IN VITRO TOXICITY TESTING OF ENVIRONMENTAL AGENTS

Current and Future Possibilities

Part B: Development of Risk Assessment Guidelines

Alan R. Kolber
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Lester D. Grant
Robert S. DeWoskin
and
Thomas J. Hughes

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PREFACE

These two volumes contain the papers presented at a North Atlantic Treaty Organization (NATO) Advanced Study Institute held on September 22-28, 1979 in Monte Carlo, Monaco. The conference was entitled "In Vitro Toxicity Testing of Environmental Agents: Current and Future Possibilities." This international conference presented an apportunity for the participants to exchange information and ideas on the current approaches (both scientific and political) for toxic assessment of environmental agents. The potential health effects of these compounds as well as future needs in the environmental research field were discussed.

The scientific content of the conference seminars included anoverview of the various cellular, subcellular, organ, animal, and genetic systems which have been used to assess the health effects of environmental agents. The scientific principles behind short-term assays and an evaluation of their applicability to health effects monitoring and analysis were investigated. Included among major topics were: (1) the biochemistry and pharmacology of selected environmental agents; (2) molecular mechanisms of carcinogenesis, mutagenesis, and transformation; (3) bacterial mutagenesis and toxicity; (4) mammalian cell mutagenesis, toxicity, and transformation; (5) in vitro carcinogens and mutagens; (6) teratogenic and other developmental toxic effects; and (7) the development of short-term neuro-behavioral toxicity assays.

The symposium specifically discussed the following scientific areas: the role of the R plasmid in the Ames/Salmonella assay; the development of new assay systems in Bacillus, E. coli, Protozoa, nematodes, maize, Tradescantia, and Drosophila; the role of mammalian cell culture lines in the detection of mutagens/carcinogens and in the elucidation of the mechanisms of mutagenesis, carcinogenesis, and transformation; the development of new short-term bioassays to detect neurotoxic and behavioral effects; the mechanisms of heavy metal toxicity on nerve tissue; the metabolism of polynuclear aromatic hydrocarbons; the toxicity of environmental mixtures (air pollutants, PCB's, coal gasification effluents, and food dyes) the mechanisms and effects of teratogens; validation of test systems and test batteries; statistical anal-

ysis of carcinogenic potency; epidemiology; and the discussion of established international environmental risk assessment programs.

The risk assessment sessions covered a broad spectrum of topics, ranging from the application of bioassay screening batteries for toxic assessment of environmental agents, to the utility of interspecies extrapolations, to discussions on the establishment of regulatory criteria and standards. A public policy session examined the interactions among energy resources, population, and the environment, and the roles played by scientists, engineers, and policymakers in monitoring and estimating the potential health effects of toxic substances in the environment. The purpose of the final session was to contribute to an improved understanding of how scientific knowledge can be utilized to formulate national and international environmental policies.

These symposium proceedings are divided into two volumes: Part A is a survey of test systems, and Part B is a survey of the development of risk assessment guidelines (see Table of Contents). It is hoped that the papers presented within these volumes will aid in the development of valid research procedures and reasonable regulatory policies for protection of our health and our environment.

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The Editors

Research Triangle Park,
North Carolina, USA
May 1982

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The Conference Organizing Committee that planned this successful NATO Advanced Study Institute consisted of the following members:

- Dr. Alan R. Kolber, Chairman Research Triangle Institute (RTI) Research Triangle Park, North Carolina, USA
- Dr. Thomas K. Wong
 Research Triangle Institute (RTI)
 (now with the National Institute of Environmental Health
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- Dr. John McLachlen
 National Institute of Environmental Health Sciences
 (NIEHS)
 Research Triangle Park, North Carolina, USA

It is also a pleasure to acknowledge the assistance of a number of people who were involved with various phases of this conference and the preparation of the resultant proceedings. These people included Ms. Susanne Moulton, Ms. Mary Beth Wilkie, and Mr. Eric Von Hofe, and Mr. Thomas J. Hughes, who assisted with the conference organization and activities at the Monte Carlo site; and Mr. Hu Burnett who was responsible for the mechanical editing of the manuscripts and production of the camera-ready masters.

The able assistance of numerous technical and administrative staff members of the Research Triangle Institute during the preparative and the editing phases of this NATO conference is also gratefully acknowledged.

The assistance, hospitality and courtesies extended by Princess Grace, Prince Ranier and the Principality of Monaco made the symposium a success and a pleasure to attend. The editors of these proceedings would finally like to thank the authors and participants. Their enthusiasm, scientific expertise, and hard work made the successful completion of these NATO symposium proceedings possible.

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- North Atlantic Treaty Organization
- National Institute of Environmental Health Sciences (USA)
- Environmental Protection Agency (USA)
- Fogerty International Center of the National Cancer Institute (USA)

DISCLAIMER

Research findings and their interpretation, as presented in these proceedings, represent the views of the individual research scientists/authors listed for each paper and should <u>not</u> be construed as representing official views or policies of any of the sponsoring organizations.

In Vitro Toxicity Testing Environmental Agents: urrent and Future Possibilities September 22-29, 1979. Monaco

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IN MEMORIAM

Alan Raymond Kolber (1939-1981)

Dr. Alan R. Kolber died on June 7, 1981, from injuries sustained in a single-engine airplane accident. He was both chairman of the Organizing Committee for this NATO Advance Research Institute and an editor for the resultant proceedings. His unique personality, his biting wit, and his keen intellect will be missed.

S ...

ABBREVIATIONS

Abbreviations for the District of Columbia and the 50 States of the United States of America (USA) appear in some tables and illustrations that are included in these proceedings volumes.

The two-letter U.S. Postal Service abbreviation is listed in front of the State name, and the approved/preferred text-form abbreviation (if any) follows the name.

	AL	Alabama	Ala.	MO	Missouri	Mo.
	AK	Alaska		MT	Montana	Mont.
	ÁZ	Arizona	Ariz.	NE	Nebraska	Nebr.
	AR	Arkansas	Ark.	NV	Nevada	Nev.
	CA	California	Calif.	NH	New Hampshire	N.H.
	CO	Colorado	Colo.	NJ	New Jersey	N.J.
	CT	Connecticut	Conn.	NM	New Mexico	N. Mex.
	DE	Delaware	Del.	NY	New York	N.Y.
	DC	District of	D.C.	NC	North Carolina	N.C.
		Columbia		ND	North Dakota	N. Dak.
ń	FL	Florida	Fla.	OH	Ohio	
	GA	Georgia	Ga.	OK	Oklahoma	Okla.
	HI	Hawaii		OR	Oregon	Oreg.
	ID	Idaho		PA	Pennsylvania	Pa.
	IL	Illinois	I11.	RI	Rhode Island	R.I.
	IN	Indiana	Ind.	SC	South Carolina	S.C.
	IA	Iowa		SD	South Dakota	S.D.
	KS	Kansas	Kans.	TN	Tennessee	Tenn.
	KY	Kentucky	Ky.	TX	Texas	Tex.
	LA	Louisiana	La.	UT	Utah	
	ME	Maine		VT	Vermont	Vt.
	MD	Maryland	Md.	VA	Virginia	Va.
	MA	Massachusetts	Mass.	WA	Washington	Wash.
	MI	Michigan	Mich.	WV	West Virginia	W. Va.
	MN	Minnesota	Minn.	WI	Wisconsin	Wis.
	MS	Mississippi	Miss.	WY	Wyoming	Wyo.
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