

A Guideline to Promote Best Practice With

Organophosphates

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Introduction

Organophosphate insecticides are currently an integral element of modern agriculture.

Accordingly, they are used regularly to control moths, ants, spiders, cockroaches, termites, fruitflies and similar insects, fleas, locusts, caterpillars, ticks, lice and grubs, to name a few, in a variety of situations.

This document has been developed due to the lack of information available on protecting the health and safety of organophosphate insecticide users. This group of users includes (but is not limited to):

- Market gardeners;

- Livestock farmers, e.g. beef, sheep;
- Orchardists/orchard workers;
- Vintners;
- Fruit and vegetable growers;
- Customs officers;
- Pest control specialists; and
- Field crop farmers, e.g. grain.

This document is primarily targeted at livestock and crop growers and farmers. However, the principles of health and safety are applicable to any workplace.

About these Guidelines

This guideline is designed to provide information on organophosphate pesticides, the nature of their toxicity, and biological monitoring of users. The information contained in this document should be used to supplement the information contained in the pamphlet *Information for Users of Organophosphates* (soon to be released).

It also discusses the various issues to be considered for effective control of health risks from these compounds. More concise guides to assist employers and users to achieve safe working practices, consistent with the requirements of the Health and Safety in Employment Act 1992, are also available.

Abbreviations

The following abbreviations are used in this guide:

- OP - organophosphate pesticide compound
- RBC - red blood cell (erythrocyte)
- AChol - acetylcholine
- AChE - acetyl cholinesterase (in RBC)
- pChE - pseudocholinesterase (in plasma)
- SNS - Sympathetic nervous system
- PSNS - Parasympathetic nervous system

A Summary of the Health and Safety in Employment (HSE) Act 1992

The principal object of the Health and Safety in Employment Act 1992 is to prevent harm to employees at work. To do this, it imposes duties on employers, employees, principals and others, and promotes excellence in health and safety management by employers. It also provides for regulations, codes of practice and industry-based guidelines.

Employers have general duties to take all practicable steps to ensure the safety of employees. In particular, they are required to take all practicable steps to:

- Provide and maintain a safe working environment;
- Provide and maintain facilities for the safety and health of employees at work;
- Ensure that machinery and equipment is safe for employees;
- Ensure that working arrangements are not hazardous to employees; and
- Provide procedures to deal with emergencies that may arise while employees are at work.

Hazard Management

Employers must have an effective method to identify and regularly review hazards in the place of work (existing, new and potential). They must determine whether the identified hazards are significant hazards and require further action.

“Significant hazard” means a hazard that is an actual or potential source of:

- Serious harm; or
- Harm (being more than trivial) where the severity of effects on a person depends (entirely or among other things) on the extent or frequency of the person’s exposure to the hazard; or

- Harm that does not usually occur, or usually is not easily detectable, until a significant time after exposure to the hazard.

Where the hazard is significant, the HSE Act sets out the steps that employers must take:

- Where practicable the hazard must be eliminated.
- If elimination is not practicable, the hazard must be isolated.
- If it is impracticable to eliminate or isolate the hazard, the employer must minimise the likelihood that employees will be harmed by the hazard.

Where the hazard cannot be eliminated or isolated, employers must:

- Ensure that protective equipment is provided, accessible and used;
- Monitor employees exposure to the hazard;
- Seek the consent of employees to monitor their health and, with their informed consent, monitor employees’ health.

Employees should be provided with the results of any health and safety monitoring. In doing so, the privacy of individual employees must be protected.

Information for Employees

Before employees begin work, their employer must inform them of:

- Hazards employees may be exposed to while at work;
- Hazards employees may create which could harm people;
- How to minimise the likelihood of these hazards becoming a source of harm to themselves and others;

- The location of safety equipment; and
- Emergency procedures.

Duties of Self-Employed People

Some people working with organophosphates are likely to be self-employed. Self-employed people also have duties under the HSE Act.

They have a responsibility for their own safety and health while at work. They must also ensure that their actions do not harm anyone else.

The following information may assist employers to meet their duties covered above.

What are Organophosphates?

The organophosphate insecticides are a large group of compounds with some common elements to their structure and the same basic mechanism of acute toxicity. However, they differ substantially in their detailed structure and their degree of toxicity. While OPs have been categorised according to structure, a more useful classification is based on acute toxicity. (See Appendix 1).

Although a number of organic phosphorus compounds were synthesised prior to 1900 it was not until the 1930s that the specific toxic properties of some, known subsequently as organophosphates, were documented in mammals. Organophosphate use in agriculture and horticulture increased in the late 1950s with the decline in popularity of the organochlorine pesticides due to concerns over their environmental persistence.

Toxicology of Organophosphates

OPs are toxic because they inhibit the actions of an enzyme in nervous tissue called acetylcholinesterase (AChE) which in turn inactivates a “neurotransmitter”, acetylcholine (AChol). It is perhaps helpful to think of this as a “double-negative” type of effect in that the OP inhibits an enzyme which itself inactivates acetylcholine, the net result being increased levels of acetylcholine. The neurotransmitter is present and necessary in various parts of the nervous system to enable transmission of stimulation either between nerves, or between nerves and various organs. It is normally released in short sharp peaks, which provide the appropriate degree of stimulus or “messenger” effect. With the increased levels of acetylcholine induced by OPs, there is greater and more sustained

stimulation, with increased “target” organ response, although at very high levels the response can decrease.

The various acute symptoms of OPs can be explained by the various sites where acetylcholine is present as a neurotransmitter and where abnormally increased levels can disturb function. These include parts of the “autonomic” nervous system, which regulates the continuous, largely “automatic” or non-voluntary function of many organs and glands in the body. This system has two arms or divisions: the sympathetic nervous system (SNS) and the parasympathetic nervous system (PSNS), which help to keep each other in check and maintain an appropriate balance. However, OPs can increase acetylcholine at various sites within these divisions, causing increased response in many organs and tissues, with resulting symptoms (Table 1).

Acetylcholine is also present in the junctions between nerves and the muscles, and in some nerve-to-nerve connections (synapses) in the brain. Increased levels at these sites can also disturb function. In more severe cases, organ response decreases which leads to some of the more serious symptoms of OP poisoning.

Symptoms of Organophosphate Poisoning

These have been classified in 2 different ways, either according to severity (mild, moderate, severe) or to the sites in the nervous system involved and similarity to other toxins (muscarinic, nicotinic and central nervous system effects).

The former system is used in Table 1.

Table 1 - Symptoms and Signs of OP Poisoning

Mild	Moderate	Severe
Increased salivation Contraction of pupil of eye (miosis) Lacrimation (tears in eye) Nausea Headache Weakness (of muscles) or tremor Dizziness	Excessive salivation Small pupil with visual disturbance Lacrimation Sweating Vomiting, diarrhoea. Headache, drowsiness. Weakness increased, muscle tremor, increased muscle tension. Disturbed gait (ataxia) Bronchoconstriction and bronchial hypersecretion Breathlessness increased	Symptoms for mild and moderate poisoning increased, plus: Depressed consciousness or coma Reduced respiration Cyanosis Convulsions Cardiac failure

The symptoms experienced by an individual may present in different combinations and sequences. The time of onset of symptoms also varies, depending mainly on the route and severity of exposure, but also with the specific OPs in some cases. OPs are generally well absorbed via the respiratory tract and the skin, as well as the gastrointestinal tract. However, in many usage situations, the greatest danger lies in skin absorption, as the actual or potential degree of skin contact generally exceeds the amount capable of entering the airways. With ingestion or very heavy inhalational overexposure, eye and lung effects can occur within minutes.

In the most common situation of predominantly skin exposure, symptoms, if occurring at all, are typically delayed at least 2-3 hours and often up to 12 hours.

A comparatively delayed onset can also occur with OPs which are either highly fat-soluble (lipophilic) or are “indirect” inhibitors of AChE, or both. In the former case, a higher percentage than usual of the OP becomes stored in fatty tissue relatively early and it may have maximum effects on AChE enzyme depression as it more slowly redistributes out again. With indirect inhibitors, the compound

must first be changed in the body to a “metabolite” which then inhibits the AChE. In either case, symptoms can be delayed for up to 24 hours and, uncommonly, even later. In some situations with onset between 12-24 hours or more it can be hard to distinguish between continued skin absorption, delayed mobilisation from fatty tissues or the indirect type of action. Many of the “indirect” OPs have this property because they have a P-S chemical grouping present rather than a P-O grouping. For most of the listed OPs, an indication is given in Appendix 1 as to whether the action is likely to be direct or indirect.

Note that some effects on the eye, skin and airways can be at least partly ‘local’, in that they can arise from direct tissue contact, rather than occurring only after absorption into the bloodstream. As such, they can be the earliest of signs. Thus, constricted pupil(s) (miosis), with impairment of one’s normal visual capacity in dim light, can be an early warning, especially if affecting just one eye (from direct contamination), when judgement of distance is also affected.

Similarly, sweating responses confined to near the area of direct skin contact can occur. With

inhalation of mists or dusts, breathlessness may occasionally be the first response due to the local action on direct contact, or even the only response.

Other Aspects of Organophosphate Toxicity

Some OPs can have a quite different toxic effect, termed “delayed neurotoxicity”. However, this has occurred with relatively few OPs, only with very high exposures or doses which were sufficient to firstly cause the more typical cholinergic symptoms of poisoning, described above. The neurotoxic effects are typically delayed between 2-4 weeks after a heavy exposure. They are most noticeable in the distal parts of the limbs (especially the feet, but also hands), and often muscle weakness is more marked than other changes such as loss of sensation.

The underlying mechanism relates to phosphorylation of a nerve cell membrane protein (termed neurotoxic esterase, or more recently neuropathy target esterase, NTE), which initiates a chain of events leading to direct nerve damage. The list of OPs which, at high doses, have caused this syndrome include chlorpyrifos, EPN, fenthion, merphos, methamidophos, mipafox, leptophos, trichloronat, trichlorphon.

It has been demonstrated that only some of the OP structural subclasses have the potential to cause these effects (at sufficient dosage).

A more complex area is the question of more subtle long-term neurological effects, such as EEG changes and/or neurobehavioural disturbances. There is good evidence that these can occur for months after exposures sufficiently severe to cause the typical “cholinergic” type of poisoning in the first phase. Thus, deficits have been noted in reaction time, attention span, memory and in tasks requiring complex cognitive processes.

More recently it has been suggested that long-term exposure, even at insufficient levels to cause the typical symptoms of the acute

illness, might cause subtle effects such as slight disturbances on neuropsychological tests of reaction time, attention and mood.

However, this remains subject to debate and ongoing research, but provides further reason for safe working practices with OPs.

Finally, there is some evidence that OPs may occasionally affect further organ systems by mechanisms other than those discussed in this document. Thus, it is known that they can react with targets in the body other than AChE, pChE, or NTE though not to the same extent. There are occasional reports of disturbed liver function tests, for example, accompanying the typical cholinergic poisoning picture.

Toxicity Differences Between the Organophosphates

The toxicity of a specific compound such as an OP is generally assessed by the amount required to produce some specific toxic effect. This is generally expressed in terms of grams or milligrams (mg, a thousandth of a gram). However, this amount will depend in part on the size of the exposed subject, and this is accounted for by defining a toxic dose in terms of mg of chemical per kg of subject weight (mg/kg). This “toxic dose” will vary according to the effect being considered, and the susceptibility of the individual (and species) being considered.

A chemical’s toxicity is often described by its ‘LD50’ value. This is the single dose estimated to be lethal to half (50%) of a group of test animals. It is, therefore, an insensitive test because it considers the final possible toxic effect rather than the first symptom, and identifies only the more sensitive half of the population rather than the most susceptible individual. There are other limitations. The test itself is only a rough estimate and results can differ, it varies with different species, and relates to a single dose rather than repetitive exposures. For these reasons a LD50 figure should not be used to provide an accurate estimate of toxicity to humans. It can, however, be used as a rough guide to the

probable relative toxicity of different chemicals to humans.

Organophosphorus compounds and other pesticides have been classified according to degree of likely hazard, by the World Health Organisation. The categories used are Extremely, Highly, Moderately and Slightly Hazardous respectively, corresponding to Classes Ia, Ib, II and III. The classification is based primarily on acute oral and/or dermal toxicity (in rats), as measured by estimates of the LD50 when given orally or by skin application (held in place on the skin for 4-48 hours). However, there is provision for altering such a classification for various reasons. These include where direct human data suggest a different categorisation is warranted, and/or when the product is highly volatile, markedly cumulative, can cause irreversible damage or is significantly allergenic. Appendix 1 outlines the hazard class of each OP active compound (not all currently registered in New Zealand), as determined by this system.

The role of the solvent vehicle as a cause of symptoms with OP exposure remains unclear. Their main influence lies in their effects on volatility of the formulation and the potential risk of increased skin absorption or of inducing dermatitis with impaired barrier function of the skin. However, they may also contribute to some symptoms such as headache and fatigue.

Hazards During Use

The percentage of the active constituent, other characteristics of the formulation, and the degree of final dilution will influence the level of exposure, as does the specific method of use and the duration. Therefore, the level of hazard can depend on a number of factors other than the toxicity classification alone.

Volatility, and hence exposures, can vary with different compounds of the same active constituent. Volatility influences the balance of vapour versus aerosol, the former being more readily inhaled and more widely

dispersed. Handling concentrates is always potentially hazardous, especially as it may be difficult to avoid splashes.

Mixing	<ul style="list-style-type: none"> Liquids are more hazardous generally than solids as liquid concentrates are absorbed more rapidly through the skin, particularly when in a solvent formulation. Water-dispersible powders are hazardous as the fine dust can be inhaled. With powders/granules, small prepared packages are best.
Spraying	<ul style="list-style-type: none"> The process of spraying results in the creation of an aerosol. Aerosols consist of small particles, which can be absorbed through the lungs. Skin exposure and absorption (even through normal looking skin) is by far the most important route of entry under most usage circumstances. Spraying methods and technique, climatic factors (e.g. wind speed, humidity) and volatility affect airborne levels in the breathing zone. Upwards directed movement and/or smaller aerosol size as with air-blast sprayers, can increase off target drift. Skin absorption also increases at higher environmental temperatures. Leaks in spraying apparatus e.g. knapsack sprayers can occur in the tubing resulting in rapid skin contamination.
Clean-up	<ul style="list-style-type: none"> Equipment becomes contaminated during the spraying process. It should therefore be hosed down. However, washing can expose the unprotected worker to the chemical hazard.
Disposal of containers	<ul style="list-style-type: none"> The diluted OP mixture can still be hazardous. Avoid brushing up against containers with skin or clothing to avoid further contamination.

Requirements for Safe Use

This section raises the main issues and principles involved in minimising risks. For detailed advice on specific practices, users may also consult the NZS 8409: 1999 *Code of practice for the management of agrichemicals*, or subsequent revisions. This is a key reference used in current training programmes relating to agrichemicals use.

Selection of Pesticides

Aim to use the least toxic OP formulation compatible with a satisfactory effect or outcome. This issue is beyond the scope of these guidelines. However, considerations should ideally include:

- Identification of need – what is the problem and what will the use of the OP achieve;
- Hazards including toxicity and environmental (spray drift, water and soil contamination, environmental persistence);
- Animal welfare. This may include the most favourable insect versus mammalian toxicity ratio and the lowest mammalian dermal toxicity;
- Least toxic other constituents; and
- Lowest feasible usage concentration.

Further information on the appropriate selection of pesticides can be obtained from the pesticide supplier, the local council and veterinarians.

Education and Training

Employees (or the self-employed) new to the industry should be provided with information on the following aspects:

- Formulations and toxicity of the chemicals including common types, components, and characteristics of various types;
- How OPs can enter the body, i.e. their high absorption rates, including via skin;

- Potential health effects (poisoning), including early warning symptoms;
- Reasons for monitoring users (see “Biological Monitoring”);
- First aid measures and antidotes; and
- Safe use, including principles of mixing/preparation, application, use of protective clothing and safe disposal.

The knowledge of existing employees should also be periodically assessed. These guidelines are designed to assist in the above. More formal detailed training programmes are offered by the several organisations around New Zealand. If you wish to be advised of these, please contact your local OSH office or refer to Appendix DD of the *Code of Practice for the Management of Agrichemicals*.

It is important to stress to users that they cannot totally rely on an initial or previous lack of symptoms as a guide to complete safety as the effects of OPs can take time to develop. Another important point to cover is that OP-induced pChE inhibition acts to substantially increase sensitivity to some muscle relaxants such as suxamethonium, used in some surgical procedures. Therefore, anaesthetists need to be informed of the nature of the user’s work.

Personal Protective Equipment (PPE)

The following factors should be considered when selecting the most appropriate protective equipment for a situation:

1. OP type and formulation.
2. Risk of exposure (concentrated or diluted chemical).
3. User comfort/preference.
4. Practicality – worksite conditions.
5. Frequency of use of protective clothing.
6. Ease of decontamination.
7. Possible health effects from contamination.

PPE advice is generally present on the label. This represents the lowest standard required

for the applications approved at registration. A higher standard may be required for some (different) applications. Specific procedures should be followed when dealing with the following situations:

- **When handling concentrates** of class 1a or 1b classification (see Appendix 1) an impervious chemical resistant suit with hood or impermeable apron must be worn. Chemical resistant gloves, boots and headwear are also required. Face and eye, and respiratory protection are also necessary. Wear overalls/ trousers over boots.
- **At other times (including spraying)**, wear full length, long-sleeved but light and comfortable clothing (such as cotton overalls). However, when spraying a highly poisonous OP, a full impermeable chemical-resistant suit with hood may be required. Always wear gloves and chemical resistant boots. Again, depending on the possible poisoning effects of the OP, impermeable headwear, face and eye protection, and respiratory protection are required. This protective equipment should be worn in all other situations where there is the potential for spray or dust to drift into the user's breathing zone. For further information on selection of protective clothing, refer to the *Code of Practice for the Management of Agrichemicals*.
- **There are no occasions when shorts, open shoes and a sleeveless shirt are adequate.**
- **When working with powders or granules**, a highly protective air purifying dust/mist respirator is required.
- Most sprayed organophosphates consist of wettable powders, dusts and other formulations, which form mists. A particulate filter suitable for toxic dusts and mists is the most appropriate filter

for these products. For those products which present the greatest risk by the release of harmful vapour, or deadly or dangerous poisons, a combination air purifying filter consisting of a particulate filter fitted over a gas filter may be the best option.

- **“Cleanup”** procedures as well as preparation may also require special skin protection.
- PPE is not required when seated in **air filtered enclosed** cabs using tractor-drawn spray equipment, provided the air filtration unit:
 - Prevents penetration of particulate material through the filter;
 - Prevents leakages past the filter; and
 - Maintains sufficient positive pressure inside the cab to prevent leakage into the cab.

Filters do require regular checks, however. Resistance of airflow can provide an indication of service life. If any doubt exists about the level of protection provided by the cab filter, then a suitable personal respirator and other protective equipment should be worn. If exiting an enclosed cab, personal protective equipment may be required if exit is made in the treatment area or exit is made during application. Users may need to carry gloves and a small respirator in the cab for use if they need to leave the cab under these conditions.

Assistance regarding **choice of appropriate respirators** is provided by publications such as:

- NZS 8409:1999 *Code of practice for the management of agrichemicals*;
- *A Guide to Respiratory Protection*, OSH, Department of Labour, 1999;

- *Guidelines for Personal Protective Equipment for Agrichemical Users*, OSH, Department of Labour, and
- *AS/NZS 1715: 1994 Selection, use and maintenance of respiratory protective devices* (a joint publication of Standards Australia and Standards New Zealand).

Care of PPE

Wearing protective clothing that is contaminated can be more hazardous than not wearing it at all. All application equipment should be cleaned regularly and at least at the completion of each day's work.

- On completion of the job, shower with waterproof protective equipment on, before undressing. Wipe impervious clothing clean while still wearing impervious gloves.
- Wash gloves daily, outside and inside, with detergent and warm water and rinse with copious amounts of water. Check for holes, and replace if necessary.
- Thoroughly scrub boots, outside and inside, with warm water and detergent. Check for holes, and replace if necessary.
- Wash other (fabric) clothing before re-use, preferably daily. If clothing is seriously contaminated, discard as solid material.
- Keeping a spare set of clothing on hand is recommended for Class Ia and Ib OPs, in the event of spills requiring immediate skin decontamination.
- The service life of a respirator depends on a number of factors including the physical properties of the organophosphate, the concentration of the organophosphate, the air flow rate and the humidity. Respirators therefore require adequate maintenance and safe storage. The OSH publication *Guidelines on Personal Protection for Agrichemical Users* and NZS 8409:1999 discuss details.

Other Work Practices

- Do not handle concentrates with bare hands. An implement is better for mixing than relying on gloves totally.
- Stand upwind when mixing or loading.
- Identify the target for spraying.
- Ensure the spray is applied in accordance with the specifications on the product label.
- Avoid spraying on windy days.
- Learn to reduce overspray, especially onto yourself.
- Be aware of other people located in the area.
- Pour liquid concentrates carefully.
- Check all joints regularly to ensure there is no leakage from equipment, especially with knapsack sprayers.
- Never attempt to clear blocked nozzles by mouth.
- Always wear gloves while working with spray equipment.
- Clean spills promptly.
- Have a water supply handy.
- Users should wash hands and clothing in soap and water immediately if any contamination occurs.
- Never eat or smoke while working, without first washing hands.
- Never transfer any OP to an unlabelled container, especially one usually used for beverages or food.

Storage and Transport

Storage buildings should conform to any local authority requirements and consents, in addition to the minimum standards specified in current legislation and regulations.

Store concentrates in a lockable area, so that they are both inaccessible to children, and other unauthorised persons.

OPs should only be stored in buildings and

places suitable for the purpose. The ideal store will depend on volumes used, but the following requirements should be met:

- Store ventilated to the outside.
- Store secure and lockable.
- Suitable fire extinguishing equipment available.
- In a position where runoff or dusts cannot reach water supplies, waterways or crops.
- An impervious floor with a sump, and drip tray for cabinets.
- Properly placarded signage (HAZCHEM).

All organophosphates in storage shall have sound and legible labels on them at all times, accurately identifying the contents.

The HAZCHEM codes for organophosphorus pesticide formulations are generally 2WE or 3WE for liquids, and 2WE for solids.

Organophosphorus pesticides formulations are classified as Class 6.1 (“Poison” or “Harmful”) and in some cases also Class 3 (flammable liquid) in the NZS 5433:1999 *Code of practice for the transport of hazardous substances*. The appropriate precautions for transport and storage of these classes are discussed in this code.

Fire, Spills and Disposal

As stated above, the HAZCHEM codes for organophosphorus pesticide formulations are generally 2WE or 3WE for liquids, and 2WE for solids. The “2” signifies that in the event of a fire, a fogging agent is best but a fine spray is satisfactory as an extinguishing agent. The “3” signifies that foam is most appropriate. It is therefore, important that appropriate firefighting equipment is available (depending on the type of organophosphorus compound being used).

Any spillage of an organophosphate compound or water used to clean up spills must be contained. For containment of spills, full

breathing apparatus and skin protection is recommended.

When disposing of organophosphates, the container should be flushed out with water and disposed of in accordance with the requirements of the local territorial authority, and the instructions on the MSDS. If no MSDS is available, all containers of liquid formulations should be triple rinsed into the spray tank then emptied. Other acceptable alternatives include:

- Returning the empty container to supplier;
- Selling the container to a firm dealing with used drums which is equipped to neutralise the organophosphate compounds; or
- Taking the container to a recognised public sanitary landfill site.

Labelling

The current labelling requirements for pesticide formulations depend on their Toxicity Classification according to the Schedule System adopted by the Toxic Substances Act 1979. These classifications are provided in the Toxic Substances Regulations 1983 or its Annotations, and also in this document. Full details of labelling requirements for each Schedule are contained in the Toxic Substances Act 1979.

NOTE: Regulations to be introduced under the Hazardous Substances and New Organisms Act (HSNO), will replace the existing legislation in this area.

Material Safety Data Sheets (MSDS)

It is the employer’s responsibility to ensure that they have adequate information available on any product that may be hazardous to themselves, their employees and other people in the place of work.

It is essential that MSDSs provide the following information:

- Details of supplying company;

- Identifying information regarding all constituents;
- Physicochemical description and properties;
- Health hazard information including toxic effects and first aid measures;
- Precautions for use, including personal protective equipment; and
- Safe handling information including instruction on:
 - Storage and transport;
 - Fire/explosion hazard; and
 - Spills and disposal.

The Occupational Safety and Health Service (OSH) has produced guidelines for the preparation of MSDS.

Technical Controls

There may be various technical options available to decrease the probability or intensity of exposure. Such important measures would be indicated where biological monitoring results or practical experience suggests increased risks are present. Engineering controls are more appropriate preventive measures in the long term than personal protective equipment. Appropriate

design of application equipment can be a key factor. However, this is beyond the scope of these guidelines.

Environmental Monitoring

Routine environmental monitoring is not advised, as biological monitoring provides a more sensitive indicator of individual risk. However, its possible role in a wider context has been discussed in the Ministry of Health publication, *Guidelines for the Investigation and Surveillance of Agrichemical Spray Drift Incidents*.

Health Surveillance

Note that OPs are one group of chemicals for which health surveillance is recommended under the *Approved Code of Practice for the Management of Substances Hazardous to Health* (MOSHH). One of the most useful tools in such surveillance is acetylcholinesterase testing in blood, a form of biological (effect) monitoring, supplemented by medical examination where indicated by the test results. Thus, such biological monitoring needs to be considered for all OPs, although whether to adopt and how frequently depends on the type of compound, its nature of use and other factors. (See “Biological Monitoring” in the following section.)

Biological Monitoring for Organophosphates in the Body

Why Monitor?

The HSE Act requires that where a hazard cannot be eliminated or isolated, such as organophosphates, then exposure to that hazard must be minimised and monitored.

The basic abnormality causing the symptoms of acute OP poisoning is inhibition of AChE at various sites within the nervous system, where it breaks down Acetylcholine (AChol). Thus the activity level (reflecting the amount of inhibition) of this enzyme is a good guide to any potential risk. However, the nervous tissue cannot be analysed directly for these levels. Instead, blood tests are used as a rough indicator or “marker” for activity levels in the nervous system. This is possible because the enzyme AChE is also present in RBCs and a similar enzyme (pChE) is present in the blood plasma. Therefore, an OP compound which has been absorbed and is beginning to affect nerve enzyme levels will be detectable by its effects on the blood enzyme levels.

These tests are useful because OPs can affect the body adversely in a “silent” fashion. This is because the basic toxic disturbance of enzyme inhibition reverses slowly. Therefore, while individual episodes of usage are often insufficient to produce enough enzyme depression to cause symptoms, if such exposures are regular or frequent enough they can cause a progressive decrease in active enzyme levels due to its slow recovery rate between each exposure. The user may, therefore, remain well and apparently unaffected for days or weeks, yet they run the risk of reaching a critical point where enzyme levels have silently dropped to a level where the next exposure could be sufficient to tip the balance and result in symptoms.

Periodic blood testing can detect this unsuspected process and act as a warning.

NOTE: The carbamate group of insecticides are similar in that they also inhibit AChE, but by a process of “carbamylation” (not “phosphorylation” as is the case with OPs). However, the carbamate-induced inhibition is much more short-lived and there is little need for (and considerably difficulty with) biological monitoring for these agents.

Who and What to Monitor (Which Users, Which Organophosphates)

It is accepted that two of the primary considerations in setting recommendations are:

- The toxicity of the OP(s), as assessed by various Classification Systems.
- The type of usage, as affecting intensity, duration and frequency of exposure.

Monitoring should be initiated in all personnel involved in direct handling, including mixers, loaders and applicators.

Factors that should influence the frequency or need for continued monitoring are:

- Frequency of use;
- Occurrence of mishaps or oversights during use;
- Changes in procedures or products;
- In the case of new workers;
- Substandard usage of personal protective equipment, or constraints on its use; and
- Past experience within the particular occupation or task.

Monitoring is an important complement to other control measures as it can help to assess the effectiveness of those measures.

How to Monitor (What Tests)

1. When monitoring a worker's exposure to organophosphate, both red cell and plasma cholinesterase levels should be determined.

Plasma enzyme (pChE) activity is generally a more sensitive test of exposure because it is more rapidly inactivated by most, though not all OPs. However, it is less specific in reflecting levels of enzyme depression in the nervous tissue, as it is a different compound from acetylcholinesterase. In some cases it may overestimate nerve tissue levels as it often recovers from inhibition and also regenerates more quickly than AChE. It is also a less specific test, in that there are a wider range of other conditions or personal characteristics that can affect the measurements (Appendix 2). It also represents only about 8% of the total cholinesterase activity of whole blood, the majority (about 92%) being due to RBC AChE.

The RBC (erythrocyte) AChE test is more specific and reliable, and various authorities have recommended that this test should form the basis for decisions on management. It is the preferred test of the two. However, it can be a somewhat conservative indicator of nerve tissue levels, particularly in the later stages of recovery. Ideally, both RBC and pChE should be done because interpretation can be aided by having the results of both tests available.

NOTE: It is recognised that in some cases complete recovery of RBC AChE may lag behind enzyme recovery in nervous tissue, because full return to normal RBC AChE depends on its re-synthesis, which in turn depends on the re-synthesis or turnover rate of RBCs themselves. This is limited to about 0.8% per day. Thus, recovery of RBC AChE, unlike that in nerve tissue, is artificially constrained. However, it is better to sometimes underestimate recovery rates of AChE in

the nervous system with the use of RBC or whole blood AChE tests, than to use pChE as the criterion, which can sometimes overestimate such recovery rates and lead to a false sense of security.

The Ellman method is recommended for the tests. The tests may be performed on separated red blood cells and plasma, or on whole blood using a procedure that is specific for AChE and pChE activity. (*Biological Monitoring of Chemical Exposure in the Workplace*, W.H.O., Geneva, 1996.)

2. The same laboratory using the same method should do cholinesterase tests for any individual. This is because there may be considerable variation in results even among different laboratories using the same method.

When to Monitor

Monitoring takes two forms – an initial test of the individual's "normal" cholinesterase activity levels before they are exposed to OPs, and periodic testing thereafter. The former test of the user's "baseline" level is very important, because of the large range of normal values between different people. Thus, if a test is only done once OP exposures have recently commenced, it can be difficult to know, in the event of a low result, to what extent this signifies OP-induced enzyme depression, on the one hand, versus a naturally low individual level on the other (See Interpretation of Results.)

1. Baseline Testing

These tests should be done only after at least 30 days freedom from exposure to OPs. They are best done, however, prior to employment or before first use of OPs. Such stringent timeframes are not required for carbamate insecticides, where inhibition of AChE is more short-lived.

At least one pre-exposure test should be done (ideally two). Many authorities recommend averaging two such tests (as a

minimum) for optimum baseline estimation.

2. Periodic Testing

Testing should be related to intensity and frequency of exposure, with the following recommendations:

- a) Periodic testing should be carried near the probable peak of the application period.
- b) Retesting should be more frequent in cases of:
 - An inexperienced user, or if there is evidence for occurrence of mishaps;
 - Substandard protective equipment or work practices;
 - A new formulation, where the method of absorption has not been thoroughly assessed; or
 - Where the extent and frequency of use is increased.

Testing of new workers may need to be on a weekly basis for the first two or three tests (provided they have been regularly exposed during this time), then monthly for two or three months. If no significant decrease is found, tests could thereafter be reduced to once per season, near to the probable peak of the application period, as recommended in 2a).

Interpretation of Results and Management of Users

Monitoring using blood tests can give only an approximate idea of nervous tissue levels and hence risks. Furthermore, the risk depends on the rate of enzyme inhibition as well as its absolute level at a point in time. (Thus, in someone regularly exposed, a gradual 70%-80% depression to 20-30% of normal levels may not always be associated with symptoms, while in previously unexposed workers, a rapid 30% drop to 70% of normal may.)

AChE % of Baseline	AChE Fall from Baseline	Significance Percentage of Baseline	Management Baseline
20% to 39%	61% to 80%	Evidence of significant exposure	(i) Retest (ii) Check work practices
40% or greater	60% or less	Increased vulnerability from subsequent exposures	(i) Remove from work (ii) Notify to OSH

NOTE: The above criteria refer to AChE. The fall from baseline and the percentage of baseline are complementary. For example, a person with a baseline of 100 may subsequently be tested after exposure to OPs and have a AChE level of 75. This is a 25% fall from baseline, and it is also 75% of the original baseline.

Two fundamental points to remember:

1. Decisions are best based on AChE levels.
2. Decisions are much easier if baseline values are available.

Criteria for Return to Work

Workers should be suspended from work when their fall from baseline is 40% or greater. They should then return to work only when the fall from baseline has partially recovered and is only 25% or less i.e. is 75% or more of the baseline.

NOTE: The above criteria relate to RBC active AChE levels, rather than whole blood levels. The relationship between the two results depends on the type of test method used, in particular whether it measures AChE specifically. However, in any case there is a

close correlation and little difference between the two test results. Therefore, the above criteria can be used for whole blood results as well.

Testing for Diagnostic Purposes

Sequential post-exposure testing in the absence of a baseline can also be used to help confirm or question the diagnosis of OP-induced illness. Recovery of enzyme levels is more rapid during the first few days of post-exposure (for some OPs at least) than subsequent rates of recovery towards the baseline. This is because for many OPs there is some degree of spontaneous reversal of enzyme inhibition (termed “reactivation”) which occurs more rapidly than the slower progress of regeneration or re-synthesis of new active enzyme to replace the permanently inhibited fraction, (i.e. recovery = reactivation + regeneration.)

A Word on Prevention

Safe work practices and AChE monitoring are the key

For further advice please contact your local OSH office. The contact details are in the ‘blue pages’ of your telephone book under Labour, Department of. Alternatively, the OSH website address is www.osh.dol.govt.nz

The New Zealand Agrichemical Education Trust may also be of assistance when developing education and training packages on safe work practices for employees. Their address is:

**The New Zealand Agrichemical
Education Trust
PO Box 10 232
Wellington
phone (04) 472 9997**

Appendix 1: W.H.O. Classification of Organophosphorus Pesticides

NOTE: This classifies the active OP constituents, not the overall formulated products of which they are a part. It is more relevant to those such as formulators working with “pure” technical OP preparations.

Class Ia “Extremely hazardous”	Direct (d) or Indirect (i) effects
chlorfenvinphos	d
chlormephos	i
chlorthiophos	
coumaphos	i
demephion (-o and -s)	
demeton (-o and -s)	d and i
dimefox	
disulfoton	i
e.p.n.	i
ethoprophos	d
fenamiphos	d
Fensulfothion	i
fonophos	i
leptophos	
mephosfolan	d
mevinphos	d
parathion	i
parathion-methyl	i
phorate	i
phosfolan	d
phosphamidon	d
prothoate	
schradan	
sulfotep	i
TEPP	d
terbufos	i
thionazin	
trichloronat	

Class Ib “Highly hazardous”	Direct (d) or Indirect (i) effects
azinphos-ethyl	i
azinphos-methyl	i
bromophos-ethyl	i
cadusafos	d
carbophenothion	i
crotoxyphos	d
demeton-S-methyl	d
demeton-S-methylsulphon	
dichlorvos	d
dicrotophos	d
dioxathion	i
edifenphos	d
ESP	
famphur	i
fenthion	i
fosmethilan	
heptenophos	d
isazofos	i
isofenphos	i
isothioate	
isoxathion	i
methamidophos	d
methidathion	i
monocrotophos	d
omethoate	d
oxydemeton-methyl	d
pirimphos-ethyl	i
propaphos	d
propetamphos	i
thiometon	i
triazophos	i
vamidothion	d

Class II “Moderately hazardous”	Direct (d) or Indirect (i) effects
chlorpyrifos	i
cyanofenphos	
cyanophos	i
dialifos	i
diazinon	i
dichlofenthion	i
dimethoate	i
dioxabenzophos	
EPBP	
ethion	i
etrimfos	
fenchlorphos	
fenitrothion	i
formothion	i
methacrifos	i
naled	d
phenthoate	i
phosalone	i
phosmet	i
phoxim	i
profenofos	d
prothiofos	i
pyraclofos	d
quinalphos	i
sulprofos	i

Class III “Slightly hazardous”	Direct (d) or Indirect (i) effects
acephate	d
azamethiphos	d
bromophos	
crufomate	
malathion	i
maldison	i
menazon	
pirimiphos-methyl	i
pyridaphenthion	i
trichlorfon	d

Class IV “Unlikely to present acute hazard”	Direct (d) or Indirect (i) effects
chlorphoxim	
chlorpyrifos methyl	
ditalmifos	
jodfenphos	
temephos	i
tetrachlorvinphos	d

Appendix 2: Sources of Variation

Extent and Sources of Variability in pChE and AChE

The wide variability between individuals in pChE and AChE can make interpretation of a single result difficult. (See further under “Monitoring”.) The pChE has greater variability than the AChE. The situation can arise where one must distinguish between a low pChE caused by OP exposure and that due to other, especially genetic, causes. An important point is that most other (non-pesticide) causes of decreased pChE are relatively mild in effect and/or clinically apparent, or extremely rare. Therefore, a severe depression in pChE in an otherwise well individual is almost always due to chemically-induced inhibition. Note that the following non-pesticide causes of pChE inhibition are not thought to make the individual more vulnerable to OPs. (It is, after all, AChE levels in the nervous system that are more relevant.) However, such people are more susceptible to the effects of certain muscle relaxant drugs such as suxamethonium; as indeed are OP workers whose pChE levels have been depressed and are not yet recovered.

Physiological Sources of Variation

There is no significant gender difference in RBC AChE activity. However, plasma pChE activity is lower in women than in men. It also decreases with oral contraceptives (and pharmacological doses of other steroids), and falls during the first trimester of pregnancy

(until about week 12). There is also some fluctuation within the menstrual cycle. Other physiological sources of variation are vigorous exercise (causing transient increases) and age, with higher pChE levels generally in young children, and increases in females again after about 60 years.

Pharmacological Sources of Variation

Drugs implicated as causing decreases in pChE include oral contraceptives, steroids, quinidine, some B-blockers, some treatments for myasthenia gravis and glaucoma, phenothiazines, MAOI's and metoclopramide.

Genetic Sources of Variation

It was thought up till recently that any individual fell into one of three different groups with regard to genetic make-up affecting pChE enzyme activity. It is now thought there may be up to 10 different groups, although only two are at all common. The “usual” group, comprising about 96% of the population, has on average a significantly higher level of pChE activity than the other groups. The next most common (or intermediate) group (nearly 4%) have on average about 77% the levels of the usual group. There are several other “atypical” groups whose average levels may be as low as about 40% or even 20% of the typical ‘normal’ level; however these groups are extremely uncommon.

Genotype	Relative pChE levels (averages)	Prevalence in population
Usual group	100%	c. 96%
Intermediate group	77%	c. 4%
Groups 3 - 5	43 - 86%	1/190 - 1/2000
Group 6- 9	22% - 74%	1/20,000 - 1/154,000
Group 10	0%	1/100,000

This data suggests that levels of pChE much below 43% of general population values are only likely to be due to individual genetic make-up on very rare occasions, and levels below 22% will almost always be due to OP exposure.

Disease as a Source of Variation

The following is not an exhaustive list of all conditions suggested as influencing pChE levels. Evidence is stronger for some than others. There is evidence that pChE production and activity is influenced by the levels and production rates of serum albumin.

pChE decrease	pChE increase
Liver disease	Recovery from liver damage
Malnutrition	Nephrotic syndrome
Hypothyroidism	Hyperthyroidism
Tuberculosis	Hyperlipoproteinemia
	Alcoholism
	Diabetes (IDDM)

RBC AChE is also uncommonly affected. It can be decreased with some forms of anaemia, but increased in haemolytic anaemia, for example.

Appendix 3: Explanation of Chosen Criteria for Return to Work

Baseline Test Results Available

It is estimated that the 'coefficient of variation' (standard deviation as a fraction of the mean) of AChE measurements in an individual is 8-11%, or roughly 10%. (This amount however, varies with the test method.) This means that a one-off measurement as much as 20% (i.e. 2 standard deviations, (SDs)) below (or above) the baseline may just reflect a normal result and one can only dismiss the possibility of its being a chance finding as less than 5% likely when measurements are more than 20% lower than the baseline. (This also varies with the number of tests used to estimate the baseline.) Thus, from a statistical point of view, one accepts that a 20% or lower result in all probability reflects a real enzyme depression. That is, only with a greater than 20% depression can the changes be recognised with some assurance as not being (entirely) due to normal variation. Thus, any level over 80% of baseline has some statistical chance of being a normal value. Furthermore, in the prolonged

recovery phase, RBC AChE depression tends, if anything, to persist longer than that in nervous tissue, so that even a real persisting depression of 20% in the former does not necessarily imply a similar abnormality still exists in the latter. For these reasons, a return of RBC AChE levels to within 80% baseline can be considered good enough to recommence work even if it might reflect a small amount of remaining AChE inhibition in nerve tissue in some cases.

In the absence of such a baseline, the pChE level and its recovery rate should not be used for decisions on when to return to work. Rather, this should be based on recovery rates of AChE (see above). However, the recovery rates of pChE have been used as a diagnostic tool in these situations, due to their more rapid return to normal. Thus, an increase of pChE of 20% or more between the time of an exposure and suspect illness, and a retest 3-5 days later, is strongly supportive of an OP effect, although it is not absolute proof.

Appendix 4: First Aid and Antidotes

The full details of clinical management are not discussed in this document, as the focus here is prevention and emergency measures. For further information, refer to NZS 8409:1999 *Code of practice for the management of agrichemicals*.

Where organophosphate poisoning is suspected, the recommended procedure is:

1. Make sure it is safe for you to help the patient. It is important to protect yourself from airborne or skin contamination. Protect yourself with adequate clothing, especially gloves, when decontaminating others.
2. Remove the person from the contaminated atmosphere.
3. Assess airway, breathing, and circulation. If breathing has stopped, begin artificial respiration (mouth-to-nose for ingestions or via resuscitube). If breathing is laboured, ensure throat is clear, tilt head back and bring tongue forward.
4. Seek medical assistance.
5. Remove any contaminated clothes, and “double-bag” them.
6. Wash contaminated skin thoroughly with plenty of cold water and soap. Continue washing skin for 10-15 minutes. Pay attention to the hair, armpits, navel, groin, ears, and other skin folds, under fingernails and the eyes if involved. Do not attempt to remove contact lenses prior to initial irrigation with water. Remove later, with clean fingers, and continue irrigation. Adequate skin decontamination is required as any insecticide present may continue to be absorbed for a few days.

With ingestion, if the person is able to drink, it is possible that small amounts of milk or food may be helpful to delay

stomach emptying, and might delay absorption of the toxin. On the other hand, large amounts of fluid may hasten stomach emptying. Do not induce vomiting, nor administer chemical antidotes unless instructed to do so by a medical professional.

Activated charcoal (orally or via nasogastric tube) may be the most useful first aid decontamination measure though its effectiveness is not always high. Gastric lavage may be helpful in symptomatic cases but only if seen at hospital early, i.e. within one hour. Induction of vomiting is not recommended as this can cause problems if poisoning becomes severe (e.g. aspiration of vomitus during coma or convulsions).

Antidotal Treatment

1. Atropine is required if symptoms are moderate or severe.
 - Oral atropine is not recommended as the tablet dose is too low and the time before effect too long.
 - If injectable atropine is not available, arrange transport to health care facility (after immediate measures).
 - If injectable atropine is available, give 2-4 mg iv or im and repeat at 15-30 minute intervals (0.05 mg/kg in children) if indicated.
 - More frequent dosing with large total daily doses may be required in severe cases.
 - Aim to achieve drying of bronchial secretions, dilation of pupils, flushing of skin and reversal of excess salivation and sweating.

- Maintain such 'atropinisation' by repeated dosage for at least 24 hours.
 - NOTE: Atropine can be risky when oxygenation is poor. If patient is cyanotic, it is better to give oxygen before atropine.
2. Pralidoxime (the chloride is preferable to the iodide) is especially indicated for severe muscle weakness (including the respiratory muscles) but also coma or respiratory depression within the first 24-36 hours. It must be administered slowly. Adults 1-2 gm. Half can be given im or iv. Remainder as a slow iv infusion.

Supportive Treatments

In resolving severe cases, observe closely for at least 48 hours for possible recurrence of toxicity. Diazepam is indicated for severe cases and/or convulsions.

The lung is the critical target organ.

Monitor for and treat:

- Bronchial secretions and bronchospasm;
- Pulmonary oedema; and
- Respiratory depression.

References

OSH Publications

Approved Code of Practice for Management of Substances Hazardous to Health

A Guide to Respiratory Protection

Guidelines on Personal Protection for Agrichemical Users

A Guide to the Safe Use of Agrichemicals in Forestry

Agrichemicals farming bulletin

Handling Farm Chemicals

Guidelines for the Preparation of Material Safety Data Sheets

Interim Guidelines for the Investigation and Surveillance of Agrichemical Spray Drift Incidents

Standards

NZS 5433:1999 *Code of practice for the transport of hazardous substances*

NZS 8409:1999 *Code of practice for the management of agrichemicals*

AS/NZS 1715:1994 *Selection, use and maintenance of respiratory protective devices*