



**Australian Pesticides &  
Veterinary Medicines Authority**

**The reconsideration of approval of the active constituent Endosulfan, registrations of products containing Endosulfan and their associated labels.**

**Draft FINAL REVIEW REPORT  
Technical Reports**

May 2004

**Australian Pesticides &  
Veterinary Medicines Authority**

**Canberra  
Australia**

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This review report for the active constituent Endosulfan and products containing Endosulfan is published by the Australian Pesticides and Veterinary Medicines Authority. For further information about this review or the Pesticides Review Program, contact:

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## **FOREWORD**

The APVMA (\*1) is an independent statutory authority with responsibility for the regulation of agricultural and veterinary chemicals in Australia. Its statutory powers are provided in the *Agricultural and Veterinary Chemicals Code Act, 1994* (Agvet Codes).

The APVMA can reconsider the approval of active constituents, the registration of chemical products or the approval of labels for containers of chemical products at any time. This is specified in Part 2, Division 4 of the Agvet Codes.

The basis for the reconsideration is whether the APVMA is satisfied that continued use of the active constituent endosulfan and products containing endosulfan in accordance with the instructions for their use:

- would not be an undue hazard to the safety of people exposed to it during its handling; and/or
- would not be likely to have an effect that is harmful to human beings; and /or
- would not be likely have an unintended effect that is harmful to animals, plants or things or to the environment; and/or
- would not unduly prejudice trade or commerce between Australia and places outside Australia.

A reconsideration may be initiated when new research or evidence has raised concerns about the use or safety of a particular chemical, a product or its label.

The process for reconsideration includes a call for information from a variety of sources, a review of that information and, following public consultation, a decision about the future use of the chemical or product.

In undertaking reviews, the APVMA works in close cooperation with advisory agencies including the Department of Health and Aging, the Department of Environment and Heritage, the National Occupational Health and Safety Commission, and State Departments of Agriculture as well as other expert advisors, as appropriate.

The APVMA has a policy of encouraging openness and transparency in its activities and community involvement in decision-making. The publication of review reports is a part of that process.

The APVMA also makes these reports available to the regulatory agencies of other countries under bilateral agreements. It is proposed that countries receiving these reports will not utilise them for registration purposes unless they are also provided with the raw data from the relevant applicant.

This document contains the draft Final Review Report – Technical Reports of *‘The reconsideration of approval of the active constituent Endosulfan, registrations of products containing Endosulfan and their associated labels’* and relates to all products containing endosulfan. The review’s findings and recommendations are based on information collected from a variety of sources. The information and technical data required by the APVMA to review the safety of both new and existing chemical products must be derived according to accepted scientific principles, as must the methods of assessment undertaken.

The draft review report containing the APVMA preliminary assessments (The NRA Review of Endosulfan, Volume I, August 1998) and the technical reports from its advisory agencies (Volume II) for all registrations and approvals relating to endosulfan are available from the APVMA website:

<http://www.apvma.gov.au/chemrev/chemrev.shtml>.

(\*1) Prior to March 2003, the APVMA was known as the National Registration Authority for Agricultural and Veterinary Chemicals (NRA). In this report, the name APVMA is generally used even when referring to the organisation prior to March 2003.

**TABLE OF CONTENTS**

|            |  |            |
|------------|--|------------|
| <b>8</b>   | <b>RESIDUES ASSESSMENT TECHNICAL REPORT</b> .....  | <b>8</b>   |
| <b>8.1</b> | <b>METABOLISM STUDIES</b> .....  | <b>8</b>   |
| 8.1.1      | Hen Studies.....   | 8          |
| 8.1.2      | Lactating Cow Studies .....  | 10         |
| 8.1.3      | Sheep.....   | 11         |
| <b>8.2</b> | <b>RESIDUE DEFINITION</b> .....  | <b>12</b>  |
| <b>8.3</b> | <b>ANALYTICAL METHODOLOGY</b> .....  | <b>12</b>  |
| 8.3.1      | Crop matrices .....  | 12         |
| 8.3.2      | Animal tissues and milk .....  | 13         |
| <b>8.4</b> | <b>STORAGE STABILITY</b> .....   | <b>14</b>  |
| 8.4.1      | Storage stability in crop matrices .....   | 14         |
| 8.4.2      | Stability of endosulfan in animal tissues and milk .....                                     | 15         |
| <b>8.5</b> | <b>CROP RESIDUE STUDIES</b> .....  | <b>16</b>  |
| 8.5.1      | Citrus fruit (oranges, mandarins, lemons) .....  | 16         |
| 8.5.2      | Pome fruit (apples, pears).....  | 22         |
| 8.5.3      | Stone fruit (peaches, nectarines, apricots).....   | 25         |
| 8.5.4      | Grapes .....   | 28         |
| 8.5.5      | Tropic/sub-tropic fruit-inedib peel (avocado, custard apple, mango, pawpaw, persimmon) ..... | 29         |
| 8.5.6      | Brassica vegetables (broccoli, cabbage, cauliflower, Brussels sprouts) .....                 | 33         |
| 8.5.7      | Cucurbits (cucumber, melons, zucchini) .....   | 36         |
| 8.5.8      | Fruiting vegetables (capsicum, eggplant, tomato, sweet corn).....                            | 40         |
| 8.5.9      | Leafy vegetables (chinese cabbage, silverbeet, lettuce).....                                 | 43         |
| 8.5.10     | Legume vegetables (beans, peas).....   | 45         |
| 8.5.11     | Pulse crops (navy beans, faba beans, cow peas, field peas, lupins, chickpeas) .....          | 47         |
| 8.5.12     | Root and tuber vegetables (beetroot, carrot, potato, sweet potato).....                      | 55         |
| 8.5.13     | Stalk and stem vegetables (celery, rhubarb) .....  | 58         |
| 8.5.14     | Cereal Crops (sorghum, wheat, barley).....   | 59         |
| 8.5.15     | Tree Nuts (macadamia).....   | 67         |
| 8.5.16     | Oilseeds (Cotton, Soyabeans, Sunflowers, Canola).....  | 68         |
| <b>8.6</b> | <b>ANIMAL TRANSFER STUDIES</b> .....   | <b>76</b>  |
| 8.6.1      | Cattle studies .....   | 76         |
| 8.6.2      | Pigs.....  | 79         |
| 8.6.3      | Sheep.....   | 80         |
| <b>8.7</b> | <b>PROCESSING STUDIES</b> .....  | <b>80</b>  |
| <b>8.8</b> | <b>RESIDUES REFERENCES</b> .....   | <b>81</b>  |
|            | <b>RESIDUES APPENDIX 1</b> .....   | <b>88</b>  |
|            | <b>RESIDUES APPENDIX 2</b> .....   | <b>91</b>  |
|            | <b>RESIDUES APPENDIX 3</b> .....   | <b>98</b>  |
|            | <b>RESIDUES APPENDIX 4</b> .....   | <b>100</b> |
| <b>9.</b>  | <b>OH&amp;S ASSESSMENT TECHNICAL REPORT</b> .....  | <b>105</b> |
| <b>9.1</b> | <b>BACKGROUND</b> .....  | <b>107</b> |
| <b>9.2</b> | <b>OCCUPATIONAL EXPOSURE STUDIES</b> .....   | <b>109</b> |
| 9.2.1      | Parameters used in exposure studies .....  | 109        |
| 9.2.2      | Exposure assessment.....   | 118        |
| <b>9.3</b> | <b>OCCUPATIONAL RISK ASSESSMENT</b> .....  | <b>128</b> |
| 9.3.1      | End use acute exposure risk assessment.....  | 129        |
| 9.3.2      | End use repeated exposure risk assessment.....   | 129        |

|             |  |            |
|-------------|--|------------|
| 9.3.3       | Re-entry risk assessment .....                       | 133        |
| <b>9.4</b>  | <b>VALIDITY OF NEW OHS STUDIES .....</b>             | <b>136</b> |
| <b>9.5</b>  | <b>OHS REFERENCES.....</b>                           | <b>137</b> |
|             | <b>OHS APPENDIX 1 .....</b>                          | <b>139</b> |
|             | <b>OHS APPENDIX 2 .....</b>                          | <b>141</b> |
|             | <b>OHS APPENDIX 3 .....</b>                          | <b>144</b> |
|             | <b>OHS APPENDIX 4 .....</b>                          | <b>149</b> |
| 10.         | ENDOCRINE DISRUPTION TECHNICAL REPORT.....           | 160        |
| <b>10.1</b> | <b>INTRODUCTION .....</b>                            | <b>160</b> |
| <b>10.2</b> | <b>US EPA AND APVMA R EPORTS.....</b>                | <b>161</b> |
| 10.2.1      | APVMA review of endosulfan.....                      | 161        |
| 10.2.2      | The US EPA Reregistration Eligibility Decision ..... | 162        |
| <b>10.3</b> | <b>IS ENDOSULFAN AN ENDOCRINE DISRUPTOR? .....</b>   | <b>164</b> |
| 10.3.1      | The toxicological database for endosulfan .....      | 166        |
| <b>10.4</b> | <b>DISCUSSION.....</b>                               | <b>176</b> |
| <b>10.5</b> | <b>CONCLUSION.....</b>                               | <b>178</b> |
| <b>10.6</b> | <b>TOXICOLOGY REFERENCES .....</b>                   | <b>180</b> |

## GLOSSARY OF TERMS AND ABBREVIATIONS

|         |   |
|---------|---|
| AAAA    | Australian Aerial Agricultural Association          |
| ACAHS   | Australian Centre for Agricultural Health & Safety  |
| ADI     | Acceptable Daily Intake                             |
| a.i.    | Active Ingredient                                   |
| ai/100L | active ingredient per 100 Litres                    |
| aPAD    | Acute Population Adjusted Dose                      |
| ATV     | All Terrain Vehicles                                |
| BCF     | Bioconcentration Factor                             |
| bw      | Body weight   |
| CAS     | Chemical Abstracts Service                          |
| CNS     | Central Nervous System                              |
| CP      | Pressure control nozzles                            |
| cPAD    | Chronic Population Adjusted Dose                    |
| C-PAS   | Centre for Pesticide Application Safety             |
| CRDC    | Cotton Research & Development Corporation           |
| CRP     | Chemical Review Program                             |
| CXL     | Codex Maximum Residue Level                         |
| d       | Days  |
| DFR     | Dislodgeable Foliar Residue                         |
| EC      | Emulsifiable concentrate                            |
| ECRP    | Existing Chemical Review Program (APVMA)            |
| EPA     | US Environmental Protection Agency                  |
| ER      | Oestrogen Receptor                                  |
| FIFRA   | Federal Insecticide, Fungicide, and Rodenticide Act |
| FFDCA   | Federal Food, Drug, and Cosmetic Act                |
| FOB     | Functional Observation Battery                      |
| FQPA    | Food Quality Protection Act                         |
| g       | Gram  |
| g ai/ha | grams of active ingredient per hectare              |
| GAP     | Good Agricultural Practice                          |
| HPA     | Hypothalamic-pituitary-adrenal                      |
| HPG     | Hypothalamic-pituitary- gonadal                     |
| HPT     | Hypothalamic-pituitary-thyroid                      |
| HRs     | Highest Residues                                    |
| IPM     | Integrated Pest Management                          |
| kg      | Kilogram  |
| L       | Litre   |
| LOAEL   | Lowest Observed Adverse Effect Level                |
| LOD     | Limit of Detection                                  |
| LOEL    | Lowest Observable Effect Level                      |
| MFL     | Maximum Feed Level                                  |
| mg      | Milligram   |
| mg/kg   | milligrams per kilogram                             |
| mL      | Millilitre  |

|         |   |
|---------|---|
| M/L     | Mixing/loading  |
| M/L/A/C | Mixing/loading/application/cleaning                       |
| MOE     | Margins of Exposure                                       |
| MRL     | Maximum Residue Limits                                    |
| NEDI    | National Estimated Dietary Intake                         |
| NESTI   | National Estimated Short Term Intake                      |
| NOAEL   | No Observed Adverse Effect Level                          |
| NOEC    | No Observable Effect Concentration                        |
| NOEL    | No Observable Effect Level                                |
| NOHSC   | National Occupational Health & Safety commission          |
| OCS     | Office of Chemical Safety                                 |
| OHS     | Occupational Health and Safety                            |
| OP      | Organophosphorus compound                                 |
| OPP     | EPA Office of Pesticide Programs                          |
| OPPTS   | EPA Office of Prevention, Pesticides and Toxic Substances |
| PAD     | Population Adjusted Dose                                  |
| PADI    | Provisional Acceptable Daily Intake                       |
| PF      | Processing Factor   |
| ppb     | Parts Per Billion   |
| PPE     | Personal Protective Equipment                             |
| ppm     | parts per million   |
| PVC     | Polyvinyl chloride  |
| RBC     | Red Blood Cell  |
| RED     | Reregistration Eligibility Decision                       |
| REI     | Restricted Entry Interval                                 |
| RfD     | Reference Dose  |
| RLEM    | Red Legged Earth Mite                                     |
| SHBG    | Sex hormone-binding globulin                              |
| STMRS   | Supervised Trial Median Residues                          |
| SUSDP   | Standards for the Uniform Scheduling of Drugs and Poisons |
| TC      | Transfer Coefficient                                      |
| TGA     | Therapeutic Goods Administration                          |
| TGAC    | Technical Grade Active Constituent                        |
| ULV     | Ultra-low Volume  |
| US EPA  | United States Environment Protection Authority            |
| WHP     | With Holding Period                                       |

## 8 RESIDUES ASSESSMENT TECHNICAL REPORT

### 8.1 METABOLISM STUDIES

#### 8.1.1 Hen Studies

Distribution, elimination and the nature of the metabolite residues in the eggs and edible tissues of the laying hen. C.M.M. Reynolds, 26 March 1996. AgrEvo U.K. Limited, Study Number TOX/94306.

Six laying hens were dosed by capsule daily for 12 consecutive days, at a mean dose level of 0.7 mg/kg bodyweight (dose range 0.65 – 0.72 mg/kg bw/day). The dose was composed of <sup>14</sup>C endosulfan<sup>1</sup> (α – endosulfan: β – endosulfan 68:32) absorbed onto ground grain contained in a gelatine capsule. This was equivalent to 11 ppm in the feed (range 9.9 – 12.5 ppm), based on mean individual bodyweights and feed intakes over the 12 day dosing period.

Excreta were collected at 24 hour intervals over the 12 day period and combined with cage washes for quantification of radioactivity. Eggs were collected twice a day over 24 hour intervals; yolks and whites were separated for quantification. At 24 hours after administration of the final dose, the hens were slaughtered and samples of skin, muscle (breast and thigh), liver, subcutaneous and abdominal fat and unlaidd eggs were collected for analysis.

Initial radioactivity was measured using LSC; TLC and HPLC were used to separate and identify various metabolites.

Elimination of radioactivity via excreta (and cage washes), accounted for a mean recovery of up to 50% of the administered dose within 24 hours after administration. By day 4, the recovered radioactivity accounted for up to 93% of the administered dose. The mean daily recovery of the administered dose was 86% in excreta over all hens during the 12 day study period.

Total radioactive residues (TRR, mg/kg endosulfan equivalents) in tissues and eggs are shown in Table 2 below.

**Table 2: TRR in hen tissues and undeveloped eggs following dosing of <sup>14</sup>C-endosulfan at 0.7 mg/kg bodyweight/day (Reynolds, 1996).**

| Tissue             | TRR (mg/kg endosulfan equivalents) |       |       |       |       |       | Mean ± SD    |
|--------------------|------------------------------------|-------|-------|-------|-------|-------|--------------|
|                    | Hen 1                              | Hen 2 | Hen 3 | Hen 4 | Hen 5 | Hen 6 |              |
| Liver              | 0.444                              | 0.423 | 0.334 | 0.393 | 0.533 | 0.671 | 0.466 ±0.119 |
| Muscle             | 0.031                              | 0.025 | 0.027 | 0.027 | 0.024 | 0.036 | 0.028 ±0.004 |
| Skin               | 0.600                              | 0.593 | 0.519 | 0.786 | 0.808 | 0.825 | 0.689 ±0.133 |
| Fat (Subcutaneous) | 0.695                              | 0.819 | 0.935 | 0.799 | 0.918 | 1.083 | 0.875 ±0.134 |
| Fat (Abdominal)    | 0.906                              | 0.876 | 1.103 | 0.952 | 0.970 | 1.035 | 0.974 ±0.084 |
| Undeveloped eggs   | 0.713                              | 0.636 | 0.995 | 0.806 | 0.610 | 0.847 | 0.768 ±0.145 |

<sup>1</sup> Labelled in the methylene bridge and in the 6,7,8,9 carbon positions of the cyclopentane ring.