

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

For the review of Temephos in the product COOPERS ASSASSIN SHEEP DIP

Report prepared by the Office of Chemical Safety
and Environmental Health (OCSEH), Therapeutic
Goods Administration *of the* Department of Health
and Ageing

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GLOSSARY OF TERMS AND ABBREVIATIONS

ai	Active ingredient
bw	Body weight
d	Day
hr	Hour
mg	Milligram
kg	Kilogram
L	Litre
mL	Millilitre
APVMA	Australian Pesticides and Veterinary Medicines Authority
ChE	Cholinesterase
DHA	Department of Health and Ageing
EC	Emulsifiable concentrate
FAISD	First Aid Instructions & Safety Directions
LC ₅₀	Lethal Concentration that kills 50% of test animals
LD ₅₀	Lethal Dose that kills 50% of test animals
MOE	Margin of Exposure
NOEL	No Observable Effect Level
OHS	Occupational health and safety
OCSEH	Office of Chemical Safety and Environmental Health
OP	Organophosphorus pesticide
PPE	Personal protective equipment

1 EXECUTIVE SUMMARY

Temephos is used to control blowfly and lice infestation on sheep. Temephos treatment usually involves various application methods including, portable and fixed plunge dipping, shower dipping and hand jetting. Workers may be occupationally exposed to temephos during mixing, loading, and applying the pesticide.

Specific occupational exposure studies using a temephos product were not available. Therefore, the OCSEH used a surrogate study, which involved a different active constituent but the same mode of application to estimate worker exposure during mixing/loading and application. Since inhalation exposure was negligible when compared to dermal exposure, the Personal Protective Equipment (PPE) for respiratory protection is not recommended for the product.

The margin of exposure (MOE) arising from repeated use of temephos was calculated by comparing the estimated dermal exposure for each task against an appropriate No Observed Effect Level (NOEL). A dermal absorption factor of 10% was estimated from an *in vitro* human epidermal penetration study with Coopers Assassin Sheep Dip containing 350 g/L temephos. A NOEL derived from a four-week oral study in human volunteers (1 mg/kg bw/day), and then adjusted for dermal absorption, was considered to be the most appropriate for an occupational risk assessment. Given that the NOEL is based on human data, a MOE equal to, or greater than 10 is considered acceptable.

The results indicated that for mixing/loading the temephos product, workers can be adequately protected if they wear a washable hat, cotton overalls buttoned to the neck and wrist, waterproof full-length bib apron, elbow-length PVC gloves, goggles and water resistant footwear. The OCSEH considers that workers applying the diluted solution by portable plunge dip, fixed plunge dip or shower dip, can be adequately protected when they wear protective waterproof clothing, a waterproof hat, elbow-length PVC gloves and water resistant footwear. For hand jetting, the MOE for workers was unacceptable with or without above PPE. Continuation of sheep treatment by hand jetting, therefore, is not supported.

Exposure to temephos when handling treated sheep was calculated from temephos residue in wool grease up to 12 weeks after sheep treatment. Results indicated low risks to workers (shearers) handling treated sheep once they are dry after treatment.

2 INTRODUCTION

Temephos is an organophosphorus insecticide, which is available in a limited range of registered products. Temephos is a contact insecticide that acts by inhibiting cholinesterase activity (an enzyme important in nerve conduction). It is mainly used as an ectoparasiticide for the control of body lice on short and long wool sheep. Temephos products are also used for the control of mosquito and midge larvae by treatment in breeding areas and for lice control on cattle.

Temephos has been under review as part of a consideration of a range of sheep ectoparasiticide products in relation to wool residues arising from handling treated animals (APVMA, 2005). Additionally, an APVMA Expert Panel, in its report on the relevance of the UK Institute of Occupational Medicine (IOM) report to sheep husbandry practices in

Australia, recommended a review into the continuing registration of temephos sheep treatment products on occupational health and safety grounds (APVMA, 2000).

At the time this review commenced only one temephos sheep treatment product was registered in Australia, namely Coopers Assassin Sheep Dip (referred to in this report as Coopers Assassin); containing 350 g/L temephos as an emulsifiable concentrate formulation.

In conducting the occupational health and safety review of Coopers Assassin, the OCSEH obtained information from the following sources: industry submissions, overseas reviews and the published literature.

3 FORMULATION AND PACKAGING

Workers likely to be exposed to the product are those involved in formulation of the end-use product (EUP) and those involved in packing, storage and transport of the EUP, as well as users. Coopers Assassin is packed in 5 L and 20 L tin plate cans with plastic overcaps. The 20 L cans are fitted with a pouring adapter that minimises splashes, drips and spills.

4 USE PROFILE

Coopers Assassin is currently registered in Australia for the control of body lice (including synthetic pyrethroid resistant strains) on wet or dry short wool sheep. It is usually applied by plunge or shower dip. However, in long wool sheep it is usually applied by hand jetting. Information regarding the use of Coopers Assassin was obtained from the product label.

4.1 Plunge and shower dipping no less than 2 weeks and up to 6 weeks off-shears

Plunge dipping is the most common mode of application although shower dipping, with either conventional shower dips or continuous replenishment shower dips, is sometimes used as an alternative to plunge dipping. Current label instructions for Coopers Assassin specify that sheep should not be dipped less than 2 weeks or more than 6 weeks off-shears, and include whole-of-flock treatment. Large numbers of sheep can be treated by dipping. Plunge and shower dipping utilise similar concentrations of temephos in the dip solution (ie. 0.35 g/L).

4.2 Jetting

Sheep are jetted predominantly for the control of body lice. Hand jetting was the recommended treatment method for Coopers Assassin on long wool sheep at the commencement of the review, although jetting is a slow and labour intensive method of application. Hand jetting is conducted using a “jetting gun” or wand, with a “comb-like” end, usually made up of 5 nozzles and a T-bar leading edge for opening fleece while jetting. The gun is connected to a motorised pressure tank (approximately 2000 L capacity). The required pressure at the hand piece is 600-700 kPa (low). A single operator can potentially jet around 500 sheep per day.

The Coopers Assassin label recommends the use of protective clothing during mixing/loading and application. Table 1 summarises the occupational use pattern for the product.

Table 1. Use pattern of Coopers Assassin

Application method	Pest	Application rate /dilution of product (concentration of ai)	Comments
Plunge dip up to 6 weeks off-shears	Body lice <i>(Bovicola ovis)</i>	100 mL per 100 L water (0.035% ai) Reinforcing 25 mL of undiluted product when dip level falls by 100 L	Plunge dipping usually occurs not more than once a year as a whole of flock treatment Sheep should be totally immersed twice in the dip solution and checked for effective wetting Sheep carrying <2 weeks or >6 weeks wool should not be dipped Work rate expected to be 300 sheep/hour (average) 500 sheep/hour (maximum) for 4 hours /day WHP - 14 days before slaughtering for human consumption and 3 months for shearing or fibre collection.
Conventional shower dip up to 6 weeks off-shears	Body lice <i>(Bovicola ovis)</i>	Initial charge 100 mL per 100 L water (0.035% ai) Reinforcing 25 mL of undiluted product when dip level falls by 100 L	Shower dipping usually occurs not more than once per year as a whole of flock treatment Dip wash is discarded after treatment of 1000 sheep Average number of sheep treated is 2000 per day. Sheep carrying <2 weeks or >6 weeks wool should not be dipped WHP - 14 days before slaughtering for human consumption and 3 months for shearing or fibre collection.
Continuous replenishment shower dip up to 6 weeks off-shears	Body lice <i>(Bovicola ovis)</i>	100 mL per 100 L water (0.035% ai)	Topping up is not recommended Inspection of treated animals is recommended to ensure sheep are wet to skin level to achieve effective treatment.

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Table 1. Use pattern of Coopers Assassin...cont'd.

Application method	Pest	Application rate /dilution of product (concentration of ai)	Comments
<p>Hand jetting (Long wool sheep; up to 9 months wool)</p>	<p>Body lice (<i>Bovicola ovis</i>)</p>	<p>100 mL per 100 L water (0.035% ai)</p>	<p>Thorough wetting of the skin from the poll to the tail is essential. Apply in a band 15-25 cm in width with some fluid sprayed into the shoulder wool.</p> <p>Approximately 0.5 L of fluid for each month of wool is required (minimum 2.5 L/sheep)</p> <p>Use a jetting gun with nozzles or a hand wand/comb to apply the chemical at a pressure of 600-700 kPa directly into the fleece of the sheep (for 4 month wool or longer, use 900 kPa)</p> <p>Work rate approximately 500 sheep/day</p> <p>WHP - 14 days before slaughtering for human consumption and 3 months for shearing or fibre collection</p>

4.3 Label restrictions

The product label specifies a withholding period (WHP) of 14 days before slaughter and a 3-month wool withholding period (or wool harvesting interval) before shearing. There is a label restraint statement against dipping within two weeks of shearing and sheep should not be plunge dipped or shower dipped more than six weeks after shearing.

5 TOXICOLOGICAL ENDPOINT SELECTION FOR OCCUPATIONAL RISK ASSESSMENT

Coopers Assassin has low acute oral toxicity, with an LD₅₀ in rats of 2610 mg/kg bw for males and 3064 mg/kg bw for females. The product exhibited low dermal toxicity in rabbits (LD₅₀ >2020 mg/kg bw, no deaths) and low inhalation toxicity in rats (LC₅₀ in excess of 2340 mg/m³, no deaths). It was not a skin irritant in rabbits after a 4-hour exposure, but caused delayed onset of local irritation if dermal exposure was prolonged for 24 hours. The formulation was a severe eye irritant in rabbits, but did not cause skin sensitisation in guinea pigs.

5.1 Selection of NOEL

In order to perform an occupational risk assessment, careful consideration needs to be given to the selection of the appropriate toxicological endpoint and duration of dosing. An inspection of all repeat-dosing studies in the database (as shown in Table 2 below) indicated that the most sensitive endpoint by all routes of administration, durations and species was cholinesterase inhibition. This endpoint is also considered relevant for an occupational risk assessment.

As humans are the species that are being protected it is appropriate that available human data, if of suitable quality, is used for risk assessment purposes. In a human study in which a NOEL was established, temephos was without any symptoms or detectable effects on plasma or red cell ChE activity when administered orally at a dose of 64 mg/person/day (~1 mg/kg bw/day) for 28 days (Hayes & Laws, 1991). Although a 28-day repeat dosing study may be considered to be too short to ensure adequate protection, it is the consistency of the endpoint in relation to the dosing duration and its occurrence in all species, which is important. Consequently, this study in humans can be used as the basis for the occupational risk assessment. Since temephos, like most organophosphorus pesticides, is almost completely absorbed from the gastrointestinal tract, no correction is required to the oral NOEL for the purpose of determining an 'internal' dose. However, since the volunteers in the study ingested the temephos, a dermal absorption factor needs to be applied to make the risk assessment relevant for the major occupational route of exposure, ie. dermal.

Table 2: Summary of NOELs / LOELs (mg/kg bw/d)

Studies	Doses used (mg/kg bw/day)	NOEL	LOEL	Effects
Rat 28-day gavage	0, 1, 10, 100	1	10	ChE inhibition
Rat 3-week dermal	0, 12, 60	12	60	Reduced body weight and increased liver and kidney weights.
Rabbit 35-day gavage	0, 0.1, 1, 10	1	10	ChE inhibition
Rabbit 3-week dermal	0, 25, 50, 75, 100	25	50	Systemic toxicity and hematological changes
Rat 99-day dietary	0, 0.1, 1, 10, 100	1 (20 ppm)	10 (200 ppm)	ChE inhibition
Rat 90-day dietary	0, 0.1, 0.3, 0.9, 18	0.1 (2 ppm)	0.3 (6 ppm)	Erythrocyte ChE inhibition
Rat 14-week dietary	0, 0.3, 0.9, 2.7	0.3 (6 ppm)	0.9 (18 ppm)	Erythrocyte ChE inhibition
Rat 90-day dietary	0, 0.05, 0.15, 0.45	0.45 (18 ppm)		No effects
Rat 2-year dietary	0, 0.5, 5, 15			Not carcinogenic. A NOEL was not established since ChE was not measured.
Rat 3-generation reproduction (dietary)	0, 2.5, 12.5	Reproduction: 12.5 (125 ppm)		No reproduction and other effects.
Rabbit developmental (gavage)	0, 3, 10, 30	Maternal: 10 Foetal: 30	30	Reduction in kidney weight None
Human 4-week oral	1 (~64 mg/person/day)	1		No effects.

The data are derived from the Consolidated Summary of Temephos (OCS, 1997).

5.2 Dermal absorption

Cross S (2006) Determination of the *in vitro* human epidermal penetration of ASSASSIN (350 g/L Temephos) (SCH 530377). Therapeutic Research Unit, Southern Clinical Division, University of Queensland, Princess Alexandra Hospital, Woolloongabba, QLD 2039. Guidelines: OECD 428 (2004)

The *in vitro* dermal penetration of Coopers Assassin Sheep Dip (350 g/L temephos, Batch No: LB-6-001) was determined in human epidermal membranes. The membranes (30 samples) were prepared from full thickness tissue of three female donors and mounted in diffusion cells for equilibrium. Damaged membranes were removed and replaced with intact membranes.

The test substance (final concentration of 350 µg/mL temephos) was applied topically to the membranes. Receptor phase was removed and replaced with fresh solution at 1, 2, 4, 8, 12 and 24 hrs. At the end of the 24 hr penetration period, the surfaces of the epidermal membranes were washed and then swabbed. Temephos residues in solutions and epidermal membranes were determined by High Pressure Liquid Chromatography using an ultraviolet detector.

Residues of temephos in all matrices were quantified.

Mean recovery of temephos was 81% of the dose. According to the study author, this recovery is consistent with values that are acceptable at the test facility. It is also consistent with APVMA guidelines for acceptable recoveries (accuracy of 70-110% and standard deviation of < 20%).

Levels of temephos residues in all samples taken from receptor solutions were under the limit of detection (LOD, i.e. 50 ng/mL). On the assumption that residues were present in the receptor solution at the LOD, the maximum total amount of temephos that could be present in the receptor solution was calculated. Together with the maximum amount bound in epidermal membrane after wash, the maximum percentage of the dose transfer across the membrane was calculated to be approximately 10%.

6 OCCUPATIONAL EXPOSURE ASSESSMENT

6.1 Sources of exposure

Plunge and shower dipping

Workers involved in plunge and shower dipping of sheep are expected to handle large volumes of dip solution (up to 4000 L per day). Exposure to the product is possible during mixing and loading the solution and when dipping (plunge and shower) the sheep in the prepared solution. The likely routes of exposure are dermal and inhalation although ocular contact could also occur from splashes and/or the generation of a spray mist during shower dipping. Workers may also be exposed to the product when removing sludge from the dip at the end of the treatment.

In most instances, mixing/loading and dipping operations are carried out by the farmer or farm employee. Mobile dipping may be conducted by contractors. Worker exposure is possible when measuring the product, initial charging of the dip, during periodic topping up (required to maintain an adequate concentration of the chemical in the dip), when dunking sheep and cleaning out the sump. Sheep are dunked twice in the dip solution using T-shaped poles. It is anticipated that the dip will be charged once or twice per day, depending on the sump capacity and the number of animals to be treated (average 2000 sheep per day).

Information obtained from regular users indicated that flock treatment on farms is generally carried out not more than once per year. It is reasonable to assume that dipping operations will take place from one to a few consecutive days (2-3 days, particularly on large farms) until all sheep are treated. Dipping contractors can be potentially exposed to temephos over longer periods.

Hand jetting

Mixer/loader exposure will be mainly through skin contamination whilst during jetting, exposure is also likely to be by the dermal route, due to the proximity of the worker to the jetting equipment and the animal during application.

Most often hand jetting is conducted by the farmer or farm employee. Workers are required to add the product and water into the pressure tank, which is agitated mechanically. The number of mixing/loading operations per day would depend on the number of animals to be treated, the capacity of the pressure tank and the container size.

At any one time, one or two workers may be involved in hand jetting operations per farm. The applicator is required to stand in close proximity to the animal to be treated and thoroughly saturate the wool by running the comb along the fleece. The pressure at which the fluid is applied is dependent on the length of wool, with higher pressure being used for longer-woolled sheep.

The product label neither limits the number of applications nor specifies a re-treatment interval. However, information obtained from regular users indicated that jetting is generally carried out not more than once per year. A single operator can potentially jet around 500 sheep per day, requiring workers to handle large volumes of jetting fluid (up to 2250 L/day).

6.2 Exposure characterization

The registrant did not provide any worker exposure studies in support of dipping or hand jetting applications of temephos for this review and there are no published data for temephos exposure during sheep treatment.

However, since commencing the review of temephos the National Farmer's Federation Limited and Australian Wool Innovations jointly submitted a study entitled, "Worker Exposure to Diazinon in Australian Sheep Industries", carried out to measure the exposure of sheep handlers to diazinon during mixing/loading of product and treating sheep by plunge and shower dipping and hand and auto race jetting (Wood, 2004). The OCSEH has used this study as surrogate data to estimate worker exposure during mixing/loading and application of temephos product (Coopers Assassin).

Exposure study

Worker Exposure to Diazinon in Australian Sheep Industries, Report no. v.3.1; June 2004 Nicholas Wood. The Centre for Pesticide Application and Safety, The School of Agronomy and Horticulture and The School of Animal Studies (University of Queensland, Gatton Campus, Gatton, QLD) in conjunction with the NSW Department of Agriculture.

The study was structured to determine exposure levels to diazinon during mixing and loading of the pesticide, application and subsequent clean up operations pertaining to the following five application techniques:

- Portable plunge dipping
- Hand jetting
- Auto race jetting
- Fixed plunge dipping
- Shower dipping

The field trial protocol was also designed to evaluate the effectiveness of the current label PPE in reducing pesticide exposure and to assess the risk of inhalation exposure during these application processes.

Diazinon emulsifiable concentrate formulation of 200 g ai/L (Virbac Jettip Sheep Jetting Fluid and Blowfly Dressing) was used during the study. The application rates of the active ingredient were made in accordance with label specifications, varying from 0.1 g diazinon/L

(plunge and shower dips, lice control) and 0.2 g diazinon/L (plunge and shower dips, sheep blowfly control) to 0.4 g diazinon/L (jetting, sheep blowfly control). Each application method was carried out three times in three separate sessions (total 15 sessions) and locations (sites). In each session, one worker prepared the working solution, 5 workers treated sheep and one worker cleaned the equipment and surroundings. The dermal and inhalation exposure of each worker was measured as they mixed/loaded or applied the solution to sheep.

All workers wore waterproof clothing underneath the following PPE:

- Washable cotton hat
- Full face-shield / or goggles and half face respirator
- Elbow-length PVC gloves, cuff folded outwards
- Cotton overall done up to neck and wrists
- Water resistant footwear/boots, worn beneath the overalls

Those involved in mixing/loading operations wore a waterproof full-length bib apron in the diazinon worker exposure study in addition to the PPE specified above.

Dermal exposure was measured using chromatographic paper patches attached to clothing. To measure exposure in workers wearing PPE, patches were located under overalls (internal patches) and exterior to waterproof clothing. To measure exposure in workers not wearing any PPE, patches were located exterior to all PPE (external patches). Cotton gloves worn on hands or inside the gloves were used to determine the amount of diazinon coming in contact with the hands.

In the study, inhalation exposure was measured using chromatographic paper patches placed in the respirators. However, the results showed that in all application methods, inhalation exposure was negligible when compared to dermal exposure. Exposure via inhalation was therefore not included in the risk assessment, and PPE for respiratory protection is not recommended in the First Aid Instructions and Safety Directions (FAISD) Handbook.

The occupational health and safety (OHS) risk to these workers was estimated from the total diazinon deposited on a worker's body following treatment of approximately 50 sheep. Total body deposition of diazinon was estimated as the sum of diazinon residues deposited on head, face, neck (front and back), chest, back, upper arms, forearms, hands, thighs, lower legs and feet of the subjects. Deposition on each of these body regions was determined by multiplying the amount of diazinon deposited per square cm of patch attached to a body region by the surface area of that region (cm²). For mixer/loaders however, the volume of diazinon solution used up following treatment of approximately 250 sheep by each treatment method was provided. This data was used to express exposure for mixer/loaders. Thus for OHS risk assessment, exposure of mixer/loaders to diazinon was expressed as the amount of diazinon deposited on the body when a solution enough to treat 250 sheep was prepared. The exposure due to inhalation during mixing/loading and application was found to be negligible.

Suitability of surrogate study

Table 3 provides a comparison of relevant parameters for evaluating the suitability for use of diazinon study as a surrogate for estimating exposure to temephos.

Parameter	Diazinon study	Temephos	Comments
Formulation	EC 200 g/L	EC 350 g/L	Both EC formulations, similar ai concentrations
Product dilution	0.01- 0.02% ai (dipping) 0.02-0.04% ai (jetting)	0.035% ai (all uses)	Similar concentrations in dilute solutions
No. of animals treated (average)	50 sheep/session (average) Extrapolated to 500 sheep/day (jetting) 2000 sheep/day (dipping)	500 sheep/day (jetting) 2000 sheep/day (dipping)	Animal species is same
Amount of spray mixed	1000-7200 L per session @	2250-4000 L/day@@	Amount of spray prepared varies according to the application method and the number of sheep being treated. It is nearly 2-fold higher in diazinon study (plunge dipping).
Amount of ai handled while mixing	0.255-1.0 kg per session	0.875-1.4 kg/day	(see above comment).
Amount of diluted product used	275-2300 L per session	2250 – 4000 L/day@@	(see above comment).

@Data derived from *Occupational Health and Safety Assessment of Diazinon Sheep Dip (OCS, 2005)*.

@@The lower limit 2250 L/day is for treatment of 500 sheep using hand jetting, while 4000 L/day is likely for 2000 sheep using shower dip.

The exposure data from this study were adopted for the OHS risk assessment of workers using the temephos product, since the application methods in the diazinon study were identical to those used for treating sheep with Coopers Assassin and since the final concentration of diazinon in the treating solution was very similar to that of temephos when Coopers Assassin is used (0.35 g/L temephos compared to 0.1- 0.4 g/L diazinon). The exposure values obtained in the diazinon study for various activities were considered comparable to those obtained if Coopers Assassin (temephos) were used. Therefore these values were used without further modification to assess the risk to workers using Coopers Assassin. Occupational exposure values during mixing/loading, treating sheep by the five application methods, and cleaning up after application are presented in Table 4.

Table 4: Dermal exposure during sheep treatment with temephos products (extrapolated from diazinon exposure data (Wood, 2004))

Application Method	Total Dermal Exposure (µg temephos) per 50 sheep	Total Dermal Exposure (µg temephos) per 500 sheep^a per 2000 sheep^b
Mixing/Loading – without PPE	78882*	78882*
Mixing/Loading - with PPE	94.6*	94.6*
Portable Plunge Dip - without PPE	6804	272160 ^b
Port. Plunge Dip – with PPE	400	16000 ^b
Hand Jetting - without PPE	136987	1369870 ^a
Hand Jetting - with PPE	63004	630040 ^a
Fixed Plunge Dip - without PPE	6293	251720 ^b
Fixed Plunge Dip - with PPE	159	6360 ^b
Shower Dip - without PPE	3558	142320 ^b
Shower Dip - with PPE	371	14840 ^b
Clean up - without PPE	9633**	9633**
Clean up - with PPE	422**	422**

*µg temephos/volume of temephos solution prepared to treat 250 sheep

**µg temephos. This is independent of the number of sheep treated

^a and ^b : Average 500 sheep/day using hand jetting and 2000 sheep/day using dipping methods, based on work rates in the use pattern.

6.3 Post-treatment exposure

No specific re-handling restrictions are indicated on product labels. Post-application exposure may occur in workers handling treated sheep (e.g. for drenching, vaccination, marking, mulesing, crutching and shearing). Coopers Assassin label specifies a WHP of 3 months before shearing or fibre collection.

A study evaluating the degradation of temephos residues in the fleece of merino sheep following treatment with Cooper Assassin (Burman et. al., 1997) was submitted by Schering-Plough. Based on the measured residue data for temephos, it was concluded that temephos residue on sheep wool did not pose an unacceptable risk to workers handling sheep once they were dry after treatment (APVMA, 2006).

7 OHS RISK ASSESSMENT

The occupational risk assessment takes into consideration the hazard of the chemical as determined by its toxicological profile, its use pattern in Australia, and worker exposure for each exposure scenario.

In order to adequately determine repeat exposure risks associated with the use of Coopers Assassin, a MOE for temephos was calculated by comparing the most appropriate NOEL

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(1 mg/kg bw/day) with exposure estimates obtained from the surrogate exposure study and a dermal absorption factor of 10% derived from an *in vitro* human epidermal penetration study. As a NOEL based on human data was used, a MOE of 10 or more is considered to be acceptable.

7.1 Risk from end-use exposure

The risk assessment is based on workers wearing the following PPE:

- Washable cotton hat
- Goggles
- Elbow-length PVC gloves, cuff folded outwards
- Cotton overalls done up to neck/wrists
- Water resistant footwear/boots, worn beneath the overalls
- Waterproof full-length bib apron in addition to the above PPE (mixer/loaders only)

In the exposure study, inhalation exposure was measured using chromatographic paper patches placed in the respirators. However, the results showed that in all application methods, inhalation exposure was negligible when compared to dermal exposure. Exposure via inhalation was therefore not included in the risk assessment, and PPE (e.g. half face respirator) for respiratory protection is not recommended in FAISD Handbook.

The margins of exposure calculated for temephos from the diazinon exposure data are presented in Table 5. The results show that the margin of exposure was acceptable for mixer/loaders wearing the above PPE (also see table 4).

During sheep treatment, eye protection is not considered essential because the diluted product is not expected to cause eye irritation. It is also considered acceptable that protective waterproof clothing and a waterproof hat are more practical PP for workers during sheep treatment and are equivalent protection to cotton overalls and a washable hat. When the specified PPE for application were worn, the MOEs (>10) were acceptable for workers treating sheep by portable plunge dipping, fixed plunge dipping or shower dipping in accordance with label restraints (i.e. more than 2 weeks and up to 6 weeks off-shears). The results also indicated an acceptable MOE for workers cleaning the treatment areas and equipment after dipping.

However, the data indicated that the MOE for workers without PPE were below the target MOE for all treatment methods, mixing/loading and cleaning.

For hand jetting, the MOEs for workers applying the product were also below 10 with specified PPE. Therefore the OCSEH is unable to conclude that this mode of application would not be an undue hazard to the safety of workers.

Table 5: Absorbed dermal doses and MOE for workers exposed to temephos during mixing/loading and treating sheep (standardised from diazinon data (Wood, 2004))

Application Method	Total Dermal Exposure (µg temephos) per 50 sheep	Total Dermal Exposure (µg temephos) per 500 sheep ^a per 2000 sheep ^b	Dermal absorbed dose (mg temephos/kg bw)	MOE	No. of sheep that can be treated to give a MOE of more than 10
Mixing/Loading – without PPE	78882*	78882*	0.1127	8.8	220
Mixing/Loading - with PPE	94.6*	94.6*	0.00014	7400	185000
Portable Plunge Dip - without PPE	6804	272160 ^b	0.389	2.57	514
Port. Plunge Dip – with PPE	400	16000 ^b	0.0229	43.7	8750
Hand Jetting - without PPE	136987	1369870 ^a	1.957	0.51	26
Hand Jetting - with PPE	63004	630040 ^a	0.900	1.11	56
Fixed Plunge Dip - without PPE	6293	251720 ^b	0.360	2.78	556
Fixed Plunge Dip - with PPE	159	6360 ^b	0.0091	110	22000
Shower Dip - without PPE	3558	142320 ^b	0.2033	4.92	984
Shower Dip - with PPE	371	14840 ^b	0.0212	47.2	9440
Clean up - without PPE	9633**	9633**	0.0138	72.7	-
Clean up - with PPE	422**	422**	0.0006	1660	-

*µg temephos/volume of temephos solution prepared to treat 250 sheep.

**µg temephos. This is independent of the number of sheep treated.

^a and ^b: Average 500 sheep/day using hand jetting and 2000 sheep/day using dipping methods, based on work rates in the use pattern.

Dermal absorbed dose (mg/kg bw/day) = Total dermal exposure (per amount of temephos mixed/loaded for 250 sheep or per 500/ 2000 sheep treated) x 10% dermal absorption ÷ 70 kg bw ÷ 1000 (mg); MOE = NOEL (1 mg/kg bw/day) ÷ Total absorbed dose (mg/kg bw/day).

7.2 Risks from post-treatment handling

Shearers and shed hands handling treated sheep and fleece may be exposed to residual temephos on treated wool (especially during shearing). Winter and spring are the peak shearing seasons, although some sheep farmers may elect to shear flocks at other times of the year. Residual pesticides are assumed to be wholly absorbed in the wool grease; consequently the route of worker exposure used for the purposes of risk assessment is dermal absorption.

Dermal exposure to temephos residues from re-handling treated sheep was calculated from temephos residue present in wool grease 1 to 12 weeks after treatment (OCS 2007, Table 6). MOEs were above 10 for all sampling times indicating low risk to workers handling treated sheep from week 1 onwards. The data was extrapolated to determine MOEs for days zero to 7 in order to determine whether in such cases it would be safe for shearers to handle treated sheep 1 or 2 days after treatment. Results indicated that risk from rehandling sheep would be low once the sheep are dry following treatment.

Table 6: Dermal exposure and MOEs for shearers handling treated sheep

	Weeks after treatment						Reference
	1	2	4	6	8	12	
Temephos residue (mg/kg wool grease)	454		366		141	139	Schering Plough (reported in APVMA 2006)
MOE for shearers	1101		1366		3546	3597	-

The amount applied was 1.4 g/sheep (9 months wool, backline/Pour-on formulation containing temephos). A NOEL of 1 mg/kg bw/day and a dermal factor of 10% were used to calculate the MOE. A MOE >10 is acceptable.

8 SAFETY DIRECTIONS AND RE-HANDLING INTERVALS

The current safety directions for temephos in the FAISD Handbook (2004) are as follows:

DIP 350 g/L or less	
207 162	Will damage the eyes
160 163 164	May irritate the nose and throat and skin
190	Repeated minor exposure may have a cumulative poisoning effect
373	Obtain an emergency supply of atropine tablets 0.6 mg
210 211	Avoid contact with eyes and skin
220 222	Do not inhale vapour
279 280 281 290 292 294 297	When opening the container and preparing dip or spray, wear cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length PVC gloves and goggles
279 282 290 291 294 298b	When using the prepared dip or spray, wear protective waterproof clothing, elbow-length PVC gloves and water resistant footwear
330 341 331 332	If clothing becomes contaminated with product, premix or wet with spray remove clothing immediately
340 341 342	If product, premix or spray on skin, immediately wash area with soap and water
340 341 343	If product premix or spray in eyes, wash it out immediately with water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360 361 363 366	After each day's use, wash gloves, goggles and contaminated clothing

Risk assessment of the temephos product indicated that mixer/loaders were adequately protected when they wore a waterproof full-length bib apron and water-resistant footwear in addition to the current PPE for mixer/loaders.

For sheep treatment, the MOEs for hand jetting were below the target MOE of 10 with or without PPE. The current safety directions for handling dilute solutions are, therefore, considered adequate except for workers treating sheep by hand jetting.

9 DISCUSSION AND CONCLUSIONS

This review focuses on the sheep dip product, Coopers Assassin, containing 350 g/L temephos. At the commencement of the review it was the only temephos product currently registered in Australia for sheep dipping and jetting. Coopers Assassin, at the commencement of the review, indicates for the control of body lice by plunge or shower dip in short wool sheep and by hand jetting in long wool sheep. Both application methods utilise similar concentrations of temephos in the dip solution (0.35 g/L).

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9.1 Dermal absorption

A 10% dermal absorption for temephos was derived from an *in vitro* human epidermal penetration assay using Coopers Assassin Sheep Dip (Cross, 2006). A limitation associated with an *in vitro* approach is that the peripheral blood flow may not be fully reproduced by conditions of the diffusion cells. Unfortunately, no *in vivo* dermal absorption study is available for a more refined evaluation. However, this estimation (10%) is supported by the available toxicology data in rats, where a ratio for oral NOEL to dermal NOEL was 1:12 (see Table 7 below), which is consistent with a dermal absorption rate of 10% in rats.

Table 7: Comparison of oral and dermal NOELs in rats

Study	Dose (mg/kg bw/day)	NOEL (mg/kg bw/day)*
Rat 28-day oral	0, 1, 10	1 (ChE inhibition)
Rat 44-day oral	0, 1, 10, 100	1 (ChE inhibition)
Rat 21-day dermal (5 d/w)	0, 12, 60	12 (lower body weight, higher liver and kidney weight)

*Data based on consolidated summary in the OCSEH toxicology assessment report on temephos (OCS, 1997).

The applicant also submitted an OHS assessment report on temephos which was prepared by Health Council of the Netherlands (2003). In this report, the estimated dermal absorption rate for temephos was less than 3% in humans, based on a biokinetic study in rats, rabbits and dogs. In this study, animals were given a single intravenous dose, or a topical application of the radio-labelled temephos. Dermal absorption rates, 38% in rats, 52% in rabbits and 5% in dogs, were calculated by dividing the percentage of the dose excreted in the urine following dermal application by that following intravenous dosing in the same species. However, the rationale for the estimation of a dermal absorption of 3% in humans was not specified in the report. Besides, limited information in the Netherlands assessment report indicates that the study was poorly conducted, with a total recovery of the radioactivity ranging from 25% to 55% in all species following intravenous administration. On the other hand, it is noted that the US EPA RED report for temephos chose the dermal absorption factor of 38% in rats from the Dutch study as the estimation for humans (USEPA, 2001).

9.2 Exposure assessment

In conducting this review, the OCSEH focused on the use-pattern information provided by the registrant and as recommended on the product label for Coopers Assassin.

In most cases, mixing/loading and dipping/jetting operations are carried out by the farmer or farm employees. Professional sheep dipping may also be carried out under contract.

Worker exposure studies for temephos or its products are not available. The OCSEH used a surrogate study to estimate worker exposure during mixing/loading and application. Surrogate studies can be used only if they are conducted according to good study guidelines and the use pattern assessed in the study closely resembles the use pattern of the chemical in question. In this regard, the diazinon study (Wood,

2004) was considered to be very suitable data as the use pattern in this study was identical to that for the temephos product and concentrations of the two actives were very similar in the respective products as well as in the final working solutions.

Exposure estimations for hand jetting were based on treatment of 500 sheep per day. For plunge and shower dipping, treatment of larger number of animals (average 2000 sheep per day), was used in exposure estimations. Similar to that in the OHS risk assessment report for diazinon (OCS, 2005), a linear extrapolation is used to convert the amount of worker's dermal exposure, from 50 sheep to the average daily workload of 500 or 2000 sheep.

This method of linear extrapolation is consistent with the observations in "The relevance to sheep husbandry practices in Australia of the UK Institute of Occupational Medicine (IOM) Report" (APVMA, 2000). It was stated that "the most important source of exposure to OPs was contact with concentrate dip". "Increased splashing with the dilute dip-wash was found to be positively associated with an increase in urinary metabolites". Hence, "a linear regression model was developed which describes the relationship between uptake of OPs as assessed by post-dipping urinary metabolite levels and exposure to both the dip-concentrate and the dip wash". Therefore, a linear extrapolation in the present assessment for temephos is considered to be reasonable, although it may be conservative in cases when the worker is not in close proximity to where the sheep treatment is taking place.

Post-application exposure to temephos may occur in workers handling treated sheep for drenching, mulesing or shearing. Shearer exposure to temephos was estimated from data obtained from residue studies, which measured temephos residue in wool, up to 12 weeks after treatment.

9.3 Risk management

Mixing/loading (Plunge/shower dipping and hand jetting)

Exposure data extrapolated from the diazinon surrogate study indicated that for mixing/loading the temephos product, workers can be adequately protected if they wear cotton overalls, waterproof full-length bib apron, elbow-length PVC gloves, goggles and water resistant footwear.

Application

For three out of the four different treatment methods, *viz.* portable plunge dip, fixed plunge dip and shower dip, the OCSEH considers that workers will be adequately protected if they wear protective waterproof clothing, a waterproof hat, elbow-length PVC gloves, and water resistant footwear. Exposure via inhalation was negligible when compared to dermal exposure, and therefore respiratory protection is not required.

Exposure data for hand jetting gave very low MOEs with or without PPE, indicating unacceptable risk (MOE 0.5-1). This high exposure is probably due to splashes during

treatment. A possibility to reduce exposure might be to wear an extra layer of waterproofing. A PVC or rubber apron over waterproof overalls could be expected to provide extra protection during treatment. However, the practicality of wearing such PPE all day in hot weather would be likely to render this proposal impractical. Further, at present there are no data available to estimate the extent of protection such aprons can provide.

For applicators the number of sheep that could be treated to achieve the target MOE ($MOE \geq 10$) was calculated for each treatment method. Results indicated that the numbers of sheep that could be treated per day by portable plunge dip, fixed plunge dip and shower dip with PPE exceed the average number of sheep normally treated per day by these methods. For hand jetting, however, the number of sheep that could be treated per day in order to achieve an acceptable MOE were very small (56 sheep per day with PPE). Treatment of such small number of animals over several days, especially on large farms where sheep numbers could exceed a thousand, is not practical and so the OCSEH is unable to conclude that this mode of application would not be an undue hazard to the safety of workers.

A proposal which could be considered is to increase the number of workers involved in treating sheep so that each individual would treat no more in a day than that specified above. However, for hand jetting the number of workers needed would be unrealistic.

Re-handling treated sheep

Exposure to temephos for workers re-handling treated sheep was calculated from temephos residue in wool grease up to 12 weeks after sheep treatment. Results indicated low risks to workers (shearers) handling treated sheep from as early as one week after treatment. The data was extrapolated to determine MOE for days 0 to 7 in order to determine whether it would be safe for shearers to handle treated sheep 1 or 2 days after treatment. Results indicated that the risk for handling the sheep after they are dry following treatment is low (Sheep ectoparasiticides review; APVMA, 2006).

9.4 Conclusions

The following conclusions are made as a result of this review:

- There is unlikely to be a risk to workers during the mixing/loading components of the preparation of the dip solution for sheep treatment when personal protective equipment is worn;
- There is unlikely to be a risk to workers treating sheep by portable plunge dipping, fixed plunge dipping or shower dipping when personal protective equipment is worn;
- It is not possible to conclude that there is unlikely to be an undue hazard to the safety of workers treating sheep by hand jetting, even when personal protective equipment is worn;

- There is unlikely to be a risk to workers re-handling temephos-treated sheep once sheep are dry following treatment.

The revised safety directions are summarised in Table 8. A quantitative OHS risk assessment has indicated the need for waterproof full-length bib apron when mixing/loading temephos product for sheep treatment.

10 RECOMMENDATIONS TO THE APVMA

Based on the OHS assessment of temephos uses in sheep treatment, the following recommendations are made to the APVMA:

1. OCSEH recommends that the APVMA NOT be satisfied that continued use of temephos products containing 350 g/L temephos in EC formulations by hand jetting in accordance with current label instructions would NOT be an undue hazard to the safety of workers.
2. OCSEH recommends that the APVMA can be satisfied that the use of temephos products containing 350 g/L temephos in EC formulations by portable plunge dipping, fixed plunge dipping or shower dipping would NOT be an undue hazard to the safety of workers provided that workers wear the PPE indicated in the amended safety directions.

In addition, the following amended Safety Directions in Table 8, which will be included in the FAISD Handbook, should be included on the product label.

Safety Directions

Table 8: Amended safety directions

DIP 350 g/L or less	
207 162	Will damage the eyes
160 163 164	May irritate the nose and throat and skin
190	Repeated minor exposure may have a cumulative poisoning effect
210 211	Avoid contact with eyes and skin
220 222	Do not inhale vapour
279 280 281 290 292 293 294 299 298b	When opening the container and preparing dip, wear cotton overalls buttoned to the neck and wrist and a washable hat, PVC or rubber apron, elbow-length PVC gloves, face shield or goggles and water resistant footwear

279 282 290 291 waterproof hat 294 298b	When using the prepared dip wear protective waterproof clothing, a waterproof hat, elbow-length PVC gloves and water resistant footwear
330 341 331 332	If clothing becomes contaminated with product or dip, premix or wet with spray remove clothing immediately
340 341 342	If product, dip or spray on skin, immediately wash area with soap and water
340 341 343	If product, dip or spray in eyes, wash it out immediately with water
350	After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water
360 361 365 366	After each day's use, wash gloves, face shield or goggles and contaminated clothing

Precautionary statement

RE-HANDLING INTERVAL: DO NOT RE-HANDLE SHEEP UNTIL DRY AFTER TREATMENT

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