

serum study were:

1. to obtain estimates of baseline levels of dioxins, PCBs, and chlorinated pesticides in serum sampled from the New Zealand population
2. to determine the relationships of organochlorine contaminant body burdens to age, sex, ethnicity, and geographic region
3. to obtain data that can be used, under the Resource Management Act 1991, to develop national environmental standards for the protection of human health and the environment from organochlorine contaminants.

Research design and methods

Between December 1996 and November 1997, samples of blood were collected from 2,925 people across the country. The serum component was separated from the blood and sent for chemical analysis to the Centres for Disease Control and Prevention, Atlanta, USA. Because only a small quantity of blood was collected from each person, it was necessary to pool individual samples of serum to obtain a sufficient volume for the full range of organochlorine analyses to be undertaken. Following extensive discussions, serum was pooled into groups according to the following criteria for region, sex, age, and ethnicity:

Region	Sex	Age	Ethnicity
Northland/Auckland	Male	15-24	Maori
Bay of Plenty/Waikato	Female	25-34	Non-Maori
Lower North Island		35-49	
South Island		50-64	
		65+	

This study was designed to establish a base-line reference of organochlorine levels for the general New Zealand population, and was not intended to identify or characterise highly exposed or at-risk populations. Therefore, any blood samples from individuals who reported that they may have been occupationally exposed were not included in the pooled samples analysed. The research design and methods followed in this study were reported in Bulletin 7 (September 1998).

Results

This section presents some of the preliminary results from the analysis of serum for organochlorines.

Low levels of dioxins were found in all pooled samples. When measured as toxic equivalents (TEQ), these levels ranged from 5.1–26.7 pg TEQ/g of serum lipid³. Within an age group, the dioxin levels found in each region were generally similar. However, in all regions, the average concentrations were found to

increase with age. This variation with age is shown in Figure 1.

The study found that little variation in dioxin levels was associated with sex or ethnicity. Thus, the dioxin levels for males and females, Maori and non-Maori were generally similar, as shown in Figure 2. The concentration in female Maori in the 50-64 year age group stands out above the other results for that age group. However, this female Maori result is based on only a small number of individual serum samples, and, therefore, may not be particularly representative of that population group.

There was an insufficient number of serum samples collected for measurements to be obtained for Maori (both male and female) in the 65+ age group. In that age group, non-Maori females had appreciably higher dioxin levels than non-Maori males. This may be because the life expectancy of women is longer than men, and the average age of the women in that age group is greater than that of the men.

Generally, the levels of dioxins measured in this study are lower than levels reported in non-occupationally exposed populations from other countries. For example, concentrations of dioxins in blood of the US population have been reported in the range 15.1–58.0 pg TEQ/g lipid.

Serum samples were also analysed for persistent organochlorine pesticides. The most commonly detected pesticides were beta-hexachlorocyclohexane (β -HCH), dieldrin, and DDE (a metabolite of the pesticide DDT). Concentrations of β -HCH and dieldrin were measured in the range <7–73.1 ng/g lipid and <8–28.4 ng/g lipid respectively⁴. DDE concentrations were typically ten to a hundred times higher – between 306–2060 ng/g lipid. For both DDE and dieldrin, the older age groups tended to have the highest concentrations in their serum, although there was more age variability for β -HCH. The variation in DDE concentration by region and age group, is shown in Figure 3.

The highest DDE levels were consistently found in the Lower North Island and South Island regions. This may reflect historic use patterns of these materials.

³ Dioxins are a family of 210 individual compounds, and generally occur in the environment, and in human tissue, as complex mixtures. To simplify the reporting of dioxin concentrations for use in risk assessment, it is common for the relative toxicity levels of each of the individual dioxin compounds to be added up to give a single value, known as the toxic equivalents (TEQ), that reflects the complete mixture. Because dioxins are lipid (fat) soluble, they accumulate in the fat of people's bodies. It is normal therefore, for data from the analysis of serum to be reported as a concentration in serum lipid. Such data is often measured in picograms (pg), where one picogram is one million millionth (1×10^{-12}) of a gram.

⁴ One nanogram (ng) is one thousand millionth (1×10^{-9}) of a gram.

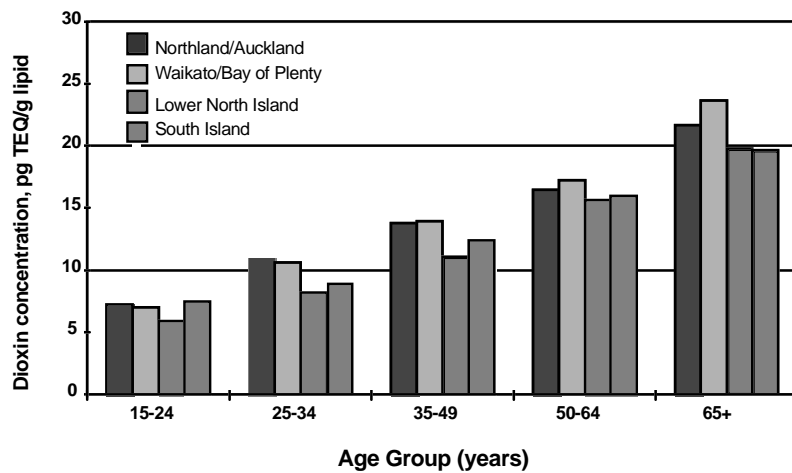


Figure 1 Average dioxin levels in serum for each region and age group

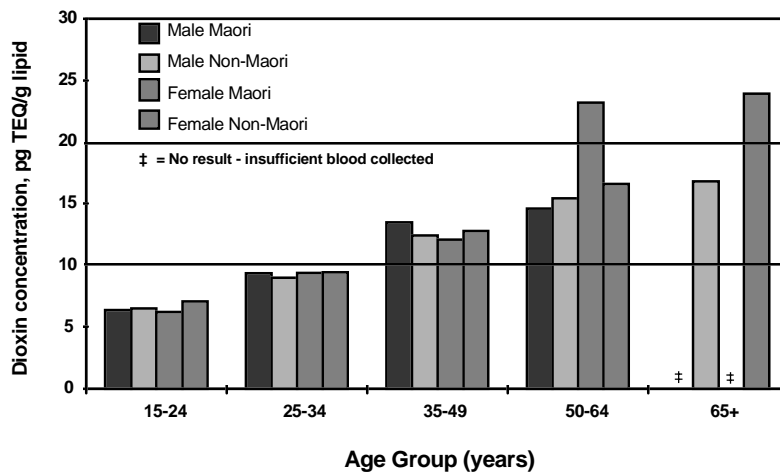


Figure 2 Average dioxin levels in serum for sex and ethnicity with each age group

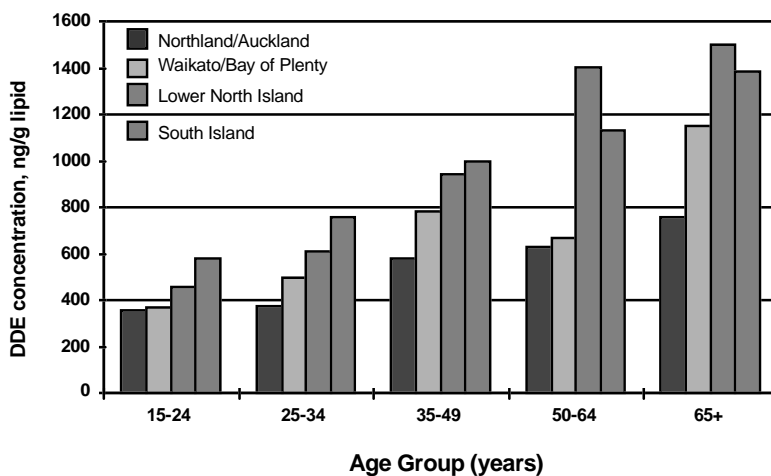


Figure 3 Average DDE levels in serum for each region and age group

Further information

A public summary of this research as well as a detailed technical report are being prepared and will shortly be available from the Ministry's web site at:

<http://www.mfe.govt.nz/issues/waste/organo.htm>.

In addition, these reports will be available on CD ROM. To order a printed copy of the public summary or a copy of the CD ROM, write to:

Ministry for the Environment
Publications
PO Box 10 362
Wellington

Phone (04) 917 7400
Fax (04) 917 7523
Email publications@mfe.govt.nz

There is a charge of \$10 for the CD ROM which will also hold the technical reports from the dietary and environmental surveys that have been undertaken (see Bulletin 7). Printed copies of the technical reports are not available.

Health effects of dioxins

How people are exposed to dioxins and the health effects of these chemicals has been well studied. This section provides a brief synopsis of our current understanding in this area.

Exposure to dioxins

Exposure to dioxins is generally of two kinds. Low level background exposures, as for the entire population, and higher exposures that are normally restricted to smaller groups of people, such as may occur in the workplace.

Exposure to dioxins for the general population

Dioxins can be found almost everywhere in our environment. Most people are exposed to very small background levels of dioxins when they consume food, and to a lesser extent, when they breath air or have skin contact with dioxin contaminated materials.

The World Health Organization (WHO) has recently revised the tolerable daily intake for dioxins, and recommended a range of 1–4 pg TEQ per kg body weight per day. Importantly, the New Zealand exposure levels are below this WHO tolerable daily intake range, and are also below dietary exposures of other countries where comparable studies have been undertaken.

For the general population, over 90% of exposure to dioxins and PCBs is through the diet, with food such as meats, dairy products and fish, usually being the predominant sources. Unborn children can be exposed to dioxins *in utero*, and nursing infants are exposed to the dioxins present in breast milk.

Dioxins in our food mainly result from its deposition from air onto pasture and its uptake by grazing animals, from where it contaminates the animal's meat and milk. Another exposure pathway results from the discharge of dioxin containing effluents to waterways, where the dioxins can then bioaccumulate in fish and shellfish. The application of waste materials, such as sewage sludge, to farm land might also enhance the entry of dioxins into food produce.

Information from studies in Europe and North America indicate a daily intake of dioxins for these regions in the order of 1-3 pg TEQ per kg body weight per day. If the "dioxin-like" PCBs⁵ are also considered, the daily TEQ intake can be two or three times higher. A recent study of the New Zealand diet has estimated the daily intake of dioxins and dioxin-like PCBs by New Zealanders to be 0.33 pg TEQ per kg body weight per day for an adult male, and 0.76 pg TEQ per kg body weight per day for an adolescent male.

Recent studies from a number of northern hemisphere countries, including the Netherlands, United Kingdom and Germany, show decreasing levels of dioxins in people's diets and their bodies. This has been attributed to measures taken since the late 1980s to reduce dioxin emissions to the environment from industrial processes, and bans on the use of certain chlorinated chemicals such as pentachlorophenol and the PCBs.

The relatively low level of dietary exposure to dioxins and PCBs in New Zealand is consistent with the low levels of these contaminants in the serum of New Zealanders (see previous article). A study of levels of organochlorines in the breast milk of New Zealand women carried out in 1987/88 also showed comparatively low levels of dioxins and PCBs. These levels were generally in the low to mid-range relative to the levels of these contaminants found in the breast milk of women from other countries. The 1987/88 study is currently being repeated (see Bulletin 7), and this should show whether dioxin levels in New Zealand have also fallen over the last decade, in line with the fall observed overseas.

Accidental and occupational exposures

Some people may be exposed to dioxins in the work place, and sometimes people have been exposed to very high levels from industrial accidents. The most well-known accident occurred in Seveso, Italy, in 1976, when an explosion at a chemical manufacturing plant sent a cloud containing 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)⁶ over the surrounding area. The exposed population has been studied closely since that time.

⁵ The PCBs are a family of 209 individual compounds, some of which induce toxic responses similar to those observed from dioxins. These PCBs are often referred to as "dioxin-like".

⁶ 2,3,7,8-tetrachlorodibenzo-p-dioxin is just one of the 210 dioxin compounds. It is often abbreviated to TCDD.

Occupational exposures have generally been associated with the manufacture or use of industrial chemicals contaminated with dioxin, including chlorophenols and the phenoxy herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). In New Zealand, the past use of pentachlorophenol in the timber industry is believed to have resulted in occupational exposure to dioxin contaminants for some timber workers. A study, published in 1992, reported that the dioxin blood serum levels of pesticide applicators involved for many years in ground-level spraying of 2,4,5-T in New Zealand were found to be significantly higher than those of a comparison group. Pentachlorophenol and 2,4,5-T are no longer used in New Zealand.

Other exposed groups that have been studied include the American servicemen who sprayed Agent Orange in Vietnam.

Toxic effects of dioxins on animals and humans

Effects on animals

The toxicity data for dioxins comes mainly from high-dose experiments on laboratory animals, such as rats and mice. Most research has been carried out on TCDD, as this is the most toxic of the dioxins. A variety of toxic effects have been reported in studies involving dosing of animals with dioxins. The animal data indicate that TCDD is one of the most toxic substances known.

Adverse effects induced in animals by administration of TCDD include neurobehavioural, developmental, reproductive and immunotoxic effects, as well as cancer.

The susceptibility of different animal species to TCDD varies widely. The characteristic signs and symptoms of lethal doses of TCDD are severe weight loss and atrophy of the thymus gland, which is involved in the immune system. Exposure to non-lethal doses of TCDD can cause a variety of adverse effects in animals, including weight loss and biochemical and degenerative changes in the liver. In many animal species, the immune system appears to be the body system that is most sensitive to TCDD.

TCDD is a very potent animal carcinogen, causing a variety of cancers in several animal species. Rats and mice that are exposed to very small amounts of TCDD in food over a period of time can develop cancers of various organs, including the liver and thyroid gland.

TCDD can also cause reproductive damage and birth defects in animals. Decreases in fertility, altered levels of sex hormones, reduced production of sperm, and

increased rates of miscarriages have been reported from various studies. Birth defects induced in animals by TCDD include cleft palate and kidney anomalies.

In general, the doses that have caused adverse effects in the animal studies are considerably higher than background human exposures for the general population.

Effects on humans

As there is a wide range of variation within different animal species in their susceptibility to dioxins, it is unclear from animal studies alone what effects dioxins might induce in exposed human populations. Therefore, it is important to consider the results of epidemiological studies of human populations. Since the most highly exposed groups of people are more likely to produce evidence of health effects associated with dioxins, epidemiological studies have focused on such groups. However, despite a wide range of studies, evidence of effects that can be clearly attributed to dioxin exposure is still quite limited. For most of the effects that have been induced in animal studies, there is little evidence of similar effects in exposed human populations.

A number of effects have been observed in people exposed to TCDD at levels higher than general background exposures as a result of acute accidental or industrial exposures. The most obvious health effect that occurs is chloracne, a skin disease characterised by acne-like lesions. Chloracne generally occurs on the face and upper body, but may occur elsewhere on the body.

Other effects to the skin, including rashes and discolouration, have been reported in people following high exposures to TCDD. Changes in blood and urine have also been observed that may indicate the occurrence of liver damage. Of the many effects evaluated in exposed human populations, most were transient and disappeared after the end of exposure. An increase in mortality from cardiovascular and non-malignant liver disease has been observed in association with high level accidental and occupational exposures.

Several studies of workers exposed to high levels of TCDD suggest that this chemical may increase the risk of cancer in people. Based on these and other studies, the International Agency for Research on Cancer concluded, in 1997, that TCDD is a human carcinogen.

Approaches to risk assessment

Ultimately, the purpose of carrying out scientific studies and obtaining information on the health effects and risks of chemicals is to determine what are “safe” or “acceptable” levels of exposure to the chemicals. Decisions on these matters, combined with information on the extent to which various uses or

levels of emission lead to exposures of people or the environment, drive public policy. In the case of organochlorine chemicals, decisions may be made on what (if any) are appropriate uses of these chemicals, or how emissions, such as discharges from incinerators and industrial processes, should be restricted and controlled.

The process of arriving at “acceptable” levels of human exposure is a complex one. Often the available information is limited or open to varying interpretation. As new information emerges, it may be necessary to revise estimates of risk associated with particular levels of exposure. This has particularly been the case with the dioxins.

Most of the information on which risk estimates are based is of two types: toxicological studies using laboratory animals and epidemiological studies of exposed human populations. Both types of study are useful and both types have their strengths and weaknesses. Animal studies have the advantages that they are carried out in controlled laboratory situations where very precise estimates of dose and comprehensive measures of the effects of those doses on the animals can be obtained. They can also be carried out on chemicals to which no humans have yet been exposed. However, they have the major disadvantage that the effects of particular chemicals on animals may be completely different to the effects on humans. Also, laboratory toxicological studies, of necessity, usually involve studies of animals at much higher exposures than those which humans normally experience.

Epidemiological studies of human populations compensate for some of the deficiencies of animal studies, since they involve the appropriate species and more relevant exposure levels. However, they also have certain disadvantages. There is usually much uncertainty about the actual levels of exposure that people receive, and it is not possible to study effects on humans in the same detail that is possible with laboratory animals. Also, if there is no exposed human population, as would be the case with a new chemical, an epidemiological study could not be carried out. Even when there is an exposed human population, it may not have been exposed for a sufficiently long period for effects, such as cancer, to have become apparent. In that situation, it is necessary to use animal toxicology studies in which cancer effects can be detected in a much shorter timeframe.

Despite the limitations of toxicological and epidemiological studies, scientists have devised a wide variety of methods of using the results of such studies to assess the potential impact of exposures on people and the environment. The application of these methodologies comprise the multidisciplinary area of risk assessment.

The following sections outline some of the key approaches to deriving an “acceptable” level of exposure considered protective of human health.

Application of uncertainty (safety) factors

This is a very traditional approach, which assumes that there is some threshold of exposure below which toxic effects are unlikely to occur. One approach is to start with either the highest dose level that, in animal studies, causes no observed toxic effect (called the no-observed-adverse-effect-level, or NOAEL) or the lowest dose level that, in animal studies, causes a toxic effect (called the lowest-observed-adverse-effect-level or LOAEL). Either the NOAEL or LOAEL is divided by an uncertainty factor, which may range from 10 to several thousand, depending on the scientific quality of the study or the nature of the effect that occurs at higher dose levels. The uncertainty factor takes into account the fact that humans may be more susceptible to toxic effects of the chemical than the animal species, and also that different people will vary in their degree of susceptibility. Some people may be more sensitive to the effects of the chemical than others.

In December 1990, the WHO established a tolerable daily intake of 10 pg TCDD per kg body weight. Since that time, additional epidemiological and toxicological data have been published. Based on the results of hormonal, reproductive and developmental effects seen at low doses in experimental animals, the WHO, in May 1998, revised the tolerable daily intake to a range of 1–4 pg TEQ per kg body weight per day. Both the earlier and the most recent assessments of the tolerable daily intake for dioxin, by WHO, were based on the application of uncertainty factors.

As mentioned, the uncertainty factor approach assumes the existence of a threshold of effect. However, for some types of effect, particularly cancer, there is uncertainty about whether such thresholds exist. This has led to the development and use of low dose extrapolation methods.

Low dose extrapolation methods

If there is no verifiable exposure threshold for the effect of a chemical, then the possibility exists that any exposure may carry some level of risk. The question is how to estimate those risks at very low levels of exposure, well below those doses that can practically be used in animal toxicology studies or have occurred in epidemiological studies. A number of methods have been developed to extrapolate from established levels of toxic response at measurable levels of exposure in toxicological or epidemiological studies, to estimating the risks associated with very low levels of exposure, such as might be associated with trace levels of organochlorines in food. These methods are usually various forms of mathematical models, some simple, some very complex. The limitation of this approach is that no-one knows the actual shape of the dose-response relationship at low levels of exposure. Different models may predict widely varying degrees of risk at low exposures. There is usually no way of distinguishing

between the different possibilities. Thus, low-dose risk estimates may vary widely depending on the mathematical model used.

Benchmark dose method

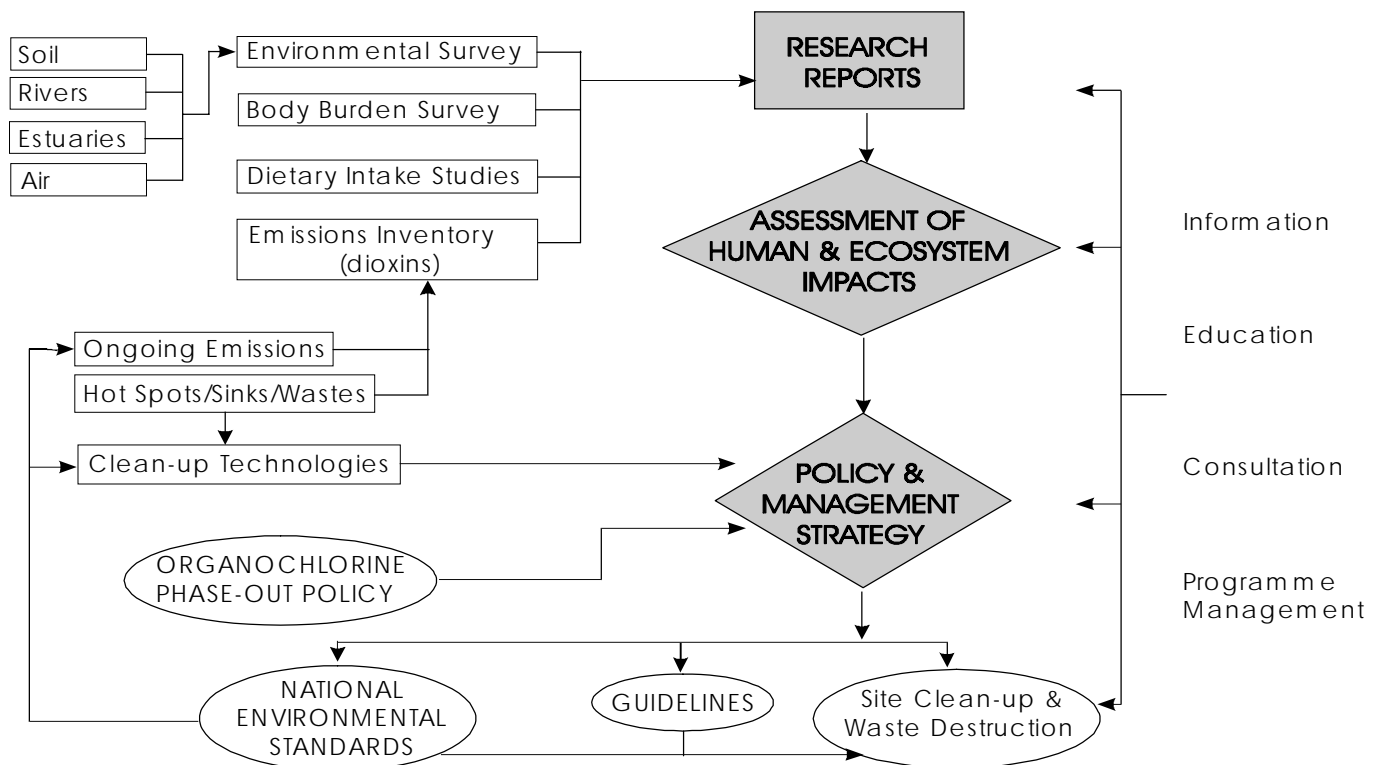
Because of the widely accepted limitations of both the conventional uncertainty factor and the low dose extrapolation approaches, a new method of deriving “safe” levels of exposure has gained favour in recent years. This is the method of deriving a benchmark dose. It uses toxicological or experimental data to derive an estimate of the dose that will cause a low percentage, say 1% or 5%, toxic response, in either animals or humans. This is the benchmark dose, which has the advantage that it is within or close to the dose or exposure range for which experimental or epidemiological data exist. An uncertainty factor can then be applied to the benchmark dose to derive an

“acceptable” level of exposure. The use of the benchmark dose avoids extrapolation into the unknown dose-response range, and the benchmark dose has more robustness and validity than a NOAEL or LOAEL.

Development of National Environmental Standards for New Zealand

Using the methodologies outline above (and others, as appropriate), and taking into account the organochlorine levels found in food, serum and environmental media in New Zealand, National Environmental Standards will be developed for organochlorines under the Resource Management Act 1991. These standards are intended to protect both human health and the environment.

Overview of the Organochlorines Programme



Public Meeting “Dioxins and Human Health”

Wellington	Thursday 24 th June 1999	BP Theatrette, Ground floor, BP Oil, 20 Customhouse Quay Wellington (entrance off Johnstone St)
New Plymouth	Monday 28 th June	Plymouth International Hotel corner of Leach and Courtenay Street, New Plymouth
Hamilton	Tuesday 29 th June	Whitiara Room, Novotel Tainui Hamilton, 7 Alma Street, Hamilton
Whakatane	Wednesday 30 th June	Tudor Room, Manor Inn, 34 Domain Road, Whakatane
Rotorua	Thursday 1 st July, Hui 10.00 am – 4.00 pm	Apumoana Kokiri, Tarawera Road, Rotorua. For further details, contact John Hohapata-Oke, Ph: 021 779 930. Fax: (07) 307 0762
Auckland	Friday 2 nd July	The Gallery, Level 3 Civic Centre, Manukau City Council, 31-33 Wiri Station Road, Manukau City (down from Rainbows End)
Dunedin	Tuesday 6 th July	Conference Room, top floor, Dunedin Public Art Gallery, 30 The Octagon, Dunedin
Christchurch	Wednesday 7 th July	Elizabeth Kelly Room, 1 st floor, Christchurch Art Centre, Corner of Hereford Street and Rolleston Avenue, Christchurch (opposite the YMCA)

All the above meetings (except the hui) **will be from 5.30 pm till 7.30 pm.** Ministry for the Environment and Ministry of Health officials will then be available for further discussions over tea and coffee.

Technical Lunch-time Seminars “Dioxins in New Zealand: A Health Risk Appraisal”

These seminars will be held from 12.30 - 1.30 pm

Wellington	Thursday 24 th June	Large Lecture Theatre, Level C, Wellington Medical School (Mein Street)
Auckland	Friday 2 nd July	Seminar Room 1, Level One, Department of Community Health, Grafton Mews, 52-54 Grafton Rd (down hill from the main medical school building), Auckland School of Medicine
Dunedin	Tuesday 6 th July	Room 036, Department of Preventive and Social Medicine, Ground Floor, Adams Building, Otago Medical School