Report to the NRA

The relevance to sheep husbandry practices in Australia of the UK Institute of Occupational Medicine (IOM) Report (*Epidemiological study of the relationship between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy, and neuropsychological abnormalities in sheep farmers and dippers).*

Expert Panel on Organophosphate Sheep Dips

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1 EXECUTIVE SUMMARY

In July 1999, the UK Institutes of Occupational Medicine (IOM) released a report titled *Epidemiological study of the relationship between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy, and neuropsychological abnormalities in sheep farmers and dippers.*

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) established an independent expert panel to review the findings of the IOM report, assess its implications for Australia, and develop recommendations to the NRA in light of this report and other recent reports.

The NRA Expert Panel reviewed the UK IOM Report and other relevant literature published since 1995. It was noted that the IOM study had design flaws and the Report was difficult to interpret as the results of two of the three phases of the study were inconclusive.

The NRA Expert Panel considered that the main findings of the IOM report were that:

- The main source of exposure to organophosphate (OP) sheep dip chemicals is associated with handling the concentrate, and therefore all practical measures should be taken to minimise worker exposure to concentrates;

- The IOM study could not establish a definitive link between OP exposure and chronic health effects.

The NRA Expert Panel found that work practices and exposure patterns differed between the UK and Australia. In Australia there were only limited data available on exposure to OP concentrates from sheep dipping, and some evidence of a lack of compliance with label recommendations for the use of personal protective equipment.

Because a link between OP exposure and long-term health effects was not completely eliminated by the IOM Report and other studies that were reviewed, the NRA Expert Panel considered it prudent to take measures to minimise user exposure to OPs in sheep dip concentrates.

The NRA Expert Panel therefore recommends that the NRA:

- maintain registration of OP-based sheep dip products, pending further findings of the Existing Chemical Review Program (ECRP);

- strengthen label warnings on registered OP sheep dips by incorporating additional statements to minimise exposure to concentrate;

- investigate the development of improved packaging/formulation to reduce worker exposure from handling of OP sheep dip concentrates;

- take initiatives to improve education and training/certification of users of OP sheep dip chemicals;

- review regulatory approaches to the following:
  - reporting of exposures and adverse reactions;
  - the review of OP sheep dips that are not currently in the ECRP;
  - recommendations for the design and use of personal protective equipment;
  - suitability of containers;

- promote research into:
  - characterising OP exposures from sheep dipping in Australia;
  - development of a predictive model for worker exposure to sheep dip chemicals in Australia;
  - procedures for the inactivation of the OPs in chemical spillages and dipping solutions;
  - the development or identification of personal protective equipment that is more practical and therefore more acceptable to workers.

Further detail on the recommendations can be found in Section 8.

2 INTRODUCTION AND TERMS OF REFERENCE OF THE NRA EXPERT PANEL

In July 1999 the UK Institute of Occupational Medicine (IOM) released a report titled *Epidemiological study of the relationship between exposure to organophosphate pesticides and indices of chronic peripheral neuropathy, and neuropsychological abnormalities in sheep farmers and dippers.* The report identified handling of organophosphate sheep dip concentrates as the main source of potential worker exposure during sheep dipping and suggested that this exposure was associated with an increased likelihood of ill-health in the groups studied.

In order to clearly assess the implications of the report, the Minister for Food Safety, UK Ministry of Agriculture, Forestry and Fisheries (MAFF) in the UK forwarded the report to its advisory committees (Committee on Toxicity Working Group on OPs (COT), Veterinary Products Committee, and Advisory Committee on Pesticides) for urgent consideration, along with any other evidence available on the possible ill-health effects of organophosphates. The committees were asked to report before the end of 1999[1].

In Australia, the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) established an independent expert panel (hereafter referred to as the NRA Expert Panel) to review the findings of the IOM Report, to assess its relevance and implications for Australian sheep husbandry and to formulate recommendations to the NRA. The NRA Expert Panel was headed by Professor JG McLean, former Pro Vice-Chancellor (responsible for Science, Engineering and Design) at Melbourne's Swinburne University of Technology. Members included experts from key organisations with an interest in sheep dip chemicals – farmers, farm workers, industry, regulatory authorities, and occupational health and safety authorities. The panel was convened in August 1999 and was asked to report to the NRA by mid February 2000. Membership and resumés of the NRA Expert Panel are included in Appendix A.

The NRA Expert Panel was asked to:

- Review:

- the UK IOM report *Epidemiological study of the relationship between exposure to OP pesticides and indices of chronic peripheral neuropathy, and neuropsychological abnormalities in sheep farmers and dippers*;

- international literature published in scientific and government reports since 1995 on the effects of organophosphate use in sheep husbandry;

- sheep husbandry practices in Australia which include the application of organophosphate pesticides.

[1] See Addendum for a brief summary of UK committee findings and Appendix I for the Executive Summary of the COT report.

- With the purpose of:

- advising on the relevance of both the findings of the UK IOM report and international literature to Australian usage of organophosphates in sheep husbandry;

- identifying the implications of this relevant material to the development of recommendations for organophosphates currently under review as part of the NRA's Existing Chemicals Review Program ie. chlorfenvinphos and diazinon;

- formulating recommendations to the NRA on risk management options for the general use of organophosphates in sheep husbandry, and specifically on chlorfenvinphos, diazinon, temephos and propetamphos.

3 BACKGROUND INFORMATION

3.1 Overview of the Toxicology of Organophosphates

Organophosphates (OPs) kill insects by interfering with the activity of the enzyme acetylcholinesterase in the nervous system. This interference results in overstimulation of the nervous system resulting in rapid twitching and then paralysis of muscles. Paralysis of muscles in the respiratory system ultimately causes death.

While the toxicity of organophosphates varies, they are all relatively toxic to humans and animals. Poisoning can occur by oral ingestion, by inhaling the spray or dust, or by absorption through the skin. The extent of poisoning is directly related to the toxicity of the compound and the quantity ingested, inhaled or absorbed through the skin. Symptoms associated with acute poisoning (in approximate order of appearance and severity) are nausea, vomiting, abdominal cramps, diarrhoea, excessive salivation, headache, dizziness, blurred vision, ocular pain, pinpoint pupils, breathing difficulty due to excessive secretions and bronchoconstriction, random jerky movements, convulsions, respiratory failure and death. Effective medical and first aid treatments are available for the immediate effects of OP poisoning.

In mammals, organophosphates tend to be rapidly absorbed and metabolised. Excretion is mainly in the urine. In laboratory studies of these compounds in mice, rats, dogs and monkeys, long-term exposure to low concentrations in the diet is associated with some reduction in cholinesterase (ChE) activity, with the degree of inhibition being largely dependent upon the potency of the particular OP and the dose administered. The weight of evidence suggests that these chemicals do not interact with genetic material, and whole-of-life studies in animals gave no indication that they would be likely to cause cancer in humans. Of the OPs used as sheep dips, there is no evidence of adverse effects on reproduction or on development of the foetus.

While it is well established that acute over-exposure to organophosphates can lead to adverse short term health effects of varying severity, recent concerns have arisen that exposure may also give rise to chronic health effects in users. There is currently little scientific evidence available to either support or refute the existence of these chronic

effects. Two different types of chronic effect have been suggested: those due to after-effects of one or more serious acute poisoning episodes and those ascribed to long-term low level exposures which do not cause acute symptoms.

A wide variety of both neuropsychological and neurological effects have been described. Some organophosphate pesticides have been reported to induce 'intermediate syndrome' after incidents of acute intoxication, often as a result of attempted suicide. This effect differs from the usual signs of poisoning seen very soon after exposure, and is observed as a delayed onset of muscular weakness affecting neck, proximal limb and respiratory muscles. It usually occurs 1 to 3 days after exposure. Another reported condition, known as organophosphate induced delayed neuropathy (OPIDN) is characterised by usually irreversible sensory and motor symptoms mainly in the lower limbs. These occur within 1-2 weeks of acute poisoning with certain OPs.

Other reported symptoms include cognitive impairment, psychiatric or neuropsychiatric disturbances, cholinesterase inhibition and various non-specific symptoms.

3.2 Relevant Events in Australia

Since the 1970s there has been a move away from the use of persistent chemicals in the sheep industry in Australia. All cyclodiene organochlorine pesticides were removed from agriculture/sheep husbandry uses in the 1980s (see Appendix B, *Organochlorines in Australia*). By 1990 the only use of these chemicals was as termiticides or for a very limited number of special uses. With the phase-out of organochlorine pesticides, there has been an increase in the use of organophosphate pesticides.

In the early 1990s occupational health concerns were raised about the safety of horticultural use of parathion-ethyl in the Goulburn Valley of Victoria.

In 1994 tribufos (formerly called DEF) was withdrawn from use as a cotton defoliant because of its potential effects on human health. Tribufos, though a relatively weak anticholinesterase compound, was shown to inhibit the enzyme neuropathy target esterase and to cause delayed neuropathic effects in animals.

In 1995/96 the Australian Commonwealth Department of Health considered the use of organophosphate sheep dips following the release of the UK Health and Safety Executive study on OP sheep-dip farmers (Stephens et al., 1995). The study raised the possibility that there could be chronic neuropsychological and neurological effects of occupational exposure to organophosphates. At this time it was noted that the findings were not new as there had been many reports of neuropsychological effects of OPs, dating back to the mid-1950s. Some of the actions taken at the time included:

- raising the issue of the neurotoxicity of OPs with the Advisory Committee on Pesticides and Health (ACPH), an expert committee within the Department of Health comprising scientists with expertise in toxicology and chemical residues;

- considering whether plasma cholinesterase inhibition is the most appropriate indicator of the toxicity of OPs or whether there may be more sensitive or relevant indicators on which to base no-observable-effect (NOEL) levels ;

- setting a NOEL for parathion-methyl based on neuropathological findings in peripheral nerves in a chronic rat study rather than on plasma cholinesterase inhibition;

- requesting further chronic toxicology studies in animals from registrants of OP pesticides, to address the potential of these chemicals to cause neurotoxic effects and the levels at which such effects might occur;

- liaising with the US Environmental Protection Agency on appropriate testing requirements for new and existing cholinesterase inhibitor pesticides.

Thirteen out of the first nineteen chemicals in the NRA Existing Chemicals Review Program (ECRP) are organophosphates (viz. mevinphos, parathion, parathion-methyl, chlorfenvinphos, chlorpyrifos, diazinon, dichlorvos, fenitrothion, monocrotophos, azinphos-methyl, azinphos-ethyl, demeton-S-methyl and fenthion).

In 1997 in New South Wales (NSW) a judge accepted that four members of a shearing team had been poisoned after being required to restrain blowfly struck sheep while they were treated on the shearing floor with a “tar” preparation which contained diazinon. On several days, their clothing had become saturated with this preparation. Symptoms included impaired memory and learning, reduced attention span and a slowed rate of information processing. As a result, the men had become unfit to continue work as shearers (McKenzie and Ors -v- Harper, Supreme Court of NSW, 8 October 1997). The full case report is included in Appendix C.

Australian sales of organophosphate sheep dips have declined over the last few years, the most significant decline occurring with diazinon, the most widely used of these chemicals. Total sales of organophosphate sheep dip products decreased from approximately $11 million in 1994 to approximately $6 million in 1998. This may be as a result of changing management practices such as the use of backline treatment as an alternative to dipping. However, it was noted that OPs are relatively inexpensive compared with other ectoparasite control options.

3.3. Australian Worker Exposure Monitoring

An overview of approaches to biological monitoring of worker exposure to organophosphate insecticides in Australia is included in Appendix D.

In response to the UK Health and Safety Executive report on UK sheep farmers (Stephens et al, 1995), a pilot study was carried out in NSW to establish the degree of exposure to organophosphate chemicals, the level of occupational hygiene and the prevalence of symptoms reported by workers in the sheep industry. It was a cross sectional study of sheep industry workers in the central western districts of NSW which was undertaken during the summer of 1996. A questionnaire was administered and blood was collected for the determination of red blood cell and plasma

cholinesterase activities. A shorter questionnaire was administered in the following winter and blood collected for "baseline" cholinesterase determinations. Urinary metabolites were not determined.

The report[2] of the study is yet to be published, but it indicated that:

- red blood cell cholinesterase was observed to decrease slightly while workers were involved in dipping;
- compliance with the use of personal protective equipment was very poor;
- only low level exposures to organophosphate compounds were detected.

As a result of these preliminary results, it is likely that further investigation of chronic low level exposures experienced by workers in the sheep industry and any associated adverse effects will be carried out.

3.4 Historical Perspective to Concerns about Chronic Toxicity of Organophosphates

Reports of possible chronic effects of OP exposure have appeared in the scientific literature for more than 50 years.

A report of a study conducted in German army personnel involved in the manufacture and handling of OPs noted psychopathological/neurological delayed lesions, for example memory difficulties, which persisted for 5-10 years (Speigelberg, 1961).

In the 1960s Australian research reported depression and schizophrenia as possible effects of chronic OP exposure, a finding which triggered much debate in the literature at the time. A study from researchers at the University of Melbourne and Prince Henry's Hospital presented brief case studies of 14 men and two women exposed to OPs for between 1.5 and 10 years. These subjects were suffering from schizophrenic and depressive reactions, with severe impairment of memory and difficulty in concentration. A limited field survey suggested that psychiatric disorders may be more common in fruit-growing areas than in towns (Gershon & Shaw, 1961).

A separate study compared schizophrenia incidence with OP sales in Australian fruit-growing areas. It was found that schizophrenia was 1.9 times more common in two areas where sales were 7.9-times higher than the reference area. However, follow-up work could not link individual cases to OP pesticide use. Also, over a larger population of 5034 growers there was no correlation between schizophrenia or depression, and pesticide sales. It was recognised that measures of exposure and effects were limited, which did not allow more than the detection of a gross effect (Stoller et al, 1965).

With the debate about the safety of OP pesticides still ongoing both in Australia and overseas, researchers at Monash University published a paper titled, "Has the time come to ban organophosphate pesticides?" (Dyer & Hanna,1974). These authors

[2] Pers. comm. R Kenyon, 1999, from draft manuscript in preparation, Scott M, McDonald A, Hazelton R Mirek A & Kenyon R "Organophosphate Exposure in Sheep Husbandry".

cautioned about the increasingly widespread use of organophosphates. Their concerns largely arose from the indications of possible mutagenicity of some of the OPs in use or being introduced at the time, including dichlorvos, oxydemeton-s-methyl, thiometon, pirimifos and thiometon. In the event, most of those OPs with positive results in tests for mutagenicity have either been withdrawn from the market or further testing has allayed health concerns.

Available data (predominantly from Japan) suggested an association between organophosphate chemical exposure, and signs and symptoms of visual system toxicity (Boyes et al, 1994). It should be noted that the bulk of the literature reporting ocular toxicity of OPs in humans was confined to Japan, with only a limited number of published reports from other countries.

4. ASSESSMENT OF THE IOM REPORT ON ORGANOPHOSPHATE SHEEP DIP USE IN UK

The original three volumes of the IOM Report together with a summary assessment prepared by staff from the Therapeutic Goods Administration (Appendix E), were considered by the NRA Expert Panel.

The IOM study attempted to address the question of whether prolonged exposure to organophosphate sheep dip may cause chronic ill-health in sheep dip users, and specifically, whether prolonged exposure leads to cumulative damage, reflected in clinically-detectable neuropathy.

The NRA Expert Panel **NOTED** that among the major challenges facing the IOM investigators was the difficulty in estimating the extent of exposure to OP sheep dips in a meaningful way. Sheep dip users had been using a variety of sheep dip products, and possibly other organophosphates in agriculture over the thirty-year period considered in the study, and estimates of exposure over this period were based on memory recall.

The NRA Expert Panel also **NOTED** that the phases 2 and 3 of the study had significant methodological flaws which made scientific interpretation difficult.

4.1 Phase 1 of the IOM Study

This phase involved one-day surveys of plunge dipping sessions at farms, and the development of a model of systemic exposure to OPs during sheep dipping.

The NRA Expert Panel **NOTED** that Phase 1 of the study was designed to:

- observe one-day sheep dipping sessions on 20 farms mostly located in the border region of England and Scotland, recording the activities performed by individuals involved in dipping operations with diazinon. These observations included: the frequency and extent of handling dip concentrate; the extent and time of contact with dip wash; protective clothing worn; smoking and eating habits.

- assess uptake of OPs by measuring levels of diazinon metabolites in urine of workers before and after dipping;
- identify the specific tasks or activities that lead to exposure and utilise the data to develop a mathematical model relating the uptake of OPs to task characteristics.

The NRA Expert Panel **CONSIDERED** that this phase of the study had been satisfactorily conducted by the IOM and that the major findings were that:

- exposure to dip concentrate (generally on the hands) was the most important source of exposure to OP sheep dip;
- the number of exposures to concentrate could be related to flock size and main task performed during dipping, that is whether workers were "chuckers", "paddlers" or "helpers/handlers"[3];
- a linear regression model was developed which described the relationship between uptake of OPs as assessed by post-dipping urinary metabolite levels and estimated exposure to both the dip concentrate and the dip wash, with a weighting for their relative importance. In the case of uptake of diazinon, exposure to concentrate was 18-times more important than exposure to dip wash.
- the use or otherwise of personal protective equipment (PPE) was a poor predictor of exposure. This was thought to be because of both poor quality equipment and poor use of equipment during the study.

The NRA Expert Panel **NOTED** that the investigators had not reported whether a dose response relationship could be found despite having urinary metabolite data on individuals who had been exposed to diazinon at concentrations of 0, 16% and 60% active ingredient. There was insufficient data in the published IOM report to perform this analysis. This is unfortunate as the establishment of a dose response would have provided robust confirmation of the exposure model put forward.

4.2 Phase 2 of the IOM Study

Phase 2 of the study was a cross-sectional field study of sheep dippers and of individuals not occupationally exposed to OPs. The final study group consisted of 612 farmers with sheep dipping experience and a control group of 53 farmers with no sheep dipping experience recruited from pig and chicken farms, combined with 107 ceramics workers from two factories. This phase was designed to examine the relationship between cumulative history of exposure to OPs and indices of effect. Symptoms were recorded in a neurological symptoms score questionnaire administered to each subject and field measurements were made of quantitative sensory thresholds (QST). The findings from the questionnaire are reported in Table 1.

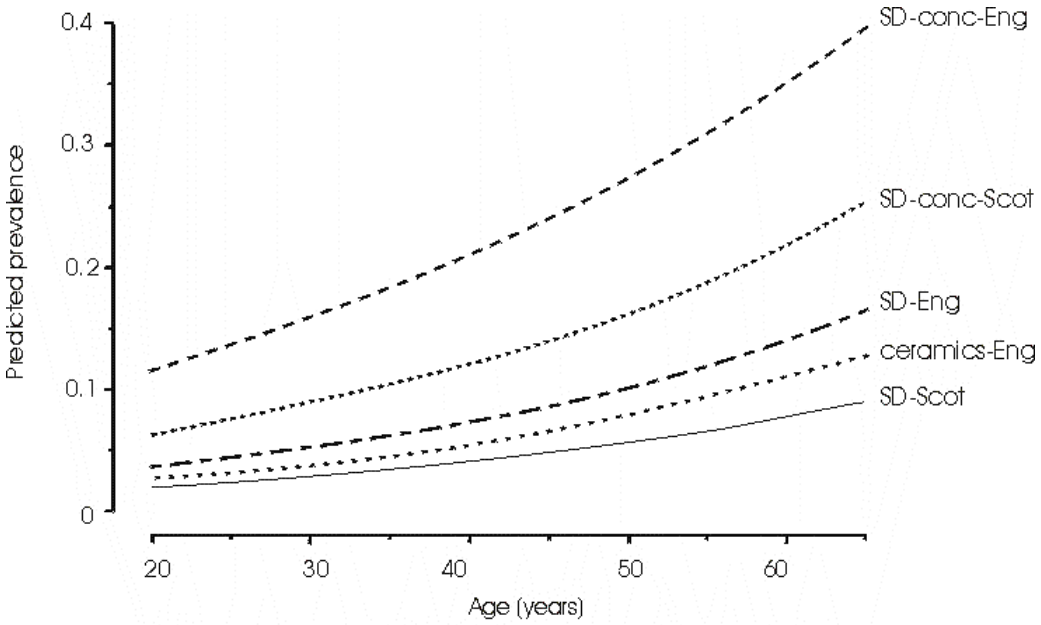
[3] These descriptions of the roles of workers apply to sheep farm workers in the UK and do not necessarily translate directly to the Australian situation.

Table 1 Prevalence of reported neuropathic symptoms by occupational group [% affected, (number)]

Type or location of symptom	Ceramics Workers	Non-Sheep-Dip Farmers	Sheep-Dip Farmers
Muscle weakness			
Hands	0	1.9 (1)	6.4 (39)
Shoulders	0	0	2.0 (12)
Feet	0	0	2.3 (14)
Legs	0	3.8 (2)	0.8 (5)
Reduced sensory function (negative sensory)			
Feet	0	3.8 (2)	5.2 (32)
Hands	0	0	2.1 (13)
Altered sensation eg numbness or pain (positive sensory)			
Feet	1.9 (2)	2.7 (3)	10 (61)
Hands	0.9 (1)	3.8 (2)	5.4 (33)
Autonomic nervous system symptoms			
Fainting	3.7 (4)	15 (8)	14 (87)
Diarrhoea	0	0	0.7 (4)
Bladder	0	0	1.8 (11)
Impotence	0	1.9 (1)	5.6 (34)
Sweating	7.5 (8)	5.7 (3)	8.2 (50)
Group size	***107***	***53***	***612***

A regression model was developed and used to predict the prevalence of symptoms from reported OP exposure. The prevalence of symptoms predicted by this model is shown in Figure 1 which graphs the predicted prevalence of symptoms for male sheep dip (SD) farmers aged 20 to 65 years under the four combinations of country (England or Scotland) and concentrate handler (ever or never). All predictions in Figure 1 are adjusted to 50 days dipping.

Figure 1 Predicted prevalence of symptoms among male sheep dippers and ceramics workers by concentrate handling and country



Predicted prevalence of symptoms among male sheep dippers (SD) and ceramics workers by concentrate handling (conc) and country.

The importance of concentrate handling was investigated by including a variable to indicate those individuals who had been principal concentrate handlers. Adjusting for concentrate handling decreased the large difference in symptom prevalence between sheep-dip farmers and ceramics workers. As seen in the Figure, sheep-dip farmers with no experience of handling concentrate were predicted to have the same prevalence of symptoms as ceramics workers of the same age, sex and country.

Among concentrate handlers there was a predicted age-related increase in symptom reporting, reaching 35% at age 60 years for English sheep dippers. A higher incidence of reporting in England compared to Scotland is also clear. The predicted prevalence of symptoms among male English ceramics workers was always marginally higher than Scottish sheep dip farmers who had never handled concentrate.

The NRA Expert Panel **NOTED** the following important findings from this phase of the study:

- sheep dippers reported higher rates of symptoms compared with non-exposed workers see Table 1);
- self-reported symptom score was related to indices of cumulative exposure to sheep dips. However the statistical significance of the relationship between cumulative exposure and symptoms was determined by the inclusion of a very small number of highly exposed individuals. The exclusion of the four most highly exposed subjects from among the 612 sheep-dip farmers resulted in the relationship being no longer statistically significant;

- there was a strong regional difference among subjects of the same age and occupational group, with a higher prevalence of reported symptoms in England compared to Scotland;
- sensory symptoms were more commonly reported than motor symptoms;
- though the IOM report showed no evidence that cumulative exposure to OPs was associated with impairment of measured sensory thresholds, the significance of this finding is equivocal because of the lack of reliability of the QST data;
- the critical exposure factor appeared to be contact with concentrate. Markedly higher rates of reported symptoms (adjusted for other factors) were reported among those who had, at some time, been principal concentrate handlers.

The NRA Expert Panel **IDENTIFIED** the following possible methodological problems in phase 2 of the study:

- organophosphate exposure for the control groups was assumed to be negligible, which may have been incorrect;
- OP exposure in the sheep dip farmers was estimated retrospectively from a questionnaire which required respondents to recall details about their working history over a thirty-year period, including: principal tasks when sheep dipping; flock size; dipping frequency and sheep dip bath types. It is difficult to assess the reliability of the exposure data thus obtained or the degree of recall bias.
- the reliability of the symptoms questionnaire is also difficult to assess. However, the NRA Expert Panel noted that all questionnaires including the neurological symptoms questionnaire were administered in the field by a trained technician using an established protocol and hence the data were likely to be reasonably reliable;
- differences in awareness of health issues associated with OPs may have biased the responses to the symptom questionnaires. It was noted that the authors concluded that there was more media coverage of the issue in England during the period of the survey and this could in part explain the differences in the reported level of symptoms between the English and Scottish sheep dip areas. Other plausible theories that could explain the regional difference in symptoms were identified by the NRA Expert Panel including genetic differences in pesticide metabolism, altered exposure to other neurotoxins, and cultural and language differences in the responses to the questionnaire;
- the control groups were inadequately matched to the sheep dipping group for age, sex and alcohol intake. These confounding factors are likely to have a significant effect on neuropathy findings and hence the cross-sectional study was seriously weakened;
- there was a disparity between the full QST data obtained from the same individuals in Phase 2 and Phase 3. The NRA Expert Panel **CONCLUDED** that the field measurements of QSTs were not sufficiently reliable to be useful in further analysis in either Phase 2 or Phase 3.

4.3 Phase 3 of the IOM Study

This phase consisted of a detailed neurological and neuropsychological study, performed in a clinic, of a sub-group of Phase-2 subjects. The study was designed to validate the results obtained in the field.

On the basis of the Phase 2 symptoms questionnaire and QST, the 79 individuals tested were classed into three groups “no neuropathy”, “possible neuropathy” or “probable/definite neuropathy”. Clear evidence of neuropathy was then independently diagnosed by a neurologist from nerve conduction changes or clinical signs detected during a detailed neurological examination.

The NRA Expert Panel **NOTED** the following important findings from this clinical phase of the study:

- only about half the 23 subjects classified as having "probable/definite neuropathy" and about 30% of the 34 individuals classified as having "possible neuropathy" on the basis of Phase 2 studies had clear evidence of neuropathy.
- the neuropathy described was predominantly of a sensory type, both symptomatically and neurophysiologically, and was characteristic of distal, chronic axonopathy with no acute features. Symptoms did not include motor neuron dysfunction. Small nerve fibre populations were affected more than large nerve fibre populations.
- autonomic nervous system symptoms (including fainting, diarrhoea, bladder function, impotence, and sweating) were commonly reported by the “no neuropathy” and “possible neuropathy” groups, but less commonly by the “probable neuropathy group”.
- the neuropathy reported in this phase apparently differed from organophosphate-induced delayed neuropathy (OPIDN) on the basis of the timecourse and symptomatology.
- the results did not show that the neuropsychological findings were related to cumulative exposure to OPs (results of two of the sixteen tests carried out were statistically significant, one indicating better and one indicating worse performance in the sheep-dip farmers).
- the IOM study authors accepted that the sampling design of the clinical study was not optimal for the characterisation of neurophysiological or neuropsychological differences between exposure groups.

The NRA Expert Panel **COMMENTED** that Phase 3 of the study had serious methodological flaws including lack of controls and poor recruitment from the initial 772 participants who were assessed in Phase 2. It was noted that only 79 (72 of whom were assessed) of the 772 attended for phase-3 clinical assessment, and these were all from the sheep-dip farmer group. No participants from the non-sheep-dip farmer group or the control (ceramic worker) group attended for in-clinic testing. Also, the sheep-dip farmers who participated in this phase of the study did not appear to be identified as to their main role in the dipping process.

The NRA Expert Panel **BELIEVED** that while the study had demonstrated a relatively high incidence of neuropathic signs in the sheep dip farmers (23/72 tested), the small sample of individuals tested in this phase prevented a realistic analysis of any relationship between neuropathy and estimated OP exposure. Thus it is possible that the combined activities of farming in general lead to an increased incidence of neuropathy compared with the general population (stated in the IOM report as being between 0.3 - 0.5%). The NRA Expert Panel did **NOT ACCEPT** that the neuropsychological tests were capable of unequivocal interpretation.

4.4 Summary of NRA Expert Panel Review of IOM Report

The NRA Expert Panel **CONSIDERED** that the main conclusions to be drawn from the IOM Report were:

- sheep-dip farmers reported symptoms more frequently than ceramics workers;
- the most important source of OP exposure (as measured by metabolites) appeared to be contact with dip concentrates; however, increased splashing with dip wash was also correlated with increased urinary metabolites;
- the highest prevalence of symptoms was reported by those who had at some time been concentrate handlers. Sheep dippers who had not handled concentrate did not report more symptoms than non-exposed (ceramic) workers. Average concentrate handling frequency, independent of duration of exposure, could explain the difference between sheep dip farmers and non-exposed workers in relation to reported symptoms;
- there was a much higher prevalence of symptoms reported by English study subjects compared to Scottish subjects;
- Quantitative Sensory Thresholds (QSTs) measured in the field in Phase 2 appeared to be quite unreliable and did not correlate with QSTs measured in the clinic in Phase 3 of the study;
- Phase 3 of the report indicated a higher incidence of clinically-detectable neuropathy in farmers who had dipped sheep compared to the general population. However, it should be noted that this group was self-selected with respect to clinic attendance;
- there was some evidence of an association between neuropathy findings and neuropsychological findings (anxiety and depression). However, it is known that psychosocial variables can significantly influence symptom reporting. Thus it is possible that this association reflects a tendency for anxious or depressed individuals to complain of neurological symptoms more readily;
- neuropsychological tests did not show any clear evidence of a statistically significant relationship between neuropsychological performance and cumulative exposure to OP sheep dips.

The IOM study was not conclusive, but did show an association between OP exposure, predominantly handling the concentrate, and reported symptoms consistent with peripheral neuropathy. That is, exposures to concentrated forms of OPs above a certain handling frequency and on a repeated basis, over even a relatively short time-scale, may be associated with increased reporting of long-term health effects. Unequivocal findings indicative of neuropathy were common in the small sample of sheep dip farmers who attended for testing in the clinic, but the absence of equivalent testing of the control groups (non-sheep dip farmers and ceramic workers) means that no firmer conclusions can be drawn.

A separate summary and analysis by Australia's National Occupational Health and Safety Commission also concluded that the IOM Report raises concerns of a relationship between neurological dysfunction and exposure to organophosphate pesticides, but the Report does not provide strong evidence of such a relationship.[4]

5. OVERVIEW OF RELEVANT TOXICOLOGICAL RESEARCH ON ORGANOPHOSPHATE PESTICIDES SINCE 1995

The following studies and reviews were considered important in this overview of relevant recent publications.

5.1 Stephens R, Spurgeon A, Beach J, Calvert I, Levy LS, Berry H & Harrington JM (1995) An investigation into the possible chronic neuropsychological and neurological effects of occupational exposure to organophosphates in sheep farmers. Institute of Occupational Health, University of Birmingham, UK. HSE Contract Research Report No. 74.

This cross-sectional study was designed to assess neuropsychological performance of 146 male sheep farmers and farm workers who had been exposed to OP sheep dips compared with a control population of 143 non-exposed quarry workers.

Farmers and workers who had been involved in sheep dipping performed significantly worse (48% ± 23%) than controls in tests to assess sustained attention and speed of information processing. A dose-relationship was evident when data was analysed by exposure groups, but there were no observed effects on short-term memory and learning. Although the effects observed were not severe, the report concluded that, as far as possible, measures should be taken to reduce exposure to organophosphates during sheep dipping.

The exposed workers were administered a questionnaire to examine the role of dippers' risk perception in relation to indices of exposure and health outcomes. While there was no relationship between attitudes and delayed and chronic effects, there was a positive correlation ($r=0.23$, $p=0.036$) between acute symptom reporting (symptoms scored 24 hours after dipping) and attitude score. Workers who reported more symptoms were somewhat more likely to perceive a higher risk from OP sheep dips. There was also a significant correlation with general health questionnaire scores such

[4] Driscoll T and Mitchell R, December 1999. This draft overview was submitted too late to be considered in detail by the NRA Expert Panel.

that those with a higher risk perception appeared to be more at risk of developing psychiatric problems. As there was no correlation between risk perception and any of the significant cognitive test outcomes, the inter-relationship between attitudes and symptoms remains undetermined.

The NRA Expert Panel **ACCEPTED** that this report raised concerns when it was published in 1995. However, it did not contain sufficient detail to establish whether there were any findings specific to farmers who handled concentrate compared to those only exposed to dip wash.

5.2 Ray D (1998) Organophosphorus esters: An evaluation of chronic neurotoxic effects. MRC Institute for Environment and Health.

This report, prepared under contract to the UK Department of Health, reviewed the available scientific and medical literature in order to assess the possibility that chronic neurotoxicity could result from exposure to OP pesticides.

It was noted that the only OPs currently approved for use as sheep dips in the UK are propetamphos and diazinon, with a number of others having been removed from the market in recent years. The author commented that the efficacy, low environmental persistence, and low costs of OP pesticides will probably ensure that they have a continuing use well into the future.

The report provided a good overview of the toxicity of the OP class of chemicals, noting that these chemicals can cause three syndromes of poisoning in humans and experimental animals, namely, acute pharmacological toxicity, the intermediate syndrome, and delayed polyneuropathy.

The author provided a tabular summary of the effects seen in 19 epidemiological and/or clinical studies of low level OP exposure (see Appendix F). Direct comparison of these studies was difficult. In some, the effects of hard work and OP exposure were closely linked, while in others overall OP exposure was from a combination of high and low level exposures. While the effects reported in these studies ranged from small to negative, it is clear that many studies did report indications of toxicity associated with low-level exposure.

The author expressed several reservations about drawing general conclusions from such a diverse data set. He also made criticisms of study design, case-control matching and endpoint suitability.

Although Ray concludes that low level exposure to OPs are not likely to be responsible for any health effects large enough to be subjectively apparent, the NRA Expert Panel **NOTED** that subtle effects (ie. not subjectively apparent) should not be dismissed.

The Ray Report noted that research in the UK could be more usefully directed to examining agent-specific effects, and that OP class effects could be evaluated in a prospective study of cases of higher exposure, such as in tropical and developing countries, where cases of frank OP poisoning were quite common. The NRA Expert

Panel believed that, for Australian use patterns for OP sheep dips, local research would be the most appropriate.

In discussing the link between OP exposure and suicide or depression, the report commented that reported studies of suicide incidence suffered from poor data analysis, an association of an unusually high level of exposure with intensive workload and probable intermittent acute poisoning (see discussion at Section 3.1).

The NRA Expert Panel **AGREED** with a number of the findings from this report:

- It appears that, for the majority of sheep farmers and farm workers, exposures associated with normal sheep dipping are low enough not to produce any frank cholinergic signs.

- Some of the main difficulties in interpreting results from neurotoxicity studies in humans after OP exposure have included:-

    - lack of definition of exposed groups in epidemiological studies;
    - lack of use of the same indices/end-points across a number of otherwise good neurobehavioural studies, thus preventing direct comparison of results;
    - the non-specific nature of signs of intoxication after low-level exposures;
    - limited consideration of known individual and socio-economic factors that may influence reporting rates; and
    - the absence of a clear theoretical or mechanistic framework to explain long-term effects.

- Observations which warrant further investigation of OP toxicity include:-

    - adaptation to OP-induced toxicity in workers which could lead to additional occupational exposure resulting from a lack of warning signs or symptoms;
    - individual susceptibility to OP-induced neurotoxicity, based on variation in such factors as blood or liver metabolic capacity;
    - the possibility of an increase in incidence of suicide and depression in situations of high or medium OP exposure;
    - the possibility of novel protein targets (in the brain and nervous system) which might form an important underlying part of the mechanism of OP-induced toxicity;
    - cholinergic excitotoxicity, a situation in which cells die as a result of prolonged activation.

5.3 ECETOC (1998) Organophosphorus pesticides and long-term effects on the nervous system. Technical Report No. 75, December 1998 (ISSN-0773-8072-75)

This report, commissioned by the European Centre for Ecotoxicology and Toxicology of Chemicals, Brussels, reviewed published evidence for neurotoxicity arising from chronic, low-level OP exposure. Their main conclusion was that there was insufficient evidence in the epidemiological literature to convince the reviewers that there is a “chronic syndrome” resulting from chronic, apparently asymptomatic exposure to

OPs. Nevertheless, they noted that continued surveillance of exposed populations would be the most appropriate course of action.

While early drafts of the report had undergone independent peer review, the NRA Expert Panel **NOTED** that members were current employees of the drug/chemical manufacturing industry. Ray (1998) considered that the ECETOC report was essentially the manufacturers' view of the hazards.

5.4 Official Group on OPs: Report to Ministers, 1988. MAFF Publications, London.

In the face of continuing public debate over whether organophosphate products damage human health, a meeting of UK Government Ministers in 1997 established a high-level group of government officials to examine government policies relating to OP products and arrangements for administering them. The overall conclusion of the UK group was that "the potential of OPs to cause ill health following long-term low-level exposure remains unknown ….. data were difficult to interpret and no firm conclusions could be drawn".

From the information published in this report, the NRA Expert Panel **NOTED**:

- the availability of a comprehensive information brochure in the UK advising sheep dippers on safety (AS29. "Sheep-Dipping" Agricultural Safety Series Leaflet, published by the Health and Safety Executive);

- the extensive list of pesticide research supported by UK government funding in the UK (309 studies);

- proposals for a greater level of inter-agency coordination of chemical management in the UK;

- the various UK poisoning reporting schemes;

- several of the recommendations of the UK group, including:
  - the views of the advisory committees dealing with various aspects of OPs should be placed in the public domain.
  - legislative changes should be made to allow exchange of documents between Departments and greater disclosure to the public.
  - various changes could be made to control OP exposure including modification of containers, disposable packaging and mandatory personal protective equipment, all designed to minimise skin contact for concentrate-handlers. Other possibilities for minimising risk could include encouraging injectable preparations, use of non-OP compounds and the use of trained contract dippers.
  - examination of the possibility of licensing users as well as purchasers of sheep dip products.

5.5 Rees H (1996) Exposure to sheep dip and the incidence of acute symptoms in a group of Welsh sheep farmers. Occup Environ Med 53: 258 – 263

Rees (1996) carried out a prospective study of 23 sheep farmers and one dipping contractor during one dipping period in 1992. The working methods of the subjects were assessed by questionnaire. The absorption of organophosphate pesticide (diazinon and propetamphos) was estimated before, immediately after, and six weeks after dipping by measuring plasma cholinesterase, erythrocyte cholinesterase, and dialkylphosphate urinary metabolites of the organophosphates. Self-reported symptoms in the subjects were recorded by questionnaire at the same time as biological monitoring. Possible confounding factors were identified by medical examination of the subjects and were reflected in the interpretation of the results where possible.

The subjects reported inadequate handling precautions and significant skin contamination with dip. Measurement of dialkylphosphate urinary metabolites did not appear to correlate with the estimates of exposure (number of sheep dipped; working practices; reported contamination). After dipping, about half the subjects reported the first occurrence or exacerbation of symptoms that might be related to OP toxicity.

However none of the subjects had symptoms or signs of the intermediate syndrome, or organophosphate-induced delayed neuropathy. Plasma and red blood cell cholinesterase activities were generally not decreased after dipping; in fact 13 out of 24 workers showed increases in red blood cell cholinesterase, which was possibly due to some technical confounding factors.

The Panel **NOTED** the author's comment that sheep dipping is strenuous and dirty work and sheep farmers find it difficult to wear personal protective equipment and avoid skin contamination with dip.

The NRA Expert Panel **CONCLUDED** that the lack of a control population and the reported technical problems limit the significance of this study. The Report failed to link self-reported OP exposure with the measured biomarkers (cholinesterase inhibition and urinary metabolites), that made it impossible to interpret the reports of OP-related symptoms.

5.6 Eyer P (1995) Neuropsychopathological changes by organophosphorus compounds - a review. Human Exp Toxicol 14: 857 - 864.

This review considered the available literature on neuropsychopathological changes after exposure to OP insecticides. It was concluded that subacute neurological sequelae following acute intoxication include the intermediate syndrome and organophosphate-induced delayed neuropathy, the latter caused by particular OPs which inhibit the neuropathy target esterase enzyme. Long-term toxic effects affecting behaviour as well as mental and visual functions appear to be occasionally observed after exposure to high doses, if these doses cause repeated clinically significant intoxications. The available data do not indicate that asymptomatic exposure to OPs is connected with an increased risk of delayed or permanent neuropsychiatric effects.

A more comprehensive review of the above reports (5.1 - 5.6) is included in Appendix F.

6. USE PATTERNS OF ORGANOPHOSPHATE ECTOPARASITICIDES IN SHEEP HUSBANDRY

6.1 Currently Registered Use Patterns

At various times, approximately fifty organophosphate compounds have been registered as agricultural chemicals, veterinary chemicals, household insecticides or human therapeutic agents in Australia. A number are no longer registered, with varying reasons for withdrawal (for example toxicological concerns, deficiencies in data, lack of a sponsor to generate data). Six OPs have been registered as sheep dips (Table 2) and four (diazinon, chlorfenvinphos, temephos and propetamphos) are currently registered for ectoparasite control on sheep.

Organophosphates which have been used for many years as human therapeutic agents include malathion for the topical treatment of lice infestation (Australia) and metrifonate (trichlorfon) administered orally for schistosomiasis (overseas countries).

Table 2 Organophosphate sheep dip chemicals in Australia*

Chemical	Registration Status	Comments
Diazinon	Currently registered as sheep dip	Under ECRP review
Chlorfenvinphos	Currently registered as sheep dip	Under ECRP review
Propetamphos	Currently registered as sheep dip	Has been prioritised in top 80 for review under ECRP
Temephos	Currently registered as sheep dip	No current sales
Carbofenothion	Withdrawn 1990 from use as sheep dip and cattle spray	
Coumaphos	Currently registered as a dog and horse wash, withdrawn from sheep and cattle dip uses in 1999.	Under Special Review. National Drugs and Poisons Schedule Committee (NDPSC) has recommended withdrawal from domestic use on toxicology grounds.

*Other OPs used as internal sheep drenches have not been included

The following Tables summarise typical use patterns derived from product labels of organophosphates registered for ectoparasite control on sheep in Australia.

Table 3 Diazinon sheep dip use patterns

Formulation Type	Concentration	Rate
Emulsifiable concentrate	200 g/L	Plunge dip, shower dip, continuous replenishment & spray race for lice &ked: 500 mL/1000 L water (0.1g ai#/L), topping up use 250 mL/500 L water. Plunge dip & shower dip for Sheep blowfly: 1 L/1000 L water (0.2 g ai./L), topping up use 500 mL/500 L water. Jetting and continuous replenishment for Sheep blowfly 2 L/1000 L water (0.4 g ai/L). Blowfly dressing: Use at 5 mL/L water (1 g ai/L).
Emulsifiable concentrate	96 g/L	Long wool sheep lice treatment and sheep blowfly suppressant. Used at 8.7 g ai./L Body lice 6 weeks to 4 months wool; 5.25 mL/sheep (0.5 g ai per sheep), 5-9 months wool 10.5 mL/sheep (1 g ai/sheep) Blowfly 6.3-10.5 mL/sheep (0.6-1.0 g ai/sheep)
Emulsifiable concentrate	93.3 g/L	Used at 1.33 g ai/L with spray applicator (0.12-0.30 g ai/sheep)
Emulsifiable concentrate	80 g/L	For sheep blowfly, lice and ked control and itchmite reduction. Initial charge: Plunge and shower dip 2.5 L/1000 L water (0.2g ai/L), continuous replenishment shower dip 5 L /1000 L water (0.4g ai/L). Topping up: plunge dip add 4 L/1000 L water added; shower dip add 1.5 L for each 500 L water added.

#ai= active ingredient

Table 4 Chlorfenvinphos sheep dip use patterns

Formulation Type	Concentration	Rate
Emulsifiable concentrate	1000 g/L	Jetting: 100 mL/200 L water (0.5 g ai/L) Hand dressing: 10 mL/12 L water (0.7 g ai/L) Lamb marking: 5 mL/10 L water (0.5 g ai /L)
Emulsifiable concentrate	138 g/L	Plunge dip Charge: 1 part product : 250 parts water Top-up: once 1000 L is dropped add 1 part product to 185 parts water Spray race Charge: 1 part product: 250 parts water Top-up: when sump drops 300 L add 1 part product to 185 parts water

Table 5 Propetamphos sheep dip use patterns

Formulation Type	Concentration	Rate
Emulsifiable concentrate	360 g/L	Body lice & ked by plunge dip, shower dip and constant replenishment dip 0.18 g ai/L Lice, ked & blowfly by plunge dip, shower dip and constant replenishment: 0.3 g ai/L Jetting: 0.36 g ai/L

Table 6 Temephos sheep dip use patterns

Formulation Type	Concentration	Rate
Emulsifiable concentrate	350 g/L	Body lice by plunge dip, shower dip and continuous replenishment dip. Initial charge: 0.35 g ai/L , topping up 0.35 g ai/L Hand jetting (up to 10 months wool): 0.35 g ai/L. Use approx 0.5 L (0.18 g) of fluid for each 1 month of wool growth.

6.2 Other Use Pattern Information

Additional use pattern information was provided by members of the NRA Expert Panel and derived from other sources including:

- the results of a survey of farmers which was carried out by the NRA in 1998 as part of the Existing Chemicals Review Program review of diazinon. Survey forms were completed by farmers who used diazinon for both agricultural and veterinary purposes. The responses from the sheep farmers have been consolidated in Appendix G.

- the NSW Agriculture brochure, "Hand Jetting Sheep" (Appendix H).

While the farmer survey was limited in scope, the material suggests that:

- plunge and spray dipping have largely been superseded as application methods for sheep ectoparasiticides. Off-shears backline treatment is now seen as preferable, with a relatively small proportion of farmers still using plunge dipping;

- the majority of farmers who responded to the (diazinon) survey indicated that they had been using the chemical for over 5 years;

- the majority of users treated their sheep only occasionally, when their sheep were affected by lice or flystrike;

- farmers reported a maximum of one application in any one year;

- while farmers considered that there were alternatives available, diazinon was regarded as relatively cheap and effective;

- most farmers reported that they were more aware of safe practices and now took more care than they had in the past;

- the use of strategies to minimise residues of the chemical in wool were common, such as long withholding periods and minimising chemical use;

- a number of farmers identified problems with handling dip concentrates. They reported that it was difficult to pour out the required amount of concentrate, there

was often spillage or splashing during pouring and lids often rusted on to metal containers;

- farmers identified hot weather and strenuous physical activity as factors limiting or discouraging the use of protective clothing.

Based on this information, verbal reports by a panel member, the IOM Report and the exposure monitoring discussed in section 3.3, the NRA Expert Panel **CONCLUDED** that there was a lack of adequate compliance with label recommendations for the use of personal protective equipment when using sheep dip chemicals in some farming situations.

6.3 Comparison of Australian and United Kingdom Use of Organophosphate Sheep Dip Chemicals

While Australia has a full range of sheep dip products and use patterns comparable to those available worldwide, Australian use patterns differ significantly from those in the UK. There are no figures on the use practices in Australia but the NRA Expert Panel felt that Table 7 summarised current practices in Australia and the UK.

Table 7 Overview of certain UK and Australian ectoparasite treatment practices*

Australia	United Kingdom
• Plunge and shower dips and jetting	• No licensed shower dip or jetting products (shower dip ineffective against sheep scab)
• Sheep scab (Psoroptes ovis) eradicated in 1890	• Sheep scab introduced 1973 (Sheep scab is very difficult to treat, highly contagious and up until 1992 was a notifiable disease with mandatory treatments in UK)
• Plunge dips 4,500 - 5,600 litres (some 9000 litres)	• Plunge dips 900 - 2,300 litres (therefore require more replenishment/reinforcement and therefore more chemical handling)
• Generally 1 dip per year	• 1-2 dips per year, unless sheep scabs present when additional dipping will be required
• Farmers/contractors dip	• Farmers/contractors (with certification requirements increase in use of contractors)
• Dipping practice - individual pushes sheep under with "rod"	• Dipping practice - large variation - standing in a pit next to dip through to highly mechanical systems
• Charging rate calculates to: 100 ppm diazinon for lice/ked; 200 ppm diazinon for fly	• Charging rate calculates to: 400 ppm diazinon for scab
• Large flock sizes	• Small flock sizes

*Information provided by AVCARE

Organophosphate sheep dips are used in Australia for control of sheep blowfly, lice and keds (the latter being of less economic importance), while in the UK they are mandatory for control of sheep scab, a condition which has been eradicated from Australia.

In Australia, sheep may be treated at varying times after shearing. If sheep are to be treated immediately off-shears, then a pour-on formulation is used rather than a dip. Products for plunge dipping are registered for use in Australia when wool growth is more than 24 hours from shearing and up to 6 weeks. If wool growth is more than 6 weeks, it is considered to be long-wool treatment and long-wool pour-on (fleece tip) or jetting is the preferred application method.

7. RELEVANCE AND IMPLICATIONS FOR AUSTRALIA

The NRA Expert Panel reviewed the UK IOM Report and other relevant literature published since 1995. It was noted that the IOM study was not carried out in accordance with the original design parameters and the Report was difficult to interpret as the results of two of the three phases of the study were equivocal.

While the findings of the IOM Report are spelled out in detail in Section 4.4 of this Report, the NRA Expert Panel **CONSIDERED** that the main conclusion of the IOM study was that, in the UK, there was an association between OP concentrate exposure and reported symptoms consistent with peripheral neuropathy. The Panel noted that an association between OP exposure and long-term health effects was not a new finding and there had been reports of chronic effects of OP exposure in the scientific literature for many years. Although the IOM study could not establish a definitive link between OP exposure and chronic health effects, such an association could not be ruled out.

After consideration of Australian use patterns and work practices, the NRA Expert Panel **INDICATED** that the following issues are relevant to Australia:

- it is likely that the main source of exposure to organophosphate sheep dips in Australia, as in the UK, is from concentrate handling. This was reinforced by comments made by Australian farmers in the survey (Appendix G). Increased exposure results from increased frequency of handling of concentrate, with every handling incident potentially leading to exposure unless protective measures are taken;

- diluted products pose lower risk and if they are used according to label directions and good hygiene, then existing controls should suffice;

- exposure patterns in Australia are variable and not necessarily equivalent to those in the UK;

- there is anecdotal evidence that the level of compliance with label recommendations for the use of personal protective equipment during sheep dipping is inadequate to protect users from low level exposure to OP concentrates.

The NRA Expert Panel **CONSIDERS** it prudent to put in place measures to minimise exposure to OP sheep dips, with particular emphasis on concentrates. Actions have therefore been recommended to minimise exposure of workers to organophosphate sheep dip chemicals and to address user non-compliance with label recommendations for personal protective equipment.

The panel **NOTED** that the NRA has recently undertaken a number of review activities relevant to organophosphate sheep dips. These activities are summarised in Appendix J.

8. RECOMMENDATIONS TO NRA

These recommendations apply to all OP sheep dips and should be taken into account where appropriate for the current ECRP reviews of chlorfenvinphos and diazinon.

8.1 Registration/approval status

- Maintain registration of existing organophosphate sheep dip products pending outcomes of ongoing ECRP reviews;

- Modify labels of all registered OP sheep dip products:

  - to meet current Labelling Code requirements;
  - adding an occupational health and safety warning about minimising worker exposure to concentrate;
  - taking into account field conditions when recommending personal protective equipment for sheep dip chemicals.

8.2 Formulation and Packaging

- Investigate the development of improved packaging/formulation to reduce worker exposure during the handling of the concentrate. Such developments may include:

  - wide neck containers;
  - containers with measures on side to avoid need for measuring in a separate vessel;
  - taps on containers;
  - metering devices on concentrate containers;
  - measures to prevent turbulence and splashing of concentrate;
  - ready-to-use products.

8.3 Education and Training

- Prepare a comprehensive information brochure advising sheep dippers on safety procedures including suitable point of sale materials outlining the hazards of OP sheep dip products and highlighting risks associated with improper use of sheep dip chemicals;

- Promote work routines for designated concentrate handlers during sheep dipping that encourage the continued wearing of appropriate personal protective equipment and full attention to chemical hygiene matters;

- Evaluate the availability, effectiveness and relevance of current training courses in ectoparasiticide use in the animal health industry;

- Foster Best Practice standards, training and documentation within the sheep industry.

8.4 Regulatory actions

- Investigate the continuing registration status of temephos sheep dip products and apply the findings of this report as appropriate;
- Give a higher priority to the review of propetamphos under the NRA's ECRP;
- Develop standards for container design to ensure minimum worker exposure when handling concentrate;
- Assess containers of registered products for human exposure potential;
- Review existing label statements for personal protective equipment with a view to ensuring practical recommendations for field use;
- Consider the practicality of a scheme for certification/licensing of users of OP sheep dip concentrates;
- Review regulatory approaches to reporting exposures and adverse reactions under Australian working conditions;
- Enhance the links with overseas programs and agencies.

8.5 Further information and/or research

- Characterise OP exposures in Australian work practices in sheep dipping (including in the cleaning out of sludge/residues from sheep dips after use);
- Develop a model which can be used to predict/monitor worker exposure to sheep dip chemicals in Australia;
- Investigate procedures for neutralising/inactivating OPs in chemical spillages and dipping solutions;
- Promote research into personal protective equipment that is more practical and therefore more acceptable to workers.

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ADDENDUM

On 30 November 1999, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) within the United Kingdom's Department of Health issued a report entitled "Organophosphates". This report looked the subject matter in a comprehensive way and included detailed consideration of the full report of the major study by the Institute of Occupational Medicine published in July 1999. While agreeing with the conclusions within the IOM report that exposure to concentrates was the major source of exposure, the Committee acknowledged that the study had significant limitations and the Committee therefore did not consider the overall findings of the report to be definitive.

The Chairman of the NRA Expert Panel has recommended that the relevant sections of the COT report be attached to this report (see Appendix I).