Contents

Foreword V
Preface XIX
List of Contributors XXI
Disclaimer XXV

Volume 1

1 Introduction 1
W.R. Külpmann
References 3

2 Requirements for Toxicological Analyses 5
F. Degel
2.1 General Aspects 5
2.2 Devices 5
2.3 Rooms and Facilities 5
2.4 Management and Technical Requirements 7
2.5 Chemicals and Reagents 8
2.6 Personnel 8
References 8

3 Materials for Investigation 11
H.J. Gibitz and F. Pluisch
3.1 Introduction 11
3.2 Judicial Preconditions for Taking and Surrendering Materials for Investigation 11
3.2.1 The Contract on Medical Treatment 12
3.2.2 Patient’s Consent 12
3.2.3 Suicidal Patients 13
3.2.4 Surrender of Materials for Investigation 14
3.3 Containers for Sampling and Storage 15
3.4 Kind of Materials
3.4.1 Urine
3.4.2 Blood, Plasma, and Serum
3.4.3 Stomach Contents
3.4.4 Other Materials
3.5 Identification of Materials
3.6 Request Form
3.7 Transport of Materials
3.8 Evaluation of Materials
3.8.1 Urine
3.8.2 Blood
3.8.3 Stomach Contents
3.8.4 Expired Air
3.9 Storage of Materials
3.10 Sampling and Storage of Materials for Forensic Investigation

References

4 Methods for Clinical Toxicological Analysis
4.1 Immunoassays
W.R. Külpmann and D. Hannak
4.1.1 Introduction
4.1.2 Selection of Materials for Investigation
4.1.3 Detection Limit and Cutoff Concentration
4.1.4 Maximal and Practical Sensitivity
4.2 Thin-Layer Chromatography
F. Degel
4.2.1 Introduction
4.2.2 Toxicological Analyses by Thin-Layer Chromatography
4.2.3 Perspectives and Limitations
4.3 High-Performance Liquid Chromatography
H. Käferstein
4.3.1 Introduction
4.3.2 Packing Materials and Separation Techniques
4.3.3 Detection
4.3.4 Conclusion
4.4 Gas Chromatography
H.H. Maurer
4.4.1 Injection
4.4.2 Chromatographic Separation and Detection
4.4.3 Conclusion
4.5 Gas Chromatography–Mass Spectrometry
H.H. Maurer
4.5.1 Outline
4.5.2 Instrumentation
4.5.3 Full Scan Mode and Selected Ion Monitoring
6.2.5 Uncertainty and Unreliability 71
6.2.6 Quality Assurance: A Practical Approach 73
W.R. Külpmann
References 75

7 Assessments of Analytical Results 77
W.R. Külpmann, M. Geldmacher-von Mallinckrodt, and J. Hallbach
7.1 Introduction 77
7.2 Technical Level: Analytical Assessment 77
7.3 Biological Level: Plausibility Check 78
7.4 Nosological Level 79
References 79

8 The Analytical Toxicological Report 81
J. Hallbach, M. Geldmacher-von Mallinckrodt, and W.R. Külpmann
8.1 Introduction 81
8.2 The Analytical Toxicological Report 81
References 87

9 Medical Interpretation 89
J. Hallbach, N. Felgenhauer, M. Geldmacher-von Mallinckrodt,
and H.H. Maurer
9.1 Overview 89
9.2 Differential Diagnosis 90
9.3 Poison Information Center 90
9.4 Interpretation of Blood, Plasma, or Serum Concentrations 90
9.5 Conclusion 91
References 92

10 Forensic Aspects 93
W.R. Külpmann
10.1 Overview 93
References 94

11 Strategy of Clinical Toxicological Investigations 95
J. Hallbach, W.R. Külpmann, H.H. Maurer, F. Pragst,
and N. Felgenhauer
11.1 Epidemiology of Poisoning 95
11.2 Diagnosis of Poisoning 96
11.3 Investigation Request 100
11.4 Clinical Toxicological Requirements 102
11.5 Documentation 105
References 105

12 Screening Procedures for “General Unknown” Analysis 107
F. Pragst, H.H. Maurer, J. Hallbach, W.R. Külpmann,
U. Staerk, F. Degel, and M. Lappenberg-Pelzer
References 105
12.1 High-Performance Liquid Chromatography with Photodiode Array Detector 108

F. Pragst

12.1.1 Sample Preparation 108
12.1.2 Chromatographic Conditions 120
12.1.3 HPLC–DAD Spectra Libraries 126
12.1.4 Identification of Metabolites 131
12.1.5 Estimation of Concentration 135
12.1.6 Application Examples 138
12.1.7 Practicability 147
12.1.8 Mechanized High-Performance Liquid Chromatography 148

J. Hallbach

12.2 Gas Chromatography 151

H. H. Maurer

12.3 Gas Chromatography–Mass Spectrometry 152

H. H. Maurer

12.3.1 Instruments and Settings 152
12.3.2 Procedure and Data Evaluation 153
12.3.3 Quality Assurance of Screening Procedures 154
12.3.4 Screening for Basic and Neutral Drugs and Poisons in Urine 156
12.3.5 Screening for Acidic Drugs and Poisons in Urine 159
12.3.6 Identification and Determination of Drugs and Poisons in Plasma 161
12.3.7 Solid-Phase Microextraction 163

W.R. Külpman and U. Staerk

12.4 Gas Chromatographic Headspace Analysis 165

F. Degel

12.4.1 Introduction 165
12.4.2 Screening Procedure 167
12.5 Color Test: Tetrabromophenolphthalein Ethyl Ester 175

M. Lappenberg-Pelzer

12.5.1 Introduction 175
12.5.2 Procedure 176
12.5.3 Medical Assessment and Clinical Interpretation 181

References 182

13 Nonopioid Analgesics and Antirheumatics 189

H. König and J. Hallbach

13.1 Detection of Nonopioid Analgesics and Antirheumatics in Serum and Urine 189

13.1.1 Screening by High-Performance Liquid Chromatography 190
13.1.2 Medical Assessment and Clinical Interpretation 194
13.1.3 Screening by Gas Chromatography 195
13.1.4 Medical Assessment and Clinical Interpretation 198
13.2 Diclofenac 199
13.2.1 High-Performance Liquid Chromatography 199
13.2.2 Gas Chromatography 199
13.2.3 Medical Assessment and Clinical Interpretation 199
13.3 Ibuprofen 200
13.3.1 High-Performance Liquid Chromatography 200
13.3.2 Gas Chromatography 201
13.3.3 Medical Assessment and Clinical Interpretation 201
13.4 Metamizole (Dipyrone) 202
13.4.1 High-Performance Liquid Chromatography 202
13.4.2 Gas Chromatography 202
13.4.3 Medical Assessment and Clinical Interpretation 202
13.5 Paracetamol (Acetaminophen) 203
13.5.1 Immunoassay 203
13.5.2 High-Performance Liquid Chromatography 204
13.5.3 Gas Chromatography 204
13.5.4 Medical Assessment and Clinical Interpretation 204
13.6 Phenazone (Antipyrine) 207
13.6.1 High-Performance Liquid Chromatography 207
13.6.2 Gas Chromatography 207
13.6.3 Medical Assessment and Clinical Interpretation 207
13.7 Salicylates 209
13.7.1 Photometry 209
13.7.2 Immunoassay 211
13.7.3 High-Performance Liquid Chromatography 211
13.7.4 Gas Chromatography 212
13.7.5 Medical Assessment and Clinical Interpretation 212

References 214

14 Analgesics: Opiates and Opioids 215

H. Käferstein
14.1 Group Assays 216
14.1.1 Immunoassay 216
14.1.2 High-Performance Liquid Chromatography 216
14.1.3 Gas Chromatography 216
14.1.4 Medical Assessment and Clinical Interpretation 216
14.2 Buprenorphine 216

W.R. Külpman
14.2.1 Immunoassay 216
14.2.2 High-Performance Liquid Chromatography 217
14.2.3 Gas Chromatography – Mass Spectrometry 217
14.2.4 Medical Assessment and Clinical Interpretation 217
14.3 Dextropropoxyphene 218

H. Käferstein
14.3.1 Immunoassay 219
14.3.2 High-Performance Liquid Chromatography 219
14.3.3 Gas Chromatography – Mass Spectrometry 221
14.3.4 Medical Assessment and Clinical Interpretation 221
14.4 Fentanyl 222
  G. Sticht, H. Käferstein, and L. von Meyer
14.4.1 Immunoassay 223
14.4.2 High-Performance Liquid Chromatography 224
14.4.3 Gas Chromatography – Mass Spectrometry 224
14.4.4 Medical Assessment and Clinical Interpretation 227
14.5 Meperidine (Pethidine) 228
  H. König
14.5.1 Immunoassay 228
14.5.2 Chromatography 229
14.5.3 Medical Assessment and Clinical Interpretation 229
14.6 Methadone 230
  H. Käferstein and A. Schmoldt
14.6.1 Immunoassay 231
14.6.2 High-Performance Liquid Chromatography: Total Methadone 231
14.6.3 High-Performance Liquid Chromatography: l- and
  d-Methadone 234
14.6.4 Gas Chromatography – Mass Spectrometry 236
14.6.5 Medical Assessment and Clinical Interpretation 238
14.7 Morphine and Morphine Derivatives 240
  H. Käferstein and G. Sticht
14.7.1 Immunoassay 243
14.7.2 High-Performance Liquid Chromatography 244
14.7.3 Gas Chromatography – Mass Spectrometry 244
14.7.4 Medical Assessment and Clinical Interpretation 247
14.8 Oxycodone 249
  F. Degel
14.8.1 Immunoassay 250
14.8.2 Chromatography 250
14.8.3 Medical Assessment and Clinical Interpretation 251
14.9 Pentazocine 252
  T. Binscheck
14.9.1 High-Performance Liquid Chromatography 253
14.9.2 Gas Chromatography – Mass Spectrometry 255
14.9.3 Medical Assessment and Clinical Interpretation 257
14.10 Tilidine 257
  T. Binscheck
14.10.1 High-Performance Liquid Chromatography 258
14.10.2 Gas Chromatography – Mass Spectrometry 259
14.10.3 Medical Assessment and Clinical Interpretation 261
14.11 Tramadol 262
  J. Hallbach and H. Käferstein
14.11.1 Immunoassay 262
14.11.2 Chromatography–Mass Spectrometry 262
14.11.3 Medical Assessment and Clinical Interpretation 263
References 266

15 Antidysrhythmic Agents 271
H. König and A. Schmoldt
15.1 Immunoassay 272
15.2 High-Performance Liquid Chromatography 273
15.3 Gas Chromatography 274
15.4 Medical Assessment and Clinical Interpretation 275
References 285

16 Antiepileptic Drugs 287
D. Hannak
16.1 Immunoassay 288
W.R. Külpmann
16.2 High-Performance Liquid Chromatography 289
D. Hannak
16.3 Gas Chromatography–Mass Spectrometry 291
J. Hallbach
16.4 Medical Assessment and Clinical Interpretation 294
D. Hannak
References 300

17 Anticoagulants 301
L. von Meyer and M. Geldmacher-von Mallinckrodt
17.1 Coumarin Derivatives Used in Therapy 302
17.1.1 General Screening Methods 302
17.1.2 High-Performance Liquid Chromatography 303
17.1.3 Medical Assessment and Clinical Interpretation 306
17.2 Rodenticide Coumarin Derivatives 309
17.2.1 General Screening Methods 309
17.2.2 High-Performance Liquid Chromatography 309
17.2.3 Medical Assessment and Clinical Interpretation 310
References 311

18 Bronchodilators 313
W.R. Külpmann
18.1 Group Assay 313
18.2 Caffeine 313
18.2.1 Immunoassay 313
18.2.2 High-Performance Liquid Chromatography 313
18.2.3 Gas Chromatography – Mass Spectrometry 314
18.2.4 Medical Assessment and Clinical Interpretation 314
18.3 Theophylline 315
18.3.1 Immunoassay 315
18.3.2 High-Performance Liquid Chromatography 315
18.3.3 Gas Chromatography – Mass Spectrometry 315
18.3.4 Medical Assessment and Clinical Interpretation 315

References 316

19 Calcium Channel Blockers 317
J. Hallbach and A. Schmoldt
19.1 Nifedipine 317
19.1.1 Introduction 317
19.1.2 High-Performance Liquid Chromatography 318
19.1.3 Medical Assessment and Clinical Interpretation 318
19.2 Verapamil 320
19.2.1 Introduction 320
19.2.2 High-Performance Liquid Chromatography 320
19.2.3 Gas Chromatography 322
19.2.4 Medical Assessment and Clinical Interpretation 324

References 325

20 Cardiac Glycosides 327
J. Hallbach
20.1 Digitoxin 327
20.1.1 Immunoassay 328
20.1.2 Medical Assessment and Clinical Interpretation 329
20.1.3 Annotations 331
20.2 Digoxin 331
20.2.1 Immunoassay 332
20.2.2 Medical Assessment and Clinical Interpretation 333
20.2.3 Annotations 336

References 336

21 Hypnotics: Barbiturates 339
W.R. Külpmann and A. Schmoldt
21.1 Detection of Barbiturates 339
21.1.1 Immunoassay 339
21.1.2 High-Performance Liquid Chromatography 340
21.1.3 Gas Chromatography 340
21.1.4 Medical Assessment and Clinical Interpretation 340
21.2 Methohexital 340

A. Schmoldt and W.R. Külpmann
21.2.1 High-Performance Liquid Chromatography 340
21.2.2 Gas Chromatography 343
21.2.3 Medical Assessment and Clinical Interpretation 345
21.3 Phenobarbital 345

W.R. Külpmann
21.3.1 Immunoassay 345
24.3.2 Outline  400
24.3.3 Procedure  401
24.4 Gas Chromatography  404
  *H.-J. Birkhahn and D. Lampe*
24.4.1 Outline  404
24.4.2 Procedure  404
24.5 Gas Chromatography–Mass Spectrometry  407
  *U. Demme*
24.5.1 Introduction  407
24.5.2 Outline  410
24.5.3 Procedure  411
24.5.4 Detailed Analytical Information on Some Relevant Drugs  414
24.6 High-Performance Thin-Layer Chromatography  422
  *U. Demme*
24.6.1 Introduction  422
24.6.2 Outline  423
24.6.3 Procedure  424
24.7 High-Performance Liquid Chromatography–Mass Spectrometry  430
  *T. Grobosch*
24.7.1 Outline  430
24.7.2 Procedure  430
24.8 Medical Assessment and Clinical Interpretation  432
  *F. Degel*
References  453

**Volume 2**

25  *β*-Receptor Blocking Drugs  455
26  Drugs of Abuse  463
27  Solvents and Inhalants  511
28  Pesticides  559
29  Antidiabetics: Proinsulin, Insulin, C-Peptide, and Oral Antidiabetics  613
30  Dyshemoglobins  623
31  Various Drugs and Toxic Agents  635
32  Chemical Warfare Agents  679
Contents

33 Biochemical Investigations in Toxicology  745
34 Therapeutic Drug Monitoring  775
35 Poisonous Plants  785
36 Poisonous Mushrooms  809
37 Venomous and Poisonous Animals  825

Appendix A  Abbreviations  835
Appendix B  Therapeutic and Toxic Concentrations of Drugs and Xenobiotics in Plasma or Serum  841
Appendix C  Biological Tolerance Values at the Workplace (BAT Values)  853
Appendix D  Antidotes  857
Appendix E  Poison Information Centers  861
Appendix F  List of Narcotic Drugs According to German Law  867

Index  877