



Chemistry Assistance Manual for Premanufacture Notification Submitters

TABLE OF CONTENTS

PREFACE	1
LIST OF TABLES	3
LIST OF FIGURES	4
THE PREMANUFACTURE NOTIFICATION (PMN) REVIEW PROCESS	5
1.1 Introduction	5
1.2 The PMN Review Process	6
1.2.1 Receipt of the PMN	11
1.3 Chemistry Review Phase	12
1.3.1 Initial Chemistry Review	13
1.3.2 Inventory Review	15
1.3.3 Preparation of the Chemistry Report	16
1.3.4 Chemical Review and Search Strategy (CRSS) Meeting	24
1.4 Hazard Evaluation	27
1.4.1 Human and Ecological Hazard Identification	27
1.4.2 Environmental Fate	31
1.4.3 Structure-Activity Team Meeting	32
1.5 Exposure Evaluation	33
1.6 Risk Assessment/Risk Management Phase	35
1.6.1 Focus Meeting	35
1.6.2 Standard Review	38
References for Chapter 1	40
List of Selected Readings for Chapter 1	42
CHEMICAL INFORMATION NEEDED FOR RISK ASSESSMENT	44
2.1 Introduction	44
2.2 Important Chemical Information	45
2.2.1 Melting Point	45
2.2.2 Octanol/Water Partition Coefficient (K_{ow} , P)	49
2.2.3 Water Solubility	59
2.2.4 Soil/Sediment Adsorption Coefficient	62
2.2.5 Henry's Law Constant	63
2.2.6 Boiling Point	65
2.2.7 Vapor Pressure	66
2.2.8 Reactivity	68
2.2.9 Hydrolysis	69
2.2.10 Spectral Data	70
2.2.11 Photolysis (Direct/Indirect)	70
2.2.12 Other Chemical Information	72
2.3 Use of Chemical Information in Assessment of PMN Chemicals	74
2.4 How EPA Obtains Physicochemical Information	74
2.4.1 General Approach	74

2.4.2	Methods of Searching for Measured Physicochemical Properties	78
2.4.3	Methods For Estimating Physicochemical Properties From Structural Analogs	80
2.4.4	Methods For Estimating Physicochemical Properties Using Computer Estimation Programs ..	81
	References for Chapter 2	83
	List of Selected Readings for Chapter 2	90
 POLLUTION PREVENTION AND PREMANUFACTURE NOTIFICATIONS		95
3.1	Introduction: Pollution Prevention	95
3.2	Pollution Prevention Initiatives within EPA's PMN Program	97
3.2.1	Optional Pollution Prevention Information (page 11 of the PMN form)	97
3.2.2	Synthetic Method Assessment for Reduction Techniques (SMART) Review	98
3.3	Considerations in Implementing Pollution Prevention Practices Prior to Submission of PMN Substances	100
	References for Chapter 3	103
	List of Selected Readings for Chapter 3	104
 THE TOXIC SUBSTANCES CONTROL ACT: HISTORY AND IMPLEMENTATION		105
A.1	Introduction	105
A.2	The Premanufacture Provisions of TSCA	108
A.2.1	Definition of "Chemical Substance" Under TSCA	109
A.2.2	Definition of "New" Chemical Substance	109
A.2.3	Section 5: Manufacturing and Processing Notices	109
A.2.4	Other Sections of TSCA Related to Section 5	112
A.2.4.1	Section 4. Testing of Chemical Substances and Mixtures	112
A.2.4.2	Section 6. Regulation of Hazardous Chemical Substances and Mixtures	112
A.2.4.3	Section 7. Imminent Hazards	113
A.2.4.4	Section 8. Reporting and Retention of Information	113
A.2.4.5	Section 12. Exports	113
A.2.4.6	Section 13. Entry into Customs Territory of the United States	113
A.2.4.7	Section 14. Disclosure of Data	114
A.3	Implementation of TSCA	114
A.3.1	The TSCA Inventory	114
A.3.2	Inventory Update Rule	116
A.3.3	Premanufacture Notification Rule and Form	116
A.3.4	Biotechnology	117
A.3.5	Exemptions	117
A.3.5.1	Test Market Exemptions	117
A.3.5.2	5(h)(3) Exemption for Research and Development	118
A.3.5.3	5(h)(4) Exemptions	118
A.3.5.4	Instant Film Exemption	118
A.3.5.5	Low Volume Exemption	118
A.3.5.6	Low Release and Exposure Exemption	119
A.3.5.7	Polymer Exemption	119
A.3.6	TSCA Section 5(e) Consent Orders and Significant New Use Rules	120
A.3.7	Polymers: The Two Percent Rule	121

A.3.8 Importing Chemical Substances	121
A.3.9 Addendum to Appendix: Inventory Reporting Regulations	121
References for Appendix	124
List of Selected Readings for Appendix	129
Index	132

PREFACE

Since the passage of the Toxic Substances Control Act (TSCA) in 1976, the Environmental Protection Agency (EPA) has received and reviewed nearly 30,000 Premanufacture Notifications (PMNs) for new chemical substances. During this period, the Agency has developed both a review process to estimate the risk attributable to a new chemical substance and a decision process to determine whether an unreasonable risk may occur if the substance is commercialized.

The information included in the PMN submissions constitutes the basis of the Agency's risk assessments. Careful consideration is given to all submitted physicochemical, environmental, and health-related data. If the PMN does not contain chemical properties or other information needed for assessment, the Agency scientists often must estimate the missing values. This leads to less accurate risk assessments than might be desirable, and may lead to regulation of substances that would not have been regulated if data had been available.

The purpose of this book is to assist submitters in the technical aspects of PMN preparation. EPA's hope is that, with this information, submitters will be able to develop more physicochemical property data and other technical information for their new substances so that the Agency's ability to perform accurate risk assessments will increase. Chapter 1 provides a discussion of the PMN review process, emphasizing its scientific aspects. Chapter 2, the heart of the book, reviews the most important physicochemical properties, including methods for measurement and estimation, and describes how EPA uses these properties to assess the risks of PMN substances. Chapter 3 discusses the Agency's pollution prevention program as it relates to the PMN program, emphasizing factors that submitters should consider in the development of new chemical substances and in their preparation of PMNs. Both references and a list

of selected reading materials containing additional information are included at the end of each chapter. Also included is an Appendix, which provides an historical overview of the factors and events leading to the passage of TSCA, a summary of the premanufacture provisions of TSCA, and a review of the Agency's implementation of TSCA.

This book is intended primarily for people in the chemical industry who are involved with the design and development of new chemical substances, and the submission of PMNs. This book is also intended for a broader audience of other individuals such as technical managers, risk assessors, and risk managers who are involved with evaluating chemical substances for potential risks. We feel that the information contained in this book will help these individuals make better risk assessment and risk management decisions.

Stephen C. DeVito, Ph.D.
Carol A. Farris, Ph.D.

Exposure, Economics, and Technology Division
Office of Pollution Prevention and Toxics U.S.
Environmental Protection Agency
Washington, DC 20460

Acknowledgment

The authors gratefully acknowledge the support and encouragement of our many EPA colleagues who rigorously reviewed this book or provided helpful comments or assistance during its preparation:

Frank S. Amato
(Eastman Kodak Company,
Rochester, NY)
Kent E. Anapolle, Ph.D.
Paul T. Anastas, Ph.D.
Charles M. Auer
Robert S. Boethling, Ph.D.
Anna C. Coutlakis
Mary E. Cushmac, Ph.D.
Gregory L. Fritz, Ph.D.
Roger L. Garrett, Ph.D.
Steven M. Hassur, Ph.D.
Carol L. Hetfield
Rebecca A. Jones
Leonard Keifer, Ph.D.
Raymond J. Kent, Ph.D.
Doyoung Lee, Ph.D.
Robert J. Lenahan.
C-T. Daniel Lin, Ph.D.
Robert L. Lipnick, Ph.D.
Gregory J. Macek
Nhan T. Nguyen
Breeda M. Reilly
William A. Silagi
Jay Tunkel, Ph.D.
(Syracuse Research Corporation,
Syracuse, NY)
Caroline D. Weeks, Ph.D.
Tracy C. Williamson, Ph.D.
Maurice G. Zeeman, Ph.D.

Disclaimer

This publication has been reviewed and approved for publication as an EPA document. Mention of trade names, commercial products, or computer programs does not constitute Agency endorsement or recommendation for use.

LIST OF TABLES

Table 1-1	Types of Submissions and Their Designators	7
Table 1-2	Acronym List: Organizational and Meeting Acronyms	8
Table 1-3	Test Data Submitted with PMNs (1979-1985)	10
Table 1-4	Technical Problems Frequently Encountered in PMN Submissions	17-21
Table 1-5	Notations Used for CRSS Meeting Notes	26
Table 1-6	The Role of Pharmacokinetics in Predicting Health Hazards	30
Table 1-7	Possible Outcomes of Focus Meeting	37
Table 2-1	Methods of Measuring Octanol/Water Partition Coefficient (K_{ow})	54
Table 2-2	Methods of Estimating Octanol/Water Partition Coefficient (K_{ow})	56
Table A-1	Sources of Office of Pollution Prevention and Toxics Information	131

LIST OF FIGURES

Figure 1-1	Office of Pollution Prevention and Toxics New Chemical (PMN) Review Process	9
Figure 2-1	Important Physicochemical Properties, Their Interrelationships, and Their Uses in Risk Assessment	46
Figure 2-2	Use of Octanol-Water Partition Coefficient (Log K_{ow}) in Risk Assessment	51
Figure 2-3	Methods for Obtaining Measured Physicochemical Property Values on Exact Structures	75-76
Figure 2-4	Methods for Identifying Analogs of PMN Substances and Their Physicochemical Properties	77