CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR ANTICOAGULANT RODENTICIDES

Preamble 8

Introduction 17

1. SUMMARY 19

1.1 General 19
1.2 Properties and analytical methods 19
1.3 Sources of human and environmental exposure 19
1.4 Environmental distribution, levels and exposures 19
1.5 Mode of action and metabolism 20
1.6 Effects on mammals and *in vitro* test systems 20
1.7 Effects on humans 21
1.8 Effects on other organisms in the laboratory and field 22
1.9 Evaluation and conclusion 22

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS 24

2.1 Identity 24
2.2 Physical and chemical properties 24
2.3 Analytical methods 34

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE 37

3.1 Natural occurrence 37
3.2 Anthropogenic sources 37

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION 38

4.1 Transport and distribution between media 38
4.1.1 Air, water and soil 38
4.1.2 Vegetation and wildlife 39
4.2 Transformation 39
4.2.1 Biodegradation 39
4.2.2 Abiotic degradation 40
4.2.2.1 Photolysis 40
4.2.2.2 Hydrolysis 40

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE 42

5.1 Environmental levels 42
5.2 General population exposure 42
5.3 Occupational exposure 42

6. MODE OF ACTION AND METABOLISM 44

6.1 Vitamin K and its antagonists 44
6.2 Metabolism 48
6.2.1 Absorption, distribution and elimination 48
6.2.2 Metabolic transformation 49
6.2.3 Retention and turnover 50

7. EFFECTS ON LABORATORY MAMMALS AND *IN VITRO* TEST SYSTEMS 53

7.1 Acute effects 53
7.1.1 Rodent species 53
7.1.2 Non-target species 55
7.2 Short-term exposure 57
7.2.1 Rodent species 57
7.2.2 Non-target species 58
7.3 Long-term exposure 59
7.4 Skin and eye irritation; sensitization 60
7.5 Reproductive toxicity and teratogenicity 60
7.6 Mutagenicity 61
7.7 Factors modifying toxicity 63
7.8 Adverse effects in domestic and farm animals 64
7.8.1 Domestic animals 64
7.8.1.1 Poisoning incidents 64
7.8.1.2 Diagnosis and treatment of poisoning 65
7.8.2 Farm animals 66

8. EFFECTS ON HUMANS 67

8.1 General population exposure 67
8.1.1 Acute poisoning 68
8.1.2 Poisoning incidents 68
8.1.3 Controlled human studies 72
8.2 Monitoring of biological effects 72
8.2.1 Effects of short- and long-term exposure 72
8.2.2 Epidemiological studies 72
8.3 Developmental effects 73

8.4 Other adverse effects 73
8.5 Methods for assessing absorption and effects of anticoagulant rodenticides 74
8.6 Treatment of anticoagulant rodenticide poisoning 76
8.6.1 Minimizing the absorption 77
8.6.2 Specific pharmacological treatment 77
8.6.2.1 Vitamin K_1 (phytomenadione) 77
8.6.2.2 Blood components 78
8.6.2.3 Phenobarbital 78
8.6.3 Response to therapy 78

9. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD 79

9.1 Laboratory experiments 79
9.1.1 Microorganisms 79
9.1.2 Aquatic organisms 79
9.1.3 Terrestrial organisms 79
9.1.3.1 Acute toxicity 79
9.1.3.2 Primary toxicity 81
9.1.3.3 Secondary toxicity 82
9.2 Field observations 84
9.2.1 Primary poisonings 84
9.2.2 Secondary poisonings 85

10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT 86

10.1 Evaluation of human health risks 86
10.2 Evaluation of effects on the environment 87

11. CONCLUSIONS AND RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH AND THE ENVIRONMENT 90

11.1 Conclusions 90
11.2 Recommendations for protection of human health and the environment 90

12. FURTHER RESEARCH 92

13. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES 93

REFERENCES 95

RESUME 111

RESUMEN 117