



SIXTH EDITION

# PATTY'S TOXICOLOGY

VOLUME 3

EDITED BY  
EULA BINGHAM  
BARBARA COHRSEN

 WILEY

# PATTY'S TOXICOLOGY

---

**Sixth Edition**

**Volume 3**

**EULA BINGHAM**  
**BARBARA COHRSEN**

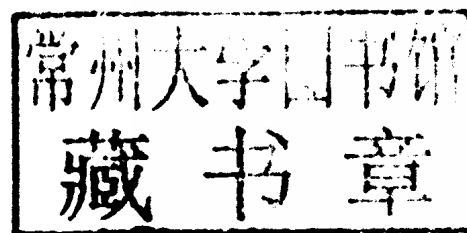
Editors

## CONTRIBUTORS

Fiorella Belpoggi  
C. Bevan  
Michael T. Borchers  
James S. Bus  
D. Chiozzotto  
Gunnar Johanson

M. Lauriola  
A. Philip Leber  
Myron A. Mehlman  
Custodio V. Muianga  
Debdas Mukerjee  
John L. O'Donoghue

Shane Que Hee  
Jon B. Reid  
Patricia Ruiz  
George M. Rusch  
Maria Szilagyi



 **WILEY**

A JOHN WILEY & SONS, INC., PUBLICATION

Copyright © 2012 by John Wiley & Sons, Inc. All rights reserved

Published by John Wiley & Sons, Inc., Hoboken, New Jersey

Published simultaneously in Canada

No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning, or otherwise, except as permitted under Section 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher, or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400, fax (978) 750-4470, or on the web at [www.copyright.com](http://www.copyright.com).

Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, (201) 748-6011, fax (201) 748-6008, or online at <http://www.wiley.com/go/permission>.

**Limit of Liability/Disclaimer of Warranty:** While the publisher and author have used their best efforts in preparing this book, they make no representations or warranties with respect to the accuracy or completeness of the contents of this book and specifically disclaim any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives or written sales materials. The advice and strategies contained herein may not be suitable for your situation. You should consult with a professional where appropriate. Neither the publisher nor author shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

For general information on our other products and services or for technical support, please contact our Customer Care Department within the United States at (800) 762-2974, outside the United States at (317) 572-3993 or fax (317) 572-4002.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic formats. For more information about Wiley products, visit our web site at [www.wiley.com](http://www.wiley.com).

***Library of Congress Cataloging-in-Publication Data:***

Patty's toxicology / edited by Eula Bingham, Barbara Cohrssen.— 6th ed.

p. : cm.

Toxicology

Includes bibliographical references and indexes.

ISBN 978-0-470-41081-3 (cloth) – ISBN 978-1-118-16581-2 (v. 1) – ISBN 978-1-118-16580-5 (v. 2)

– ISBN 978-1-118-16579-9 (v. 3) – ISBN 978-1-118-16577-5 (v. 4) – ISBN 978-1-118-16578-2 (v. 5)

– ISBN 978-1-118-16576-8 (v. 6)

I. Bingham, Eula. II. Cohrssen, Barbara. III. Patty, F. A. (Frank Arthur), 1897–1981. IV. Title: Toxicology.

[DNLM: 1. Occupational Medicine. 2. Occupational Diseases. 3. Poisons. 4.

Toxicology. WA 400]

613.6'2–dc23

2012002020

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

# **PATTY'S TOXICOLOGY**

---

**Sixth Edition**

**Volume 3**

**Organic Halogenated Hydrocarbons**

**Aliphatic Carboxylic Acids**

**Ethers**

**Aldehydes**

**Ketones**

## Contributors

---

**Fiorella Belpoggi**, DBS, Cesare Maltoni Cancer Research Center, Ramazzini Institute, Italy

**C. Bevan**, Ph.D., DABT, CJB Consulting, LLC, Loveland, Ohio

**Michael T. Borchers**, Ph.D., Kettering Laboratory, University of Cincinnati, Cincinnati, Ohio

**James S. Bus**, Ph.D., DABT, Dow Chemical Co., Midland, Michigan

**D. Chiozzotto**, Ph.D., Cesare Maltoni Cancer Research Center, Ramazzini Institute, Italy

**Gunnar Johanson**, DrMedSc, Institute of Environmental Medicine (IMM), Stockholm, Sweden

**M. Lauriola**, Ph.D., Cesare Maltoni Cancer Research Center, Ramazzini Institute, Italy

**A. Philip Leber**, Ph.D., DABT, Consultant, Akron, Ohio

**Myron A. Mehlman**, Ph.D., University of Texas Medical Branch at Galveston, Princeton, New Jersey

**Custodio V. Muianga**, Ph.D., MPH, Center for Industrial Studies, Safety, and Environment, Eduardo Mondlane University, Mozambique

**Debdas Mukerjee**, Ph.D., US Environmental Protection Agency, Cincinnati, Ohio

**John L. O'Donoghue**, VMD, Ph.D., DABT, University of Rochester, Honeoye Falls, New York

**Shane Que Hee**, Ph.D., Department of Environmental Health Sciences, School of Public Health, University of California at Los Angeles, Los Angeles, California

**Jon B. Reid**, Ph.D., DABT, Kettering Laboratory, University of Cincinnati, Cincinnati, Ohio

**Patricia Ruiz**, Ph.D., Agency for Toxic Substance and Disease Registry, Atlanta, Georgia

**George M. Rusch**, Ph.D., DABT, FATS, Risk Assessment and Toxicology Services, Bridgewater, New Jersey

**Maria Szilagyi**, DABT, US Environmental Protection Agency, Washington, DC



# Preface

---

In this Preface to the Sixth Edition, we acknowledge and note that it has been built on the work of previous editors. We especially need to note that Frank Patty's words in the Preface of the second edition are cogent:

This book was planned as a ready, practical reference for persons interested in or responsible for safeguarding the health of others working with the chemical elements and compounds used in industry today. Although guidelines for selecting those chemical compounds of sufficient industrial importance for inclusion are not clearly drawn, those chemicals found in carload price lists seem to warrant first consideration.

When available information is bountiful, an attempt has been made to limit the material presented to that of a practical nature, useful in recognizing, evaluating, controlling possible harmful exposures. Where the information is scanty, every fragment of significance, whether negative or positive, is offered the reader. The manufacturing chemist, who assumes responsibility for the safe use of his product in industry and who employs a competent staff to this end, as well as the large industry having competent industrial hygiene and medical staffs, are in strategic positions to recognize early and possibly harmful exposures in time to avoid any harmful effects by appropriate and timely action. Plant studies of individuals and their exposures regardless of whether or not the conditions caused recognized ill effects offer valuable experience. Information gleaned in this manner, though it may be fragmentary, is highly important when interpreted in terms of the practical health problem.

While we have not insisted that chemical selection be based on carload quantities, we have been most concerned about agents (chemical and physical) in the workplace that are toxicological concerns for workers. We have attempted to

follow the guide as expressed by Frank Patty in 1962 regarding practical information.

This edition includes toxicological information on flavorings, metal working fluids, pharmaceuticals, and nanoparticles which were not previously covered, and reflects our concern with their technology and potential for adverse health effects in workers. It also continues to include the toxicology of physical and biological agents which were in the Fifth Edition. In the workplace of this new century, physical agents and human factors continue to be of concern as well as, nanotechnology. Traditionally, the agents or factors such as ergonomics, biorhythms, vibration, heat and cold stress were centered on how one measures them. Today, understanding the toxicology of these agents (factors) is of great importance because it can assist in the anticipation, recognition, evaluation and control of them. The mechanisms of actions and the assessment of the adverse health effects are as much a part of toxicology as dusts and heavy metals. As noted in Chapter 74 in Volume 5, the trend in toxicology is increasingly focused on molecular biology, mechanisms of action, and, molecular genetics.

The thinking and planning of this edition was a team effort by Barbara and Eula based on the framework that was established for the Fifth Edition by us and Charles H. Powell who died in September 1998. The three of us have had a long professional association with the Kettering Laboratory: Charles H. Powell received his ScD., Barbara Cohrsen received a MS, and Eula Bingham, has been a lifetime faculty member. Many of the authors were introduced to us through this relationship and association.

We are grateful for the help of our expert contributors, many of whom we have known for 10, 20 or 30 years, to complete this edition. The team effort was fostered between

the current editors by many of the first contributors to Patty's such as Robert A. Kehoe, Francis F. Heyroth, William B. Deichmann, and Joseph Treon, all of whom were at the University of Cincinnati, Kettering Laboratory, sometime during their professional lives.

The authors have performed a difficult task in a short period of time for a publication that is as comprehensive as this one is. We want to thank Meghan Lobaugh whose assistance is greatly appreciated. We would like to express

our deep appreciation and thanks to everyone who has helped us with this publication.

EULA BINGHAM, Ph.D

*Kettering Laboratory, Cincinnati Ohio*

BARBARA COHRSEN, MS

*San Francisco, California*

## USEFUL EQUIVALENTS AND CONVERSION FACTORS

1 kilometer = 0.6214 mile  
 1 meter = 3.281 feet  
 1 centimeter = 0.3937 inch  
 1 micrometer =  $1/25,4000$  inch = 40 microinches  
     = 10,000 Angstrom units  
 1 foot = 30.48 centimeters  
 1 inch = 25.40 millimeters  
 1 square kilometer = 0.3861 square mile (U.S.)  
 1 square foot = 0.0929 square meter  
 1 square inch = 6.452 square centimeters  
 1 square mile (U.S.) = 2,589,998 square meters  
     = 640 acres  
 1 acre = 43,560 square feet = 4047 square meters  
 1 cubic meter = 35.315 cubic feet  
 1 cubic centimeter = 0.0610 cubic inch  
 1 cubic foot = 28.32 liters = 0.0283 cubic meter  
     = 7.481 gallons (U.S.)  
 1 cubic inch = 16.39 cubic centimeters  
 1 U.S. gallon = 3,7853 liters = 231 cubic inches  
     = 0.13368 cubic foot  
 1 liter = 0.9081 quart (dry), 1.057 quarts  
     (U.S., liquid)  
 1 cubic foot of water = 62.43 pounds (4°C)  
 1 U.S. gallon of water = 8.345 pounds (4°C)  
 1 kilogram = 2.205 pounds

1 gram = 15.43 grains  
 1 pound = 453.59 grams  
 1 ounce (avoir.) = 28.35 grams  
 1 gram mole of a perfect gas  $\approx$  24.45 liters  
     (at 25°C and 760 mm Hg barometric pressure)  
 1 atmosphere = 14.7 pounds per square inch  
 1 foot of water pressure = 0.4335 pound per  
     square inch  
 1 inch of mercury pressure = 0.4912 pound per  
     square inch  
 1 dyne per square centimeter = 0.0021 pound per  
     square foot  
 1 gram-calorie = 0.00397 Btu  
 1 Btu = 778 foot-pounds  
 1 Btu per minute = 12.96 foot-pounds per second  
 1 hp = 0.707 Btu per second = 550 foot-pounds  
     per second  
 1 centimeter per second = 1.97 feet per minute  
     = 0.0224 mile per hour  
 1 footcandle = 1 lumen incident per square foot  
     = 10.764 lumens incident per square meter  
 1 grain per cubic foot = 2.29 grams per cubic meter  
 1 milligram per cubic meter = 0.000437 grain per  
     cubic foot

To convert degrees Celsius to degrees Fahrenheit:  $^{\circ}\text{C} (9/5) + 32 = ^{\circ}\text{F}$

To convert degrees Fahrenheit to degrees Celsius:  $(5/9) (^{\circ}\text{F} - 32) = ^{\circ}\text{C}$

For solutes in water: 1 mg/liter  $\approx$  1 ppm (by weight)

Atmospheric contamination: 1 mg/liter  $\approx$  1 oz/1000 cu ft (approx)

For gases or vapors in air at 25°C and 760 mm Hg pressure:

To convert mg/liter to ppm (by volume):  $\text{mg/liter} (24,450/\text{mol. wt.}) = \text{ppm}$

To convert ppm to mg/liter:  $\text{ppm} (\text{mol. wt.}/24,450) = \text{mg/liter}$



**CONVERSION TABLE FOR GASES AND VAPORS<sup>a</sup>**  
*(Milligrams per liter to parts per million, and vice versa;  
 25°C and 760 mm Hg barometric pressure)*

Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter
1	24,450	0.0000409	39	627	0.001595	77	318	0.00315
2	12,230	0.0000818	40	611	0.001636	78	313	0.00319
3	8,150	0.0001227	41	596	0.001677	79	309	0.00323
4	6,113	0.0001636	42	582	0.001718	80	306	0.00327
5	4,890	0.0002045	43	569	0.001759	81	302	0.00331
6	4,075	0.0002454	44	556	0.001800	82	298	0.00335
7	3,493	0.0002863	45	543	0.001840	83	295	0.00339
8	3,056	0.000327	46	532	0.001881	84	291	0.00344
9	2,717	0.000368	47	520	0.001922	85	288	0.00348
10	2,445	0.000409	48	509	0.001963	86	284	0.00352
11	2,223	0.000450	49	499	0.002004	87	281	0.00356
12	2,038	0.000491	50	489	0.002045	88	278	0.00360
13	1,881	0.000532	51	479	0.002086	89	275	0.00364
14	1,746	0.000573	52	470	0.002127	90	272	0.00368
15	1,630	0.000614	53	461	0.002168	91	269	0.00372
16	1,528	0.000654	54	453	0.002209	92	266	0.00376
17	1,438	0.000695	55	445	0.002250	93	263	0.00380
18	1,358	0.000736	56	437	0.002290	94	260	0.00384
19	1,287	0.000777	57	429	0.002331	95	257	0.00389
20	1,223	0.000818	58	422	0.002372	96	255	0.00393
21	1,164	0.000859	59	414	0.002413	97	252	0.00397
22	1,111	0.000900	60	408	0.002554	98	249.5	0.00401
23	1,063	0.000941	61	401	0.002495	99	247.0	0.00405
24	1,019	0.000982	62	394	0.00254	100	244.5	0.00409
25	978	0.001022	63	388	0.00258	101	242.1	0.00413
26	940	0.001063	64	382	0.00262	102	239.7	0.00417
27	906	0.001104	65	376	0.00266	103	237.4	0.00421
28	873	0.001145	66	370	0.00270	104	235.1	0.00425
29	843	0.001186	67	365	0.00274	105	232.9	0.00429
30	815	0.001227	68	360	0.00278	106	230.7	0.00434
31	789	0.001268	69	354	0.00282	107	228.5	0.00438
32	764	0.001309	70	349	0.00286	108	226.4	0.00442
33	741	0.001350	71	344	0.00290	109	224.3	0.00446
34	719	0.001391	72	340	0.00294	110	222.3	0.00450
35	699	0.001432	73	335	0.00299	111	220.3	0.00454
36	679	0.001472	74	330	0.00303	112	218.3	0.00458
37	661	0.001513	75	326	0.00307	113	216.4	0.00462
38	643	0.001554	76	322	0.00311	114	214.5	0.00466

# CONVERSION TABLE FOR GASES AND VAPORS (Continued)

(Milligrams per liter to parts per million, and vice versa;  
25°C and 760 mm Hg barometric pressure)

Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter
115	212.6	0.00470	153	159.8	0.00626	191	128.0	0.00781
116	210.8	0.00474	154	158.8	0.00630	192	127.3	0.00785
117	209.0	0.00479	155	157.7	0.00634	193	126.7	0.00789
118	207.2	0.00483	156	156.7	0.00638	194	126.0	0.00793
119	205.5	0.00487	157	155.7	0.00642	195	125.4	0.00798
120	203.8	0.00491	158	154.7	0.00646	196	124.7	0.00802
121	202.1	0.00495	159	153.7	0.00650	197	124.1	0.00806
122	200.4	0.00499	160	152.8	0.00654	198	123.5	0.00810
123	198.8	0.00503	161	151.9	0.00658	199	122.9	0.00814
124	197.2	0.00507	162	150.9	0.00663	200	122.3	0.00818
125	195.6	0.00511	163	150.0	0.00667	201	121.6	0.00822
126	194.0	0.00515	164	149.1	0.00671	202	121.0	0.00826
127	192.5	0.00519	165	148.2	0.00675	203	120.4	0.00830
128	191.0	0.00524	166	147.3	0.00679	204	119.9	0.00834
129	189.5	0.00528	167	146.4	0.00683	205	119.3	0.00838
130	188.1	0.00532	168	145.5	0.00687	206	118.7	0.00843
131	186.6	0.00536	169	144.7	0.00691	207	118.1	0.00847
132	185.2	0.00540	170	143.8	0.00695	208	117.5	0.00851
133	183.8	0.00544	171	143.0	0.00699	209	117.0	0.00855
134	182.5	0.00548	172	142.2	0.00703	210	116.4	0.00859
135	181.1	0.00552	173	141.3	0.00708	211	115.9	0.00863
136	179.8	0.00556	174	140.5	0.00712	212	115.3	0.00867
137	178.5	0.00560	175	139.7	0.00716	213	114.8	0.00871
138	177.2	0.00564	176	138.9	0.00720	214	114.3	0.00875
139	175.9	0.00569	177	138.1	0.00724	215	113.7	0.00879
140	174.6	0.00573	178	137.4	0.00728	216	113.2	0.00883
141	173.4	0.00577	179	136.6	0.00732	217	112.7	0.00888
142	172.2	0.00581	180	135.8	0.00736	218	112.2	0.00892
143	171.0	0.00585	181	135.1	0.00740	219	111.6	0.00896
144	169.8	0.00589	182	134.3	0.00744	220	111.1	0.00900
145	168.6	0.00593	183	133.6	0.00748	221	110.6	0.00904
146	167.5	0.00597	184	132.9	0.00753	222	110.1	0.00908
147	166.3	0.00601	185	132.2	0.00757	223	109.6	0.00912
148	165.2	0.00605	186	131.5	0.00761	224	109.2	0.00916
149	164.1	0.00609	187	130.7	0.00765	225	108.7	0.00920
150	163.0	0.00613	188	130.1	0.00769	226	108.2	0.00924
151	161.9	0.00618	189	129.4	0.00773	227	107.7	0.00928
152	160.9	0.00622	190	128.7	0.00777	228	107.2	0.00933

**CONVERSION TABLE FOR GASES AND VAPORS (Continued)**  
*(Milligrams per liter to parts per million, and vice versa;  
 25°C and 760 mm Hg barometric pressure)*

Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter
229	106.8	0.00937	253	96.6	0.01035	227	88.3	0.01133
230	106.3	0.00941	254	96.3	0.01039	278	87.9	0.01137
231	105.8	0.00945	255	95.9	0.01043	279	87.6	0.01141
232	105.4	0.00949	256	95.5	0.01047	280	87.3	0.01145
233	104.9	0.00953	257	95.1	0.01051	281	87.0	0.01149
234	104.5	0.00957	258	94.8	0.01055	282	86.7	0.01153
235	104.0	0.00961	259	94.4	0.01059	283	86.4	0.01157
236	103.6	0.00965	260	94.0	0.01063	284	86.1	0.01162
237	103.2	0.00969	261	93.7	0.01067	285	85.8	0.01166
238	102.7	0.00973	262	93.3	0.01072	286	85.5	0.01170
239	102.3	0.00978	263	93.0	0.01076	287	85.2	0.01174
240	101.9	0.00982	264	92.6	0.01080	288	84.9	0.01178
241	101.5	0.00986	265	92.3	0.01084	289	84.6	0.01182
242	101.0	0.00990	266	91.9	0.01088	290	84.3	0.01186
243	100.6	0.00994	267	91.6	0.01092	291	84.0	0.01190
244	100.2	0.00998	268	91.2	0.01096	292	83.7	0.01194
245	99.8	0.01002	269	90.9	0.01100	293	83.4	0.01198
246	99.4	0.01006	270	90.6	0.01104	294	83.2	0.01202
247	99.0	0.01010	271	90.2	0.01108	295	82.9	0.01207
248	98.6	0.01014	272	89.9	0.01112	296	82.6	0.01211
249	98.2	0.01018	273	89.6	0.01117	297	82.3	0.01215
250	97.8	0.01022	274	89.2	0.01121	298	82.0	0.01219
251	97.4	0.01027	275	88.9	0.01125	299	81.8	0.01223
252	97.0	0.01031	276	88.6	0.01129	300	81.5	0.01227

<sup>a</sup>A. C. Fieldner, S. H. Katz, and S. P. Kinney, "Gas Masks for Gases Met in Fighting Fires," *U.S. Bureau of Mines, Technical Paper No. 248*, 1921.

# **PATTY'S TOXICOLOGY**

---

**Sixth Edition**

**Volume 3**

**Organic Halogenated Hydrocarbons**

**Aliphatic Carboxylic Acids**

**Ethers**

**Aldehydes**

**Ketones**

# Contents

---

<b>40</b>	<b>Halogenated One-Carbon Compounds</b>	<b>1</b>
	Jon B. Reid, Ph.D., DABT and Custodio V. Muianga, Ph.D., MPH	
<b>41</b>	<b>Saturated Halogenated Aliphatic Hydrocarbons Two to Four Carbons</b>	<b>61</b>
	Jon B. Reid, Ph.D., DABT and Custodio V. Muianga, Ph.D., M.P.H	
<b>42</b>	<b>Unsaturated Halogenated Hydrocarbons</b>	<b>129</b>
	Fiorella Belpoggi, DBS, D. Chiozzotto, Ph.D., and M. Lauriola, Ph.D.	
<b>43</b>	<b>Dibenzo-<i>p</i>-Dioxins: 2,3,7,8-Tetrachlorodibenzo-<i>p</i>-Dioxin</b>	<b>231</b>
	Shane Que Hee, Ph.D.	
<b>44</b>	<b>Halogenated Biphenyls</b>	<b>247</b>
	Debdas Mukerjee, Ph.D. and Patricia Ruiz, Ph.D.	
<b>45</b>	<b>Halogenated Benzenes</b>	<b>323</b>
	A. Philip Leber, Ph.D., DABT and James S. Bus, Ph.D., DABT	
<b>46</b>	<b>Organic Chlorofluoro Hydrocarbons</b>	<b>359</b>
	George M. Rusch, Ph.D., DABT, FATS	
<b>47</b>	<b>Miscellaneous Chlorinated Hydrocarbon Pesticides</b>	<b>429</b>
	James S. Bus, Ph.D., DABT and A. Philip Leber, Ph.D., DABT	
<b>48</b>	<b>Aliphatic Carboxylic Acids: Saturated</b>	<b>471</b>
	Maria Szilagyi, DABT	
<b>49</b>	<b>Aliphatic Carboxylic Acids: Unsaturated</b>	<b>533</b>
	Maria Szilagyi, DABT	

<b>50</b>	<b>Ethers</b>	<b>589</b>
	Myron A. Mehlman, Ph.D.	
<b>51</b>	<b>Aldehydes and Acetals</b>	<b>655</b>
	Michael T. Borchers, Ph.D.	
<b>52</b>	<b>Acetone</b>	<b>735</b>
	Gunnar Johanson, DrMedSc	
<b>53</b>	<b>Ketones of Four or Five Carbons</b>	<b>753</b>
	John L. O'Donoghue, VMD, Ph.D., DABT	
<b>54</b>	<b>Ketones of Six to Thirteen Carbons</b>	<b>807</b>
	John L. O'Donoghue, VMD, Ph.D., DABT	
<b>55</b>	<b>Monohydric Alcohols: C<sub>1</sub> to C<sub>6</sub></b>	<b>915</b>
	C. Bevan, Ph.D., DABT	



## Halogenated One-Carbon Compounds

Jon B. Reid, Ph.D., DABT and Custodio V. Muianga, Ph.D., MPH

Chlorinated methanes (also ethanes) are among the most widely used and useful chemical compounds. There are potentially 26 compounds with other multiple halogen substitutions. Eleven important or representative compounds were selected to discuss in this chapter. The physical states vary from colorless gases: methyl chloride and methyl bromide; colorless liquids: methyl iodide, methylene chloride, methylene bromide, chloroform, bromoform (heavy), and carbon tetrachloride; and a yellow solid, iodoform, and colorless solid; carbon tetrabromide. The main use of methyl chloride is in the manufacture of silicone while methylene chloride, chloroform, and carbon tetrachloride have been used as solvents, paint removers, degreasers, cleaning compounds, and chemical intermediates. The following table provides toxicity information (reference doses, RfD;

reference concentrations, RfC; oral slope factors (carcinogen), OSF; and inhalation unit risks (carcinogen), IUR) from Integrated Risk Information Service (IRIS) (1). It can be seen that the RfDs (oral exposure for lifetime) for the chemicals that have been evaluated are in the order of  $10^{-2}$  to  $10^{-3}$  mg/kg/day. The inhalation RfCs (inhalation exposure) for chemicals that have been evaluated are  $10^{-2}$  to  $10^{-3}$  mg/m<sup>3</sup>. For the chemicals indicated as either probable human carcinogens or methylene chloride, chloroform, bromoform, and likely to be a human carcinogen, carbon tetrachloride, the OSF (per mg/kg/day) are in the order of  $10^{-2}$  to  $10^{-3}$ . The IURs for the chemicals evaluated are of the order of  $10^{-5}$  to  $10^{-6}$  per  $\mu\text{g}/\text{m}^3$ . Fluorene compounds are not included in this chapter as they represent a very special case of halogenated compounds.

Chemical	RfD (mg/kg/day)	RfC (mg/m <sup>3</sup> )	Cancer Description	OSF (Per mg/kg/day)	IUR (Per $\mu\text{g}/\text{m}^3$ )	References
Methyl chloride	None	9E-2 Brain	Not classified	None	None	Toxicological Review (2001)
Methyl bromide	1.4E-3	5E-3 Nasal	Not classified	None	None	No Toxicological Review
Methyl iodide	None	None	None	None	None	No Toxicological Review
Methylene chloride	6E-2 Liver	None	Probable human	7.5E-3	4.7E-7	No Toxicological Review
Methylene bromide	None	None	None	None	None	None
Chloroform	1E-2 Liver	None	Probable human	RfD 1E-2	2.3E-5	Toxicological Review (2001)
Bromoform	2E-2 Liver	None	Probable human	7.9E-3	1.1E-6	No Toxicological Review
Iodoform	None	None	None	None	None	No Toxicological Review
Carbon tetrachloride	4E-3 Serum SDH	1E-1	Likely human	7E-2	6E-6	Toxicological Review (2010)
Carbon tetrabromide	None	None	None	None	None	No Toxicological Review
Methylene chlorobromide	None	None	None	None	None	No Toxicological Review

Several of the compounds listed in the above table are receiving attention because of their presence as disinfection by-products (DBPs): products formed in reaction with chlorine, ozone, chlorine dioxide, or chloramines with naturally occurring organic matter in drinking water. A comprehensive review was provided in *Mutation Research* (2) in conjunction with the International Agency for Research on Cancer (IARC) review (3). The trihalomethanes (THMs)—chloroform, bromoform, bromodichloromethane, and chlorodibromomethane—are regulated by the U.S. EPA at a level of 80 µg/L (for total halomethanes) and are included in 600 drinking water DBPs. Together, the THMs and haloacetic acids (HHAs) are the two most prevalent classes of DBPs formed in chlorinated drinking water, accounting for approximately 25% of the halogenated DBPs. Of concern is the demonstrated human carcinogenicity of many of the DBPs. The World Health Organization (WHO) (4) in *Trihalomethanes in Drinking-Water* (background document for development of *WHO Guidelines for Drinking-Water Quality*) provides a thorough discussion of four compounds considered the most common forms of halomethanes present in drinking water. These are chloroform, bromodichloromethane, dibromochloromethane, and bromoform. These compounds are liquids at room temperature, relatively to extremely volatile, and only slightly soluble in water.

As in the previous editions, this chapter includes relevant information provided in earlier editions along with updated information from several sources including National Toxicology Program (NTP), IRIS, and the Agency for Toxic Substances and Disease Registry (ATSDR) websites.

## 1.0 Methyl Chloride

### 1.0.1 CAS Number

[74-87-3]

### 1.0.2 Synonyms

Chloromethane; monochloromethane

### 1.0.3 Trade Names

Artic; RCRA waste number U045; R40, Refrigerant R40, R-40; UN 1063

### 1.0.4 Molecular Weight

50.49

### 1.0.5 Molecular Formula

CH<sub>3</sub>Cl

### 1.0.6 Molecular Structure



## 1.1 Chemical and Physical Properties

Physical state	colorless gas
Melting point	−97°C
Boiling point	−24.2°C
Solubility	0.9 g/100 mL water at 20°C; 7.8 g/100 mL ethanol at 20°C; soluble in ethyl ether, chloroform, and acetone
Autoignition temperature	634°C
Flash point	<0°C
Flammability limits	8–19% in air

1 mg/L = 484 ppm and 1 ppm = 2.06 mg/m<sup>3</sup> at 25°C, 760 Torr

### 1.1.1 General

Methyl chloride is a natural and ubiquitous constituent of the oceans and atmosphere. Major sources of release of methyl chloride to the air include tropical plants (5–7), wood-rotting fungi, and soil from wood-rotting fungi. It is estimated that up to 99% of methyl chloride released to the environment is from natural sources, such as chemical reactions that occur in the oceans or chemical reactions that occur from combustion of grass, wood, charcoal, and coal. An anthropogenic source of methyl chloride may be cigarette smoke, about 5% in the United States, as estimated by Novak et al. (8). Novak et al. collected smoke samples from burning cigarettes in special smoking adaptors into 2 L canisters, and analyzed the smoke for chloromethane using gas chromatography. The chloromethane concentrations were about 30–500 ppmv (1.5–5.3 mg/cigarette) compared with about 500 pptv (parts per trillion) in typical urban air.

Methyl chloride has also been detected in surface waters, drinking water, groundwater, and soil as well as in industrial leachate. It is an impurity in vinyl chloride.

### 1.1.2 Odor and Warning Properties

Methyl chloride has a faint sweet odor. Charcoal used in most organic respirator cartridges and canisters is not totally effective as a sorbent.

## 1.2 Production and Use

Methyl chloride has been used in rubber adhesives and other rubber solutions; in the pharmaceutical industry; as a paint and varnish remover; in solvent degreasing; in aerosol

formulations; in food and drug processing; in the plastics industry; in hair sprays, insecticides, and spray paints; as a cosolvent or vapor pressure depressant; as a blowing agent for flexible polyurethane foams; as a cleaning solvent for printed circuit boards; as a stripper solvent for photoresists; as a solvent for cellulose acetate fiber; in plastic film; in protective coatings; in chemical processing; as a carrier solvent for herbicides and insecticides; to extract heat-sensitive, naturally occurring substances such as cocoa, edible fats, spices, and beer hops; for decaffeinating coffee; as a refrigerant; in oil dewaxing; as a dye and perfume intermediate; in the textile industry; as a postharvest fumigant for strawberries; as a grain fumigant; for degreening citrus fruits; as an industrial solvent; in low-temperature extraction; as a solvent for oil, fats, bitumen, esters, resins, and rubber; in coating photographic films; as a food additive; in synthetic fibers and leather coatings; as a spotting agent; and in organic synthesis.

Methyl chloride is a ubiquitous environmental contaminant because it is produced in very large quantities by fire, fungi, terrestrial plants, seaweed, algae, and possibly other organic processes. An estimated  $5 \times 10^6$  tons is produced annually by global biological processes. Less than 1% of environmentally occurring methyl chloride is the result of industrial processes.

Most industrially produced methyl chloride is consumed as a chemical intermediate, primarily in methylating reactions. However, published reports of human exposure have primarily been the result of its previous use as a refrigerant gas and as a blowing agent for plastic foams. Both of these uses have virtually disappeared, although it is possible that some methyl chloride may be present in old refrigeration systems and foams.

Because methyl chloride has a sweet odor that is not noticeable at dangerous concentrations, it must be used in closed or well-ventilated systems, preferably with continuous monitoring to prevent excessive exposure. Inhalation is the only significant route of toxic exposure. Respirators containing activated charcoal have only limited capacity for removing the gas.

Methyl chloride has been identified in at least 172 of the 1467 current or former EPA National Priorities List (NPL) hazardous waste sites.

### 1.3 Exposure Assessment

Many people are likely exposed to low levels of chloromethane because of its presence in the air due to natural processes (approximately 99% of the methyl chloride released into the environment) and as a by-product of the chlorination of drinking water supplies and other industrial processes (approximately 1%). Background concentrations are around  $1.2 \mu\text{g}/\text{m}^3$  (0.6 ppb) (9). Air concentrations of chloromethane measured in several U.S. cities averaged slightly below 1 ppb. In urban

areas, mean and median concentrations generally seem to be slightly higher,  $1.0\text{--}2.31.2 \mu\text{g}/\text{m}^3$  (0.5–1.1 ppb), with highest values found up to 15 ppb for individual measurements. Humans are exposed to methyl chloride in ambient air. The concentrations of methyl chloride are slightly higher in the air of urban/suburban sites than rural remote sites. WHO summarized workplace exposure concentrations in the United States reported by NIOSH (range  $0.2\text{--}44.2 \text{mg}/\text{m}^3$  (0.1–21.4 ppm)) and in the Netherlands (range  $62\text{--}186 \text{mg}/\text{m}^3$  (30–90 ppm)).

Methyl chloride has been occasionally detected in water, soil, and biota. A maximum concentration of  $44 \mu\text{g}/\text{L}$  was measured in a drinking water well. Groundwater in the United States ranged from nondetectable up to  $100 \mu\text{g}/\text{L}$ , found at a former waste site of a chemical factory. In surface water samples in North America, the concentrations ranged from not detectable up to  $224 \mu\text{g}/\text{L}$ , the highest value reported. Methyl chloride was detected in soils at 34 waste sites and in sediments at 13 waste sites in the United States. The ATSDR Toxicological Profile (10) and the WHO *Concise International Chemical Assessment* (9) provide a detailed description of exposure assessment of methyl chloride.

#### 1.3.1 Air

As discussed in the ATSDR profile for methyl chloride (10) in air, methyl chloride can be analyzed by NIOSH Method 1001, using gas chromatography (GC) with flame ionization detector, for a range of  $66\text{--}670 \text{mg}/\text{m}^3$  (11). Methyl chloride can also be trapped cryogenically from an aliquot of air collected into an evacuated canister followed by determination using GC with either electron capture or mass spectrometric detection (12).

#### 1.3.2 Background Levels

Background concentrations are around  $1.2 \mu\text{g}/\text{m}^3$  (0.6 ppb) (9).

#### 1.3.3 Workplace Methods

NIOSH Method 1001 is recommended for determining workplace exposures to methyl chloride (11).

#### 1.3.4 Biomonitoring/Biomarkers

The ATSDR profile (10, 13) indicates several analytical methods in the analytical section. Several studies have unsuccessfully attempted to correlate exposure levels in air with urinary excretion of S-methylcysteine. Use of blood and breath analysis to monitor exposure levels immediately after exposure was of limited value.

**1.3.4.1 Blood.** No analytical methods were found for blood.