic activity in S. cerevisiae. The test system used was induction of (1) back mutation and (2) mitotic gene conversion. Given directly to yeast, cyclophosphamide showed no genetic effect. After oral application to BD rats the urine showed medium mutational activity but strong convertogenic activity up to a 100-fold increase of induced convertants. In the host-mediated assay (injection of yeast into the ventral cavity), cyclophosphamide was only weakly active.

Mutagenicity testing in S. cerevisiae.

Siebert, D., and G. Eisenbrand.

Genetic Effects of Some New Bifunctional and Water-Soluble Analogs of the Anti-Cancer Agent 1,3-Bis(2-chloroethyl)-1-nitrosourea (BCNU) in S. cerevisiae. MUTAT. RES., XLII: 45-50, 1977. 10 refs.

A series of 1-(2-chloroethyl)-1-nitrosoureas were examined for their genetic activities. BCNU was simultaneously tested as an established, clinically used reference compound. A diploid strain of S. cerevisiae, heteroallelic at the gene loci ade2 and trp5 was used as a test system for the induction of mitotic gene conversion (intragenic recombination).

Mutagenicity testing in S. cerevisiae.

Siebert, D., F. K. Zimmermann and E. Lemperle.

Genetic Effects of Fungicides. MUTAT. RES., X: 533-543, 1970. 39 refs. Fourteen fungicides have been tested for genetic activity on diploid cells of the ascomycete S. cerevisiae. The test system used was induction of: (1) mitotic gene conversion at 2 different loci; and (2) cytoplasmic respiratory-deficient mutants. Two fungicides turned out to be strongly active in inducing mitotic gene conversion when applied as commercial preparations; Orthophaltan and Polyram-combi and poly-ethylenebis. Cignolin, used in dermatology, did not induce mitotic gene conversion but induced cytoplasmic respiratory-deficient mutation at frequencies close to 100%. With four more fungicides, only a weak apparent induction of gene conversion could be observed: Antracol, Basfungi and polypropylenebis, Dithane-Ultra and Captan.

Mutagenicity testing in S. cerevisiae.

Simmon, V. F., and R. G. Tardiff.

Mutagenic Activity of Drinking Water Concentrates. Source unknown.

An abstract concerned with drinking water concentrates.

Mutagenicity testing by procedure of Ames (Salmonella).

Skopek, T. R., et al.

A Quantitative Forward Mutation Assay in Salmonella typhimurium Using 8-azaguanine Resistance as a Genetic Marker. PROC. NAT. ACAD. SCI., Preprint. 15 refs.

A quantitative forward mutation assay has been developed using S. typhimurium in which resistance to the purine analog 8-azaguanine (8AG) is used as a genetic marker. Resistance to 8AG results from the loss of xanthine-guanine-phosphoribosyl transferase (XGPRT), an enzyme responsible for the transport and phosphoribosylation of xanthine, guanine, and 8 AG. Here we present the assay protocol, the concentration dependent toxicity and mutagenicity of four known mutagens. β -propiolactone (β PL) and reconstruction experiments tested the assay for possible bias. The relative merits of forward versus reverse mutation assays are discussed.

Mutagenicity testing by procedure of Ames (Salmonella).

Speck, W. T., and H. S. Rosenkranz.

Mutagenicity of Azathioprine. CANCER RES., XXXVI: 108-109, 1976. 9 refs.

Azathioprine is mutagenic for S. typhimurium. Demonstration of this mutagenic effect requires a period of anaerobic incubation of the bacteria with the test agent.

Mutagenicity testing by procedure of Ames (Salmonella).

Speck, W. T., A. B. Stein and H. S. Rosenkranz.

Mutagenicity of Metronidazole: Presence of Several Active Metabolites in Human Urine. J. NAT'L CANCER INST., LVI: 283-291, 1976. 10 refs.

Mutagenic activity was found in the urine of 10 patients given therapeutic dosages of metronidazole orally or per vagina. Paper chromatographic separation revealed that mutagenicity in the urine was associated with unmodified metronidazole and at least four of its known urinary metabolites. Activity was also recovered in a region of the chromatogram heretofore not assigned to a metronidazole metabolite.

Mutagenicity testing by procedure of Ames -- Salmonella.

Stolz, D. R., R. D. Bendall and C. T. Miller.

Mutagenic Effect of Nialamide on Salmonella typhimurium. MUTAT. RES., XL: 305-308, 1977. 6 refs.

The mutagenicity of an antidepressant drug, nialamide, was studied with S. typhimurium TA1535-8. Nialamide was mutagenic for strain TA1535 in the absence of rat liver extracts.

Mutagenicity testing by procedure of Ames (Salmonella).

Straus, D. S.

Induction by Mutagens of Tandem Gene Duplications in the glyS Region of the Escherichia coli Chromosome. GENETICS, LXXVIII: 823-830, 1974. 24 refs.

Four mutagens have been found to increase the frequency of tandem gene duplications in the glyS region of the E. coli chromosome. This result was obtained by quantitating the spontaneous and mutagen-induced reversion frequency of a glycyl-tRNA synthetase (gly-S) mutant. Following mutagenesis, as many as 0.2% of the survivors were observed to contain duplications in the gly-S region. In addition, several classes of stable revertants of the glyS mutant have been identified.

Mutagenicity testing in E. coli.

Tanooka, H.

Development and Applications of Bacillus subtilis Test Systems for Mutagens, Involving DNA-Repair Deficiency and Suppressible Auxotrophic Mutations. MUTAT. RES., XLII: 19-32, 1977. 27 refs.

A mutagen-tester of B. subtilis was constructed and tested with known carcinogens. The parental strain HA101 of Okubo and Yanagida carrying suppressible nonsense mutations in his and met genes was transformed to carry an excision-repair deficiency mutation. The constructed strain TKJ5211 showed a 20-30-fold higher sensitivity for His⁺ reversion than the parental strain when treated with UV and UV-mimetic chemicals but unchanged mutation frequency with X-rays and methyl methanesulfonate. The tester strain was used in a spot test of 30 selected chemicals and

also for testing with liver homogenate activation. The results showed an almost equivalent but somewhat broader detection spectrum than the *S. typhimurium* TA100 system. Another test method used a pair of *E. subtilis* strains differing in their DNA-repair capacity, i.e., the most UV-sensitive mutant HU-15 and a wild-type strain, to detect repair-dependent DNA damage produced by chemicals. Spores could be used in either test.

Mutagenicity testing in *Salmonella* (Ames) and *B. subtilis*.

Tazima, Y., T. Kada and A. Murakami.

Mutagenicity of Nitrofuran Derivatives, Including Furfylfuramide, a Food Preservative. *MUTAT. RES.*, XXXII: 55-80, 1975. 113 refs.

Strong mutagenic as well as carcinogenic activities were revealed for several nitrofuran derivatives and these caused doubt about the use of furfylfuramide as a food preservative.

Mutagenicity testing in *Salmonella* (Ames) and *E. coli* and *B. subtilis*.

Teranishi, K., K. Hamada and H. Wantanabe.

Quantitative Relationship Between Carcinogenicity and Mutagenicity of Polyaromatic Hydrocarbons in *Salmonella typhimurium* Mutants. *MUTAT. RES.*, XXXI: 97-102, 1975. 14 refs.

Mutagenic activities of various polyaromatic hydrocarbons in air pollutants, which are different in carcinogenic activities from each other, were examined with a set of four strains of *S. typhimurium*. All the compounds tested were converted to frameshift mutagens when they were metabolized by rat liver homogenate. There was a clear quantitative correlation between carcinogenicity and mutagenicity of PAHs tested in strain TA1538 using the rat liver enzyme induced with both dibenz(a,h)-anthracene and phenobarbital. On the other hand, such a correlation was not obvious in strain TA1537.

Mutagenicity in *Salmonella*, procedure of Ames.

Terrasso, M.

Analysis of Samples From Industrial Sources in Houston Ship Channel Area.
Analysis of data

Mutagenicity procedure of Ames (*Salmonella*).

Ueno, Y., and K. Kubota.

DNA-Attacking Ability of Carcinogenic Mycotoxins in Recombination-Deficient Mutant Cells of *Bacillus subtilis*. *CANCER RES.*, XXXVI: 445-451, 1976. 24 refs.

Thirty mycotoxins and five chemically modified toxins were tested for DNA-attacking ability in the rec assay using the recombination-deficient mutant of *B. subtilis* M45 (rec-) and the parent strain.

Six Penicillium toxins, five Aspergillus toxins and two Fusarium toxins were positive. Among these 13 compounds, eight have been reported to be carcinogenic in animals.

Correlation between the rec effect and in vivo carcinogenicity of mycotoxins is discussed.

Mutagenicity testing in Bacillus subtilis.

Venitt, S., and C. T. Bushell.

Mutagenicity of the Food Color Brown FK and Constituents in Salmonella typhimurium. MUTAT. RES., XL: 309-316, 1977. 11 refs.

The food color Brown FK is a mixture of p-sulphophenylazo derivatives of m-toluylenediamine and m-phenylenediamine and is used in the UK for coloring kippers. Brown FK and its constituents were assayed for mutagenicity in S. typhimurium TA1535, TA1537 and TA1538. Samples of brown typhimurium TA1535, TA1537 and TA1538. Samples of brown FK from three manufacturers were mutagenic in TA1538 when activated by a rat-liver supernatant fraction.

Mutagenicity testing by procedure of Ames (Salmonella).

von Borstel, R. C., and S. Igali.

Mutagenicity Testing of Antischistosomal Thioxanthenones and Indazoles on Yeast. J. TOXIC. ENVIRON. HEALTH, I: 281-291, 1975. 27 refs.

Two antischistosomal thioxanthenones, and four antischistosomal indazoles have been tested for mutagenicity on stationary phase cells of the yeast Saccharomyces cerevisiae. It was shown that, although there are some gaps in the data, hycanthone and IA-6 are mutagenic at pH 7.0, hycanthone is mutagenic at 5.9 and none of the other compounds is mutagenic at either pH. An excision-repair deficient strain of yeast is no more sensitive than other strains. It was found from time-concentration studies on lethality that an inverse relation held: cells exposed to a mutagenic compound are more sensitive when time of exposure was varied and concentration of the compound was held constant, and cells exposed to a nonmutagenic compound are more sensitive when concentration is varied and time of exposure held constant. When the compounds were tested on growing cells of yeast in rich media, none of the compounds is mutagenic, although some are lethal. The kinetic behavior in reversion of yeast exposed to these compounds shows marked departures from similar reversion studies where yeast is exposed to radiation, implicating different physiological mechanisms for the alteration or responses of yeast cells exposed to the different mutagens.

Mutagenicity testing in yeasts.

Voogd, C. E.

The Mutagenic Action of some Nitrothiazoles and Nitrophenols. MUTAT. RES., XXXVIII: 117, 1976.

An abstract

Mutagenicity testing in Klebsiella pneumoniae.

Wang, C. Y., K. Murasaka and G. T. Bryan.

Mutagenicity of Nitrofurans, Nitrothiophenes, Nitropyrroles, Nitroimidazole, Aminothiophenes, and Aminothiazoles in Salmonella typhimurium. CANCER RES., XXXV: 3611-3617, 1975. 30 refs.

Thirty-two heterocyclic compounds, including 24 nitroheterocycles, and seven aminoheterocycles and derivatives and one thiophene lacking in a nitro group were tested for mutagenic activity in S. typhimurium TA98 and TA100. All the nitroheterocycles, including nitrofurans, nitrothiophenes, nitropyrroles and one nitroimidazole, were mutagenic in TA100. Thirteen were also mutagenic in TA98, 5-Nitro-2-furoic acid, a noncarcinogen, was mutagenic in TA100. Seven carcinogenic nitroheterocycles, aminothiophenes and aminothiazole derivatives, and one thiophene without a nitro group were not mutagenic. Both TA98 and TA100 were uvrB and lacked the ability of excision repair of DNA. Among the 24 mutagenic nitroheterocycles, only 13 compounds exhibited bacterial killing effects, suggesting that more than one mechanism may be involved in the interaction of nitroheterocycles with bacterial DNA.

Mutagenicity testing by procedure of Ames (Salmonella).

Weekes, U., and D. Brusick.

In Vitro Metabolic Activation of Chemical Mutagens. II. The Relationships Among Mutagen Formation, Metabolism and Carcinogenicity for Dimethylnitrosamine and Diethylnitrosamine in the Livers, Kidneys and Lungs of balb/cj, C₅₇BL/6J and RF/J Mice. MUTAT. RES., XXXI: 175-183, 1975. 23 refs.

The metabolic activation of dimethylnitrosamine and diethylnitrosamine to mutagenic intermediates was studied using an in vitro genetic assay which measured the relative concentration and rate of formation of the active intermediates. Microsomal preparations from the livers, lungs and kidneys of male mice were compared for their ability to activate the two carcinogens to mutagens. It was demonstrated that quantitative differences in activation could be detected between organs of the three strains and that different organs have characteristic activation kinetics. Activation kinetics for microsomal metabolism of DMNA by liver, lung and kidney tissues of male and female mice were also compared.

Mutagenicity testing by procedure of Ames (Salmonella).

Wheeler, L. A., et al.

Association of Salmonella Mutants With Germfree Rats: Site Specific Model to Detect Carcinogens as Mutagens. PROC. NAT. ACAD. SCI. USA, LXXII: 4607-4611, 1975. 23 refs.

An association of the histidine auxotroph of S. typhimurium (strain TA1538) within the gastrointestinal tract of otherwise germfree Sprague-Dawley rats is maintained during periods of observation lasting as long as 7 months.

Mutagenicity testing by procedure of Ames (Salmonella).

Wislocki, P. G., et al.

Mutagenicity and Cytotoxicity of Benzo[a]pyrene Arene Oxides, Phenols, Quinones, and Dihydrodiols in Bacterial and Mammalian Cells. *CANCER RES.*, XXXVI: 3350-3357, 1976. 43 refs.

Twenty-nine benzo[a]pyrene derivatives were tested for mutagenic activity without metabolic activation in *S. typhimurium* strains TA98, TA100 and TA1538 and in Chinese hamster V79 cells.

Mutagenicity testing by procedure of Ames (Salmonella) and in mammalian cells.

Wlodkowski, T. J., and H. S. Rosenkranz.

Mutagenicity of Sodium Hypochlorite for *Salmonella typhimurium*. *MUTAT. RES.*, XXXI: 39-42, 1975. 14 refs.

Sodium hypochlorite, a standard household item, induces base-substitution mutations in *S. typhimurium*. Because of its potent bactericidal effect the mutagenicity of hypochlorite could best be demonstrated by short-term exposure to this chemical followed by the addition of ascorbic acid to decompose the hypochlorite.

Mutagenicity testing by procedure of Ames (Salmonella).

Wong, J. J., and D. P. H. Hsieh.

Mutagenicity of Aflatoxins Related to Their Metabolism and Carcinogenic Potential. *PROC. NATL. ACAD. SCI. USA*, LXXIII: 2241-2244, 1976. 41 refs.

Aflatoxins and their animal biotransformation products were screened for carcinogenic potential by using the Ames' in vitro detection system for carcinogens as bacterial mutagens. Aflatoxinol, aflatoxins Q1, B2 and P1, G2, B2a and G2a were all less active than aflatoxin B1. No compound possesses activity in the absence of the rat liver preparation. The relative mutagenic potency observed with this in vitro system qualitatively correlates with in vivo carcinogenic data.

Mutagenicity testing by procedure of Ames (Salmonella).

Wood, A. W., et al.

Mutagenic and Cytotoxic Activity of Benzo[a]pyrene 4,5-, 7,8-, and 9,10-oxides and the Six Corresponding Phenols. *PROC. NAT. ACAD. SCI. USA*, LXXII: 3176-3180, 1975. 30 refs.

The benzo[a]pyrene 4,5-, 7,8-, and 9,10-oxides and the six corresponding phenols have been tested for mutagenic and cytotoxic activity in bacteria and in a mammalian cell-culture system.

Mutagenicity testing by the procedure of Ames (Salmonella) and in mammalian cells.

Wood, A. W., et al.

Mutagenicity and Cytotoxicity of Benzo[a]pyrene Benzo-Ring Epoxides.

CANCER RES., XXXVI: 3358-3366, 1976. 34 refs.

Four benzo-ring epoxides of the environmental carcinogen benzo[a]pyrene (BP) were tested for mutagenic and cytotoxic activity in three strains of *S. typhimurium* and in Chinese hamster V79 cells.

Mutagenicity testing by the procedure of Ames (Salmonella) and in Chinese hamster cells.

Yahagi, T., et al.

Mutagenicities of Nitrofurantoin Derivatives on a Bacterial Tester Strain With an

R Factor Plasmid. MUTAT. RES., XL: 9-14, 1976. 12 refs.

Many nitrofurantoin derivatives are known to be mutagenic on *E. coli* WP2 but not on *S. typhimurium* TA1535, TA1536, TA1537 or TA1538. Ames and coworkers recently obtained a new tester strain of *S. typhimurium*, TA100, by putting an R factor plasmid, pKM 101, into TA1535. It was found that all the mutagenic nitrofurantoin derivatives previously found to be mutagenic on *E. coli* WP2 were mutagenic on this new strain TA100.

Mutagenicity testing by procedure of Ames (Salmonella and *E. coli*).

Yahagi, T., et al.

Mutagenicity of Carcinogenic Azo Dyes and Their Derivatives. CANCER

LETTERS, I: 91-96, 1975. 18 refs.

The mutagenicity of N,N-dimethyl-4-aminoazobenzene and N-methyl-4-aminoazobenzene and their derivatives was shown on *S. typhimurium* TA100 and TA98. S-9 Mix, obtained from rat liver after injection of polychlorinated biphenyl, was obligatory for their mutagenic action. N-Acetoxy-N-methyl-4-aminoazobenzene and N-benzo-yloxy-N-methyl-4-aminoazobenzene and their 4'-methoxycarbonyl derivatives were also mutagenic on TA100 and TA98 and did not require metabolic activation by S-9 Mix. It is suggested that the carcinogenic effects of azo dyes may involve modification of DNA.

Mutagenicity testing by procedure of Ames (Salmonella).

Yahagi, T., et al.

Relationship Between the Carcinogenic and Mutagenic or DNA-Modifying

Effects of Nitrofurantoin Derivatives, Including 2-(2-furyl)-3-(5-nitro-2-furyl) Acrylamide, a Food Additive. CANCER RES., XXXIV: 2266-2273, 1974. 42 refs.

The mutagenic and DNA-modifying effects of 27 nitrofurantoin derivatives were studied by means of several rapid microbial assay methods. The mutagenic effects were tested with the use of *E. coli*, B/r WP2 try- and WP2 try-, her-; and with *S. typhimurium*. TA1535, TA1536, TA1537, and TA1538.

Mutagenicity testing by procedure of Ames (Salmonella and in *E. coli*).

Yielding, L. W., W. E. White, Jr., and K. L. Yielding.

Production of Frameshift Mutations in Salmonella by a Light Sensitive Azide Analog of Ethidium. MUTAT. RES., XXXIV: 351-358, 1976. 12 refs. Frameshift mutations have been produced in specific repair-negative Salmonella tester strains by photoaffinity labeling technique using ethidium azide. Reversions requiring a +1 addition or a -2 deletion were especially sensitive. Mutagenesis was reduced by the simultaneous addition of non-mutagenic ethidium bromide, and was prevented by photolysis of the azide prior to culture addition. Identical tester strains active in DNA excision repair were not mutagenized by the azide. Mutagenicity testing by procedure of Ames (Salmonella).

Zetterberg, G., et al..

The Influence of pH on the Effects of 2,4-D (2,4-dichlorophenoxyacetic acid, Na SALT) on Saccharomyces cerevisiae and Salmonella typhimurium. MUTAT. RES., XLII: 3-18, 1977. 17 refs.

The genetic effects of 2,4-D have been investigated in cells of the yeast S. cerevisiae and of the bacterium S. typhimurium in experiments in vitro and in vivo. Experiments in vitro showed that the killing of both yeast and bacteria is dependent on the pH in the treatment solution of 2,4-D. A dose-dependent increase of the frequency of mitotic gene conversion and mitotic recombination in yeast was observed at pH 4.5 and 4.3. In experiments in vitro with two strains of Salmonella no significant increase of the number of revertants to prototrophy was obtained. The positive correlation between survival of cells and dissociation of 2,4-D in the pH region 2.8-5.0 indicates that the cells are unable to take up dissociated 2,4-D. Therefore the survival is high at a high pH when most 2,4-D is in dissociated form, and the survival is low at a relatively low pH when more of the 2,4-D is in its undissociated form. No genetic effects were induced by oral administration of tolerable doses of 2,4-D in host-mediated assays using mice as hosts and yeast or Salmonella as indicator cells.

Mutagenicity testing in Salmonella (Ames) and S. cerevisiae.

Zimmer, D. M., and B. K. Bhuyan

Mutagenicity of Streptozotocin and Several Other Nitrosourea Compounds in Salmonella typhimurium. MUTAT. RES., XL: 281-288, 1976. 18 refs.

The following nitrosourea compounds were compared for their ability to induce mutation in the histidine-requiring auxotroph S. typhimurium hisG45: MNU, streptozotocin and its analogs SZA1 and SZA2 and the antitumor drugs BCNU, CCNU and DCNU. At equitoxic doses SZ, SZA1, SZA2 and MNU were almost equally mutagenic causing 150, 42, 140 and 170 mutants/106 survivors at 20% lethal dose, although on a weight basis, SZ was the most mutagenic of the compounds tested. Our results show that these nitrosoureas, in common with many other drugs used in cancer chemotherapy, are highly mutagenic.

Mutagenicity testing by procedure of Ames (Salmonella).

Zimmermann, F. K.

Induction of Mitotic Gene Conversion by Mutagens. MUTAT. RES., XI: 327-337, 1971. 55 refs.

Mitotic gene conversion generates wild-type alleles from a pair of differently inactive alleles combined in a heteroallelic diploid. If the inactivity of those alleles causes a nutritional requirement, production of wild-type recombinants by mitotic gene conversion can be followed, in the yeast *S. cerevisiae*, by simply plating cells on selective media. Mitotic gene conversion can be induced by a large variety of mutagens: ionizing radiation, UV irradiation, methylating, ethylating, propylating and butylating agents, as well as by other alkylating agents such as ethyleneimines, nitrogen mustards, lactones, epoxides, sultones, metabolic derivatives of carcinogenic, aromatic amines, deaminating nitrous acid, radical-producing hydroxyurea and the acridine mustard 2-methoxy-6-chloro-9-(2-chloroethylaminopropylamino) acridine.

Mutagenicity in yeasts.

OTHER ASSAY SYSTEMS FOR ENVIRONMENTAL CARCINOGENS AND/OR MUTAGENS

Arenaz, P., and B. K. Vig.

Induction of Somatic Mosaicism in the Soybean by Some Carcinogens. GENETICS, LXXXIII: s3, 1976.

An abstract.

Carcinogenicity testing in plants.

Arlett, C. F.

Mutation Testing With Cultured Mammalian Cells. LAB. PRACT., XXI: 420-423, 1972. 15 refs.

Cultured mammalian cells can provide material for mutagenicity testing which is relevant to man. The 8-azaguanine resistance system in Chinese hamster cells which has been studied in detail is especially convenient for laboratory study because mutations may be scored on the basis of simple colony counts. A description of the system and its potential for use in routine mutagenicity testing is provided.

Arlett, C. F., et al.

A Comparison of the 8-azaguanine and Ouabain-Resistance Systems for the Selection of Induced Mutant Chinese Hamster Cells. MUTAT. RES., XXXIII: 261-278, 1975. 36 refs.

Mutagenicity testing -- hamster cells.

Benedict, W. F.

Morphological Transformation and Chromosome Aberrations Produced by Two Hair Dye Components. NATURE, CCLX: 368-369, 1976. 12 refs.

A possible carcinogenic hazard from hair dyes has been suggested recently by mutagenicity studies using the Salmonella tester strains developed in Ames' laboratory.

Mutagenicity testing noted by chromosome breaks and rearrangement (mouse cell line).

Bhattacharya, A. K.

Chromosome Damage Induced by Semicarbazide in Spermatocytes of a Grasshopper. MUTAT. RES., XL: 237-242, 1976. 7 refs.

Semicarbazide hydrochloride (0.1M in glass-distilled water), on injection, showed mutagenic action on the spermatocyte chromosomes of the grasshopper, Spathosternum presiniferum. Aberrations such as chromatid and chromosome breaks, translocations, fragments and bridges were encountered. The sex chromosome and the long autosomes were affected. Semicarbazide, perhaps, reacts with DNA and the chromosome in a way similar to that of hydroxylamine and hydrazines.

Mutagenicity testing - grasshopper spermatocytes.

Bond, D. J.

A System for the Study of Meiotic Non-Disjunction Using Sordaria bervicollis. MUTAT. RES., XXXVII: 213-220, 1976. 13 refs.

S. bervicollis is potentially useful in studying abnormal chromosome segregation, e.g., meiotic non-disjunction.

Does this system have a potential as a rapid screen for carcinogenic substances?

A system is described for the study of abnormal chromosome segregation in Sordaria brevicollis. The system utilizes two complementing alleles of the b₁ locus on linkage group II. Abnormal asci containing black disomic asco-spores were detected which fall into two main categories. (a) Non-disjunctive asci in which the disomic spores were present together with an equal number of abortive (nulloromic) spores and (b) asci in which an extra replication of the chromosomes had occurred resulting in pseudo-wild types being formed without accompanying spore abortion. Calculations indicate that the non-disjunction frequencies at the first and second divisions of meiosis are 4.25×10^{-4} and 4.35×10^{-4} respectively. It is suggested that the system is potentially a valuable one both for the study of meiotic non-disjunction and other causes of aneuploidy.

Mutagenicity testing -- meiotic non-disjunction in S. brevicollis.

Boyd, J. B., et al.

Mutagen sensitivity in X-linked Mutants of D. melanogaster. GENETICS, LXXXIII: s9, 1976.

An Abstract.

Mutagenicity testing -- Drosophila melanogaster.

Brewen, J. G., P. Nettesheim and K. P. Jones.

A Host-Mediated Assay for Cytogenetic Mutagenesis: Preliminary Data on the Effect of Methyl Methane-sulfonate. *MUTAT. RES.*, X: 645-649, 1970. 5 refs.

Two necessary prerequisites for easy performance of meaningful quantitative cytogenetic studies on the effect of potential mutagenic agents on mammalian cells are a homogeneous population of cells and the ability to expose these cells to the agents in vivo.

Mutagenicity testing -- cytogenic studies using small lymphocytes.

Bridges, B. A.

Modifications of Cellular Mutagenicity Test Procedures. *LAB. PRACT.*, XXI: 424, 1972. 4 refs.

In the host-mediated assay, cells are introduced into a mammalian host which is treated (by another route) with the agent being tested. After some hours the mammal is killed and the cells recovered and tested in vitro for the presence of newly-induced mutants.

The host-mediated assay is only as good as the cell system it utilizes, and although in principle any cellular system could be used, so far results and descriptions of technique have only been published for Salmonella and Neurospora (Legator and Mallin, 1971).

Bridges, B. A., J. Huckle and M. J. Ashwood-Smith.

X-Ray Mutagenesis of Cultured Chinese Hamster Cells. *NATURE*, CCXXVI: 184-185, 1970. 7 refs.

The development of quantitative systems for the detection of induced gene mutations in cultured mammalian cells is likely to facilitate work on hazards from environmental mutagens and on the mechanisms involved in mutagenesis.

Mutagenicity testing - Chinese hamster cells.

Capizzi, R. L., et al.

The Detection of Chemical Mutagens Using the L5178Y/Asn-murine Leukemia in Vitro and in a Host-Mediated Assay. *CANCER RES.*, XXXIV: 3073-3082, 1974. 45 refs.

The induction of asparagine-independent mutants by the action of known chemical mutagens on the asparagine auxotrophy of the murine leukemia L5178Y (L5178Y/Asn-) was studied.

Mutagenicity testing in murine leukemia cells.

Carver, J. H., W. C. Dewey and L. E. Hopwood.

X-Ray-Induced Mutants Resistant to 8-azaguanine. 1. Effects of Cell Density and Expression Time. MUTAT. RES., XXXIV: 447-464, 1976. 43 refs.

This study has attempted to define more clearly the optimal experimental procedures in regard to cell density and expression time which are necessary to avoid many of the problems inherent in the AG assay. With culturing conditions of the assay protocol better understood, the system holds promise as a useful tool in investigations of environmental mutagens (chemical as well as X and UV-radiation).

Mutagenicity testing in Chinese hamster ovary cells.

Carver, J. H., W. C. Dewey and L. E. Hopwood.

X-Ray-Induced Mutants Resistant to 8-azaguanine. II. Cell Cycle Dose Response. MUTAT. RES., XXXIV: 465-480, 1976. 48 refs.

These experiments were undertaken to compare the sensitivity of G₁ and S phase to mutation induction by ionizing radiation. The data indicate that there are no significant differences in response between these two phases. Relative to radiation protection standards, doubling dose estimates from cultured cells agrees reasonably well with in vivo studies. Chinese hamster cells.

Cole, J., and C. F. Arlett.

Ethyl Methanesulphonate Mutagenesis with L5178Y Mouse Lymphoma Cells: A Comparison of Ouabain, Thioguanine and Excess Thymidine Resistance. MUTAT. RES., XXXIV: 507-526, 1976. 32 refs.

We have performed a limited number of host-mediated assays with these cells. It is clear that while resistance can be induced for all three selective agents, many deficiencies of the system are apparent. TdR toxicity is particularly affected by the passage of cells through the host-compare the possible influence of growth rate on TdR resistance discussed. There is a much larger inherent variability following treatment in the mouse in both spontaneous and induced levels of resistant cells. In view of the fact that we elected to use the subcutaneous route to administer the EMS, we are unable to assume that the dose per cell in the peritoneal cavity is constant. Differences in penetration from one mouse to another may well be responsible for the variability in the induced frequency of resistant variants.

Mutagenicity assayed in mouse lymphoma cells.

Dean, B. J., and D. Blair.

Dominant Lethal Assay in Female Mice After Oral Dosing With Dichlorvos or Exposure to Atmospheres Containing Dichlorvos. MUTAT. RES., XL: 57-72, 1976. 18 refs.

This communication describes the assay of dominant lethal mutations in female mice after oral dosing or inhalation exposure to dichlorvos.

De Marco, A., et al.

Environmental Mutagens and Environmental Factors that can Modify Their Action. MUTAT. RES., XXIX, 253-454, 1975.

An abstract concerned with mutagens in the environment and environmental factors that may increase the frequency of induced mutations.
Mutagenesis testing in Drosophila melangaster.

De Serres, F. J., and H. V. Malling.

Measurement of Recessive Lethal Damage Over the Entire Genome and at Two Specific Loci in the ad-3 Region of a Two Component Heterokaryon of Neurospora crassa. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., II: 311-342, 1971. 23 refs.

Lethal mutations over the entire genome and in the ad-3 region described in the following sections are designed primarily for research programs where the investigator will not only want to obtain precise quantitative data on mutation induction but will also want to determine the spectrum of recessive lethal mutations.

Mutagenicity testing in Neurospora crassa.

Ehling, U. H.

Mutagenicity Testing and Risk Estimation With Mammals. MUTAT. RES., XLI: 113-122, 1976. 67 refs.

Mammalian test systems are currently used for mutagenicity screening. The necessity and the limitations of standardizing these methods are discussed for the dominant-lethal assay. The development of standards for the controlled use of chemical mutagens should be guided by the experience accumulated in radiation genetics. Two methods, the measurement of specific-locus mutation rates in mice and the direct determination of the phenotypic damage of dominant genes affecting the skeleton of mice, are recommended for the assessment of the hazard of chemical mutagens.

Fahmy, O. G., and M. J. Fahmy.

Mutagenic Selectivity of Carcinogenic Nitroso Compounds. II. N,N-dimethylnitrosamine. CHEM.-BIOL. INTERACT., XI: 395-412, 1975. 24 refs.

The genetic properties of the hepatocarcinogen N,N-dimethylnitrosamine (DMN) were examined in Drosophila for the assessment of the role of dose, cellular metabolism and genic target in its mutagenicity.

Mutagenicity testing in Drosophila.

Hollaender, A., ed.

Chem. Mutagens: Prin. Methods Their Detect., Vol. II. New York: Plenum Press, 1971.

Measurement of Recessive Lethal Damage Over the Entire Genome and at Two Specific Loci on the Ad-3 Region of a Two-Component Heterokaryon of Neurospora crassa

Aspergillus

Higher Plants

Procedures for Culturing Diploid Cells and Preparation of Meiotic Chromosomes from Dwarf Species of Hamsters

Induction and Analysis of Gene Mutations in Mammalian Cells in Culture

Inducing Mutations with Chemicals in Habrobracon

The Detection of Mutations in Drosophila melanogaster

Root Tips for Studying the Effects of Chemicals on Chromosomes

Cytogenetic Studies in Animals

Specific Locus Mutation in Mice

Dominant Lethal Mutations in Mammals

The Host-Mediated Assay, a Practical Procedure for Evaluating Potential Mutagenic Agents in Mammals

Human Population Monitoring

Huberman, E., and L. Sachs.

Mutability of Different Genetic Loci in Mammalian Cells of Metabolically Activated Carcinogenic Polycyclic Hydrocarbons. PROC. NAT. ACAD. SCI. USA., LXXIII: 188-192, 1976. 25 refs.

The relationship between carcinogenesis and mutagenesis in mammalian cells has been determined with 10 polycyclic hydrocarbons with different degrees of carcinogenicity.

Mutagenicity testing -- mammalian cells.

Huberman, E., et al.

Identification of Mutagenic Metabolites of Benzo[a]pyrene in Mammalian Cells. PROC. NAT. ACAD. SCI. USA, LXXIII: 607-611, 1976. 27 refs.

The mutagenicity of benzo[a]pyrene and 15 of its derivatives, which included phenols, the benzo[a]pyrene-4,5-epoxide (the K-region epoxide), dihydrodiols, two isomeric 7,8-diol-9,10-epoxides, a 6-methyl derivative, and a 6-hydroxymethyl derivative, were tested with Chinese hamster V79 cells in order to identify the mutagenic metabolites of benzo[a]pyrene. Mutations were characterized by resistance to ouabain or 8-azaguanine.

Mutagenicity testing in mammalian cells.

Huberman, E., et al.

Mutagenicity to Mammalian Cells of Epoxides and Other Derivatives of Polycyclic Hydrocarbons. PROC. NAT. ACAD. SCI. USA, LXVIII: 3195-3199, 1971. 25 refs.

The cytotoxicity and mutagenicity of several polycyclic hydrocarbons and their K-region derivatives were tested in a clone of Chinese hamster

cells; the production of clones resistant to 8-azaguanine was used as the marker for mutagenesis.
Mutagenicity testing -- mammalian cells.

Jorgenson, T. A., et al.

Mutagenic Studies of Aziridine Derivatives Derived from Various Diamines.

MUTAT. RES., XXXI: 115-122, 1975. 10 refs.

Various aziridine derivatives derived from diamines were studied in several biological systems to evaluate their effects on reproduction and as potential mutagens. Considerable variations in the biological activities of these compounds were seen among animal species and among the varied chemical structures. In general, mutagenic responses paralleled the antifertility effects in mice and houseflies and the anticancer effects in mice. The lack of an antifertility effect by N,N'-bis(aziridinylacetyl) 01, 8-octamethylenediamine in the rat was quite unexpected in view of its chemosterilant activity in houseflies and mice.

Mutagenicity testing in Coturnix coturnix japonica.

Kamra, O. P.

On the Different Mutagenic Activities of N-alkyl-N'-nitro-N-nitrosoguanidines in Higher Plants. MUTAT. RES., XIII: 327-335, 1971. 38 refs.

Mechanisms of action and the differential mutagenic activities of nitrosoguanidines in higher plants are discussed.

Mutagenicity testing in barley.

Kilbey, B. J., F. J. de Serres and H. V. Mallng.

Identification of the Genetic Alteration at the Molecular Level of Ultraviolet Light-Induced ad-3B mutants in N. crassa. MUTAT. RES., XII: 47-56, 1971. 19 refs.

The correlation between complementation pattern and genetic alteration at the molecular level found previously by Mallng and de Serres among NA- and EMS-induced ad-38 mutants, was also found among UV-induced mutants. Mutants with non-polarized patterns resulted mainly from base-pair substitutions, whereas mutants with polarized complementation patterns and noncomplementing mutants are derived from a variety of genetic alterations.

Mutagenicity testing in Neurospora crassa.

Kirkland, D. J., and S. Venitt.

Cytotoxicity of Hair Colourant constituents: chromosome Damage Induced by Two Nitrophenylenediamines in Cultured Chinese Hamster Cells. MUTAT. RES., XL: 47-56, 1976. 15 refs.

Two aromatic amines are constituent dyes of many widely used proprietary hair colorants. Both compounds were cytotoxic to CHMP/E cells following 5 days continuous exposure.
Mutagenicity testing in hamster cells.

Legator, M. S., et al.

Cytogenetic Studies in Rats of Cyclohexylamine, a Metabolite of Cyclamate. SCIENCE, CLXV: 1139-1140, 1969. 10 refs.
Cyclohexylamine, the major known metabolite of cyclamate, was tested in vivo for possible cytogenetic effects. In rats injected with this metabolite, there was a direct relation between dose concentration and percentage of spermatogonial and bone marrow cells showing chromosomal breaks. Single chromatid breaks predominated with infrequent exchange figures.

Levin, W., et al.

Carcinogenicity of Benzo[a]pyrene 4,5-,7,8-, and 9,10- Oxides on Mouse Skin. PROC. NAT. ACAD. SCI. USA, LXXIII: 243-247, 1976. 31 refs.
Benzo[a]pyrene and three arene oxides of benzo[a]pyrene have been tested for carcinogenicity in mice by topical application of each compound once every 2 weeks for 60 weeks. The carcinogenic activities of the three arene oxides of benzo[a]pyrene were not correlated with their stabilities or mutagenic activities.
Mutagenicity testing in animals.

Liwerant, I. J., and L. H. Pereira Da Silva.

Comparative Mutagenic Effects of Ethyl Methane-Sulfonate, N-methyl-N'-nitro-N-nitrosoguanidine, Ultraviolet Radiation and Caffeine on Dictyostelium discoideum. MUTAT. RES., XXXIII: 135-146, 1975. 22 refs.
A high frequency of morphogenetic mutants of D. discoideum can be induced by treatment with MNNG under conditions which result in relatively low cell killing. Six temperature-sensitive growth mutants induced by this treatment were isolated by replica plating. Among these, five showed spontaneous reversion rates of 10^{-4} to 10^{-5} . The mutagenic activity of EMS, measured for the induction of both morphogenetic and temperature-sensitive mutants, was weaker than that of MNNG and UV radiation. High frequencies of morphogenetic mutants were obtained only with doses of UV irradiation and that resulted in high killing of cells or spores. Caffeine, at concentrations that slightly decreased the growth rate of amoebae in axenic medium, induced morphogenetic defects and also enhanced the mutagenic effect of UV irradiation. However, all the aggregateless clones derived from caffeine treatment that were studied reverted to the wild-type phenotype after a variable number of clonal re-isolations.
Mutagenicity testing in Dictyostelium discoideum.

Lyon, M. F., R. J. S. Phillips and A. G. Searle.

A Test for Mutagenicity of Caffeine in Mice. MOL. GEN. GENET., XCIII: 7-13, 1962. 22 refs.

1. The results are given of an experiment comparing the specific locus mutation and rates in male and in female mice having 0.1% caffeine dissolved in their drinking-water up to the age of 10 weeks. Their parents had the same treatment from the time of mating, so that tested germcells might be exposed to caffeine during embryonic development.
2. The mutation rates in males and females did not differ significantly from each other, nor from the known spontaneous rate; thus, there was no evidence for induction of mutations by the caffeine treatment. Neither was there evidence for the induction of dominant lethals following caffeine treatment of males.
3. The treatment did not noticeably affect reproduction, but some mice developed aggressive tendencies towards their cage-mates. Some mice were kept on 0.1% caffeine throughout life: they continued to breed satisfactorily on the whole.

Mutagenicity testing in mice.

Machemer, L., and D. Lorke.

Evaluation of the Mutagenic Potential of Cyclohexylamine on Spermatogonia of the Chinese Hamster. MUTAT. RES., XL: 243-250, 1976. 26 refs.

In a cytogenetic study on the spermatogonia of Chinese hamster, cyclohexylamine (neutral sulphate) was evaluated for mutagenic effects in comparison with an untreated control group and a group treated with the mutagenic compound cyclophosphamide, by assessing spermatogonial metaphases of treated Chinese hamster for chromosomal structural changes.

Mutagenicity testing in Chinese hamster cells.

Maier, P., and W. Schmid.

Ten Model Mutagens Evaluated by the Micronucleus Test. MUTAT. RES., XL: 325-338, 1976. 38 refs.

Ten mutagenic compounds were subjected to the micronucleus bone marrow test in the mouse. Dose-effect curves were established for all compounds. With the exception of CTX, COLC and AM, the drugs also were subjected to chromosome analyses on Chinese hamster fibroblasts in vitro.

Mutagenicity testing by micronucleus test.

Manual of the First Annual Course in the Principles and Practices of Genetic Toxicology. Galveston, Texas: Clinical Cancer Center, The University of Texas Medical Branch, 1976.

Includes papers contributed by:

Bacterial Systems -- T. Matney; B. N. Ames, J. McCann and E. Yamasaki
Body Fluid and Tissue Analysis -- M. S. Legator, T. G. Pullin and T. H. Connor;

Cell Transformation Technique -- B. R. Brinkley and G. M. Fuller
Cytogenetics -- T. S. Hsu and F. E. Arrighi; D. J. Kilian and D.
Picciano; W. Schmid; E. Weber, K. Bidwell and M. S. Legator
Dominant Lethal and Translocation Test - S. Green; A. Leonard
Drosophila -- S. Zimmering
Environmental Mutagenicity Information Center
Host Mediated Assay -- M. S. Legator; R. Fahrig
Mammalian Cells -- R. J. Klebe
Specific Locus Test -- A. G. Searle

Murnik, M. R.

Mutagenicity of Widely Used Herbicides. SCIENCE, LXXXIII: s54, 1976.
An abstract.
Mutagenicity testing in *Drosophila melanogaster*.

Ong, T.-M., and H. V. Mallng.

Microsomal Activation of Dimethylnitrosamine to Metabolites Mutagenic in
Neurospora crassa. MUTAT. RES., XXXI: 195-196, 1975. 12 refs.
Studies were carried out to determine if the metabolites formed during
incubation DMN in the liver microsome system could induce adenine-3
(ad-3) mutations in *Neurospora crassa*.
Mutagenicity testing in *Neurospora crassa*.

Scalera, S. E., and O. G. Ward.

A Quantitative Study of Ethyl Methanesulfonate-Induced Alkylation of *Vicia*
faba DNA. MUTAT. RES., XII: 71-79, 1971. 27 refs.
A report of the results of a qualitative and quantitative investigation of the
alkylation products formed by the in vitro treatment of *Vicia faba* root tip
DNA with EMS.
Mutagenicity testing in *Vicia faba*.

Sung, Z. R.

Mutagenesis of Cultured Plant Cells. GENETICS LXXXIV: 51-57, 1976. 12
refs.
Experiments were designed to study the effectiveness of the chemical
mutagens ethylmethane sulfonate and nitrosoguanidine on plant cells
growing in liquid suspensions. The compounds tested usually increased
mutation frequency by one order of magnitude over the spontaneously
occurring rate, although the increase ranged from one to 140-fold. Cell
killing was found to be directly correlated with mutation frequency.
Mutagenicity testing in plant culture.

Urwin, C., J. C. Richardson and A. K. Palmer.

An Evaluation of the Mutagenicity of the Cutting Oil Preservative Groton BK. MUTAT. RES., XL: 43-46, 1976. 7 refs.

The micronucleus test in rats was used to investigate the mutagenic potential of Groton BK, a preserving agent used in industrial cutting oils.

Micronuclei testing.

Valencia, R. A.

Discussion paper: The Use of Drosophila for Mutagenesis Screening. ANN. N. Y. ACAD. SCI., CCLXIX: 34-36, 1975.

A discussion of mutagenic screening with Drosophila.

Wild, D.

Mutagenicity Studies on Organophosphorus Insecticides. MUTAT. RES., XXXII: 133-150, 1975. 50 refs.

This study uses a variety of screening methods.

Zimmering, S.

Utility of Drosophila for Detection of Potential Environmental Chemical Mutagens. ANN. N. Y. ACAD. SCI., CCLXIX: 26-33, 1975. 52 refs.

The purpose of the communication is to describe some of the advantages of Drosophila in testing chemicals for mutagenicity in traditional ways and to explore the possibilities of expanding its role to include testing of substances derived directly from humans or the human environment.

Mutagenicity testing in Drosophila.

REPORTS, LETTERS AND WORKSHOPS

Ames, B. N.

Letters: Carcinogenicity Tests. SCIENCE, CXCI: 241-245, 1976. 26 refs.

A letter to the Editor regarding carcinogenicity testing and the relationship of mutagenicity to carcinogenicity.

Ames, B. N., J. McCann and C. Sawyer.

Letters: Mutagens and Carcinogens. SCIENCE, CXCI: 132-133, 1976. 6 refs.

In reply to Andrew Sivak's comments regarding the use of the Ames' test and the correlation or lack of it between mutagenicity and carcinogenicity.

Auerbach, C.

Mutation Research in Microorganisms. MUTAT. RES., V: 198-199, 1968.
The main object of the meeting was to bring together workers engaged in the same problems in different countries and on different organisms and not always publishing in the same journals.

Auerbach, C.

Repair and Mutation in Microorganisms. MUTAT. RES., X: 168, 1970. 1 ref.
A brief report of a meeting held in Pisa on mutation in microorganisms.

Auerbach, C.

Symposium No. 2: Mutagenesis Introduction by the Chairman. GENETICS, LXXVIII: 77-79, 1974.
Chairperson's opening remarks on mutagenicity.

Brookes, P., and F. J. de Serres.

Report of the Workshop on the Mutagenicity of Chemical Carcinogens. MUTAT. RES., XXXVIII: 155-160, 1976.
The workshop was organized by the U.S. and the Japanese Environmental Panels in the U.S.-Japan Cooperative Medical Science Program to review the status of experiments in the U.S. and Japan to determine the correlation between carcinogenic and mutagenic activity.

Center for the Biology of Natural Systems. (Commoner, B.)

Reports on EPA Grant No. R-804395-01-0, "Studies to Improve the Reliability and Sensitivity of Bacterial Mutagenesis as a Screen for Environmental Carcinogens," St. Louis, Missouri: Washington University, April-November, 1976.

Committee 17, Environmental Mutagen Society. Report of the Committee. Environmental Mutagenic Hazards. SCIENCE, CLXXXVIII: 503-514, 1975.

The characteristics of mutational screens such as bacterial, fungal, plant, insect, mammalian cell culture and animal tests are discussed relative to the feasibility of using them as screens for chemicals entering the environment.

de Serres, F. J.

Mutagenicity of Chemical Carcinogens. MUTAT. RES., XLI: 43-50, 1976.
7 refs.

During the past three years, two collaborative studies were started in the U.S. and Japan to study the correlation between carcinogenic and mutagenic activity. The objective of the collaborative studies was to test known chemical carcinogens, non-carcinogenic structural analogs and other non-carcinogens, with a variety of assay systems for mutagenicity. A series of reports of meetings and workshops.

de Serres, F. J.

The Correlation Between Carcinogenic and Mutagenic Activity in Short-Term Tests for Mutation-Induction and DNA Repair. MUTAT. RES., XXXI: 203-204, 1975.

An editorial. A report of three workshops which discussed testing, particularly short-term, and the correlation between carcinogenic and mutagenic activity.

Goetz, P.

Symposium on the Mutagenicity Testing of Environmental Contaminants. MUTAT. RES., XXXI: 129-130, 1975.

A report on Czechoslovakian symposium dealing with environmental mutagens.

Hollaender, A.

Opening Remarks. ANN. N. Y. ACAD. SCI., COLXIX: 1-3, 1975.
Remarks on mutagens and potential carcinogens.

Knaap, A. G. A. C., P. G. N. Kramers, and F. H. Sobels.

Workshop on Chemical Mutagenesis in the Netherlands. MUTAT. RES., XXXVIII: 239, 1976.

Notes on the mutagens workshop in the Netherlands in 1975.

Ramel, C.

Mutagenicity Research and Testing in Sweden. MUTAT. RES., XXXIII: 79-86, 1975. 22 refs.

A survey is given of Swedish legislation for control chemicals in the environment.

An outline is given of the organization of the Environmental Toxicology Unit of the Wallenberg laboratory, University of Stockholm.

As examples of projects under joint investigation, results on polychlorinated biphenyl (PCB) and on vinyl chloride are briefly described.

Rubin, H.

Letters: Carcinogenicity Tests. SCIENCE, CXCI: 241, 1976. 11 refs.
A letter to the editor regarding carcinogenicity testing.

Sermonti, G.

"Ettore Majorana" Centre for scientific culture, international school of general genetics (A NATO Adv. Study Inst.). MUTAT. RES., XXXVIII: 161-162, 1976.

A course in environmental mutagenesis emphasized the use of bacteria and other microorganisms as the most sensitive, specific and short-term approach to the evaluation of chemical mutagenesis.

On the other hand, Drosophila had several distinct advantages, in that it permits the assessment of the total genetic spectrum and does not require activating systems, as do some bacterial systems.

Test systems for mutagenicity range from short-term assays on bacteria and eukaryotic microorganisms to tests for recessive lethals in Drosophila, to cytological observations on somatic and germ cells in vivo and in vitro, to dominant lethal and specific locus tests in rodents.

Sivak, A.

The Ames Assay. SCIENCE, CXCI: 272-273, 1976. 6 refs.

The Ames assay will continue to be useful as one of a battery of first-step prescreens for chemical agents that may have the potential for interacting with cellular genomes. However, the implication that positive results in this microbial mutagenesis system will correspond to carcinogenicity in experimental animals or in humans does not appear, at present, to be substantiated.

The European Environmental Mutagen Society.

Abstracts of Papers presented at the 5th Annual Meeting, Florence, Italy, 1975. 64 abstracts.

University of Alberta, et al.

Workshop on Mutagenesis and Predictive Carcinogenesis. Edmonton, Alberta, Canada, 1977.

The Workshop is designed to provide a detailed appreciation of techniques used in screening for environmental mutagens and potential carcinogens, together with background understanding of the problems involved.

EVALUATION OF ASSAY SYSTEMS FOR ENVIRONMENTAL CARCINOGENS AND/OR MUTAGENS

Bartsch, H.

Predictive Value of Mutagenicity Tests in Chemical Carcinogenesis, MUTAT. RES., XXXVIII: 177-190, 1976. 68 refs.

Although there are still many problems involved in the interpretation of results of mutagenicity testing in terms of evaluating the carcinogenicity of chemicals, short-term tests can already be used in detecting possible cancer-causing agents with a sensitivity which did not exist ten years ago. They could thus be a powerful tool, when used in combination with epidemiological studies, in environmental control.

Bochkov, N. P., et al.

System for the Evaluation of the Risk from Chemical Mutagens for Man: Basic Principles and Practical Recommendations. MUTAT. RES., XXXVIII: 191-202, 1976. 23 refs.

A testing system is recommended that permits: (1) reduction in cost and time, (2) analysis of gene and chromosome mutations in germ and somatic cells, (3) evaluation of mutagenic effects of a chemical substance and its metabolites, (4) guarantee of the minimal variability between separate experiments and (5) evaluation of the dose-effect relationship.

Bridges, B. A.

Evaluation of Mutagenicity and Carcinogenicity Using a Three-Tier System. MUTAT. RES., XLI: 71-72, 1976. 6 refs.

The first tier contains short-term screening tests with sub-mammalian systems, the second tier contains short- and longer-term tests with whole mammals, and the third tier involves a risk-benefit evaluation which may entail further more specialized testing procedures and experiments on the detailed metabolism of the agent in vivo.

Bridges, B. A.

Short Term Screening Tests for Carcinogens. NATURE, CCLXI: 195-200, 1976. 81 refs.

There are short term tests with a high predictive value for mammalian carcinogens. Many of them are based on the ability to detect damage to DNA in bacteria or mammalian cells after metabolic activation by microsomal enzymes. They will enable provisional safety assessments to be made of industrial and environmental chemicals.

Commoner, B.

Mutagenesis: A Probe for Carcinogenicity. HOSP. PRACT., (March): 43-44, 50, 1975.

A number of substances that are powerful carcinogens in laboratory animals are inactive as bacterial mutagens. Carcinogenic activity of a given substance often varies with the test species or even within a species, so it is difficult to arrive at a meaningful definition of carcinogenic activity, especially as it relates to people.

Commoner, B.

Reliability of Bacterial Mutagenesis Techniques to Distinguish Carcinogenic and Noncarcinogenic Chemicals. Report to the U.S. Environmental Protection Agency, Office of Research and Development, April, 1976. Washington, D.C.: U.S. Environmental Protection Agency, 1976. 5 refs.

The purpose of these investigations was to determine the reliability with which an expanded Salmonella mutagenesis test system can distinguish between those organic chemical substances that cause cancer in laboratory animals and those that do not. One Hundred organic compounds were tested, 50 presumptive carcinogens and 50 noncarcinogens.

In general the results indicate that the Salmonella mutagenesis system can be used to distinguish, with a high degree of reliability, that the statistical reliability needs to be improved for application to environmental samples and the steps that need to be taken to improve the test.

Commoner, B.

Tests of the Reliability With Which the Bacterial Mutagenesis Technique Can Distinguish Between Carcinogenic and Noncarcinogenic Synthetic Organic Chemicals. Report to the Environmental Protection Agency, Contract No. 68-01-2471, May, 1976. 13 refs.

Tests were made of 100 organic compounds, 50 presumptive carcinogens and 50 noncarcinogens. The results indicate that the Salmonella mutagenesis system can be used to distinguish, with a high degree of reliability, between presumptive carcinogens and noncarcinogens, in populations of test samples with two classes of compounds in equal proportions. The results also show that the statistical reliability of the system needs to be improved for application to those populations of environmental samples in which the proportion of active substances may be relatively low, as well as the steps needed to make the improvements.

Conference on Occupational Carcinogenesis.

Discussion. Carcinogenesis in the Metal Industry. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 496-504, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Chemical Carcinogenesis (I). Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 473-480, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Chemical Carcinogenesis (II). Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 481-488, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Current Concepts of Carcinogenesis. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 460-472, 1976.

Conference on Occupational Carcinogenesis.

Discussion. High-Risk Industrial Groups: Identification, Education and Surveillance. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 508-612, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Methodologies for Risk Assessment. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 513-516, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Prevention of Occupational Cancer-Toward an Integrated Program of Governmental Action. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 491-495, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Radiation and Particulate Matter. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 505-507, 1976.

Conference on Occupational Carcinogenesis.

Discussion. Recent Approaches to the Control of Carcinogenic Exposures. Conference on Occupational Carcinogenesis, N. Y. Academy of Sciences, New York, May, 1975. In ANN. N. Y. ACAD. SCI., CCLXXI: 489-490, 1976.

Dean, B. J.

A Predictive Testing Scheme for Carcinogenicity and Mutagenicity of Industrial Chemicals. MUTAT. RES., XLI: 83-88, 1976. 4 refs.
A general discussion. Mutagenicity screening.

de Serres, F. J.

Perspective in a Period of Transition. MUTAT. RES., XXXVIII: 355-358, 1976.

During the past year there have been two major developments that will have an enormous impact on the work of this Society in the near future. The first was the identification of many environmental and industrial chemicals as carcinogens and the widespread belief that a high percentage (80-90%) of human cancer is a result of such exposures. The second was a demonstration of a high correlation between carcinogenic and mutagenic activity in newly developed short-term tests for mutagenicity. The latter finding has enormous implications for the first, because it opens up the possibility to utilize the short-term tests not only to identify potential mutagens in our environment but potential carcinogens as well.

de Serres, F. J.

Prospects for a Revolution in the Methods of Toxicological Evaluation. MUTAT. RES., XXXVIII: 165-176. 39 refs.

There is a realization that many man-made chemicals have potent mutagenic activity and there is concern over their effects on man. Genetic toxicology focuses on biological activity harmful to man and his offspring.

de Serres, F. J.

The Utility of Short-Term Tests for Mutagenicity MUTAT. RES., XXXVIII: 1-2, 1976. 3 refs.

A thesis based on the need to screen environmental chemicals for mutagenicity. Short-term tests should be considered assays for potential mutagenic activity in man and as a highly efficient mechanism both for screening activity of environmental agents and establishing priorities for further testing.

de Serres, F. J.

The Utility of Short-Term Tests for Mutagenicity in the Toxicological Evaluation of Environmental Agents. MUTAT. RES., XXXIII: 11-15, 1975.

By using the short-term tests to establish priorities for testing in higher organisms, we can develop a more extensive data base from tests on hundreds of compounds.

Drake, J. W.

Environmental Mutagenesis: Evolving Strategies in the USA. MUTAT. RES., XXXIII: 65-72, 1975.

The "Committee 17" report made recommendations regarding the screening of environmental mutagens and the use of the resulting data. It is important to employ highly sensitive tests which detect heritable genetic damage of all possible molecular types. Mutagens of artificial origin which are being considered for continued production must be characterized with respect to level and pattern of distribution and persistence in the environment. Finally, the Committee laid out specific recommendations concerning maximum permissible exposures to environmental mutagens.

Epler, J. L.

Panel 4: Synfuel Utilization: Environmental and Health Effects. For publication in: PROC. SYMP. MANAGEMENT OF RESIDUALS FROM SYNTHETIC FUELS PRODUCTION, Denver, Colorado, 1976. 11 refs. A discussion of mutagenicity screening.

Kolata, G. B.

Chemical Carcinogens: Industry Adopts Controversial "Quick" Tests. SCIENCE, CXCII: 1215-1217, 1976.

In support of the Ames Test (Salmonella mutagens) as a screen for environmental chemical carcinogens.

Legator, M. S., and S. Zimmering.

Integration of Mammalian, Microbial and Drosophila Procedures for Evaluating Chemical Mutagens. MUTAT. RES., XXIX: 181-188, 1975. 23 refs.

The incorporation of a mutagenicity protocol as a part of an overall toxicological program required or advocated by regulatory agencies in the U.S. has yet to be realized.

Three screening procedures for environmental carcinogens are discussed.

Purchase, I. F. H., et al.

Evaluation of Six Short-Term Tests for Detecting Organic Chemical Carcinogens and Recommendations for Their Use. NATURE, CCLXIV: 624-627, 1976. 18 refs.

Six short-term tests for detecting carcinogenicity have been evaluated using 120 compounds, of which half were carcinogens and the rest non-carcinogens. The results obtained indicate that the Ames test and a "cell transformation" assay are both sufficiently sensitive to carcinogenicity, or the lack of it, in the compounds studied to enable them to be employed for detecting potential carcinogens. The consequences of using short term tests under various screening conditions have been explored. In order to have confidence in the results obtained for new or previously untested compounds it is important to use such tests in a carefully controlled manner.

Sobels, F. H.

Some Thoughts on the Evaluation of Environmental Mutagens. MUTAT. RES., XXXVIII, 361-366, 1976. 10 refs.

Chemical compounds in ever-increasing variety and kind are constantly being introduced into the human environment. Some of these may adversely affect the genetic material. Such effects deserve attention not only for reasons of protecting the genetic constitution of future generations, but are also of prime and direct concern to the present, in view of the striking concordance between the carcinogenic and mutagenic potential of most chemicals. That is, recent results with microbial assay systems and with Drosophila have convincingly demonstrated that the great majority of compounds capable of producing malignant transformation are also effective in inducing genetic changes in the form of heritable mutations. A task of immediate concern thus becomes one of how such genetic and carcinogenic hazards can be avoided and how adequate regulations to minimize exposure should be formulated.

Stich, H. F., et al.

The Search for Relevant Short-Term Bioassays for Chemical Carcinogens: the Tribulation of a Modern Sisyphus. CAN. J. GENET. CYTOL., VII: 471-492, 1975. 26 refs.

Based on a good correlation between carcinogenicity and mutagenic activity, several rapid microbial bioassays for chemical carcinogens have been recently developed. We would like to suggest, that these microbial tests should be followed by bioassays using cultured human cells of the "average" man, and of persons with elevated cancer risk or increased susceptibility to carcinogenic agents.

Zeigler, E., and J. Springer.

Storage and Statistical Evaluation of Microbial Mutagenicity Data. MUTAT. RES., XXXI: 337, 1975.

An abstract. Statistical evaluation of the Ames Test (Salmonella).

MISCELLANEOUS

Auerbach, C.

The Effects of Six Years of Mutagen Testing on Our Attitude to the Problems Posed by It. *MUTAT. RES.*, XXXIII: 3-10, 1975. 22 refs. Progress has been amazingly rapid both in technical means for the detection of mutagens and in the understanding of the basic process of mutagenesis. There has also been much feedback in both directions, to the profit of both areas of research.

Auerbach, C.

History of Research on Chemical Mutagenesis. *CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT.*, II: 1-19, 1973. 4 refs.

Auerbach, C.

Some Old Problems in Mutagenesis and Their Bearing on Mutagen Testing. *MUTAT. RES.*, XLI: 3-6, 1976.

The paper points up some problems that, after having been discussed for many years, now gain new importance through their relevance for mutagen testing.

Bender, D. F., M. L. Peterson, and H. Stierli, eds.

Physical, Chemical and Microbiological Methods of Solid Waste Testing. Report to the U.S. Environmental Protection Agency Office of Research and Monitoring, Cincinnati, Ohio, May, 1973. Cincinnati, Ohio: Office of Research and Monitoring, National Environmental Research Center, 1973. 20 refs.

This publication is a compilation of methods used by the Solid Waste Research Laboratory of the National Environmental Research Center in Cincinnati, Office of Research and Monitoring, U.S. Environmental Protection Agency, to perform various physical, chemical, and microbiological analyses in the field of solid waste management.

Berenblum, I.

Possible Relationships Between Mutagenesis and Carcinogenesis. *ENVIRON. SCI.: AN INTERDISCIPLINARY MONOGRAPH SERIES*, 177-183, 1972. 20 refs.

A discussion of chemical carcinogens in reference to the relationship between mutagens and carcinogens.

Bridges, B. A.

Environmental Genetic Hazards -- The Impossible Problem? *ECOLOGIST*, I: 19-21, 1971.

Environmental pollution and attendant genetic hazards.

Bridges, B. A.

The Mutagenicity of Captan and Related Fungicides. MUTAT. RES., XXXII: 3-34, 1975. 70 refs.

Review of chemical mutagenesis in bacteria, eukaryotic cells, higher organisms, etc., and recommendations.

Bridges, B. A.

A Review of the Committee 17 Report. MUTAT. RES., XXXI: 255-257, 1975.

Environmental mutagenesis -- EMS Committee.

Bridges, B. A.

Screening for Environmental Agents Causing Genetic Damage: Introduction. LAB. PRACT., XXI: 411-412, 1972. 7 refs.

A substantial proportion of disease in man can be attributed to genetic damage to cells, both somatic and germ cells. Heritable mutations can be induced by both radiations and chemicals. It is likely that safety requirements for food additives, pharmaceuticals, pesticides and environmental pollutants will in future include tests for mutagenicity. The following four papers describe simple cellular systems which detect heritable genetic damage.

Bridges, B. A.

The Three-Tier Approach to Mutagenicity Screening and the Concept of Radiation Equivalent Dose. MUTAT. RES., XXVI: 335-340, 1974. 3 refs.

A three-tier approach to mutagenicity screening is proposed, based on 3 general principles. The object would be to carry out experiments designed to give a quantitative indication of the potential risk to man followed by a risk-benefit assessment. It is suggested that one way of comparing the effect of one agent with that of another might be to express it as a radiation-equivalent dose (in RADEQUIV units).

Bridges, B. A., and J. G. Stamper.

Hypothetical Dose-Response Curves for Chronic Exposures to Mutagens or Carcinogens Subject to Simple Enzymatic Detoxification in the Mammalian Body. MUTAT. RES., XXXIII: 87-91, 1975. 6 refs.

Dose-response curves for chemical carcinogenesis and mutagenesis in the whole mammal may be influenced (a) by processes affecting the delivery of the applied dose to the DNA of the target cell or (b) by processes affecting the response of the cell to the initial DNA damage.

Care of the Environment in Scandinavia, Special Issue, SCAND. REV., LXIV: 1976.

Chadwick, K. H., and H. P. Leenhouts.

The Correlation Between Mutation Frequency and Cell Survival Following Different Mutagenic Treatments. THEOR. APPL. GENE., XLVII: 5-8, 1976. 21 refs.

A direct mathematical relationship between mutation frequency per survivor and cell survival is derived from theoretical considerations of the molecular effects of radiation in a cell. The mathematical relationship is independent of the way in which the lesion which leads to mutations and cell death is induced, so the analysis has consequently been applied to other mutagenic treatments such as UV light and chemicals. It is concluded that, although the lesions induced by chemicals may not be the same as those induced by radiation, it is probable that for the chemicals considered common basic damage to the DNA molecule is implicated as the critical lesion.

Clark, A. M.

Naturally Occurring Mutagens. MUTAT. RES., XXXII: 361-374, 1976. 50 refs.

Naturally occurring mutagens have usually been discovered as a result of outbreaks of disease in agriculture livestock, or as a result of epidemiological studies of cancer of the liver in man. Subsequent work has then shown that the toxic agents responsible often have mutagenic properties. Commonly the toxic agent itself does not show high biological activity, but after ingestion it is converted by metabolic processes into the active mutagen or carcinogen.

Clarke, C. H.

Giant Hogweed Sap: Another Environmental Mutagen. MUTAT. RES., XXXI: 63-64, 1975. 10 refs.

The sap of the Giant Hogweed (Heracleum mentagazianum) causes severe blistering of human skin on exposure to sunlight. The active principles are furocoumarins. In view of the fact that 8-methoxypsoralen plus long wavelength ultraviolet light (LUV) has been shown to be mutagenic in bacteria tested in an E. coli, fluorescent light is also used.

Commoner, B.

Cancer as an Environmental Disease. HOSP. PRACT., (February): 82-84, 1975.

Prevention of disease is one of the most powerful motivations for improving the environment; and among the growing roster of environmental diseases, one is beginning to emerge as predominant: cancer.

Commoner, B.

Carcinogens in the Environment. CHEM. TECHNOL., (February): 76-82, 1977. 9 refs.

It would appear that the opportunity now exists to develop a new strategy for controlling the growing problem of environmental cancer. It would begin with detecting presumptive carcinogens in environmental samples, identifying them and tracing their movements in the environment by means of screening based on bacterial mutagenesis. Then by determining the mutagenicity of human urine samples it may be possible to determine which of these presumptive carcinogens represent carcinogenic risks to people. With such information in hand, it would be possible to reduce this risk by tracing environmental carcinogens back to their origins, and then taking the final, and most difficult step -- regulating environmental emissions-that will, at last, prevent the disease.

Commoner, B.

Comments on Measures of Mutagenic Activity. Unpublished, St. Louis, Missouri: Washington University, 1976.

There is at present a good deal of confusion regarding the terms in which the mutagenic activity of a substance should be measured in the Ames test. By using the same data, Sivak seemingly demonstrates the reverse. The question arises, then, as to whether the latter measure is, in fact, a valid index of the comparative mutagenic activity of different compounds in the Salmonella system.

Drake, J. W.

The Molecular Basis of Mutations. San Francisco: Holden-Day, 1970.

This book presents a broad outline of what is understood about mutational mechanisms and also to emphasize many of the doubtful areas.

Drake, J. W., and R. H. Baltz.

The Biochemistry of Mutagenesis. ANN. REV. BIOCHEM., XLV: 11-37, 1976. 228 refs.

A review of mutagenesis.

Drake, J. W., and W. G. Flamm.

The Molecular Basis of Mutation. ENVIRON. SCI.: AN INTER-DISCIPLINARY MONOGRAPH SERIES, 15-26, 1972.

Introduction toward the understanding of the mutation process.

Elias, P. S.

The Medical Significance of Marine Pollution by Organic Chemicals. PROC. R. SOC. LOND, B., CLXXXIX: 443-458, 1975. 13 refs.
A discussion of mutagenicity and carcinogenicity relative to chemical pollutants.

Epstein, S. S.

Environmental Determinants of Human Cancer. CANC. RES., XXXIV: 2425-2435, 1974. 85 refs.
A general discussion of chemical carcinogens.

Epstein, S. S., and M. S. Legator.

The Mutagenicity of Pesticides. Cambridge, Mass.: MIT Press, 1971.
This monograph is based on the Report of the Advisory Panel on Mutagenicity of Pesticides to the Secretary's Commission on Pesticides and Their Relationship to Environmental Health, HEW (GPO, December 1969).

Farber, E.

Chemical Carcinogenesis. CURR. RES. ONCOLOGY, 95-123, 1972. 30 refs.
A discussion of chemical carcinogenesis.

Fishbein, L.

Atmospheric Mutagens. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT. IV: 219-319, 1976. 606 refs.
Comparative data (where available) has been presented on the relative amounts, residues, and transport in the atmosphere of a spectrum of mutagenic and potential mutagenic agents from diverse categories, including anthropogenic sources of air pollution, pesticidal and industrial use categories and their degradation products, as well as a number of naturally occurring pollutant and aerosol contributors.

Fishbein, L.

Atmospheric Mutagens. I. Sulfur Oxides and Nitrogen Oxides. MUTAT. RES., XXXII: 309-330, 1976. 144 refs.
A discussion of atmospheric chemical contaminants.

Fishbein, L.

Industrial Mutagens and Potential Mutagens. I. Halogenated Aliphatic Derivatives. MUTAT. RES., XXXII: 267-308, 1976. 242 refs.

A discussion of potential industrial mutagens from the standpoint of environmental toxicology.

Flamm, W. G.

A Tier System Approach to Mutagen Testing. MUTAT. RES., XXVI: 329-333, 1974. 20 refs.

This approach to testing involves the employment of a hierarchical system of tests that is referred to as a tier system. The first tier is a prescreen, utilizing microbial organisms coupled to mammalian metabolic activation systems. Substances found to be mutagenic are presumed mutagens and subjected to further testing. Substances positive in both tier one and two are assumed to be mutagens in the qualitative sense.

Fraser, F. C.

Non-Scientific Influences on Decisions Concerning Human Chemical Exposure - a personal commentary. MUTAT. RES., XXXIII: 93, 1975. It would be nice if interests based on economic, political or emotional involvement had no opportunity to influence the judgement of those who formulate policy decisions relating to environmental hazards.

Gelboin, H. V.

Carcinogens, Enzyme Induction and Gene Action. ADV. CANCER RES., X: 1-81, 1967. 203 refs.

A large segment of this review concerns the effect of polycyclic hydrocarbons and drugs on the level of certain enzyme activities.

Gletten, F., U. Weekes and D. Brusick.

In Vitro Metabolic Activation of Chemical Mutagens. 1. Development of an In Vitro Mutagenicity Assay Using Liver Microsomal Enzymes for the Activation of Dimethylnitrosamine to a Mutagen. MUTAT. RES., XXVIII: 113-122, 1975. 22 refs.

Qualitative and quantitative assays were developed to study the in vitro enzymatic activation of dimethylnitrosamine (DMNA) to its mutagenic form. A comparison between two inbred mouse strains using the in vitro activation assay demonstrated that this technique might be a useful tool in quantitatively measuring differences in genetically influenced levels of DMNA metabolism in individual animals and their tissues.

Harnden, D. G.

Chromosome Abnormalities and Predisposition Towards Cancer. PROC. ROY. SOC. MED., LXIX: 41-43, 1976. 22 refs.

A short essay on chromosome damage.

It seems reasonable to suggest that a chromosome damaging agency whether chemical, physical or biological should be regarded as a potential carcinogen, but the induction of chromosome damage does not necessarily mean that malignancy will ensue.

Heddle, J. A.

The Regulation of Human Exposure to Mutagens Amidst Scientific Controversy. MUTAT. RES., XXXIII: 103-105, 1975.

Three topics central to the problem of regulating human exposure are (1) the impact of an increased mutation rate upon the human population, (2) the shape of the dose response curve, and (3) the adequacy of procedures used to identify compounds that are mutagenic in man.

Hirschhorn, K.

Discussion paper: The Role of Cytogenetics in Mutagenesis Testing. ANN. N. Y. ACAD. SCI., CCLXIX: 12-15, 1975. 9 refs.

A discussion pertaining to cytogenic testing of mutagens.

Hollaender, A., ed.

Chem. Mutagens: Prin. Methods Their Detect., Vol. I. New York: Plenum Press, 1971.

Molecular mechanisms of mutations

Correlation between teratogenic and mutagenic effects of chemicals in mammals

The mutagenicity of chemical carcinogens: Correlations, problems and interpretations

Effects on DNA: Chemical methods

Physical-chemical methods for the detection of the effect of mutagens on DNA

Effects on DNA: Transforming principle

Mutagen screening with virulent bacteriophages

Prophage induction in lysogenic bacteria as a method of detecting potential mutagenic, carcinogenic, carcinostatic and teratogenic agents

The detection of chemical mutagens with enteric bacteria

Mutagenesis studies with E. coli mutants with known amino acid (and base-pair) changes

Mutation induction in yeast

Hollaender, A., ed.

Conclusion. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., II: 607-610, 1971.

Summary and conclusions on the work presented in this volume.

Measurement of recessive lethal damage over the entire genome and at two specific loci in the ad-3 region of a two-component heterokaryon of Neurospora crassa

Aspergillus
 Higher plants
 Procedures for culturing diploid cells and preparation of meiotic chromosomes from dwarf species of hamsters
 Induction and analysis of gene mutations in mammalian cells in culture
 Inducing mutations with chemicals in *Habrobracon*
 The detection of mutations in *Drosophila melanogaster*.
 Root tips for studying the effects of chemicals on chromosomes
 Cytogenetic studies in animals
 Specific locus mutation in mice
 Dominant lethal mutations in mammals
 The host-mediated assay, a practical procedure for evaluating potential mutagenic agents in mammals.
 Human population monitoring

Hollaender, A., ed.

Chem. Mutagens: Prin. Methods Their Detect.; Vol. III. New York: Plenum Press, 1973.
 History of research on chemical mutagenesis
 Observations on meiotic chromosomes of the male mouse as a test of the potential mutagenicity of chemicals in mammals.
 Techniques for monitoring and assessing the significance of mutagenesis in human populations
 Specific-locus mutational assay systems for mouse lymphoma cells
 Approaches to monitoring human populations for mutation rates and mutation rates and genetic disease
 Repair of chemical damage to human DNA
Tradescantia stamen hairs: A radiobiological test system applicable to chemical mutagenesis
 Detection of genetically active chemicals using various yeast systems
 Total reproductive capacity in female mice: Chemical effects and their analysis
 Insect chemosterilants as mutagens
 The literature of chemical mutagenesis

Hollaender, A., ed.

Chem. Mutagens: Prin. Methods Their Detect., Vol. IV. New York: Plenum Press, 1976.
 Cytological methods for detecting chemical mutagens
 The micronucleus test for cytogenetic analysis
 Numerical sex-chromosome anomalies in mammals: Their spontaneous occurrence and use in mutagenesis studies
 The function of *Drosophila* in genetic toxicology testing
 Plant test systems for detection of chemical mutagens
 The use of indirect indicator systems to detect mutagenic activity in human subjects and experimental animals
 Carcinogenic and mutagenic N-nitroso compounds
 Atmospheric mutagens
 Cytogenetic surveillance of industrial populations

Hong, S.-J., and L. H. Piette.

Electron Spin Resonance Spin-Label Studies of Intercalation of Ethidium Bromide and Aromatic Amine Carcinogens in DNA. *CANCER RES.*, XXXVI: 1159-1171, 1976. 48 refs.

These studies have demonstrated the feasibility of the spin-label technique as a powerful tool for providing not only clear-cut evidence of physical binding but also information such as base-preferential binding and the postbinding structural changes of the host DNA molecule. Moreover, carcinogenic and mutagenic activity of most of the carcinogens used were found to persist even after attachment of the nitroxide reporter on the respective ligand molecule.

We believe that the technique is a highly promising tool in studying these very important aspects.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 1. Lyon, France: IARC, 1972.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 2: Some Inorganic and Organometallic Compounds. Lyon, France: IARC, 1973.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 3: Certain Polycyclic Aromatic Hydrocarbons and Heterocyclic Compounds. Lyon, France: IARC, 1973.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 4: Some Aromatic Amines, Hydrazine and Related Substances, N-nitroso Compounds and Miscellaneous Alkylating Agents. Lyon, France: IARC, 1974.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 5: Some Organochlorine Pesticides. Lyon, France: IARC, 1974.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 6: Sex Hormones. Lyon, France: IARC, 1974.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 7: Some Antithyroid and Related Substances, Nitrofurans and Industrial Chemicals. Lyon, France: IARC, 1974.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 8: Some Aromatic Azo Compounds. Lyon, France: IARC, 1975.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 9: Some Aziridines, N-, S- and O- Mustards and Selenium. Lyon, France: IARC, 1975.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 10: Some Naturally Occurring Substances. Lyon, France: IARC, 1976.

IARC Monographs.

Evaluation of Carcinogenic Risk of Chemicals to Man. Vol. 11: Cadmium, Nickel, Some Expoxides, Miscellaneous Industrial Chemicals and General Considerations on Volatile Anaesthetics. Lyon, France: IARC, 1976.

Janerich, D. T., and C. E. Lawrence.

Epidemiological Strategies for Identifying Carcinogens. MUTAT. RES., XXXIII: 55-63, 1975. 20 refs.

Neither epidemiological techniques, nor laboratory techniques, seem to be providing specific new developments which could lead to a so-called "break-through." It has been said that, as much as 85% of human cancer is due to environmental factors. This statement is based on indirect evidence or deductive reasoning processes which intuitively balance evidence for the operation of genetic factors against evidence for the operation of environmental factors.

Kilbey, B. J.

The British Experience in Environmental Mutagenesis: An Exercise in Collaboration. MUTAT. RES., XXXIII: 73-77, 1975.

At the outset of the present expansion of interest in the study of environmental mutagenesis, suggestions were made which led to the establishment

of three mutation test methods as the normal means for screening new chemicals for their mutagenicity.

There are various reasons for this change but the most important of them are, first, that the original three test systems have on occasions proved to be surprisingly insensitive and second, it is now clear that to pass every compound through this screen of three tests would be prohibitively expensive as well as extremely time-consuming.

The next and very important stage in the collaboration between those concerned with governmental control and those concerned with testing will come when the draft guidelines are released for discussion and comment to industry.

Kubinski, H., N. R. Morin and P. E. Zeldin.

Increased Attachment of Nucleic Acids to Eukaryotic and Prokaryotic Cells Induced by Chemical and Physical Carcinogens and Mutagens. CANCER RES., XXXVI: 3025-3033, 1976. 49 refs.

Significantly enhanced attachment to Ehrlich ascites and *E. coli* cells was observed for radioactive DNA and RNA in the presence of chemical mutagens and ultimate carcinogens. In some instances, formation of nucleic acid-protein adducts by these compounds further (or similarly) enhanced the binding. DNA irradiated with ultraviolet light in the presence of a protein bound more efficiently than either an unirradiated mixture of these two macromolecules or DNA irradiated alone. The spectrum of compounds tested and found active in this system includes alkylating agents, aromatic amines, and carcinogenic metals. Precarcinogens and nonultimate carcinogenic chemicals, as well as tumor-promoting agents, did not increase the binding. However, addition of extracts from mouse or rat livers activated precarcinogenic and proximate carcinogenic chemicals and resulted in enhanced cellular attachment of indicator nucleic acids in their presence. Possible usefulness of this test system for fast and efficient screening for environmental carcinogens and mutagens, as well as possible relevance of the observed phenomena to in vivo effects of chemical and physical carcinogens, is considered.

Legator, M. S.

Chemical Mutagens. ANN. REV. MED., XXIII: 413-428, 1972. 32 refs.
A review on chemical mutagens discussing:

What is a mutation?

Molecular basis for mutation

Repair and mutation process

The role of nonmammalian systems in assessing potential mutagenic hazards to man.

Procedures recommended for evaluation of mutagenic agents

Interpretation of results

Significance of an increase in mutation rate-medical implications

Population monitoring

Correlation between carcinogenicity and mutagenicity

Legator, M. S., and W. G. Flamm.

Environmental Mutagenesis and Repair. ANN. REV. BIOCHEM., XLII: 683-708, 1973. 84 refs.

A review of chemical mutagens, mutations, genetic damage and repair, listing procedure.

Legator, M. S., and S. J. Rinkus.

The Chemical Environment and Mutagenesis, a Preprint. Division of Environmental Toxicology and Epidemiology, University of Texas Medical Branch, Galveston, Texas. 53 refs.

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Summary

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Chemical mutagenesis testing

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Lieberman, M. W.

Discussion paper: Quantitative Aspects of Using DNA Repair to Detect Mutagens and Carcinogens. ANN. N. Y. ACAD. SCI., CCLXIX: 37-42, 1975. 19 refs.

The observation that mammalian cells can repair damage to their DNA by chemical carcinogens and mutagens has prompted much research on the role of DNA repair mechanisms in mutagenesis and carcinogenesis. This communication stresses three aspects of the quantitative aspects of detection.

Mutagenicity testing using DNA repair - mammalian cells.

Malling, H. V.

Monitoring of Chemical Mutagens in Our Environment. ENVIRON. SCI.: AN INTERDISCIPLINARY MONOGRAPH SERIES, 27-39. 1972. 39 refs.

A discussion of monitoring of chemical mutagens in man's environment.

Matter, B. E.

Problems of Testing Drugs for Potential Mutagenicity. MUTAT. RES., XXXVIII: 243-258, 1976. 71 refs.

The problem of chemically induced genetic damage has begun to alarm both the scientific community and the general public. Mutagenicity testing, to

a certain degree, is necessary for chemicals entering the environment. As to feasibility, although a great number of relatively simple and practical methods are available, the evaluation of mutagenic effects at present is an extremely complex and difficult task.

Miller, J. A.

Carcinogenesis by Chemicals: An Overview - G. H. A. Clowes Memorial Lecture. CANCER RES., XXX: 559-576, 1970. 175 refs.
An overview of chemical carcinogenesis.

Miller, J. A., and E. C. Miller.

Chemical Carcinogenesis: Mechanisms and Approaches to Its Control. J. NAT'L CANCER INST., XLVII: 5-14, 1971. 36 refs.
A discussion of the history, mechanisms and possible controls of chemical carcinogenesis in man.

Mohn, G. R., and J. Ellenberger.

Genetic Effects of Cyclophosphamide, Ifosfamide and Trofosfamide. MUTAT. RES., XXXII: 331-360, 1976.
A discussion of mutagenicity systems in reference to specific chemicals.

Montesano, R., and H. Bartsch.

Mutagenic and Carcinogenic N-nitroso Compounds: Possible Environmental Hazards. MUTAT. RES., XXXII: 179-228, 1976. 5 refs.
A thorough discussion on mutagenicity and carcinogenicity.

Morgan, K., P. J. Hastings and R. C. von Borstel.

A Potential Hazard: Explosive Production of Mutations by Induction of Mutators. ENVIRON. HEALTH PERSPECT., (December): 207-210, 1973.

Potentially the genetically most hazardous events that could result from exposure to environmental mutagens are the induction of mutators. An overall enhancement of spontaneous mutation rates would lead to the creation of deleterious mutations which could persist almost indefinitely in the expanding human species. The relative frequencies of induction of antimutators and mutators are not known. Nor do we as yet fully understand the mechanism(s) by which mutators enhance the induction of mutations. Furthermore, the spectra of activities of spontaneous and induced mutators need to be characterized in order to anticipate more adequately the societal burdens which would be caused by the resulting "explosions" of genetic damage.

Narahashi, T.

In-Vitro Screening Methods Evaluating the Neurotoxic Potential of Pesticides. Report to the U.S. Environmental Protection Agency, Office of Research and Developmental Health Effects Research Laboratory, Research Triangle Park, N. C., January, 1976. Research Triangle Park, N.C.; Environmental Protection Agency, 1976. 6 refs.

Neurotoxicity is manifested as stimulation and/or paralysis of spontaneous discharges of the nerve cords. The techniques involved in this experiment are rather simple, and require only reasonable amounts of conventional electrophysiological equipment.

The order of potency of various insecticides in stimulating the crayfish abdominal nerve cord is given.

Neel, J. V.

Evaluation of the Effects of Chemical Mutagens on Man: The Long Road Ahead. PROC. NAT. ACAD. SCI., LXVII: 908-915, 1970. 49 refs.

By analogy with the problem of evaluating the genetic risks of radiation, it appears that it will be difficult to assess the mutagenicity for man of the wide range of chemicals to which populations are exposed.

Nichols, W. W.

Somatic Mutation in Biologic Research. HEREDITAS, LXXXI: 225-236, 1975. 71 refs.

In the last few years rapid progress has been made in several labs in the area of a possible etiologic role of somatic mutation in carcinogenesis and aging. Studies such as metabolic activation of an initial carcinogen to its active form, the genetic effects of tumor viruses, studies of DNA repair mechanisms, specific chromosomal patterns observed with banding techniques, and epidemiologic studies produce a strong probability of the involvement of mutational events in the initiation of malignancy.

Similarly in aging, the observations that human fibroblast-like cells exhibited a finite lifespan in culture made it apparent that this could serve as one model to study cellular and molecular mechanisms of senescence in the absence of many of the complexities and variables found in the intact organism. Chromosomal mutations can be examined throughout the lifespan of these cells. In addition, specific locus mutations can be examined by somatic cell genetic techniques and various types of DNA repair can be studied. In this way a profile of genetic damage can be obtained sequentially with increasing chronologic age of these cells in an effort to estimate the role of somatic mutation as an etiological or modifying event of senescence in vitro.

Occupational Safety and Health Administration. Final Rules Set for Exposure to Carcinogens. CHEM. ENGN. NEWS, (Feb. 11): 12-13, 1974.

A description of the rules and regulations set up by the Occupational Safety and Health Administration concerning 14 chemical carcinogens.

Ong, T.-M.

Aflatoxin Mutagenesis. *MUTAT. RES.*, XXXII: 35-53, 1975. 108 refs.
A review of mutagenesis, carcinogenesis and teratogenesis of aflatoxin.

Pellizzari, E. D.

Development of Analytical Techniques for Measuring Ambient Atmospheric Carcinogenic Vapors. Report to the Environmental Sciences Research Laboratory, Office of Research and Development, U. S. Environmental Protection Agency, Research Triangle Park, N. C., November 1975. Research Triangle Park, N. C.: Environmental Protection Agency, 1975. 51 refs.

Analytical techniques and instrumentation, developed during the previous contract year, were perfected and evaluated for the collection and analysis of carcinogenic and mutagenic vapors occurring in ambient air. The areas of investigation included (a) the performance of a sorbent cartridge sampler for hazardous vapors occurring at concentrations of ng/m; (b) the design, fabrication, and performance of a portable field samples; and (c) the identification of hazardous and background pollutants from several geographical areas in the Continental U.S.

Rall, D. P.

Difficulties in Extrapolating the Results of Toxicity Studies in Laboratory Animals to Man. *ENVIRON. RES.*, II: 360-367, 1969. 13 refs.

Careful studies with laboratory animals usually will predict the possibility of irreversible toxicity. There are hazards in irreversible toxicity. Laboratory animals are unlikely to aid in a clinically useful way in the prediction of low-incidence toxicities. There is an urgent need for implementation of a well-devised scheme for monitoring clinical drug use in the general population. No biological process is perfect, therefore there must be an effective monitoring system for chemical or drug toxicity at the clinical level.

Schöneich, J.

Safety Evaluation Based on Microbial Assay Procedures. *MUTAT. RES.*, II: 360-367, 1969. 13 refs.

Careful studies with laboratory animals usually will predict the possibility of irreversible toxicity. There are hazards in irreversible toxicity. Laboratory animals are unlikely to aid in a clinically useful way in the prediction of low-incidence toxicities. There is an urgent need for implementation of a well-devised scheme for monitoring clinical drug use in the general population. No biological process is perfect, therefore there must be an effective monitoring system for chemical or drug toxicity at the clinical level.

Schöneich, J.

Safety Evaluation Based on Microbial Assay Procedures. MUTAT. RES., XLI: 89-94, 1976. 13 refs.

Microorganisms play a major role in mutation research and mutagenicity screening for environmental chemicals. However, it should not be forgotten that the main aim of testing is to prevent the induction of mutations in man. It is uncommon for results obtained with bacteria to be extrapolated to man. However, in mutagenicity testing the situation is different. The ultimate target of chemical mutagens is DNA, which has the same four bases and the same structure in all living systems. There is evidence that the principal steps in the repair systems of DNA lesions in man are likely to be the same as in bacteria.

Shafer, N., and R. W. Shafer.

Potential of Carcinogenic Effects of Hair Dyes. N. Y. ST. J. MED., LXXVI: 394-396, 1976. 26 refs.

Hair dyes contain many of the same compounds that are known to cause cancer. Many chemicals can be absorbed into the body through the skin. Experiments were conducted on laboratory animals to ascertain if application of common commercial hair dyes can produce mammary cancer. These tests are in progress.

Sirover, M. A., and L. A. Loeb.

Infidelity of DNA Synthesis In Vitro: Screening for Potential Metal Mutagens or Carcinogens. SCIENCE, CXCIV: 1434-1436, 1976. 19 refs.

Thirty-one metal salts have been studied for their ability to affect the accuracy of DNA synthesis in vitro. All ten salts of metal carcinogens decreased the fidelity of DNA synthesis. Of the three metals which beforehand were considered to be possible mutagens or carcinogens, only one decreased fidelity. In contrast, 17 noncarcinogenic metal salts did not affect fidelity even when present at concentrations that were clearly inhibitory.

Snape, F.

Automating Pollution Measurements. AM. LAB., VIII: 51-58, 1976. 12 refs.

The importance and purpose of measuring pollution.

Sobels, F. H.

Charlotte Auerbach and Chemical Mutagenesis. MUTAT. RES., XXIX: 171-180, 1975. 63 refs.

A review of the conceptual contributions of Charlotte Auerbach to the field of chemical mutagenesis.

Stanford Research Institute.

Examples of Mutagenesis Procedures in Use at Stanford Research Institute.

Menlo Park, California: Stanford Research Institute.

Manual includes information on procedures being employed by SRI:

Microbial mutagenesis

Mammalian tissue culture and cytogenetic assays for mutagenesis

Mammalian mutagenesis (dominant lethal, translocation test)

Statistical procedure for evaluation of dominant lethal data

Sutton, H. E., and M. I. Harris

Mutagenic Effects of environmental Contaminants. ENVIRON. SCIENCES:
AN INTERDISCIPLINARY MONOGRAPH SERIES. New York: Academic
Press, 1972.

Introduction: Genetic toxicology

Gene mutation as a cause of human disease

The Molecular basis of mutation

Monitoring of chemical mutagens in our environment

The Detection of mutations with non-mammalian systems

A Bacterial system for detecting mutagens and carcinogens

The Need to detect chemically induced mutations in experimental animals

Chromosome mutations in man

The Detection of increased mutation rates in human populations

Monitoring somatic mutations in human populations

Pesticidal, industrial, food additive and drug mutagens

Mutagenicity of biologicals

Possible relationships between mutagenesis and carcinogenesis

Interrelations between carcinogenicity, mutagenicity and teratogenicity

Train, R. E.

Environmental Cancer. SCIENCE, CXCV: 443, 1977.

An editorial on environmental cancer.

Ulmer, N. S.

Physical, Chemical, and Microbiological Methods of Solid Waste Testing; Four
Additional Procedures. Report to the National Environmental Research
Center, Office of Research and Development, U. S. Environmental
Protection Agency, Cincinnati, Ohio, March, 1974. Cincinnati, Ohio:
Environmental Protection Agency, 1974. 12 refs.

A description of four additional chemical methods used by the Solid and
Hazardous Waste Research Laboratory to analyze solid wastes and solid
waste related materials.

Wagoner, J. K.

Occupational Carcinogenesis: The Two Hundred Years Since Percivall Pott.

ANN. N. Y. ACAD. SCI., CCLXXI: 1-4, 1976. 30 refs.

A summary history of occupational carcinogenesis.

Wassom, J. S.

The Literature of Chemical Mutagenesis. CHEM. MUTAGENS: PRIN. METHODS THEIR DETECT., III: 271-287, 1973. A discussion of the presentation, accumulation and sources of the literature of chemical mutagenesis.

Wilson, J. G.

Interrelations Between Carcinogenicity, Mutagenicity, and Teratogenicity. ENVIRON. SCI.: AN INTERDISCIPLINARY MONOGRAPH SERIES, 185-195, 1972. 20 refs.

A discussion of the three processes.

Wilson, K. W.

The Laboratory Estimation of the Biological Effects of Organic Pollutants. PROC. R. SOC. LONDON SER. B, CLXXXIX: 459-477, 1975.

The laboratory estimation of the toxic effects of organic pollutants relies on successive investigations of increasing sensitivity. Acute toxicity tests are useful in providing an index of relative toxicity between compounds but are of limited value for making ecological predictions. Many factors can influence the assessment of acute toxicity, with chemical stability of the test solutions and the species of test organisms employed being perhaps the most important of these. Many sub-lethal tests are also of limited value because the importance of the measured response for the well-being of the animal community as a whole is not established. The basic requirements of sub-lethal techniques are discussed, especially in relation to compounds which may exert their toxic action through accumulation in the tissues in the long term. The possibility of relating the toxicity of a compound to its chemical structure is considered.

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16. ABSTRACT A rapidly growing store of data is available relative to the potential mutagenicity and carcinogenicity of new products of chemical substances manufactured for commerce in recent years. Literature regarding mixtures, such as chemical wastes, however, is scarce and hard to find. A literature review was undertaken to assess feasibility of using bacteria as screening agents to detect environmental carcinogens. Mutagenicity data were included in the study because growing experimental evidence indicates that most chemical carcinogens are mutagens, and many mutagens may be carcinogens. This investigation found that bacterial mutagenesis can be used to initiate a series of studies designed to screen for potential mutagens and carcinogens in mixed chemical wastes. This report was submitted in fulfillment of Grant No. R-804586 by the University of Houston under partial sponsorship of the U.S. Environmental Protection Agency. This report covers the period 15 June 1976 to 14 April 1977. Work was completed as of 1 May 1977.		
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