6. Gili, J. M., and Ros, J., "Study and Cartography of the Benthic Communities of Medes Islands (NE Spain)." *Mar. Ecol.*, **6**, 219 (1985).
7. Shevtsova, L. V., and Ponurko, Ya. V., "Zoobenthos and Zooperiphyton in the Irtysh-Karaganda Canal." *Hydrobiological J.* (USSR), **21**, 18 (1985).
8. Veylande, G. Kh., and Liyepa, R. A., "Bacterial and Protozoan Benthos of Small Rivers of Lativia." *Hydrobiological J.* (USSR), **21**, 79 (1985).
9. Coomans, A., *et al.*, "Nematodes from a Freshwater Pool on a Coral Island in the Solomon Islands." *Hydrobiologia* (Den.)., **123**, 265 (1985).
10. Kownacki, A., "Stream Ecosystems in Mountain Grassland (West Carpathians)." *Acta Hydrobiol.* (Poland), **24**, 375 (1982).
11. Gray, J. S., "Nitrogenous Excretion by Meiofauna from Coral Reef Sediments: Mecor 5." *Mar. Biol.* (G. B.), **89**, 31 (1985).
12. Herman, P. M. J., and Heip, C., "Secondary Production of the Harpacticoid Copepod *Paronychocamptus nanus* in a Brackish-water Habitat." *Limnol. Oceanogr.*, **30**, 1060 (1985).
13. Yingst, J. Y., and Rhoads, D. C., "The Structure of Soft-Bottom Benthic Communities in the Vicinity of the Texas Flower Garden Banks, Gulf of Mexico." *Estuarine Coastal and Self Science*, **20**, 569 (1985).
14. Probert, P. K., "Disturbance, Sediment Stability, and Trophic Structure of Soft-bottom Communities." *J. Mar. Res.*, **42**, 893 (1984).
15. Decho, A. W., *et al.*, "Meiofauna-sediment Interactions Around Subtropical Seagrass Sediments Using Factor Analysis." *J. Mar. Res.*, **43**, 237 (1985).
16. Watzin, M. C., "Interactions Among Temporary and Permanent Meiofauna: Observations on the Feeding and Behavior of Selected Taxa." *Biol. Bull.*, **169**, 397 (1985).
17. Bell, S. S., and Woodin, S. A., "Community Unity: Experimental Evidence for Meiofauna and Macrofauna." *J. Mar. Res.*, **42**, 605 (1984).
18. Phillips, F. E., and Fleeger, J. W., "Meiofauna Meso-scale Variability in Two Estuarine Habitats." *Estuarine, Coastal and Shelf Science*, **21**, 745 (1985).
19. Woodhead, P. M. J., and Jacobson, M. E., "Epifaunal Settlement, The Processes of Community Development and Succession Over Two Years on an Artificial Reef in the New York Bight." *Bull. Mar. Sci.*, **37**, 364 (1985).
20. McLachlan, A., "The Biomass of Macro- and Interstitial Fauna on Clean and Wrack-covered Beaches in Western Australia." *Estuarine, Coastal and Shelf Science*, **21**, 587 (1985).
21. Carman, K. R., and Thistle, D., "Microbial Food Partitioning by Three Species of Benthic Copepods." *Mar. Biol.* (W. Ger.), **88**, 143 (1985).
22. Alongi, D. M., and Tenore, K. R., "Effect of Detritus Supply on Trophic Relationships Within Experimental Benthic Food Webs. I. Meiofauna-Polychaete (*Capitella capitata* (Type I) Fabricius) Interactions." *J. Exp. Mar. Biol. Ecol.* (Neth.), **88**, 153 (1985).
23. Gee, J. M., *et al.*, "Effects of Organic Enrichment on Meiofaunal Abundance and Community Structures in Sublittoral Soft Sediments." *J. Exp. Mar. Biol. Ecol.* (Neth.), **91**, 247 (1985).
24. Shiells, G. M., and Anderson, K. J., "Pollution Monitoring Using the Nematode/Copepod Ratio a Practical Application." *Mar. Pollut. Bull.* (G. B.), **16**, 62 (1985).
25. Gee, J. M., *et al.*, "Field Experiments on the Role of Epibenthic Predators in Determining Prey Densities in an Estuarine Mudflat." *Estuarine, Coastal and Shelf Science*, **21**, 429 (1985).
26. Fitzhugh, G. R., and Fleeger, J. W., "Goby (Pisces: Gobiidae) Interactions with Meiofauna and Small Macrofauna." *Bull. Mar. Sci.*, **36**, 436 (1985).
27. Bell, G., and Wolfe, L. M., "Sexual and Asexual Reproduction in a Natural Population of *Hydra pseudoligactis*." *Can. J. Zool.*, **63**, 851 (1985).
28. Lonsdale, D. J., and Levinton, J. S., "Latitudinal Differentiation in Embryonic Duration, Egg Size, and Newborn Survival in a Harpacticoid Copepod." *Biol. Bull.*, **168**, 419 (1985).
29. Ebsary, B. A., "Two New Aquatic Species of *Ironus* Bastian, 1865 (Nematoda: Ironidae) from Canada." *Can. J. Zool.*, **63**, 1368 (1985).
30. Chengalath, R., "The Rotifera of the Canadian Artic Sea Ice, with Description of a New Species." *Can. J. Zool.*, **63**, 2212 (1985).
31. Smith, M. E., "Naididae (Oligochaeta) as Hosts for Mermithid Nematodes (Enoplida: Mermithidae)." *Can. J. Zool.*, **63**, 1459 (1985).
32. Brattey, J., *et al.*, "Metazoan Parasites and Commensals of Five Crab (Brachyura) Species from Eastern Canada." *Can. J. Zool.*, **63**, 2224 (1985).
33. Turner, H. M., "Parasites of Eastern Oysters from Subtidal Reefs in a Louisiana Estuary with a note on their Use as Indicators of Water Quality." *Estuaries*, **8**, 323 (1985).
34. Li, L., and Desser, S. S., "Three New Species of *Octosporella* (Protozoa: Coccidia) from Cyprinid Fish in Algonquin Park, Ontario." *Can. J. Zool.*, **63**, 1859 (1985).
35. Li, L., and Desser, S. S., "The Protozoan Parasites of Fish from two Lakes in Algonquin Park, Ontario." *Can. J. Zool.*, **63**, 1846 (1985).
36. Khan, R. A., "Pathogenesis of *Trypanosoma murmanensis* in Marine Fish of the Northwestern Atlantic Following Experimental Transmission." *Can. J. Zool.*, **63**, 2141 (1985).

Human health effects assays

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CURRENT APPROACH

Discussion of the exponential increase in environmental toxicological information and an approach for organizing and using the information was presented by Lu and Wassom.[1] A user's guide to the Registry of Toxic Effects of Chemical Substances (RTECS) was published by NIOSH[2] that defines the record layouts and describes the types of data contained in the computer tape version of the 1984 Edition of the RTECS.[3] A text summarizing information on approximately 800 toxic chemicals was edited by Sittig.[4] Milestone publications concerning fundamentals of toxicology with environmental applications included the works of Gentile,[5] Ashby,[6] Mortelmans,[7] Thacker,[8] and Ruppert.[9] Brusick and Auletta[10] discussed the developmental status of bioassays in genetic toxicology reviewed by the U. S. Environmental Protection Agency (EPA) Gene-Tox Work Groups.

A risk assessment and risk management approach was suggested as the proper framework for decision making concerning hazardous substances in the multimedia environment.[11] Monitoring human populations for genetic damage was suggested to prevent or reduce the risk of exposure.[12] Guiney[13] presented an overview of methodologies and procedures useful to relative health risk evaluation for hazardous waste mixtures

and emphasized that more understanding of structure-activity relationships, pharmacokinetic factors, and mechanisms of toxicity were required to adequately address health risk assessment. Sobels[14] evaluated proposed EPA guidelines for mutagenicity risk assessment.

A methodology was developed for assessment of carcinogen risk to the U. S. population because of drinking water containing trace levels of volatile organic compounds (VOCs).[15] Methodologies for determining potential health effects of complex hazardous wastes using *in vivo* and *in vitro* techniques,[16] and of drinking water supplies were developed.[17] The necessity of linking *in vivo* and *in vitro* genotoxicity results with epidemiological data on cancer incidence was discussed in detail by Stich and Rosin.[18] Two hundred carcinogens were assigned hazard rankings based on epidemiological, experimental, and supportive evidence from short-term tests, metabolism and pharmacokinetics, and structure-activity correlations.[19] Human risk analysis for 2,4,6-trichlorophenol in water was discussed by Gowda *et al.*,[20] and for TCDD-contaminated soil by Schaum.[21] For each of the five exposure pathways for TCDD, factors describing contact rate, absorption fraction, and exposure duration were presented along with equations for calculating cancer risk.

Calculation of cancer risk in animals was found to depend on experimental design, dosing regime, length of study time, and age of animals at time of dosing.[22] Littlefield *et al.*[23] found differences in tumor responses of genetically-homogeneous versus genetically-heterogeneous mice and emphasized the importance of gene distribution in risk estimation studies.

Risk assessment is one task for carcinogenicity prediction and battery selection (CPBS) method for using results of short-term tests to screen for chemicals most likely to cause cancer.[24] The CPBS method was applied to data compiled under the Gene-Tox Program of the U. S. EPA as a demonstration of the method on a typical data base.[25] Assembly and analysis of a genotoxicity data base for predicting carcinogens was discussed by Palajde and Rosenkran.[26] The application of cluster analysis for results of short-term tests as a methodology for carcinogen discrimination was investigated by Benigni and Giuliani[27] and Pet-Edwards *et al.*[28]

Methods and approaches for determining exposure and response to carcinogens for risk assessment were addressed by Ricci and Molton.[29] Specific methods for estimating exposure to chemical substances in the ambient environment were presented by Freed *et al.*[30] The sizes of populations potentially exposed to chemicals were discussed by Dixon *et al.*[31] Berenbaum[32] demonstrated that, as a result of synergistic interactions between carcinogens, the dose-response curve for added risk caused by any individual carcinogen will generally be steeper at lower doses than at higher doses, and consequently the risk at low environmental levels will be higher than would be expected from a linear response.

Irr *et al.*[33] reported on a workshop of the Genetic Toxicology Association on statistical analysis of cytogenetics test systems. Critical sample size for determining statistical significance was discussed by Sylwester and Albertini,[34] Mann *et al.*,[35] and Whorton.[36] Algorithms for tests of homogeneity and trend with medians were presented by Thakur.[37] Stiratelli[38] discussed parametric approaches to analysis of results of *in vivo* cytogenetic studies, while Wahrendorf *et al.*[39] presented a nonparametric approach to the statistical analysis of mutagenicity data. Data from 1111 controls from assays run over 11 years were examined by Salsburg and Holden[40] to determine a most powerful statistical procedure for detecting a mutagenic effect. A Monte-Carlo simulation, performed by Dickinson[41] to evaluate the power of the Terpstra-Jonckheere test for monotonic trend as applied to binary data, showed that the choice of the number and spacing of treatment levels can be critical factors in determining the power of the test.

A computer program CASE (computer automated structure evaluator) that analyzes molecules and their associated biological activity based on statistical tests of significance for the *Salmonella typhimurium* assay was introduced by Klopman.[42] Thakur[43] described alternative sources to general purpose statistical packages for the more adventurous investigator by providing more specialized, appropriate, and accurate methods for analysis of certain types of data.

A book covering basics of toxicology was written for the general public, "The Dose Makes the Poison: A Plain-Language Guide to Toxicology."[44]

TEST SYSTEMS

A number of references were published reviewing test methods and evaluation procedures for short-term mutagenicity and carcinogenicity testing.[45–48] Ishidate[49] presented a compilation of data from the National Institute of Hygienic Sciences in Tokyo representing results from Chinese hamster lung fibroblast assays for nearly 600 chemicals. A recent conference sponsored by NIH concerning human environmental mutagen and carcinogen exposure monitoring methods and research needs for epidemiological evaluation of health risks was discussed by Sheridan and de Serres.[50]

Sobels[51] presented a review of six collaborative studies in an evaluation of comparative mutagenesis results of European and American testing programs. Conclusions included identification of the L5178Y mammalian point mutation assay system as showing the greatest detection capability and selection of chromosomal aberration assays for optimal complement to Salmonella assays. Additional discussion of these comparative mutagenesis results were presented by Sobels.[52] Mohn and van Zeeland[53] investigated the relationship between quantitative mutagenic activity detection in bacterial, mammalian cell and animal-mediated assays, and found that while there was no indication of an absolute correlation between dose and mutant induction between bacterial and mammalian cells, ranking of mutagenic potency of five ethylating agents was maintained. Bacterial cell and animal-mediated assay results indicated that relative ranking order of mutagenic potency observed *in vitro*, whether from bacterial or mammalian cell assays, was not necessarily representative of activity *in vivo*.

Lehmann[54] reviewed recombinant DNA techniques currently being used for the study of DNA repair and mutagenesis. Lee[55] described results of recombinant DNA methods for distinguishing mechanisms of mutagen action. The use of recombinant DNA technology for evaluation of molecular level mechanisms for gene alteration and mutagenesis was also described by Mekler *et al.*,[56] who encouraged the further development of such methods for genotoxicity studies.

The use of micronuclear counts (MNC) in peripheral blood lymphocytes for identification of individuals with high frequencies of chromosome abberations was reported by Norman

et al.[57] With the use of logistic regression analysis, the MNC was an effective predictor of the presence of cells with chromosomal abberation and may prove valuable in chromosome damage screening. Morley *et al.*[58] described methods for the measurement of *in vivo* mutations and *in vitro* mutagenesis in human lymphocyte cells. Parker *et al.*[59] demonstrated that care must be taken in the interpretation of changes in sister chromatid exchange (SCE) frequencies in lymphocytes of less than a factor of two as these changes may simply represent changes in the composition of lymphocyte sub-populations and/or in their rates of proliferation *in vitro*. SCE differences in humans as a function of race and sex were reevaluated by Margolin and Shelby.[60] Although there is substantial evidence to indicate that females average approximately 0.5 SCE/cell higher than males within a normal, healthy adult population, data concerning differences in the heterogeneity of four racial groups from earlier studies require independent verification in a larger study. Baseline SCE frequencies in newborns and three other age groups from 1 to 75 years were evaluated by Das *et al.*,[61] with results indicating that SCE frequency was definitely age-dependent. SCE frequency was found to fall from 8.97 per cell in newborns to a low value of 5.1 per cell for the 1- to 5-year age group before increasing as individuals go through the aging process. The advantages of the SCE assay for chemical carcinogen studies were described by Manoharan and Banerjee.[62]

An investigation of an *in vitro* cytotoxicity test, more sensitive than that currently available, was conducted by Fauris *et al.*[63] using toxic samples directly assayed on 11 human cell subcellular targets. The rapidity of cellular RNA synthesis was the most sensitive measure for many pollutants. This quantitative test does not require preliminary concentration of toxic contaminants in water, and in the case of polluted river water, requires the sample to be diluted. The test was shown to be applicable to surface, ground, drinking and bottled mineral waters. Athwal and Sandhu[64,65] described a short-term assay using a human/mouse monochromosomal hybrid cell line, R3-5, for detection of induced aneuploidy in mammalian cells. A single human chromosome is transferred into mouse cells, which are then subjected to chemical treatment. The human chromosome is easily identified by differential staining procedures, and the frequency of 0 and 2 human chromosome occurrences in progeny of hybrid cells provides a direct measure of aneuploidy as a result of chemical assault.

The use of Chinese hamster ovary (CHO) cytotoxicity test and the Ames assay for the identification of potentially hazardous wastes was reported by Andon *et al.*[66] A new technique of coupling thin layer chromotography with the Ames procedure was described for coke plant, herbicide manufacturing, and oil refining waste. A CHO triple auxotroph based assay was described and validated by Taylor *et al.*[67] using nine known mutagens. The test was shown to be a useful supplemental mammalian assay for assessment of mutagenic activity of weakly mutagenic metal compounds. SCE and chromosome aberration tests in CHO cells were evaluated in a interlaboratory study for use as reliable and repeatable large-scale chemical screening methods by Galloway *et al.*[68] Results were favorable for standard protocol used between the labs, and modifications and refinements used to improve test resolution were described.

A number of new assay methods and assay procedures were reported. Ruiz-Rubio *et al.*[69] described a L-aribinose forward mutation assay for the sensitive detection of oxidative mutagens acting at A-T base pairs, suggesting that this assay could replace the set of specific tester strains generally used in the histidine reverse mutation assay for general screening of genotoxic agents. An assay using umu operon induction in *Salmonella typhimurium* strain TA1535 caused by DNA-damaging agents was described by Oda *et al.*[70] The umu test was verified with 38 chemicals, 31 of which are known animal carcinogens, indicating that this method can detect many DNA-damaging agents that require detection with several tester strains in the Ames assay. The test was also described as being applicable to environmental samples containing amino acids and nutrients such as urine, blood serum, and foodstuffs. Ehrlich *et al.*[71] described methods for preliminary evaluation of primary sites of cell damage upon chemical attack using yeast cell growth and RNA synthesis data.

Comparison of an automated bacterial mutagenicity assay with conventional plate assays using 36 carcinogenic and non-carcinogenic chemicals was described by Falck *et al.*[72] The system used automated computer-controlled preparation methods selectable by the user and bases revertant quantitation on growth curve data, measured as turbidity with a vertical-pathway photometer. Results of the system were comparable with the Ames test, suggesting the potential use and reliability of automated bacterial mutagenicity testing systems. A colorimetric bacterial assay for genotoxic potential measurements was described by Quillardet and Hornung.[73,74] The test is based on a measure of the induction of sfiA, a gene controlled by the general repressor of cell repair systems in *E. coli*. The simple assay correlated quantitatively with the Ames assay for 90% of these compounds with the use of 83 compounds within a range of chemical classes. The assay was suggested for use as a primary screening tool or as part of a battery of short-term assays for carcinogen detection. Procedures for further refinement and simplification of test procedures are described.

A number of miscellaneous cell and whole organism assays were described for use in toxicity/mutagenicity/carcinogenicity determinations. A summary of methods and results are presented in Table 1.

ENVIRONMENTAL SAMPLES

Numerous problems are associated with assessing human health risks from drinking contaminated water.[94] A survey of 1565 organic chemicals identified as contaminants in drinking water was conducted to develop a data base on carcinogenicity, mutagenicity, and tumor-promoting activity of these chemicals.[95] The role of asbestos cement pipes and factors involved in release of asbestos fibers in distribution systems were recently discussed.[96]

The preparation of environmental samples for conducting health effects assays is summarized in Table 2. Results of assays dealing with drinking waters and surface waters; potential groundwater source samples; and industrial and municipal samples and wastes and other environmental samples; are presented in Tables 3, 4, and 5, respectively.

SPECIFIC CHEMICALS

Information concerning assays of individual organic chemicals or classes of chemicals and individual inorganic chemicals

Table 1—Miscellaneous cell and whole organism assays used for genotoxic evaluation of environmental chemicals.

Assay	Endpoint	Chemical(s)	Comments	Reference
Mammalian primate cells	Cell structural effects	Water samples	Gross field tests system	75
Protozoa (*T. pyriformis*)	EC50	57 chemicals of environmental interest	EC50 values related to K_{ow} of the chemicals	76
Onion (*Allium cepa*)	Chromosomal aberrations	Polluted river	Evaluated effect of break-point chlorination on mutagenic activity	77
Plant tissue cultures	Chromosomal aberrations	2,4-D, MH, NMU, kinetin	Non-linear dose-response results observed for all compounds	78
Tradescantia stamen system	Somatic mutation induction	EMS, NEU, NMU, NEDA, NDMA	Three dose-response curves observed for chemicals tested	79
Fruit fly *Drosophila melanogaster*	Chromosome mutation		Measures induction by transpositions by a number of chemical and radiation agents	80
Rainbow trout gonad cell (RTG)	DNA repair repression	MNNG, 4NQO, methylthimidine	Method modification for assay sensitivity enhancement	81
Fish cell cultures (RTG and blue gill fry)	Cell death, mitotic inhibition, chromosomal damage, stimulatory effects	Marine sediments	Contaminated sediment extracts known to contain PAHs, PCBs, chlorinated hydrocarbons and metals	82
Rainbow trout embryo	Toxicity, tumor promotion	Aflatoxin B1, MNNG	Sensitive assay limited by exposure difficulty for slightly soluble carcinogens	83
Whole organism fish assay (*Cyprinodon variegatus*)	Presence of antiviral antibodies in spleen suspension	Various environmental carcinogens	Development of a number of micro techniques because of small size of tester organism	84
Whole organism fish assay (*Gambusia affinis*)	Metabolically activated BaP derivatives	Benzo(a)pyrene	BaP derivatives and DNA alteration detected within 2 days of exposure	85
Whole organism mussel assay	Chromosomal aberration	Benzo(a)pyrene	Genotoxic chemical detection in field situation described	86
Rat liver foci assay	γ-glutamyltranspeptidase positive foci	Benzo(a)pyrene, 2- and 4-acetylaminofluorene	2-acetylaminofluorene and BAP shown to be active in assay	87
Isolate perfused rat liver system	Metabolically activated BaP derivatives	Benzo(a)pyrene	Bioluminescence test for genotoxic agents 1000-fold more sensitive than Ames test	88
Mice host-mediated assay	Mutagenicity in Ames assay using tester strains TA1538, TA98 and TA100	Benzo(a)pyrene		89
In vivo rat hepatocyte repair assay	Unscheduled DNA synthesis	BT, 2AAF	Description of practical factors affecting assay sensitivity and reproducibility	90
Mouse spot test	Tumor promotion on mouse coat application area	60 chemical database	Comparison between *in vivo* assay and Ames bacterial mutation assay provided for 60 chemical agents	91
Fertility assessment test	Mice reproduction	Theophylline	Description of "Fertility Assessment by Continuous Breeding" (FACB) protocol and results for test compound	92
Dominant lethal assay	Mice or rat early death and reproduction effects	Review of results for 140 chemicals	Review of results of assay for 140 test chemicals by USEPA Work Group of Gene-Tox Program	93

Table 2—Preparation of environmental samples for health effects assays evaluation.

Type of sample	Method	Reference
Drinking water	Amberlite XAD-4 resin used for isolation and concentration of classes of organic constituents, including PAH and THM compounds	97
Drinking water, wastewater, wastewater residues	Concentration/fraction of mutagens using XAD-2 and XAD-7 in specially designed columns, solvent extraction of resins; fractionation via a coupled bioassay/analytical method	98
Sludges from municipal sewage treatment	Milling procedure for isolating mutagenic residue organics; fractionation via HPLC	99, 100
Aqueous environmental samples	Application of Ames assay to parent residue extracts and to major subfractions obtained by reverse phase and/or normal phase HPLC	101
Aqueous environmental samples—suspended sediment samples	Portable filtration and column-adsorption system for on-site use; fractionation of organic solutes	102
Drinking water samples	Concentration/fractionation on SEP-Pak® C18 catridges and XAD-2 resins for organics and TOX; Ames assay with tester strain TA98 and TA100	103

that have been evaluated for public health impacts is presented in Tables 6 and 7, respectively.

SPECIAL ASPECTS OF HEALTH EFFECTS ASSAYS

A number of studies were described that dealt with the practical aspects of microbial health assays in terms of quality control, assay costs, laboratory safety and experimental methods and data interpretation. Zeiger *et al.*[200] indicated that, based on analysis of an extensive *Salmonella* assay database consisting of 941 samples and 799 chemicals using tester strains TA98, TA100, TA1535, and TA1537 with and without S-9 activation, a sequential testing scheme initially using strain TA100 be adopted for reduction in cost and effort.

Laboratory safety concerns during toxicity and health effects testing were expressed by several authors, who presented a review of basic principles of laboratory safety, personal protective equipment, adequate laboratory design and hazardous materials disposal and guidelines for safe laboratory operations,[201] along with appropriate design and operational considerations for a limited-access facility for use in laboratory genetic toxicity testing.[202]

Quality control/quality assurance considerations in the Ames test were addressed by Williams[203] in an ASTM standard reference manual on "Quality Assurance for Environmental Measurements." Detailed quality control procedures were outlined to increase the confidence and interlaboratory comparability of mutagenicity data. Reproducibility of Ames assay results for 63 chemicals using *Salmonella* strains TA98, TA100, TA1535, TA1537 and TA1538 and *E. coli* WP2 uvrA cells in intra- and interlaboratory studies indicated that *Salmonella* results were useful for overall judgement of compound mutagenicity, while *E. coli* results exhibited a high degree of variability among labs.[204] Positive mutagenic response in *Salmonella* predicted carcinogenicity for up to 83% of the chemicals, while 75% of the carcinogens were shown as mutagens. Rat and mice tumor studies indicated that species-specific carcinogenicity could not be predicted from mutagenicity tests using species specific S-9 activation preparations.

Effects of solvent type on measured mutagenicity of 1,1,3-trichloro-, 1,1,3,3-tetrachloro-, pentachloro- and hexachloroacetones were discussed by Nestmann *et al.*[205] Results using acetone and DMSO as a compound carrier indicated that hexachloracetone produced variable solvent-dependent mutagenic response, was mutagenic by itself, but was non-mutagenic in acetone, and produced enhanced mutagenicity in DMSO. The authors recommended screening chemicals with a range of solvents and using additional solvents for confirmation of existing mutagenicity results to identify chemicals requiring further study. Additional mutagenicity test bias was discussed because of a lack of control plates being routinely run in the Ames assay quantifying the survival rate of treated and untreated samples that indicate the toxic effect of treatment independent of mutagenic effects.[206] Data interpretation limitations of the conventional two-fold rule for Ames mutagenicity assessment were evaluated by Carnes *et al.*[207] They suggested the use of a 95-percentile method, comparing test results to the 95 percentile of accumulated historical data for spontaneous mutation frequency, in lieu of the two-fold method, to increase the reliability and sensitivity of Ames assay results for mutagenic potential detection.

Limitations in the optimal use of sister chromatid exchange (SCE) induction *in vivo* in the fish *Nothobranchium rachowi* caused by unreliable staining techniques were discussed by van de Kerkhoff and van der Gaag.[208] Methods for sample preparation, staining and HCl post-treatment for assay reliability improvement were described. The feeding behavior of the fly *Drosphilia* was examined by Gollapudi *et al.*[209] Reduced mutational yields from mutagens fed to the flies in conjunction with 5-bromo-2-deoxyuridine (BrdUrd), a chemical demonstrating effectiveness in altering radiation and chemically induced genetic damage, could be linked simply to reduced feed uptake. The need to quantitate feed uptake for adequate effect assessment was emphasized.

Effects of chemical characteristics on mutagenic activity detection were addressed by Pagano and Zeiger[210] and McCoy *et al.*[211] Pagano and Zeiger[212] investigated the effect of mutagenic chemical storage on mutagenic activity determinations and found no significant difference between freshly prepared solutions of a number of chemical mutagens (4-nitro-o-phenylenediamine, 4-nitroquinoline-N-oxide, benzo(a)pyrene, and 2-aminoanthracene) and those stored at −20 to −80°C using strain TA100 with and without S-9 activation. Sodium azide did however show an increasing mutagenic response upon

Table 3—Results of health effects assays with drinking waters and surface waters.

Type of sample	Assay	Comments	Reference
Drinking water	Fluctuation test	Formation of direct-acting mutagens in surface sources after chlorination	104
Drinking water	Rat	Weak mutagenic activity detected in urine with concentrated samples	105
Drinking water	Humans: chromosome aberrations; sister chromatid exchange	Arsenic exposure at a mean level of 0.109 mg/L for at least 5 years did not result in significant effects compared with control individuals	106
Drinking water	Fish (*Poecilia reticulata*), Protozoa (*Tetrahymena pyriformis*), Bacteria (*Escherichia coli*), Ames (*Salmonella typhimurium*)	Extracts from seeds of the tree *Moringa oleifers* Lam., used for coagulation of drinking water in the Sudan were toxic to fish, protozoa, and bacteria; however, no mutagenic effects were observed	107
River water, Kyoto City, Japan	Ames (TA1538)	Neutral and basic fractions contributed 98% of total mutagenic activity of XAD-extract	108
Pond water	Ames (TA98 and TA100)	Aniline transformation products generated during incubation of pond water with wastewater sludge inoculum had mutagenic potential towards TA98 and TA100; nitrosobenzene and azo products postulated as causative agents	109
Drinking water, Spring Lake Reservoir	*Tradescantia* micronucleus test	Mutagenicity of water from tap fluctuated with mutagenicity of lake water	110
Drinking water, surface water	Ames	Preozonization produced direct acting frameshift mutagens that were adsorbed on XAD-8 sorbent; mutagenicity of the water was dependent on the ozone dose	111
Drinking water	Ames	GAC extracted organics using XAD resins can be separated into nonpolar compounds and polar compounds	112
Drinking water	Ames	Preliminary concentration procedures are needed to evaluate mutagenic activity of drinking water before and after treatment	113
Drinking water	Human bladder cancer	Increasing risk of bladder cancer with duration of exposure to chlorinated surface water was detected and was consistent across the sexes	114
Drinking water	Human cancer	No convincing evidence was found in a case-control study for increased cancer risk in humans from imbibed asbestos	115
Reclaimed water (imported river water, stormwater, and reclaimed wastewater)	Ames	Stormwater and reclaimed wastewater yielded highest levels of mutagenicity; concentrates of imported river water yielded lowest levels	116
Freshwater alga	*Salmonella typhimurium* forward mutation assay	Algal cell extracts for algae exposed to benzo(a)pyrene were mutagenic after 1 day growth	117
Drinking water disinfectants	Chromosomal aberrations in mice; sperm-head abnormalities in mice	Oral administration of chlorine at pH 8.5 induced increases in sperm-head abnormalities; no evidence of other effects with monochloramine, chlorine dioxide, sodium chlorite, or sodium chlorate	118
Drinking water	Ames (TA98 and TA100)	Majority of mutagens were products of chlorination step; granular activated carbon was effective in removing waterborne mutagens	119
Drinking water	Human cancer	Evaluation of epidemiological studies linking disinfection of drinking water and human cancer	120
Drinking water	Human cancer	Evaluation of chemicals found in drinking water supplies and incidence of human cancer	121
Drinking water	Ames	Although PAH compounds were found to increase in water as a result of passage through asphaltlined distribution pipes, mutagenicity did not correlate with either transit of water or levels of PAH compounds in water	122

Table 4—Results of health effects assays with potential groundwater source samples.

Type of sample	Assay	Comments	Reference
Soil in land treatment system	General toxicological aspects	Potential health effects from land treatment of wastewater were examined; organics, trace elements, nitrate, and sodium were considered	123
Coal pile runoff	Ames Chinese hamster ovary	Some solvent extracts of high-sulfur coals were both mutagenic and clastogenic; extracts from low sulfur coal were not mutagenic; solvent: water-mixture extracts of the coals were not mutagenic	124
Soil	Ames	After addition of municipal wastewater organic extract to a clay loam soil, mutagenic activity decreased	125
Effluents from nightsoil treatment plants	Ames (TA98 and TA100)	Effluents exposed to UV light and fortified with nitrate demonstrated increased mutagenicity over samples without nitrate fortification	126
Soils	*Salmonella typhimurium; Aspergillus nidulans*	Agricultural soils had an inherent level of mutagenic activity which was not detected by GC/MS analysis alone; mutagenic activity may be related to past history of agricultural practices, including biocide applications, fertilization, and cultivation	127
Soil humic substances	Ames	Mutagenic compounds were generated when humic structural compounds were chlorinated	128

freezing. McCoy *et al.*[211] evaluated the effect of nitropyrene cell permeability on mutagenic activity and found that nitropyrenes are mutagenic to *E. coli* strains that have increased cell permeabilities to large molecules.

Mannironi *et al.*[212] found that a temperature of 42°C, rather than the traditional temperature of 37°C, improved the activities of mice S-9 liver fractions, and was suggested for use in liver microsomal assays to improve reliability and sensitivity of these mutagenicity tests. The pH of agar plates used for Ames assays was important for assay response results, with pH levels below 7.0 resulting in strong responses for positive control chemicals while producing negative results for some mutagens.[213] Gutierrez *et al.*[214] indicated that SCE formation was independent of oxygen status in BrdUrd independent SCE

Table 5—Results of health effects assays with industrial and municipal samples and wastes and other environmental samples.

Type of sample	Assay	Comments	Reference
Petroleum wastes, combined API separator/slop oil emulsion solids waste	*S. typhimurium* *B. subtilis* *A. nidulans*	Neutral extract fraction of waste induced maximum genotoxic response in *S. typhimurium* and *A. nidulans* haploid bioassay; acid extract fraction of waste induced maximum response in *B. subtilis* DNA repair assay	129
Municipal wastewater, chlorinated	Fish; Ames	Papillomas on fish, positive for mutagenicity	130
Municipal wastewater with industrial contributions	Ames	Mutagenicity associated with industrial contribution; chlorination of secondary effluent did not substantially increase mutagenic activity	131
Creosote and coal tar	Ames-taped plate assay	Volatile mutagens were detected in both samples	132
Petroleum refinery effluents	Ames; Sister Chromatid Exchange	Mutagenic activity present in particulate fraction	133
Iron foundry castings operation effluents	Hamsters	No effluent samples were found to be carcinogenic at the concentration used	134
Petrochemical effluents and sediment samples in discharge site	Ames	No mutagenic activity	135
Pulp and paper mill effluents	*S. cerevisiae*	9 of 20 compounds identified were positive for genetic activity	136
Softwood kraft pulp, spent liquor-bleaching process	Ames	Mutagenicity evident when treated with chlorine	137
Coal slurry transport water	Ames	Nonvolatile mutagenic agents were not detected in either raw or chlorinated slurry wastewaters	138
Coal gasification wastewater	Ames	Solvent-extracted and steam-stripped coal gasification wastewaters did not contain mutagenic activity	139
Pulp and paper mill effluents	Bioassay battery	Bibliography concerning hazards to people within and outside a plant	140

Table 6—Health effects assays of specific organic chemicals or classes of chemicals of environmental concern.

Chemical	Assay	Comments	Reference
Aldicarb sulfoxide/aldicarb sulfone mixture	Growth and cholinesterase activity	At 4.8 ppm in drinking water, no detectable ill-effects	141
Amino acids	Ames	Three aromatic amino acids formed direct-acting and frameshift mutations by irradiation in an aqueous nitrite solution	142
Aromatic amines	Ames	Mutagenic responses less with increased alkoxy substitution	143
Benzene, toluenes, xylenes, and phenols	—	Review of toxicology, genetic activity and metabolism	144
Benzo(a)pyrene (BP)	Hepatic mixed-function oxidase system of rainbow trout	Demonstrated hepatocarcinogenicity of BP in an aquatic species	145
Benzo(a)pyrene (BP)	Cloned mice tumor cells	Investigation of role of metabolism in BP carcinogenesis	146
Benzidine	Ames	Mutagenesis inhibited by nucelophiles	147
Carbon tetrachloride	—	Health assessment document	148
Chlorinated benzenes	—	Health assessment document	149
Chlorinated phenols	Mice and rats	Study indicated low toxicity of most chlorinated phenols ingested in drinking water	150
Chlorinated styrenes	Ames	None of the chlorostyrenes were mutagenic	151
Chlorinated hydrocarbons	Excretion and tissue distribution in rats and pharmacokinetic and subchronic studies in monkeys	Investigation to provide metabolic data on four common drinking water contaminants	152
3-(2-Chloroethoxy)-1,2-dichloropropene (CP)	Ames	CP, a residual organic concentrated from drinking water, shown to be a promutagen	153
Chloroform and bromodichloromethane ($CHCl_3$ and $CHBrCl_2$)	Liver	$CHCl_3$ and $CHBrCl_2$, most common haloorganic contaminants of chlorinated drinking water, increased incidence of hepatic neoplastic nodules in female rats when administered in drinking water	154
Chlorophenols, chlorocatechols, and chloroguaiacols	Chinese hamster cells V79	Several compounds were mutagenic	155
Epichlorohydrin	—	Health assessment document	156
Formaldehyde	—	Bibliography concerning health effects	157
Halocarbons	Target organ effects	Summaries of target organ effects of three halocarbons found as drinking water contaminants	158
Humic acids	*In vivo* formation of mutagens in rats	Reaction of chlorine with natural aquatic humic material likely source of mutagen formation in drinking water	159
Humic acids	Subchronic study with rats and thyroxide activity in monkeys	Summary of toxicological research with chlorine dioxide and chlorinated humic acids	160
Humic acids	Subchronic study with rats	Increased incidence and severity of hematuria in rats administered with chlorinated humic acids in drinking water	161
Humic acids	Ames	Identification of chemicals responsible for mutagenicity formed during water chlorination	162
Methylene chloride	—	Health assessment document	163
Monohalomethanes	Ames; rat and mice	NIOSH recommends monohalocarbons be considered as potential carcinogens	164
N-Hydroxylamines and N-Hydroxy-carbamates	Ames and *Escherichia coli* WP2uvrA	Study of mutagenicity of nitrogen-containing compounds and their N-oxidized derivatives	165
Nitrated polycyclic aromatic hydrocarbons (Nitrated PAHs)	—	Nitrated PAHs with perpendicularly oriented nitro groups exhibited little or no direct-acting bacterial mutagenicity	166
Nitrated polycyclic aromatic hydrocarbons (Nitrated PAHs)	Ames	Nitration increased light-mediated mutagenic activity of PAHs	167
Nitriloacetic acid (NTA)	Ames	NTA, a substitute for polyphosphates in laundry detergents, increased mutagenicity of chromium compounds	168

(Table 6 Continued)

Table 6—(Continued)

Chemical	Assay	Comments	Reference
Nitriloacetic acid (NTA)	Sister chromatid exchange (SCE)	NTA did not increase frequency of SCE, but increased frequency of SCE induced by treatment with insoluble metal salts	169
N-Nitroso compounds	—	Review of n-nitroso compounds as environmental carcinogens	170
Phthalic acid esters and metabolites	Ames	Investigation of mutagenic potential with and without mammalian enzymatic metabolic activation system	171
Polycyclic aromatic hydrocarbons	Ames	Strain TA97 (new tester strain) more susceptible to mutation than either TA98 or TA100 by many of the PAHs tested; Noncarcinogens (for example, pyrene and perylene) highly mutagenic to TA97	172
Pyrene	Ames	Pyrene mutagenic when S9 present	173
Tetrachloroethylene, trichloroethylene, and 1,1,1-trichloroethane	Toxicity to human and monkey cells	Tetrachloroethylene more toxic than trichloroethylene and 1,1,1-trichloroethane	174
Tetrachlorohydroquinone (TCH), a pentachlorophenol (PCP) metabolite	Human fibroblasts	In evaluation of mutagenic/carcinogenic potential of PCP, the metabolite TCH should be considered	175
Trichloroethylene (TCE)	Rat metabolism	Investigation of the absorption and disposition of TCE administered orally	176
Trichloroethylene (TCE)	—	Review of metabolism and carcinogenicity of TCE	177
Trichloroethylene, trichloroethanol, and chloral hydrate	*Aspergillus nidulans*	Investigation of mutagenicity of TCE and two possible metabolic products	178
Toluene	—	Review of toxicological effects of toluene	179
Vinyl acetate and acetaldehyde	DNA damage in human leucocytes	Both chemicals induced DNA cross-links in human leucocytes	180

Table 7—Health effects assays of specific inorganic chemicals of environmental concern.

Chemical	Assay	Comments	Reference
Arsenic	Chinese hamster ovary cells	Study of growth inhibition and cytotoxic effects produced one organic and two inorganic forms of arsenic	181
Arsenic	—	Bibliography concerning toxicity and carcinogenicity of arsenic and arsenic compounds	182
Arsenic	—	Review of mutagenicity of inorganic arsenic	183
Beryllium	—	Health assessment document	184
Cadmium	—	Bibliography concerning toxicity of cadmium	185, 186
Cadmium	—	Evaluation of the mutagenicity and carcinogenicity of cadmium	187
Cadmium	Mouse mononuclear phagocytic system	Effects of chronic ingestion of cadmium chloride administered in drinking water	188
Chromium	Ames	Investigation of the mutagenicity of soluble trivalent chromium compounds	189
Fluoride	Chromosome aberration and sister chromatid exchange	Sodium fluoride, at concentrations up to 60 times the level normally used in drinking water for prevention of dental decay, failed to induce chromosome aberrations and sister chromatid exchanges	190
Fluoride	Toxicity to postnatally developing rat kidney	Kidney of suckling rat largely unresponsive to sodium fluoride toxicity; renal sensitivity increased abruptly after weaning	191
Mercury	—	Review of mercury health effects	192
Metals	—	Review of mediation of mutagenicity and clastogenicity of heavy metals by physiochemical factors (for example, pH)	193
Metal ions	Ames and *Escherichia coli* WP2 uvrA pKm 101	Study of mutagenicity of metal ions	194

(Table 7 Continued)

Table 7—(Continued)

Chemical	Assay	Comments	Reference
Metal derivatives	Ames	A new strain of *Salmonella typhimurium*, TA102, was shown to be sensitive to Cr(VI) compounds but insensitive to As(III, As(IV), Cd, Ni, Pb, and Hg (known or suspected carcinogens in man) and to Cr(III)	195
Metal salts	*Saccharomyces cerevisiae*	Study of genotoxic effects of potassium dichromate, sodium arsenate, cobalt chloride, and lead nitrate	196
Nickel	—	Bibliography concerning toxicity and carcinogenicity of nickel	197
Nitrates	Micronuclei and chromosomal aberrations in bone marrow cells of rats and mice	Study of *in vivo* mutagenic activity of sodium nitrate	198
Selenium	—	Review of genotoxicity of selenium	199

production occurrences, but that increased oxygen tensions produced increased SCE production in BrdUrd dependent cases.

The effects of the source of S-9, that is, rat or human liver tissue, on mutagenic potential determinations of aflavotoxin B1, 3-methylcholanthrene, cigarette smoke condensate, 2-aminoaanthracene, and 2-aminofluorene were evaluated by Beaune.[215] The first three compounds were less mutagenic with activation with human S-9 than with rat S-9, while the last two compounds showed opposite results. Human liver S-9 clearly provided different results than commonly used rat liver S-9. It was suggested that human S-9 may represent a valuable tool for the investigation of mutagenicity, and perhaps carcinogenicity, of chemicals in man. Milling and Maddock[216] found that fish and mammalian S-9 activation systems performed identically in their evaluation of metabolism-dependent genotoxic PAH chemicals.

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REFERENCES

1. Lu, P. Y., and Wassom, J. S., "Information Science in Toxicology." Oak Ridge National Laboratory, Oak Ridge, Tenn. (1985).
2. Lewis, R. J., and Sweet, D. V., "Registry of Toxic Effects of Chemical Substances (RTECS), 1984 Edition. User's Guide to the RTECS Computer Tape." DHEW/DF-85/0001A, Natl. Inst. Occupational Safety and Health, Cincinnati, Ohio (1985).
3. Sweet, D. V., *et al.*, "Registry of Toxic Effects of Chemical Substances (RTECS), 1984 Edition." DHEW/DF-85/001, Natl. Inst. Occupational Safety and Health, Cincinnati, Ohio (1985).
4. "Handbook of Toxic and Hazardous Chemicals and Carcinogens." Marshall Sittig (Ed.), Noyes Publications, Park Ridge, N. J. (1985).
5. Gentile, J. M., "Back to the Basics: A Review of Three Books Fundamental to the Study of Environmental Mutagenesis." *Environ. Mutagenesis,* **7,** 609 (1985).
6. Ashby, J., "Fundamental Structural Alerts to Potential Carcinogenicity or Noncarcinogenicity." *Environ. Mutagenesis,* **7,** 919 (1985).
7. Mortelmans, K. E., "Cellular Systems and Toxicity Testing: An Overview." *Environ. Mutagenesis,* **7,** 135 (1985).
8. Thacker, J., "The Molecular Nature of Mutations in Cultured Mammalian Cells: A Review." *Mutation Res.*, **150,** 431 (1985).
9. Ruppert, P. H., "Neurobehavioral Consequences of Postnatal Exposure to Toxicants." EPA-600/D-85-022, Health Effects Research Laboratory, Research Triangle Park, N. C. (1985).
10. Brusick, D., and Auletta, A., "Developmental Status of Bioassays in Genetic Toxicology: A Report of Phase II of the U. S. Environmental Protection Agency Gene-Tox Program." *Mutation Res.*, **153,** 1 (1985).
11. "Risk Assessment and Management: Framework for Decision Making." EPA-600/9-85-002, U. S. EPA, Washington, D. C. (1984).
12. Ward, J. B., "Issues in Monitoring Population Exposures." EPA-600/D-85-008, U. S. EPA, Research Triangle Park, N. C. (1985).
13. Guiney, P. D., "Use of Predictive Toxicology Methods to Estimate Relative Risk of Complex Chemical Waste Mixtures." *Hazardous Waste and Hazardous Materials,* **2,** 2, 177 (1985).
14. Sobles, F. H., "Personal Comments on 'Environmental Protection Agency' Proposed Guidelines for Mutagenicity Risk Assessment." *Mutation Res.*, **147,** 211 (1985).
15. Cothern, C. R., *et al.*, "Techniques for Assessment of the Carcinogenic Risk to the U. S. Population Due to Exposure from Selected Volatile Organic Compounds from Drinking Water Via the Ingestion, Inhalation and Dermal Routes." U. S. EPA, Washington, D. C. (1984).
16. Lewtas, J., and Andon, B., "In Vivo/In Vitro Approach to the Toxicological Assessment of Hazardous Waste." EPA-600/D-84-151, U. S. EPA, Research Triangle Park, N. C. (1984).
17. Clark, R. M., *et al.*, "Use of Toxic Screening Models for Drinking Water Utility Management." EPA-600/D-84-266, U. S. EPA, Cincinnati, Ohio (1984).
18. Stich, H. F., and Rosin, M. P., "Towards a More Comprehensive Evaluation of a Genotoxic Hazard in Man." *Mutation Res.*, **150,** 43 (1985).
19. Anderson, E. L., *et al.*, "Methodology for Ranking the Degree of Hazard Associated with Exposure to Carcinogens and Other Toxic Chemicals." EPA-600/D-85-040, U. S. EPA, Washington, D. C. (1985).
20. Gowda, T. P. H., *et al.*, "A Comprehensive Study of Risk

Assessment for a Hazardous Compound of Public Health Concern." *Water, Air, Soil Pollut.*, **24,** 189 (1985).
21. Schaum, J., "Risk Analysis of TCDD Contaminated Soil." EPA-600/8-84-031, U. S. EPA, Washington, D. C. (1984).
22. Littlefield, N. A., and Gaylor, D. W., "Influence of Total Dose and Dose Rate in Carcinogenicity Studies." *J. Toxicol. Environ. Health,* **15,** 545 (1985).
23. Littlefield, N. A., *et al.*, "Influence of Genetic Composition of Test-Animal Populations on Chronic Toxicity Studies Used for Risk Estimation." *J. Toxicol. Environ. Health,* **15,** 357 (1985).
24. Chankong, V., *et al.*, "The Carcinogenicity Prediction and Battery Selection (CPBS) Method: A Bayesian Approach." *Mutation Res.*, **153,** 135 (1985).
25. Pet-Edwards, J., *et al.*, "Application of the Carcinogenicity Prediction and Battery Selection (CPBS) Method to the Gene-Tox Data Base." *Mutation Res.*, **153,** 187 (1985).
26. Palajda, M., and Rosenkranz, H. S., "Assembly and Preliminary Analysis of a Genotoxicity Data Base for Predicting Carcinogens." *Mutation Res.*, **153,** 79 (1985).
27. Benigni, R., and Giuliani, A., "Cluster Analysis of Short-Term Tests: A New Methodological Approach." *Mutation Res.*, **147,** 139 (1985).
28. Pet-Edwards, J., *et al.*, "Cluster Analysis in Predicting the Carcinogenicity of Chemicals Using Short-Term Assays." *Mutation Res.*, **153,** 167 (1985).
29. Ricci, P. F., and Molton, L. S., "Regulating Cancer Risks." *Environ. Sci. Technol.*, **19,** 473 (1985).
30. Freed, J. R., *et al.*, "Methods for Assessing Exposure to Chemical Substances. Volume 2. Methods for Assessing Exposure to Chemical Substances in the Ambient Environment." EPA-560/5-85-002, U. S. EPA, Washington, D. C. (1985).
31. Dixon, D. A., *et al.*, "Methods for Assessing Exposure to Chemical Substances. Volume 4. Methods for Enumerating and Characterizing Populations Exposed to Chemical Substances." EPA-560/5-85-004, U. S. EPA, Washington, D. C. (1985).
32. Berenbaum, M. C., "Consequences of Synergy between Environmental Carcinogens." *Environ. Res.*, **38,** 310 (1985).
33. Irr, J. D., *et al.*, "Introduction to the Genetic Toxicology Association Workshop on Statistical Analysis of Cytogenetics Test Systems." *Environ. Mutagenesis,* **7,** Supplement 4, 3 (1985).
34. Sylwester, D., and Albertini, R. J., "Confidence Intervals and Sample Size Calculations to Compare Variant Frequencies." *Environ. Mutagenesis,* **7,** Supplement 4, 31 (1985).
35. Mann, R. C., *et al.*, "Critical Sample Sizes for Determining the Statistical Significance of Mutation Frequencies." *Mutation Res.*, **143,** 93 (1985).
36. Whorton, E. B., Jr., "Some Experimental Design and Analysis Considerations for Cytogenetics Studies." *Environ. Mutagenesis,* **7,** Supplement 4, 9 (1985).
37. Thakur, A. K., "Tests of Homogeneity and Trend with Medians." *Environ. Mutagenesis,* **7,** Supplement 4, 23 (1985).
38. Stiratelli, R. G., *et al.*, "Parametric Approaches to the Analysis of In Vivo Cytogenetics Studies." *Environ. Mutagenesis,* **7,** Supplement 4, 43 (1985).
39. Wahrendorf, J., *et al.*, "A Nonparametric Approach to the Statistical Analysis of Mutagenicity Data." *Mutation Res.*, **147,** 5 (1985).
40. Salsburg, D., and Holden, H. E., "A Statistical Examination of Historical Controls for Mouse Bone Marrow Cytogenetic Assays." *Environ. Mutagenesis,* **7,** Supplement 4, 55 (1985).
41. Dickinson, A. W., "An Empirical Study of the Power of the Terpstra-Jonckheere Test Using Binary Data." *Environ. Mutagenesis,* **7,** Supplement 4, 17 (1985).
42. Klopman, G., *et al.*, "Computer Analysis of Toxicological Data Bases: Mutagenicity of Aromatic Amines in *Salmonella* Tester Strains." *Environ. Mutagenesis,* **7,** 625 (1985).
43. Thakur, A. K., "Some Readily Available Computer Programs for Special Types of Statistical Analyses." *Environ. Mutagenesis,* **7,** Supplement 4, 73 (1985).
44. Barrons, K. C., "Correcting Toxicological Misconceptions." *Chem. Eng. New,* **63,** 6, 27 (1985).
45. "Handbook of Mutagenicity Procedures. Second Edition." B. J. Kilbey *et al.* (Eds.), Elsevier Science Publishers, Amsterdam, The Netherlands (1984).
46. "Microbial Tests for Mutagenicity/Carcinogenicity." K. Traul (Ed.), Van Nostrand Reinhold, Farmingdale, N. Y. (1985).
47. "Evaluation of Short-Term Tests for Carcinogens." J. Ashby *et al.* (Eds.), Elsevier Science Publishers, Amsterdam, The Netherlands (1985).
48. Gentile, J. M., "International Study of Short Term Tests—Phase 2." *Environ. Mutagenesis,* **7,** 805 (1985).
49. "Chromosome Aberration Tests in vitro." M. Ishidate, Jr. (Ed.), Natl. Inst. of Hygienic Sciences, Tokyo, Japan (1985).
50. Sheridan, W., and de Serres, F. J., "Report of the Conference on DNA Adducts: Dosimeters to Monitor Human Exposure to Environmental Mutagens and Carcinogens." *Mutation Res.*, **147,** 59 (1985).
51. Sobels, F. H., "Studies in Comparative Chemical Mutagenesis." *Environ. Mutagenesis,* **7,** 759 (1985).
52. Sobels, F. H., "A Comprehensive Exercise in Comparative Mutagenesis with Exciting Outcome, or, How Good Are Mutation Assays in Predicting Carcinogens?" *Mutation Res.*, **147,** 1 (1985).
53. Mohn, G. R., and van Zeeland, A. A., "Quantitative Comparative Mutagenesis in Bacteria, Mammalian Cells, and Animal-Mediated Assays: A Convenient Way of Estimating Genotoxic Activity in Vivo?" *Mutation Res.*, **150,** 159 (1985).
54. Lehmann, A. R., "Use of Recombinant DNA Techniques in Cloning DNA Repair Genes and in the Study of Mutagenesis in Mammalian Cells." *Mutation Res.*, **150,** 61 (1985).
55. Lee, W. R., "Molecular Mechanisms of Mutagenesis Determined by the Recombinant DNA Technology." CONF-8506137-11, Univ. of Washington, Seattle, Wash. (1985).
56. Mekler, Ph., *et al.*, "The Use of Recombinant DNA Technology to Study Gene Alteration." *Mutation Res.*, **153,** 13 (1985).
57. Norman, A., *et al.*, "Screening Human Populations for Chromosome Aberrations." *Mutation Res.*, **143,** 155 (1985).
58. Morley, A. A., *et al.*, "Methods for Study of Mutations and Mutagenesis in Human Lymphocytes." *Mutation Res.*, **147,** 363 (1985).
59. Parkes, D. J. G., *et al.*, "Changes in Spontaneous SCE Frequencies as a Function of Sampling Time in Lymphocytes from Normal Donors and Cancer Patients." *Mutation Res.*, **147,** 113 (1985).
60. Margolin, B. H., and Shelby, M. D., "Sister Chromatid Exchanges: A Reexamination of the Evidence for Sex and Race Differences in Humans." *Environ. Mutagenesis,* **7,** Supplement 4, 63 (1985).
61. Das, B. C., *et al.*, "Baseline Frequency of Sister-Chromatid Exchanges (SCE) in Newborn Lymphocytes and Its Relationship to In Vivo Aging in Humans." *Mutation Res.*, **144,** 85 (1985).
62. Manoharan, K., and Banerjee, M. R., "Measurements of Chemical Carcinogen-Induced Sister Chromatid Exchanges in a Whole Organ in Vitro." *Mutation Res.*, **147,** 165 (1985).
63. Fauris, C., *et al.*, "Rapidity of RNA Synthesis in Human Cells. A Highly Sensitive Parameter for Water Cytotoxicity Evaluation." *Water Res.*, **19,** 677 (1985).
64. Athwal, R. S., and Sandhu, S. S., "Mammalian Cell Culture Assay to Quantitate Chemically Induced Aneuploidy: Use of a Monochromosomal Human/Mouse Cell Hybrid." EPA-600/D-85-019, U. S. EPA, Research Triangle Park, N. C. (1985).
65. Athwal, R. S., and Sandhu, S. S., "Use of a Human × Mouse Hybrid Cell Line to Detect Aneuploidy Induced by Environmental Chemicals." *Mutation Res.*, **149,** 73 (1985).
66. Andon, B., *et al.*, "Evaluation of Chemical and Biological Methods for the Identification of Mutagenic and Cytotoxic Hazardous

Waste Samples." EPA-600/D-84-150, U. S. EPA, Research Triangle Park, N. C. (1984).
67. Taylor, R. T., *et al.*, "Induced Reversion of a Chinese Hamster Ovary Triple Auxotroph: Validation of the System with Several Mutagens." *Mutation Res.*, **151,** 293 (1985).
68. Galloway, S. M., *et al.*, "Development of a Standard Protocol for In Vitro Cytogenetic Testing with Chinese Hamster Ovary Cells: Comparison of Results for 22 Compounds in Two Laboratories." *Environ. Mutagenesis,* **7,** 1 (1985).
69. Ruiz-Rubio, M., *et al.*, "Oxidative Mutagens Specific for A·T Base Pairs Induce Forward Mutations to L-arabinose Resistance in *Salmonella typhimurium.*" *Mutation Res.*, **147,** 153 (1985).
70. Oda, Y., *et al.*, "Evaluation of the New System (*umu*-test) for the Detection of Environmental Mutagens and Carcinogens." *Mutation Res.*, **147,** 219 (1985).
71. Ehrlich, W., *et al.*, "Investigation of a Test System for the Rapid Differentiation of Nuclear and Cytoplasmic Damage in Eucaryotes." *Ecotoxicol. Environ. Safety,* **9,** 71 (1985).
72. Falck, K., *et al.*, "Mutascreen®, An Automated Bacterial Mutagenicity Assay." *Mutation Res.*, **150,** 119 (1985).
73. Quillardet, P., *et al.*, "The SOS Chromotest, A Colorimetric Bacterial Assay for Genotoxins: Validation Study with 83 Compounds." *Mutation Res.*, **147,** 79 (1985).
74. Quillardet, P., and Hofnung, M., "The SOS Chromotest, A Colorimetric Bacterial Assay for Genotoxins: Procedures." *Mutation Res.*, **147,** 65 (1985).
75. Novinson, T., "Water Toxicity Field Test System." Dept. Navy, Washington, D. C. (1984).
76. Yoshioka, Y., *et al.*, "Testing for the Toxicity of Chemicals with *Tetrahymena pyriformis.*" *Sci. Total Environ.*, **43,** 149 (1985).
77. Al-Sabti, K., and Kurelec, B., "Chromosomal Aberrations in Onion (*Allium cepa*) Induced by Water Chlorination By-Products." *Bull. Environ. Contam. Toxicol.*, **34,** 80 (1985).
78. Kallak, H. I., and Vapper, M. A., "Plant Tissue Culture as a Model System for Mutagenicity Testing of Chemicals." *Mutation Res.*, **147,** 51 (1985).
79. Tano, S., and Yamaguchi, H., "Effects of Several Nitroso Compounds on the Induction of Somatic Mutations in Tradescantia with Special Regard to the Dose Response and Threshold Dose." *Mutation Res.*, **148,** 59 (1985).
80. Clark, S. H., and Chovnick, A., "A Selective Screen for Transposable Element Mobilization in *Drosophila melanogaster.*" *Environ. Mutagenesis,* **7,** 439 (1985).
81. Walton, D. G., *et al.*, "Increased Response of the Rainbow Trout Gonad Cell Unscheduled DNA Repair Assay." *Bull. Environ. Contam. Toxicol.*, **34,** 340 (1985).
82. Kocan, R. M., *et al.*, "Cytotoxicity/Genotoxicity: The Application of Cell Culture Techniques to the Measurement of Marine Sediment Pollution." *Aquat. Toxicol.*, **6,** 165 (1985).
83. Hendricks, J. D., *et al.*, "Rainbow Trout Embryos: Advantages and Limitations for Carcinogenesis Research." *Natl. Cancer Inst. Monograph,* **65,** 129 (1984).
84. Meador, C. B., *et al.*, "Serological Alterations in Carcinogen-Exposed Teleosts: Procedures for Preparation and Analysis of Samples from Small Fish." *Natl. Cancer Inst. Monograph,* **65,** 211 (1984).
85. Batel, R., *et al.*, "DNA Damage by Benzo[a]pyrene in the Liver of Mosquito Fish *Gambusia affinis.*" *Sci. Total Environ.*, **41,** 275 (1985).
86. Al-Sabti, K., and Kurelec, B., "Induction of Chromosomal Aberrations in the Mussel *Mytilus galloprovincialis* Watch." *Bull. Environ. Contam. Toxicol.*, **35,** 660 (1985).
87. Pereira, M. A., and Herren-Freund, S. L., "Liver Initiation Assay: The Rat Liver Foci Bioassay of Carcinogens and Noncarcinogens." EPA-600/D-85-045, U. S. EPA, Cincinnati, Ohio (1985).
88. Ben-Itzhak, J., *et al.*, "The Formation of Genotoxic Metabolites of Benzo[a]pyrene by the Isolated Perfused Rat Liver, as Detected by the Bioluminescence Test." *Mutation Res.*, **147,** 107 (1985).
89. Glatt, H., *et al.*, "Host-Mediated Mutagenicity Experiments with Benzo[a]pyrene and Two of Its Metabolites." *Mutation Res.*, **156,** 163 (1985).
90. Ashby, J., *et al.*, "An Assessment of the In Vivo Rat Hepatocyte DNA-Repair Assay." *Mutation Res.*, **156,** 1 (1985).
91. Styles, J. A., and Penman, M. G., "The Mouse Spot Test: Evaluation of Its Performance in Identifying Chemical Mutagens and Carcinogens." *Mutation Res.*, **154,** 183 (1985).
92. Gulati, D. K., *et al.*, "Theophylline: Reproduction and Fertility Assessment in CD-1 Mice When Administered in Drinking Water/Feed." NTP-85-096, Environ. Health Res. and Testing, Inc., Lexington, Ky. (1985).
93. Green, S., *et al.*, "Current Status of Bioassays in Genetic Toxicology—The Dominant Lethal Assay." *Mutation Res.*, **154,** 49 (1985).
94. McDonald, M. E., "Acid Deposition and Drinking Water." *Environ. Sci. Technol.*, **19,** 772 (1985).
95. Papa, P. A., *et al.*, "Survey of Organic Drinking Water Contaminants: Carcinogens, Mutagens, and Tumor Promoters (Revised)." SRI International, Menlo Park, Calif. (1984).
96. Natl. Tech. Inf. Serv., "Asbestos in Drinking Water. 1977–November 1985 (Citations from the Selected Water Resources Abstracts Data Base)." NTIS, Springfield, Va. (1985).
97. Ben-Poorat, S., *et al.*, "Evaluation of Methods for the Isolation or Concentration of Organic Substances from Water Using XAD-4 Quaternary Resin." EPA-600/1-85-020, U. S. EPA, Washington, D. C. (1985).
98. Tabor, M. W., and Loper, J. C., "Analytical Isolation, Separation, and Identification of Mutagens from Nonvolatile Organics of Drinking Water." *Inter. J. Environ. Anal. Chem.*, **19,** 281 (1985).
99. Tabor, M. W., and Loper, J. C., "Isolation of Mutagenic Compounds from Sludges and Wastewaters." *Environ. Sci. Res.*, **32,** 269 (1985).
100. Tabor, M. W., and Loper, J. C., "New Methods to Extract Sludges: Preparation of Residue Organics to Isolate Mutagenic Components." In "Concentration Techniques for Collection and Analysis of Organic Chemicals for Biological Testing of Environmental Samples." I. H. Suffet and M. Malaiyandi (Eds.), American Chemical Society, Washington, D. C. (1985).
101. Tabor, M. W., and Loper, J. C., "Mutagen Isolation Methods: Fractionation of Residue Organics from Aqueous Environmental Samples." In "Concentration Techniques for Collection and Analysis of Organic Chemicals for Biological Testing of Environmental Samples." I. H. Suffet and M. Malaiyandi (Eds.), American Chemical Society, Washington, D. C. (1985).
102. Leenheer, J. A., and Noyes, T. I., "A Filtration and Column-Adsorption System for Onsite Concentration and Fractionation of Organic Substances from Large Volumes of Water." Geological Survey Water Supply Paper 2230, U. S. Geological Survey, Alexandria, Va. (1984).
103. Monarca, S., *et al.*, "Microscale Fluctuation Assay Coupled with Sep-Pak® Concentration as a Rapid and Sensitive Method for Screening Mutagens in Drinking Water." *Water Res.*, **19,** 10, 1209 (1985).
104. Monarca, S., *et al.*, "Detection of Mutagens in Unconcentrated and Concentrated Drinking Water Supplies Before and After Treatment Using a Microscale Fluctuation Test." *Chemosphere,* **14,** 1069 (1985).
105. Monarca, S., *et al.*, "Mutagenicity and Organic Halogen Determination in Body Fluids and Tissue of Rats Treated with Drinking Water and Pulp Mill Bleachery Effluent Concentrates." *Chemosphere,* **13,** 1271 (1984).
106. Vig, B. K., "Chromosome Studies on Human Subjects Exposed to Arsenic in Drinking Water." EPA-600/1-84-023, U. S. EPA, Washington, D. C. (1984).

107. Grabow, W., *et al.*, "Toxicity and Mutagenicity Evaluation of Water Coagulated with *Moringa oleifera* Seed Preparations Using Fish, Protozoan, Bacterial, Coliphage, Enzyme and Ames *Salmonella* Assays." *Water S. A.*, **11,** 9 (1985).
108. Makuoka, S., *et al.*, "Mutagenic Activity in Organic Concentrate from Nishitakase River Water in Kyoto City, and Its Fractions Separated by Using Liquid-liquid Fractionation and Thin Layer Chromatography." *Water Res.*, **19,** 249 (1985).
109. Lyons, C. D., *et al.*, "Persistence and Mutagenic Potential of Herbicide-derived Aniline Residues in Pond Water." *Bull. Environ. Contam. Toxicol.*, **35,** 696 (1985).
110. Ma, T.-H., *et al.*, "Mutagenicity of Drinking Water Detected by the *Tradescantia* Micronucleus Test." *Can. J. Genetics Cytology,* **27,** 143 (1985).
111. Van Hoof, F., *et al.*, "Formation of Mutagenic Activity During Surface Water Preozonization and Its Removal in Drinking Water Treatment." *Chemosphere,* **14,** 501 (1985).
112. Loper, J. C., *et al.*, "Mutagenic Residues Recovered from Granular Activated Carbon After Its Use in Drinking Water Treatment." EPA-600/D-85-026, U. S. EPA, Cincinnati, Ohio (1985).
113. Monarca, S., *et al.*, "Mutagenicity Assessment of Different Drinking Water Supplies Before and After Treatments." *Bull. Environ. Contam. Toxicol.*, **34,** 815 (1985).
114. Cantor, K. P., *et al.*, "Drinking Water Source and Risk of Bladder Cancer: A Case-Control Study." EPA-600/D-85-007, U. S. EPA, Research Triangle Park, N. C. (1985).
115. Polissar, L., *et al.*, "Case-Control Study of Asbestos in Drinking Water and Cancer Risk." *Am. J. Epid.*, **119,** 456 (1984).
116. Nellor, M. H., *et al.*, "Health Effects of Indirect Potable Water Reuse." *J. Am. Water Works Assoc.*, **77,** 7, 88 (1985).
117. Schoeny, R., *et al.*, "Mutagenicity of Algal Metabolites of Benzo(a)pyrene for *Salmonella typhimurium.*" *Environ. Mutagenesis,* **7,** 839 (1985).
118. Meier, J. R., *et al.*, "Evaluation of Chemicals Used for Drinking Water Disinfection for Production of Chromosomal Damage and Sperm-Head Abnormalities in Mice." *Environ. Mutagenesis,* **7,** 201 (1985).
119. Loper, J. C., *et al.*, "Continuous Removal of Both Mutagens and Mutagen-Forming Potential by an Experimental Full-Scale Granular Activated Carbon Treatment System." *Environ. Sci. Technol.*, **19,** 333 (1985).
120. Craun, G. F., "Basic Epidemiologic Considerations for Evaluating Associations Between the Disinfection of Drinking Water and Cancer in Human Populations." EPA-600/D-84-250, U. S. EPA, Cincinnati, Ohio (1984).
121. Bull, R. J., "Toxicological Data on Selected Hazardous Chemicals and Possible Extrapolation to Man." EPA-600/D-84-261, U. S. EPA, Research Triangle Park, N. C. (1984).
122. Basu, D. K., *et al.*, "Water Distribution System as a Potential Source of Mutagens in Drinking Water." EPA-600/1-84-019, U. S. EPA, Research Triangle Park, N. C. (1984).
123. Kowal, N. E., "Health Effects of Land Treatment: Toxicological." EPA-600/1-84-030, U. S. EPA, Cincinnati, Ohio (1985).
124. Stahl, R. G., *et al.*, "Use of the Ames Test to Evaluate the Mutagenicity of Compounds in Runoffs from Model Coal Piles." In "Toxicity Screening Procedures Using Bacterial Systems." D. Liu and B. J. Dutka (Eds.), Marcel Dekker, Inc., New York, N. Y. 457 (1984).
125. Plewa, M. J., and Hopke, P. K., "The Effect of Soil on the Mutagenic Properties of Wastewater." WRC Research Report No. 95, Illinois Water Research Center, U. S. Dept. Interior, Washington, D. C. (1984).
126. Ohta, T., *et al.*, "Formation of Mutagens from Digested Night-Soil Effluent by Photochemical Reaction." *Environ. Poll.*, **36,** 251 (1984).
127. Brown, K. W., *et al.*, "Mutagenicity of Three Agricultural Soils." *Sci. Total Environ.*, **41,** 173 (1985).
128. Sato, T., *et al.*, "Chlorinated Products from Structural Compounds of Soil Humic Substances." *Sci. Total Environ.*, **43,** 127 (1985).
129. Donnelly, K. C., *et al.*, "Evaluation of the Hazardous Characteristics of Two Petroleum Wastes." *Hazardous Waste and Hazardous Materials,* **2,** 191 (1985).
130. Grizzle, J. M., *et al.*, "Papillomas on Fish Exposed to Chlorinated Wastewater Effluent." *J. Natl. Cancer Inst.*, **73,** 1133 (1984).
131. Meier, J. R., and Bishop, D. F., "Evaluation of Conventional Treatment Processes for Removal of Mutagenic Activity from Municipal Wastewaters." *J. Water Pollut. Control Fed.*, **57,** 999 (1985).
132. Bos, R. R., *et al.*, "Detection of Volatile Mutagens in Creosote and Coal Tar." *Mutation Res.*, **156,** 195 (1985).
133. Metcalfe, C. D., *et al.*, "Genotoxic Activity of Particulate Material in Petroleum Refinery Effluents." *Bull. Environ. Contam. Toxicol.*, **35,** 240 (1985).
134. Shellenberger, T. E., *et al.*, "Carcinogenic Potential of Condensed Pyrolysis Effluents from Iron Foundry Casting Operations. Volume 3 and Volume 4." Borriston Labs., Inc., Temple Hills, Md. (1985). (NTIS Nos. PB85-215192/WEP and PB85-215200/WEP).
135. Nikunen, E., "Toxic Impact of Effluents from Petrochemical Industry." *Ecotoxicol. Environ. Safety,* **9,** 84 (1985).
136. Nestmann, E. R., and Lee, E. G.-H., "Genetic Activity in *Saccharomyces cerevisiae* of Compounds Found in Effluents of Pulp and Paper Mills." *Mutation Res.*, **155,** 53 (1985).
137. Kringstad, K. P., *et al.*, "Studies on the Chlorination of Chlorolignins and Humic Acid." *Environ. Sci. Technol.*, **19,** 427 (1985).
138. Sayler, G. S., *et al.*, "Enhanced Reuse Potential of Coal Slurry Transport Water: Toxic Organics Assessment and Removal (Phase 2)." RR-106, UT/PUB-R01-1034-75-001-85, Tennessee Water Resources Research Center, Knoxville, Tenn. (1984).
139. Stetter, J. R., *et al.*, "Chemical and Toxicological Studies of Coal Gasification Wastewater Circulated Through a Cooling Tower." DOE/MC/49533-1698, ANL/SER-3, Argonne National Lab., Ill. (1984).
140. Natl. Tech. Inf. Serv., "Pulp and Paper Mill Effluents: Toxicity to Humans, 1976–July, 1984 (Citations from the Paper and Board, Printing, and Packaging Industries Research Associations Data Base)." NTIS, Springfield, Va. (1984).
141. DePass, L. R., *et al.*, "Aldicarb Sulfoxide/Aldicarb Sulfone Mixture in Drinking Water of Rats: Effects on Growth and Acetylcholinesterase Activity." *J. Toxicol. Environ. Health,* **16,** 163 (1985).
142. Suzuki, J., *et al.*, "Formation of Mutagens by Photolysis of Amino Acids in Neutral Aqueous Solution Containing Nitrite or Nitrate Ion." *Chemosphere,* **14,** 493 (1985).
143. Shahin, M. M., *et al.*, "Comparisons of Mutation Induction by Six Monocyclic Aromatic Amines in *Salmonella typhimurium* Tester Strains TA97, TA1537, and TA1538." *Environ. Mutagenesis,* **7,** 535 (1985).
144. Dean, B. J., "Recent Findings on the Genetic Toxicology of Benzene, Toluene, Xylenes, and Phenols." *Mutation Res.*, **154,** 153 (1985).
145. Hendricks, J. D., *et al.*, "Hepatocarcinogenicity of Benzo(a)pyrene to Rainbow Trout by Dietary Exposure and Intraperitoneal Injection." *J. Natl. Cancer Inst.*, **74,** 839 (1985).
146. Selkirk, J. K., *et al.*, "Role of Metabolism in Benzo(a)pyrene Carcinogenesis." CONF-8506137-13, Oak Ridge National Laboratory, Oak Ridge, Tenn. (1985).
147. Josephy, P. D., *et al.*, "Inhibition of Benzidine Mutagenesis by Nucleophiles: A Study Using the Ames Test with Hamster Hepatic S9 Activation." *Mutation Res.*, **143,** 5 (1985).
148. Derosa, C. T., *et al.*, "Health Assessment Document for Carbon Tetrachloride." EPA-600/8-82-001F, U. S. EPA, Cincinnati, Ohio (1984).
149. Peirano, W. B., "Health Assessment Document for Chlorinated Benzenes." EPA-600/8-84-015F, U. S. EPA, Cincinnati, Ohio (1985).

150. Borzelleca, J. F., *et al.*, "Toxicological Evaluation of Selected Chlorinated Phenols." EPA-600/D-84-234, U. S. EPA, Cincinnati, Ohio (1984).
151. Tarkpea, M., *et al.*, "Mutagenicity, Acute Toxicity, and Bioaccumulation Potential of Six Chlorinated Styrenes." *Bull. Environ. Contam. Toxicol.*, **35,** 525 (1985).
152. Smith, C. C., *et al.*, "Investigation of the Metabolism of Chlorinated Hydrocarbons in Subhuman Species." EPA-600/1-85-001, U. S. EPA, Research Triangle Park, N. C. (1985).
153. Distlerath, L. M., *et al.*, "Metabolic Activation of 3-(2-Chloroethoxy)-1,2-Dichloropropene: A Mutagen Structurally Related to Diallate, Triallate, and Sulfallate." *Environ. Mutagenesis,* **7,** 303 (1985).
154. Tamasonis, C. F., *et al.*, "Lifetime Toxicity of Chloroform and Bromodichloromethane when Administered Over a Lifetime in Rats." *Ecotoxicol. Environ. Safety,* **9,** 233 (1985).
155. Hattula, M.-L., and Knuutinen, J., "Mutagenesis of Mammalian Cells in Culture by Chlorophenols, Chlorocatechols, and Chloroguaiacols." *Chemosphere,* **14,** 1617 (1985).
156. U. S. Environ. Prot. Agency "Health Assessment Document for Epichlorohydrin." EPA-600/8-83-032F, U. S. EPA, Research Triangle Park, N. C. (1984).
157. Natl. Tech. Inf. Service, "Formaldehyde. June 1976–July 1985 (Citations from the Energy Data Base)." NTIS, Springfield, Va. (1985).
158. Condie, L. W., "Target Organ Toxicology of Halocarbons Commonly Found Contaminating Drinking Water." EPA-600/D-85-172, U. S. EPA, Cincinnati, Ohio (1985).
159. Kopfler, F. C., *et al.*, "Reactions of Chlorine in Drinking Water, With Humic Acids and 'In Vivo.'" EPA-600/D-84-196, U. S. EPA, Cincinnati, Ohio (1984).
160. Condie, L. W., and Bercz, J. P., "Target Organ Effects of Disinfectants and Their By-Products." EPA-600/D-85-025, U. S. EPA, Research Triangle Park, N. C. (1985).
161. Condie, L. W., *et al.*, "Subchronic Toxicology of Humic Acid Following Chlorination in the Rat." *J. Toxicol. Environ. Health,* **15,** 305 (1985).
162. Meier, J. R., *et al.*, "Identification of Mutagenic Compounds Formed During Chlorination of Humic Acid." *Mutation Res.,* **157,** 111 (1985).
163. Bayard, S., *et al.*, "Health Assessment Document for Dichloromethane (Methylene Chloride). Final Report." EPA-600/8-82-004F, U. S. EPA, Research Triangle Park, N. C. (1985).
164. Natl. Inst. for Occupational Safety and Health, "Current Intelligence Bulletin 43: Monohalomethanes (Methyl Chloride CH_3Cl, Methyl Bromide CH_3Br, Methyl Iodide, CH_3I)." DHHS/PUB/NIOSH-84-117, Natl. Inst. for Occupational Safety and Health, Cincinnati, Ohio (1984).
165. Pai, V., *et al.*, "Mutagenicity of N-hydroxylamines and N-hydroxycarbamates towards Strains of *Escherichia coli* and *Salmonella typhimurium.*" *Mutation Res.,* **151,** 201 (1985).
166. Fu, P. P., *et al.*, "The Orientation of the Nitro Substituent Predicts the Direct-Acting Bacterial Mutagenicity of Nitrated Polycyclic Aromatic Hydrocarbons." *Mutation Res.,* **143,** 173 (1985).
167. White, G. L., *et al.*, "Effect of Nitro Substitution on the Light-Mediated Mutagenicity of Polycyclic Aromatic Hydrocarbons in *Salmonella typhimurium* TA98." *Mutation Res.,* **144,** 1 (1985).
168. Loprieno, N., *et al.*, "Increased Mutagenicity of Chromium Compounds by Nitriloacetic Acid." *Environ. Mutagenesis,* **7,** 185 (1985).
169. Montaldi, A., *et al.*, "Interaction of Nitrictriacetic Acid with Heavy Metals in the Induction of Sister Chromatid Exchanges in Cultured Mammalian Cells." *Environ. Mutagenesis,* **7,** 381 (1985).
170. Koonanuwatchaidet, P., "N-Nitroso Compounds: Environmental Carcinogens." *J. Sci. Soc. Thailand,* **10,** 207 (1984).
171. Agarwal, D. K., *et al.*, "Mutagenicity Evaluation of Phthalic Acid Esters and Metabolites in *Salmonella typhimurium* Cultures." *J. Toxicol. Environ. Health,* **16,** 61 (1985).
172. Sakai, M., *et al.*, "Mutagenicity of Polycyclic Aromatic Hydrocarbons and Quinones on *Salmonella typhimurium* TA97." *Mutation Res.,* **156,** 61 (1985).
173. Matijašević, Z., and Zeiger, E., "Mutagenicity of Pyrene in Salmonella." *Mutation Res.,* **142,** 149 (1985).
174. Mochida, K., and Saito, K., "Toxicity Assessment of Tetrachloroethylene, Trichloroethylene, and 1,1,1-trichloroethane Using Human and Monkey Cells." *Bull. Environ. Contam. Toxicol.,* **35,** 593 (1985).
175. Witte, I., *et al.*, "DNA-damaging Properties and Cytotoxicity in Human Fibroblasts of Tetrachlorohydroquinone, A Pentachlorophenol Metabolite." *Mutation Res.,* **145,** 71 (1985).
176. D'Souza, R. W., *et al.*, "Oral and Intravenous Trichloroethylene Pharmokinetics in the Rat." *J. Toxicol. Environ. Health,* **15,** 587 (1985).
177. Kimbrough, R. D., *et al.*, "Trichloroethylene: An Update." *J. Toxicol. Environ. Health,* **15,** 369 (1985).
178. Crebelli, R., *et al.*, "Mutagenicity of Trichloroethylene, Trichloroethanol, and Chloral Hydrate in *Aspergillus nidulans.*" *Mutation Res.,* **155,** 105 (1985).
179. Fishbein, L., "An Overview of Environmental and Toxicological Aspects of Aromatic Hydrocarbons. II. Toluene." *Sci. Total Environ.,* **42,** 267 (1985).
180. Lambert, B., *et al.*, "DNA Cross-links in Human Leucocytes Treated with Vinyl Acetate and Acetaldehyde in Vitro." *Mutation Res.,* **146,** 301 (1985).
181. Belton, J. C., and Benson, N. C., "Growth Inhibitory and Cytotoxic Effects of Three Arsenic Compounds on Cultured Chinese Hamster Ovary Cells." *J. Environ. Sci. Health,* **A20,** 37 (1985).
182. Natl. Tech. Inf. Serv., "Toxicity of Arsenic. July 1984–June 1985 (Citations from the Energy Data Base)." NTIS, Springfield, Va. (1985).
183. Jacobson-Kram, D., and Montalbano, D., "The Reproductive Effects Assessment Group's Report on the Mutagenicity of Inorganic Arsenic." *Environ. Mutagenesis,* **7,** 787 (1985).
184. Elias, R., *et al.*, "Health Assessment Document for Beryllium. Review Draft." EPA-600/8-84-026A, U. S. EPA, Research Triangle Park, N. C. (1984).
185. Natl. Tech. Inf. Serv., "Cadmium Pollution. November 1980–April 1983 (Citations from the NTIS Data Base)." NTIS, Springfield, Va. (1985).
186. Natl. Tech. Inf. Serv., "Cadmium Pollution. May 1983–May 1985 (Citations from the NTIS Data Base)." NTIS, Springfield, Va. (1985).
187. Anderson, L. D., *et al.*, "Updated Mutagenicity and Carcinogenicity Assessment of Cadmium: Addendum to the Health Assessment Document for Cadmium (May 1981)." EPA-600/8-81-023, U. S. EPA, Washington, D. C. (1984).
188. Vredevoe, D., *et al.*, "Recovery of the Murine Mononuclear Phagocytic System Following Chronic Exposure to Cadmium." *Environ. Res.,* **37,** 373 (1985).
189. Langerwerf, J. S. A., *et al.*, "A Comparison of the Mutagenicity of Soluble Trivalent Chromium Compounds with That of Potassium Chromate." *Ecotoxicol. Environ. Safety,* **9,** 92 (1985).
190. Thomson, E. J., *et al.*, "The Effect of Fluoride on Chromosome Aberration and Sister-Chromatid Exchange Frequencies in Cultured Human Lymphocytes." *Mutation Res.,* **144,** 89 (1985).
191. Daston, G. P., *et al.*, "Toxicity of Sodium Fluoride to the Postnatally Developing Rat Kidney." *Environ. Res.,* **37,** 461 (1985).
192. Clarkson, T., *et al.*, "Mercury Health Effects Update: Health

Issue Assessment." EPA-600/8-84-019F, U. S. EPA, Research Triangle Park, N. C. (1984).
193. Babich, H., *et al.*, "The Mediation of Mutagenicity and Clastogenicity of Heavy Metals by Physicochemical Factors." *Environ. Res.*, **37**, 253 (1985).
194. Arlauskas, A., *et al.*, "Mutagenicity of Metal Ions in Bacteria." *Environ. Res.*, **36**, 379 (1985).
195. Marzin, D. R., and Phi, H. V., "Study of the Mutagenicity of Metal Derivatives with *Salmonella typhimurium* TA102." *Mutation Res.*, **155**, 49 (1985).
196. Kharab, P., and Singh, I., "Genotoxic Effects of Potassium Dichromate, Sodium Arsenite, Cobalt Chloride and Lead Nitrate in Diploid Yeast." *Mutation Res.*, **155**, 117 (1985).
197. Natl. Tech. Inf. Serv., "Toxicity of Nickel. 1970–June 1985 (Citations from the NTIS Data Base)." NTIS, Springfield, Va. (1985).
198. Luca, D., *et al.*, "Chromosomal Aberrations and Micronuclei Induced in Rat and Mouse Bone Marrow Cells by Sodium Nitrate." *Mutation Res.*, **155**, 121 (1985).
199. Shamberger, R. J., "The Genotoxicity of Selenium." *Mutation Res.*, **154**, 29 (1985).
200. Zeiger, E., *et al.*, "Strategies to Reduce the Cost of Mutagenicity Screening with the *Salmonella* Assay." *Environ. Mutagenesis*, **7**, 901 (1985).
201. Nemchin, R. G., and Brusick, D. J., "Basic Principles of Laboratory Safety." *Environ. Mutagenesis*, **7**, 947 (1985).
202. Inmon, J., *et al.*, "Design of a Limited-Access Facility and Safety Program for a Genetic Toxicology Laboratory." *Am. Ind. Hyg. Assoc. J.*, **46**, 303 (1985).
203. "Quality Assurance for Environmental Measurements." J. K. Taylor and T. W. Stanley (Eds.). STP 867, ASTM, Philadelphia, Pa. (1985).
204. Dunkel, V. C., *et al.*, "Reproducibility of Microbial Mutagenicity Assays: II. Testing of Carcinogens and Noncarcinogens in *Salmonella typhimurium* and *Escherichia coli*." *Environ. Mutagenesis*, **7**, Supplement 5, 1 (1985).
205. Nestmann, E. R., *et al.*, "Solvent Interactions with Test Compounds and Recommendations for Testing to Avoid Artifacts." *Environ. Mutagenesis*, **7**, 163 (1985).
206. Tilly, W. G., "Dead Cells Don't Form Mutant Colonies: A Serious Source of Bias in Mutation Assays." *Environ. Mutagenesis*, **7**, 225 (1985).
207. Carnes, B. A., *et al.*, "A Quantitative Comparison of a Percentile Rule with a 2-Fold Rule for Assessing Mutagenicity in the Ames Assay." *Mutation Res.*, **147**, 15 (1985).
208. van de Kerlehoff, J. F. J., and van der Gaag, M. A., "Some Factors Affecting Optimal Differential Staining of Sister-Chromatids in vivo in the Fish *Nothobranchius rachowi*." *Mutation Res.*, **143**, 39 (1985).
209. Gollapudi, B. B., *et al.*, "The Role of Feeding Rejection in Drosophila Mutation Assays." *Mutation Res.*, **144**, 13 (1985).
210. Pagano, D. A., and Zeiger, E., "The Stability of Mutagenic Chemicals Stored in Solution." *Environ. Mutagenesis*, **7**, 293 (1985).
211. McCoy, E. C., *et al.*, "Mutagenicity of Nitropyrenes for *Escherichia coli:* Requirement for Increased Cellular Permeability." *Mutation Res.*, **142**, 163 (1985).
212. Mannironi, C., *et al.*, "Studies of the Optimal Temperature for the Liver Microsomal Assay with Mice S9 Fractions." *Mutation Res.*, **147**, 231 (1985).
213. Popkin, D. J., and Prival, M. J., "Effects of pH on Weak and Positive Control Mutagens in the Ames Salmonella Plate Assay." *Mutation Res.*, **142**, 109 (1985).
214. Gutierrez, C., *et al.*, "BrdUrd-dependent Sister-Chromatid Exchanges are Increased at High Oxygen Tension." *Mutation Res.*, **142**, 213 (1985).
215. Beaume, P., *et al.*, "The Salmonella/Mammalian Microsome Mutagenicity Test: Comparison of Human and Rat Livers as Activating Systems." *Mutation Res.*, **156**, 139 (1985).
216. Milling, D. M., and Maddock, M. B., "Activation of Polycyclic Aromatic Hydrocarbons by Hepatic S-9 from a Marine Fish." *Bull. Environ. Contam. Toxicol.*, **35**, 301 (1985).

Detection and occurrence of waterborne viruses

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OCCURRENCE AND DISTRIBUTION OF VIRUSES

Vasconcelos and Anthony[1] attempted to isolate enteric viruses from both marine and fresh waters in the Seattle area. They were unable to detect any viruses, but indicated that the work of others suggests that viral infections can be acquired through contact with recreational waters. Lucena *et al.*[2] conducted a similar type of study in Barcelona. Enteric viruses were isolated from wastewater effluent samples, two rivers, and the water at two beaches. Polioviruses were detected in all types of the water samples.

Akin[3] reported that the U. S. experience has indicated that properly treated drinking waters do not contain viruses. In support of this statement Akin mentioned that no viruses were found in a survey of 54 water supplies in the U. S. or in two other, extensively studied, water systems. However, the results of Keswick *et al.*[4] indicated that the matter of viruses in potable waters is a viable concern. Keswick and his co-workers detected rotavirus in 3 of 26 finished water samples. Guttman-Bass and Fattal[5] studied the quality of drinking water in 30 rural settlements in Israel. Of 111 samples tested, three were positive for viruses. Viruses were also detected by Slade[6] in chalk well water. The chalk aquifer is an important source of water for southern and eastern England.

Krikelis *et al.*[7] found enteroviruses and adenoviruses in urban wastewater effluents of Athens, Greece. Williams[8] reported that it should not be surprising to isolate complexes of rotaviruses in fecally contaminated water because he detected viral aggregates or complexes in stool specimens. The complexes were associated with membranes, a behavior which has also been noted for parvovirus-like particles. Rotaviruses were also isolated from stool specimens by Shusheng *et al.*[9]

VIRUS DETECTION

Guttman-Bass *et al.*[10] studied the effectiveness of several types of positively and negatively charged filters for concentrating poliovirus from Jerusalem tap water. The authors reported that optimal percent recovery efficiencies were in the area of 90% for Balston and Cox filters. Shields *et al.*[11] experimented with a two-step filtration procedure to concentrate