Human Health Risk Assessment of Organophosphate Pesticides in Sri Lanka

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by

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DECLARATION

The work described in this thesis, unless otherwise acknowledged, has not been previously submitted for a degree or diploma in any university, and contains no material previously published or written by another person, except where due reference is made in the thesis itself.

Jeevani P. Marasinghe

DEDICATION

This piece of work is dedicated to my lovely little children Oshani and Dinuka, loving husband Vajira, loving parents and brothers, loving parents-in law, brothers in law and sister in law for their great encouragement, patience and numerous help.

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ABBREVIATIONS

AChE- Acetylcholin esterase

ADI- Acceptable Daily Intake

APAD- Acute Population Adjusted Dose

ARfD- Acute Reference Dose

BW, bw - Body weight

ChE- Cholin esterase

CI_A- Chlorpyrifos Intake in Breathing Air

CNS- Central Nervous System

CPAD- Chronic Population Adjusted Dose

CRfD- Chronic Reference Dose

DCI- Dietary Chlorpyrifos Intake

ECID- Equivalent Chlorpyrifos Ingested Dose

EED – Estimated Exposure Dose

FAO- Food and Agricultural Organiztion

GV- Guideline Value

HQ- Hazard Quotient

IPCS- International Programme on Chemical Safety

JMPR- Joint FAO/WHO Meeting on Pesticide Residues

LOAEL –Lowest Observed Adverse Effect Level

LOQ- Limit of Quantification

LOQ- Limit of Quantification

MF – Modifying Factor

MOE – Margin of Exposure

MRL- Maximum Residue Limit

NOAEL – No Observed Adverse Effect Level

OP- Organophosphates

OPIDP- OP induced polyneuropathy

RBC- Red blood cells

RfD – Reference Dose

SF- Safety Factor

TCP-3,5,6-trichloro-2-pyridinol

TDCI- Total Dietary Chlorpyrifos Intake

UF – Uncertainty Factor

USEPA – United States' Environmental Protection Agency

WHO – World Health Organization

ABSTRACT

Organophosphate (OP) pesticides cause a high morbidity and mortality in Sri Lanka due to intentional poisoning as well as accidental and occupational exposure. However exposure in the farming community and general population to OP at low levels goes unreported. Therefore the objectives of this study were to assess the health risks in farmers and the general population from low level exposure to OP pesticide in Sri Lanka and populations elsewhere using reported data and Guideline Values developed by regulatory agencies such as World Health Organization and U.S. Environmental Protection Agency. Clorpyrifos was identified as the principal pesticide of concern. The exposure was calculated in common units ng/kg body weight/day and presented as plots of cumulative probability and evaluated at the median (0.50 probability) and high (0.95 probability) exposure levels. The Guideline values of the regulatory agencies were used to characterise the health risk as Hazard Quotient.

The reported TCP levels (specific metabolite of chlorpyrifos) and residue data were collected from Sri Lanka and the other countries and the exposure dose (Equivalent Chlorpyrifos Ingested Dose, ECID in ng/kg/day) and the dose in the diet (Total Dietary Chlorpyrifos Intake, TDCI in ng/kg/day) were calculated. Similarly the ECID were calculated for the international populations.

The baseline and occupational (post application) ECID in Sri Lankan farmers were from 1.0 to 1600 ng/kg bw/day and 2500 to 11000 ng/kg/day respectively. The TDCI in an average diet in Sri Lanka varied from 50 to 1800 ng/kg bw/day. The TDCI in an average diet in India ranged from 7.0 to 380.0 ng/kg/day. The farmers and occupationally exposed workers in US were calculated with an occupational ECID

range of 150 to 210000 while the adults were in the range of 100 to 1200 ng/kg/day in nonoccupational situations. The European adults were observed with ECID levels from 0.80 to 2100 ng/kg/day. Australian pest control applicators had an occupational ECID ranging from 1100 to 37000 ng/kg/day. The farmers and children in Thailand had levels in between 20 to 4600 ng/kg/day and 30 to 1800 ng/kg/day respectively.

The baseline ECID in Sri Lankan farmers were comparable with the TDCI calculated with an average diet suggesting dietary exposure is a main pathway of exposure in farmers as well as the general population. The TDCI levels at the median (0.50 probability) and high (0.95 probability) exposure levels were higher than the levels found in India. The ECID in Sri Lankan farmers at baseline were comparable with the nonoccupationally exposed groups of adults in USA, Italy and Germany and the Thai children. At the high exposure level (0.95 probability) the ECID levels were below the levels observed in the Thai farmers. The median ECID (0.5 probability) in Sri Lankan farmers at occupational exposure (post application) were comparable with the levels in Australian pest control applicators.

With the Sri Lankan population and farmers at baseline the HQ using CRfD, indicated a high level of risk at the high exposure level (0.95 probability). The median Sri Lankan farmers at occupational exposure (post application) were at marginal risk with $HQ_{0.50}$ of 1.3 and the high exposure group at a higher risk of $HQ_{0.95}$ 2.2 (5% of the farmers). Thai farmers in the high exposure group were at a high risk of effects with a $HQ_{0.95}$ of 15.3 using CRfD. A similar risk was observed with the Thai children with $HQ_{0.95}$ of 16.6 using the CPAD. Five percent of the other occupationally exposed groups of US farmers, pest control applicators, manufacturing workers and Australian pest control

operators were at high risk of the adverse effects at high exposure levels (0.95 probability).

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1.0 INTRODUCTION

1.1 Background

Sri Lanka is a tropical, agricultural country with a moderate annual temperature pattern and a rainfall pattern spread throughout the year. It provides a good environment for high bio-diversity as well as agriculture. The average yearly temperature for the country ranges from 26^0 C to 28^0 C, while the annual rainfall varies from less than 1000 mm to over 2500 mm in dry and wet zones.

The last census, carried out in 2001, recorded an estimated human population of 18.8 million (Department of Census and Statistics, Sri Lanka, 2006, pp. 1-22). The economically active population (those aged 10 years and above) was 7.5 million according to the Labour Force Survey (Ministry of Finance and Planning, Sri Lanka, 2007, pp. 8-17), 65% of whom were male. About 2.2 million of the population are engaged in agriculture.

Agriculture is the predominant industry in many districts, except for districts in the western province where the services and industry sectors are high. The highest involvement in agriculture is recorded in the (see Figure 2.1.1), Uva, North Central and Central provinces, with a total of nine provinces in the country. Rice, tea, rubber and coconuts are grown extensively throughout the country. Rice is the staple food and the paddy (rice) crop is grown during the two monsoonal rainy seasons ‘yala’ (south-west monsoon from May to October) and ‘maha’ (north-east monsoon from December to March). The extent of rice cultivation in the year 2002 was 7.5 % of the total land area (Ministry of Finance and Planning, Sri Lanka, 2009, p.4). Tea, rubber and coconuts are the major export crops in Sri

Lanka and covered 6% of the total land area in 2002. Vegetables, fruits and other seasonal crops are grown throughout the country. Floriculture is a developing industry in many parts of the island.

Pesticides play a major role in controlling a variety of pests in agricultural crops in Sri Lanka. There are several hundred recommendations regarding pesticide usage for different crop-pest combinations (Ministry of Agriculture & Lands, Sri Lanka, 1997, pp. 1-76; Department of Agriculture, Sri Lanka, 2008, pp.1-6). There is a range of active ingredients used, with 29, 89 and 37 herbicides, insecticides and fungicides registered for use in the country. In the year 2000, the chemical categories that saw the highest use were amides, dithiocarbamates and organophosphates. Nearly 6000t of pesticides were imported for pest control purposes in agriculture during the year 2006 (Department of Agriculture, Sri Lanka, 2006). Although pesticides are used in vector control for public health programmes the volumes used are significantly lower when compared to their use in the agricultural sector. Most of the pesticides used in public health are in the pyrethroid group.

All activities involving the importation and use of pesticides in Sri Lanka are regulated by the Office of the Registrar of Pesticides, under the Control of Pesticides Act No. 33 of 1980 and its amendment No. 06, enacted in 1994. This requires that any of the pesticide products in use within the country should be registered under the Act. The pesticides included in the WHO Hazard Class Ia, Ib (Table 1.1.1; WHO, 2002. p.3) and the organochlorine pesticides including persistent organic pollutants (POP) are banned in the country under the conditions of a gazette notification (Gazette No.1190/24, 2001). At present, the highest toxic class registered for regular use in Sri Lanka is classified under the WHO Hazard Class II. Chlorpyrifos,

dimethoate, diazinon and profenofos are some of the organophosphate insecticides included in this class that are commonly used for crop protection in Sri Lanka.

Table 1.1.1 WHO Recommended Classification of Pesticides by Hazard

Class	**LD_{50} for the rat(mg/kg body weight)**			
	Oral		Dermal	
	Solids[a]	Liquids[a]	Solids[a]	Liquids[a]
Ia Extremely hazardous	5 or less	20 or less	10 or less	40 or less
Ib Highly hazardous	5-50	20-200	10-100	40-400
II Moderately hazardous	50-500	200-2000	100-1000	400-4000
III Slightly hazardous	Over 500	Over 2000	Over 1000	Over 4000

[a]The terms "solids" and "liquids" refer to the physical state of the active ingredient being classified (Source: WHO, 2002, p.3)

Despite the knowledge of the risks of handling pesticides, farmers tend to apply pesticides without proper protective measures. They find the personal protective measures inconvenient to wear in the hot and humid climate, expensive, limited in availability and liable to interfere with work (Chandrasekara, 1989; Van der Hoek et al, 1998).

Occupational exposure to pesticides in Sri Lanka has been recorded in many instances (Jeyaratnam et al., 1982; Jeyaratnam et al., 1987; De Alwis, 1989; Jeyaratnam et al., 1990; Sivayoganathan et al., 1995; Van der Hoek, 1998; Aponso et al., 2002; Smit et al., 2003). The majority of the poisonings were caused by organophosphates (Jeyaratnam et al., 1982; Eddleston, 2005; Ministry of Healthcare & Nutrition, Sri Lanka, 2006, pp. 29--44). Among the causes of hospital deaths, the toxic effects of pesticides were the sixth most prominent in 2006 (Ministry of Healthcare & Nutrition, Sri Lanka, 2006, pp.29-44). Although the majority of the cases were due to intentional poisoning, mainly suicides, it would be expected

there would be many observable adverse effects due to long-term and occupational exposure to pesticides. The data is not a true reflection of the problem since many cases are not diagnosed properly due to the complexity of the symptoms and an incomplete recording system.

Investigations have shown that incidences of overexposure are common within spraying situations and overdosing are often due to failure to follow the label instructions on safety (Chandrasekara et al., 1989; Nugaliyadde et al., 2001). Application of pesticides to harvested fruits and vegetables and harvesting before completion of the pre-harvest interval (PHI) also contribute to pesticide exposure (Chandrasekara et al, 1989). Overuse of pesticides can result in high residue levels in commodities and in the immediate environment, such as soil, biota and aquatic systems. It has been reported that significant pesticide residues are found in tea, vegetables and water bodies (Gunawardena et al., 1987, p.221; Guruge et al., 2001; Eramudugolla, 2002, p.29; Department of Agriculture, Sri Lanka, 2003, pp. 1-2; Aponso et al., 2003; Wickramarachchi et al., 2005; Wickramarachchi (cited in Bandara, 2007, p.20); Aravinna et al., 2004; Aravinna et al, 2.005; De Alwis et al., 2006; Aravinna et al., 2008, p.135; Magamage, 2008; Department of Agriculture, Sri Lanka, 2008, pp.4; Department of Agriculture, Sri Lanka, 2009, pp. 3-5).

The importance of developing programmes for the monitoring, research and protection of the natural environment and human health from short term and long term exposure to pesticides and their residues is clear from the evidence available. However very few risk assessments (Aponso et al., 2002; Smit et al., 2003; Samarawickrema et al., 2008) on chronic poisoning and exposure to low doses of pesticides have been conducted in Sri Lanka, particularly on the organophosphates which are responsible for most of the reported deaths and hospital admissions. No studies have evaluated the health risk as a result of dietary exposure to

organophosphates. The need for risk assessment of the adverse effects of organophosphates on human health is important because;

- It would provide information on the status of people in Sri Lanka with respect to exposure to pesticides. This is particularly important because a high proportion of the population is engaged in agriculture.
- It would help in planning further research in public health to ensure resources are directed to the highest priority problems.
- It would be useful in implementing risk management measures.
- It would help predict the relationship of pesticides to diseases in epidemic situations.

1.2 Objectives

The basic aim of this study was to assess the adverse health risks resulting from short term and long term exposure to organophosphate pesticides with Sri Lankan and international populations in general, using probabilistic risk assessment techniques. Accordingly, the following objectives will be addressed:

- Identify the organophosphates used in Sri Lanka and evaluate their relative importance in terms of the amount used and the frequency of occurrence of residues (this resulted in the identification of chlorpyrifos as the pesticide of significance and the subsequent objectives are focused on this substance).
- Evaluate the exposure dose of chlorpyrifos experienced by the Sri Lankan population, including farmers, via food, surface water and other sources expressed as probabilistic distributions.

- Evaluate the dose experienced by populations elsewhere in the world expressed as probabilistic distributions.
- Evaluate the exposure dose at 0.50 (the median) and 0.95 (the high exposure) probability levels using the Guideline Values of adverse health effects established by regulatory agencies.
- Characterise risk as a Hazard Quotient (HQ) using exposure data derived from the objectives above and Guideline Values from various sources.

2.0 LITERATURE REVIEW

2.1 The Sri Lankan Environment

2.1.1 Geographical location and topography

Sri Lanka is located in the Indian Ocean to the south east of India. It is 880 km north of the equator and lies between latitudes 5^0 55' and $9^0$50' and longitudes 70^0 42' and 81^0 52' east. The land area of the island is 65,610 km^2 and it is about 430 km from North to South and 220 km from East to West. Despite its relatively small size, Sri Lanka has a vast range of elevations from sea level to the highest mountain of Piduruthalagala at a height of 2,524 m. The coastal belt around the island is about 30 m above sea level. The central highlands consist of a high plateau containing some of Sri Lanka's highest mountains. Rivers rise in the central highlands and flow in a radial pattern, towards the sea. Mahaweli, the longest river, is 335 km long. The tropical forest occupied 23% of the total land area in 2001 (Department of Census & Statistics, Sri Lanka, 2006, pp. 1-819).

2.1.2 Climate

Sri Lanka has three main climatic zones: a wet zone (23.4% of the total land area), dry zone (63.6% of the total land area) and an intermediate zone (13% of the total land area). The climate in Sri Lanka is generally hot and humid. The mean temperature varies in the northeast coastal areas from 29^0 C (a maximum up to 37^0C) to 15.8^0C (frosty in winter weather) in the central highlands. Monsoon, convection and depression rains occur

throughout the year. In the monsoonal wind influenced seasons, which are called '*yala*' and '*maha*', the rainfall is exceptionally high (2500mm). The south-west monsoon occurs during the '*yala*' season (May to October) in which the wet zone in the south-western and the central regions get more rain. The '*maha*' season (December to March) which accompanies the north-east monsoon gives more rainfall (1250mm) to the north-east parts of the island. There are two inter-monsoonal seasons following each of the monsoons when rains and thunderstorms can occur in many parts of the island (Ministry of Disaster Management and Human Rights, Sri Lanka, 2008).

2.1.3 Human Population

The total population in Sri Lanka is 18.8 million with an annual growth rate of 1.2 % (Department of Census and Statistics, Sri Lanka, 2006, pp.1-22). The sex ratio is 99.2: 100 males to females. The life expectancy at birth is 72 yrs. The city of Colombo is the most densely populated district out of the twenty five districts in the country, with 3330 persons per km^2. The urban, rural and estate population (people living in the tea estate areas) percentages are 14.6 %, 80.0 % and 5.4 % respectively. The literacy rate of the population aged 10 yrs and over is 91.1%. The labour force participation rate is 46.6 % of the total population.

2.1.4 Agriculture in Sri Lanka

In the 2002, the prominent plantation crops tea, rubber and coconuts were cultivated in a total land area of 394836 ha, 6% of the total land area in the country (Ministry of Finance

and Planning, 2009, p.20). As a wetland crop, paddy (rice) is cultivated in all the districts. About 497053 ha of land area (7.5 % of the total land) was cultivated with paddy throughout the country in 2002 (Ministry of Finance and Planning, 2009, p.4). The pattern of crop distribution in 2001 is given in Figure 2.1.1 (Department of Census and Statistics, 2006). Up-country and low-country vegetables are grown on a large scale in certain parts in the wet and dry zones of the country. Amongst them some of the popular vegetables are beans, cabbage, carrot, tomato, eggplant, okra, cucurbits, capsicum, leafy vegetables and leeks. Other consumables include pumpkin, radish, knoh-khol, leafy vegetables, beet-root etc. The major fruit crops of banana, pineapple, mango, papaya and passionfruit are grown over a large area of land and in home gardens, while avocado, rambutan, durian, mangosteen, jack pear and some other fruits are grown to a lesser extent.

Some of the major seasonal crops grown in Sri Lanka are millet, maize, cowpea, green gram, black gram, sesame, ground nuts, manioc, sweet potato, red onion, potato, chilli, ginger and turmeric. A few other crops such as sorghum, meneri, soy bean, dhal, big onion and mustard are grown in small scale in the dry zone (Ministry of Finance & Planning, 2009).

2.1.5 Food consumption and drinking water

Rice with vegetable curries is the staple food among the majority of the Sri Lankan population. Average rice consumption per year by an average person is about 100kg (Central Bank of Sri Lanka, 2005). Among the numerous vegetables available beans, eggplant, cabbage and pumpkin are the most popular according to a survey carried out by

the central bank. ‘Mukunuwenna’ (*Alternanthera sissilis*) and ‘gotukola’ (*Centella asiatica*) are the most consumed leafy vegetables. The vegetable curries are prepared with coconut, chilli and onion which are essential ingredients in curry preparation. Fish is consumed according to availability in the area. In coastal areas people get enough marine fish for food, whilst in rural areas associated with reservoirs, people have access to freshwater fish. Dried anchovy and other dried fish are popular among the general population. Some people, especially in rural areas, tend to eat rice and curry for each of their three meals of the day.

The census carried out in 2001 reported that the major drinking water sources in Sri Lanka are protected wells (50.1% households) and tap water (26.9% households) (Department of Census and Statistics, Sri Lanka, 2006, pp. 1-22). However, a considerable population (9.9% households) derives water from unprotected wells. Tube wells, rivers, tanks and streams contributed 9.8% of household supplies.

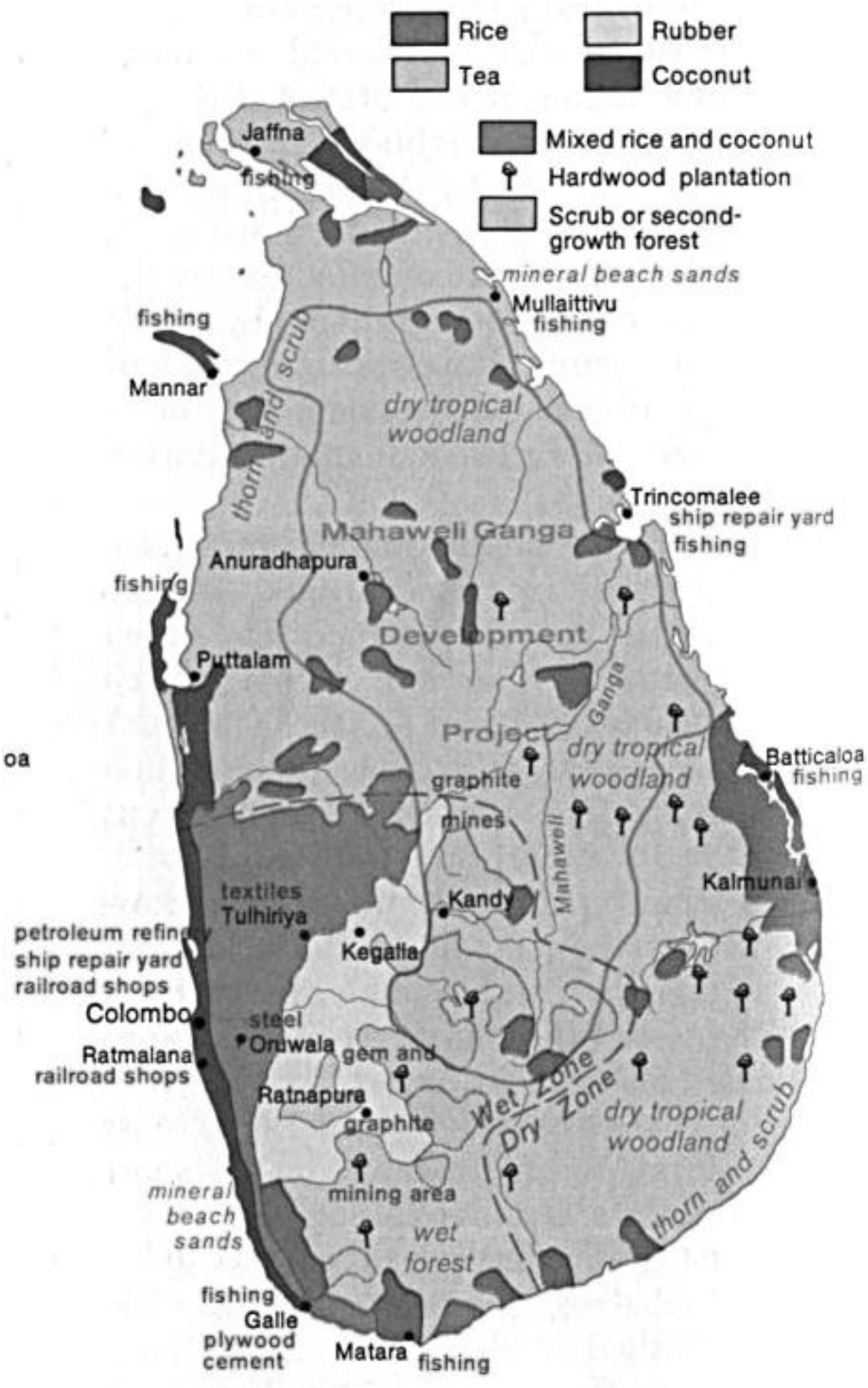

Figure 2.1.1 Crop Distribution Pattern in Sri Lanka

Source: Department of Census and Statistics, 2006

2.1.6 Public Health in Sri Lanka related to pesticides

Morbidity and mortality

The annual health statistics in the year 2006 categorize the indoor morbidity (hospital admissions) in fifty three broad disease groups and the rest in an undiagnosed group. The total number of discharged patients in this year was recorded as 4,463,011 and 36, 345 deaths were recorded (Ministry of Healthcare & Nutrition, Sri Lanka, 2006, pp. 29-44).

Poisoning

Poisoning is one of the leading causes of deaths in Sri Lanka ranking sixth, in the year 2006 (Ministry of Healthcare & Nutrition, Sri Lanka, 2006, pp. 29-44). Poisonings include those that occur bypesticides, drugs and non-medicinal substances, with the toxic effects of pesticides causing 17,518 hospital admissions and 1,242 deaths in 2006. The organophosphate and carbamate pesticides were the leading causes of morbidity (13,222 cases) and mortality (860 deaths) among pesticide poisonings in 2006. Other pesticides accounted for4296 cases and 382 deaths. Poisoning cases due to pesticides were recorded from all the districts in the country. The highest number of cases was reported from the districts where agriculture is the prominent industry.

Vector Borne diseases

Dengue Haemorrhagic Fever is a vector-borne disease transmitted by mosquitoes currently of concern. The number of cases has increased throughout the years from 1996 to 2006.

from 1294 cases in 1996, to 5646 cases in 2006, a 4 fold increase (Ministry of Healthcare & Nutrition, 2006). However the mortality rate has been reduced from 4.1 to 0.2 over the same period. Most of the cases occurred in the Western province, especially from Colombo district.

Malaria is no longer a leading cause of morbidity or mortality in Sri Lanka. It is in a controlled situation with a significant and rapid decline in both morbidity and mortality, from 58,863 cases in the year 2000 to 2,275 cases in 2006 and 111 deaths to 1 death over the same period (Ministry of Healthcare & Nutrition, Sri Lanka, 2006). The majority of cases were reported from the districts in the dry zone where monthly mean temperature range in between 21^0 C (minimum) to 37^0 C (maximum) and rainfall ranges between 0 mm to 350 mm.

2.2 Pesticide Usage in Sri Lanka

2.2.1 Pest control using pesticides

Pesticide usage has become an essential part of agriculture in Sri Lanka, despite the integrated pest management practices carried out at cultivation with many crops. Integrated Pest Management is a way of controlling pests using a combination of pest control methods but with minimum usage of pesticides. Household and public health pest control strategies also rely on pesticides to a great extent.

In agriculture, insecticides, herbicides and fungicides are recommended for pest control mainly in paddy, vegetables, fruits and export crops. However most of the pesticides are

recommended in paddy and vegetable cultivations (Ministry of Agriculture & Lands, Sri Lanka, 1997 pp. 1-76; Department of Agriculture, 2008; see Table 2.2.1). There are usually several pesticides recommended for a specific pest, offering many options to the farmer.

Pesticides are used in mosquito control programmes in Sri Lanka to some extent. In the areas where malaria transmission has been established, residual insecticide spray activities are carried out for the control of mosquitoes. Most chemicals are used on sites near human habitation. When interviewed on 15 May 2008, Dr G K Manuweera (Registrar of Pesticides, Sri Lanka) explained that the major insecticides currently in use in Sri Lanka for vector control are pyrethroids that are comparatively less toxic to mammals. Furthermore, the only organophosphate in use is fenitrothion. Another preventive measure taken to control mosquitoes are insecticide treated nets which are being distributed among the population in the areas where disease is spreading. Many people use mosquito repellent coils, sprays, aerosols and so on to prevent mosquito bites, since mosquitoes are an important vector.

2.2.2 Pesticide industry and regulation

Sri Lanka does not manufacture any of the synthetic pesticides used within the country. Pesticides are imported by multinational companies, as bulk formulations or technical materials to formulate locally. The Office of the Registrar of Pesticides, attached to the Department of Agriculture, regulates all the activities related to the import, distribution and use of pesticides. The regulatory decisions are taken under the Control of Pesticides Act No.33 of 1980 and its amendment No. 06 of 1994. All the pesticides imported are

registered at the Office of the Registrar of Pesticides after passing through a tiered evaluation process using a technical data base. Apart from regulation, the Office of the Registrar of Pesticides disseminates awareness and training programmes on pesticides among dealers and farmers. These facts were verbally confirmed (G.K.Manuweera 2008, pers. Comm., 15 May).

Table 2.2.1 Pesticides Recommended in Paddy and Vegetable Pests Control in Sri Lanka

Crop	Insecticides	Herbicides	Fungicides
Rice	carbofuran, diazinon, phenthoate, fenthion, chlorpyrifos, benfucarb, dimethoate, carbaryl, quinalphos, carbosulfan, fipronil, imidacloprid	glyphosate, MCPA, pretilachlor, propanil, oxyfluorfen, butachlor, fenoxaprop-p-ethyl, 2,4-D, sulfonylurea, bispyribac-sodium	kasugamycin, tebuconazole, carbendazim, edifenfos, pencycuron, pthalide
Vegetables	diazinon, carbosulfan, chlorfluazuron, thiodicarb, methomyl, chlorpyrifos, dimethoate, phenthoate, profenofos, carbofuran, carbaryl, imidacloprid, prothiofos, fenthion, oxydemeton-methyl, acephate, fipronil, quinalphos, etofenprox	glyphosate, diuron, alachlor, oxyfluorfen, metalachlor, metribuzin,	carbendazim, copper, mancozeb, azoles, chlorothalonil, captan, sulphur, propineb, oxadixyl

Sources: Ministry of Agriculture & Lands, Sri Lanka, 1997, pp.1-76; Department of Agriculture, 2008

2.2.3 Pesticides usage profile

The volumes and the expenditure on insecticides, herbicides and fungicides imported to the country in 2001 and 2006 are given in Table 2.2.2 (Department of Agriculture, Sri Lanka 2001, 2006). The total volumes imported in 2001 and 2006 were 3823.55 t and 5957.25 t respectively.

Table 2.2.2 Annual Imports of Pesticides (Broad Category) in Sri Lanka

	2001		**2006**	
Tech. Material	Volume (t or kL)	USDx1000	Volume (t or kL)	USDx1000
Insecticides	90.25	1084.09	128.38	1161.29
Herbicides	270.40	1252.54	207.94	950.53
Fungicides	5.30	76.26	0.40	12.36
Formulations				
Insecticides	848.50	3321.50	1576.41	7543.23
Herbicides	2055.70	7513.70	3197.06	10859.68
Fungicides	553.40	1790.20	847.06	3194.63

Source: Department of Agriculture, Sri Lanka, 2001, 2006

The pesticide categories currently registered in Sri Lanka belong to hazard classes II, III and IV of the WHO Hazard Classification (Table 1.1.1; WHO, 2002, p.3). According to the national policy recorded in the Gazette of the Democratic Socialist Republic of Sri Lanka (Extraordinary) No.1190/24 of 29.06.2001, the pesticides in Schedule I.I and II.II belonging to the World Health Organization Hazard Classes Ia and Ib (WHO, 2002, p.3) cannot be marketed for pest control purposes in agriculture in Sri Lanka. All organochlorine pesticides are banned by the same notification. Organophosphates,

carbamates, pyrethroids, nitroguanidines, phenoxy hormones, triazines, amides, inorganics and dithiocarbamates are some of the popular categories currently in registration (Sumith, 2005, pp. 1-21).

The pesticides usage profile in the country shows that WHO Hazard Class II is the highest toxicity level currently in use. Many of the pesticides ranked in this level are oragnophosphate insecticides. Chlorpyrifos, dimethoate, diazinon and profenofos are four organophosphates recommended by the Department of Agriculture for insect control in many crops in Sri Lanka which are popular among the farmers (see Table 2.2.3 and Figure 2.2.1; Department of Agriculture, Sri Lanka, 2002, 2003, 2004, 2005, 2006). Chlorpyrifos is also recommended for termite control. However, in Sri Lanka its usage was restricted to agricultural purposes from 2004 (Office of the Registrar of Pesticides, Sri Lanka, 2004).

Table 2.2.3 Annual Imports of Organophosphate Insecticides in Sri Lanka

Common name	**Volume (t or kL)**				
	2002	**2003**	**2004**	**2005**	**2006**
Chlorpyrifos	248	327	197	346	267.7
Dimethoate	105.6	159.5	172.8	219.7	162.3
Diazinon	0	24	12	24.1	11
Profenofos	37	32.2	75	71.8	82.6

Sources: Department of Agriculture, Sri Lanka, 2002, 2003, 2004, 2005, 2006

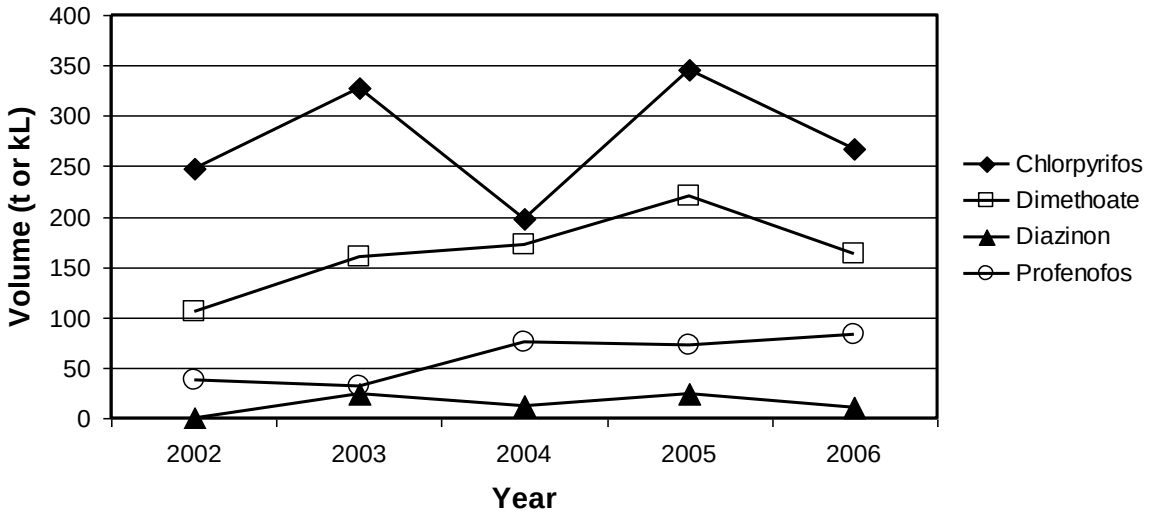

Figure 2.2.1 Organophosphate Insecticides-Import Pattern over Time in Sri Lanka

2.2.4 Problems encountered with pesticides

According to the health statistics in Sri Lanka, poisoning is a leading cause of death and hospital admissions with OPs and carbamates being the cause for most concern (Ministry of Healthcare & Nutrition, Sri Lanka, 2006, pp. 29-44). Over 17000 pesticide poisoning cases have been recorded in 2006, of which 75% were due to the toxicity of organophosphates and carbamates. However, the true figure may be higher than this, as some of the data is not recorded in hospitals. Although the amount of intentional poisonings as part of suicide attempts is significantly higher, it is also expected that there are a considerable number of unreported cases of occupational or long terms exposure(Van der Hoek et al., 1998; De Silva et al., 2006). In a review of pesticide poisoning from 1988-1997 carried out by the National Poisons Information Centre in Colombo, out of total incidences od pesticides poisoning cases reported in the centre (3740) which were enquiries on seeking antidotes and advices, 32% and 2% were for accidental and occupational poisonings respectively

(Fernando, 2002). De Silva et al. (2006) describes the urgent need of studies on occupational and environmental exposure with reference to the problems in developing countries.

Although Sri Lankan farmers have access to education programmes on strategies for the use and hazards of pesticides, it is frequently reported that occupational exposure occurs due to improper handling (Aponso et al., 2003; Smit et al., 2003; Aponso et al., 2002; Jeyaratnam et al., 1990; Chandrasekara, 1989; De Alwis, 1989; Van der Hoek, 1998; Jeyaratnam et al., 1987; Jeyaratnam et al., 1982). Aponso et al., (2002) reported the presence of a metabolite of chlorpyrifos in urine samples of a group of farmers in the Kandy district, who were occupationally exposed to chlorpyrifos. In another investigation with some farmers exposed to organophosphates, Vander Hoek et al., (1998) found a significant decline of acetyl cholinesterase levels with symptoms of chronic exposure. Further environmental and occupational exposure was studied in pregnant mothers and foetuses in a farming community in Sri Lanka (Samarawickrema et al., 2008).

It appears that most of the farming community are not following proper safety procedures while using pesticides. This may be ascribed to many factors including inconvenience, discomfort when wearing personal safety equipment in a hot and humid climate, expense and difficulties in accessing information (Chandrasekara, 1989, Van der Hoek et al., 1998). Despite the instructions given on pesticide labels, indiscriminate usage of pesticides is often reported with overdosing of crops (Chandrasekara et al., 1989; Nugaliyadde et al., 2001). In addition, commodities are sprayed with chemicals after harvesting (Chandrasekara et al., 1989) or harvested before the completion of the pre-harvest interval.

Pesticide residues have been detected in food commodities and water bodies in Sri Lanka. Aravinna et al. (2008) reported the presence of chlorpyrifos and profenofos in bean and cabbage crops collected from farming areas, with some of the samples exceeding Maximum Residue Limits (MRL) of chlorpyrifos. Chlorpyrifos and several other pesticides were found in the leafy vegetable, mukunuwenna (*Alternanthera sissilis*) (De Alwis et al., 2006). Some of the samples exceeded the MRL of chlorpyrifos specified by the Sri Lankan standard institute (De Alwis et al., 2006). Furthermore, none of these pesticides are recommended for use on this crop (Ministry of Agriculture & Lands, Sri Lanka, 1997, pp. 1-76; Department of Agriculture, Sri Lanka, 2008). Aponso et al. (2003) monitored chlorpyrifos, diazinon, profenofos and dimethoate residues in dry zone reservoirs, some of which are used as sources of drinking water. Chlorpyrifos was also detected in protected and unprotected wells in an agricultural area in the dry zone (Eramudugolla, 2002, p.29). In the studies of Wickramarachchi et al. (2005), higher residual concentrations of chlorpyrifos were reported in dry zone water tanks. The investigations by the Department of Agriculture in Sri Lanka (2003, 2008, and 2009) found the organophosphates chlorpyrifos, profenofos, quinalphos, dimethoate and diazinon in rice, several vegetables and in water.

2.3 Organophosphate Pesticides

2.3.1 Chemical structure and properties

Organophosphates (OPs) are organic compounds derived from acid containing phosphorus (Ecobichon, 1982, pp. 171-250). These compounds are used as pesticides, plasticizers, oil additives, lubricants and warfare agents. Among the OP pesticides are insecticides, herbicides, fungicides and others (Eto, 1974). All the OP insecticides are esters, amides or thiol derivatives

of the pantavalent phosphorus acid. Despite this specificity as insecticides, many of them are responsible for causing acute and chronic toxicities in humans (Ecobichon, 1982, pp. 171-203).

The general structure of an OP compound is given in Figure 2.3.1. The chemical, physical and biological properties of OP compounds vary according to the R_1, R_2 and x groups attached to the phosphorus atom. R1 and R2 are simple alkyl or aryl groups and X (the leaving group) can be aliphatic, aromatic or heterocyclic (IPCS, 1986, pp.1-86).

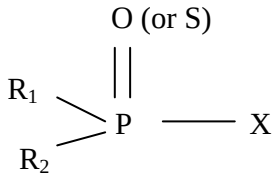

Figure 2.3.1 General Structure of Organophosphorus Compound

2.3.2 Mechanism of action- Acetylcholinesterase (AChE) inhibition

The OP compounds with easily displaceable X groups are good insecticides or rather potent cholinesterase inhibitors (Ecobichon, 1982, pp. 171-250). The reason behind this is their ability to phosphorylate the acetylcholinesterase (AChE) enzyme in the nervous system of insects generating an insecticidal activity. AChE is one of the hydrolytic enzymes for the neurotransmitter acetylcholine, which is found at the synaptic vesicles of the nerve endings. After an impulse transmission between two nerves, acetylcholine released by the vesicle into the synapse is rapidly hydrolysed by AChE before the second impulse comes. Therefore the inhibition of AChE affects nervous function, leading to severe and often lethal damage in the organism (Eto, 1974).

2.3.3 Human toxicology

Similarly, after entering into a human body, OP can irreversibly inhibit the AChE enzyme in the central and peripheral nervous systems, causing cholinergic syndrome within hours of exposure (Dyro, 2006; Lotti, 1991). Inhibition can occur in any place where the AChE enzyme is present, particularly in red blood cells (RBC), nicotinic and muscarinic receptors in nerve, muscles and gray matter in the brain. Inhibition of plasma cholinesterase will damage central, sympathetic and parasympathetic nervous systems due to its inactivation at the sites of white matter in the CNS, pancreas and heart (Dyro, 2006). Cholinergic syndrome appears only when AChE is inhibited by more than half of its base level, more than 90% inhibition can cause death of a poisoned person (Lotti, 1991). In some cases when acutely poisoned symptoms can persist for a few days, which can ultimately lead to respiratory failure, in the 'intermediate syndrome' caused by OPs (Senanayake et al.,1987).

When poisoned by some of OPs (eg: chlorpyrifos) it may take more than ten days or few weeks to show symptoms of poisoning depending on the strength and duration of the exposure. This is known as delayed polyneuropathy which results from inhibition of the neuropathy target esterase (NTE) enzyme (Dyro, 2006).

Although the mechanism of toxicity for organophosphates is thought to be the same, there are some differences in clinical symptoms found in acute poisoning of individual pesticides to humans (Eddleston et al., 2005). This finding further suggests the differences in OP toxicity between humans and animals. Accordingly, Slotkin et al. (1999, 2004 and 2008) state that different pesticides in the organophosphate class can be cause different development outcomes through neurotoxicity, some OPs may pose a greater risk of neurotoxicity than others at the

same level of exposure. Further, the developmental neurotoxicity of organophosphates occurs at doses below the threshold level which show symptoms of intoxication, or even lower than that those required for cholinesterase inhibition.

The effects of chronic organophosphate exposure are not well studied. The importance of proper studies on chronic exposure is suggested (De Silva et al., 2006). According to a review on studies of chronic toxicity of OP compounds (Ray et al., 2001), there is evidence of chronic low level exposure affecting neuro-behavioural performance in humans. Thus these effects may be caused by other mechanisms rather than AChE inhibition. Furthermore, animal studies have shown a variety of effects upon exposure to OP levels below thosecausing AChE inhibition. However, AChE inhibition by organophosphates is used in many studies as the standard biomarker for exposure and risk assessment (Smit et al., 2003; Karabay, 2004).

2.3.4 Chlorpyrifos

Usage, chemical and physical properties

Chlorpyrifos is a broad spectrum organophosphorus phosphorothionate insecticide (CASRN 2921-88-2), widely used for domestic and agricultural pest control in many countries. In Sri Lanka it is recommended for termite control and other insect pest control in paddy, coconut, vegetable and fruit crops (Ministry of Agriculture & Lands, Sri Lanka, 1997, pp.1-76)

The chemical name of chlorpyrifos is O, O-diethyl-O-(3, 5, 6-trichloro-2-pyridiyl) phosphorothioate (see Figure 2.3.2, WHO, n.d).

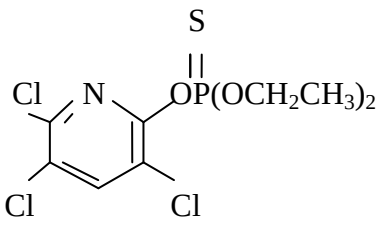

Figure 2.3.2 Chemical Structure of Chlorpyrifos

The relative molecular mass of chlorpyrifos is 350.6. It is readily soluble in organic solvents and slightly soluble in water (0.4 ppm). In exposure to UV light in the presence of water, it hydrolyses into 3, 5, 6-trichloro-2 pyridinol (TCP) and further decomposition can take place. Alkaline water (above pH 8) favours hydrolysis (JMPR, 1972). TCP is the major metabolite of chlopyrifos. Chlorpyrifos is less persistent in soil than TCP. The half life in soils varies with the pH level. The half lives of chlorpyrifos in acidic and alkaline soils are 23-28 and 7-16 days respectively while TCP has half-lives of 42-49 and 64-117 days in acidic and alkaline soil (Baskaran et al., 2006). Thus, the metabolite has a much greater leaching potential than chlorpyrifos (Baskaran et al., 2006). Chlorpyrifos has a low solubility in water (Kulkarni et al, 2000). Hydrolysis is the dominant removal process. (Liu et al., 2001). The major metabolites found in water are TCP and O, O- diethyl phosphorothioic acid (Macalady et al., 1983). Upon absorption chlorpyrifos residues can be retained by plants and animals (JMPR, 1972). Therefore tolerance limits are established for edible crops and meat.

Metabolic degradation and excretion in mammals

Chlorpyrifos is metabolically activated by microsomal P450 enzymes into its oxon metabolites in insects and vertebrates (JMPR, 1999). Metabolic activation mainly takes place in the liver. The oxon metabolites are more potent inhibitors of cholinesterase than chlorpyrifos itself. Chlorpyrifos and its oxon are further metabolised into 3, 5, 6,-trichloro-2-pyridinol (TCP) and dialkyl phosphates. Almost all the chlorpyrifos absorbed in humans is converted to equimolar amounts of TCP and alkyl phosphate metabolites (Nolan et al., 1984; Griffin et al., 1999). In humans, 70% of the oral and 3% of the dermal dose of chlorpyrifos is excreted via urine as TCP (Nolan et al, 1984). The elimination half life of TCP is 27 hours (oral and dermal). Thus, the highest levels of TCP are found in blood 6 hrs post oral administration and 24 hours post dermal administration. Also, chlorpyrifos is excreted as dialkylphosphates in urine. Thus, 93% and 1% of the orally and dermal absorbed dose was recovered in urine in a study with half lives of 15.5 and 30 hours respectively (Griffin et al., 1999). About half (53%) of the dermal dose was recovered from skin washings. Elimination half lives of dialkylphosphate metabolites are 15.5 and 30 hours for orally and dermally absorbed chlorpyrifos respectively. It has been shown that the younger population is more likely to absorb Chlorpyrifos than adults (Barr et al, 2005). Accordingly, children aged 6-11 years were found to have a significantly higher concentration of TCP than adolescents and, similarly, adolescents had significantly higher concentrations of TCP than adults. The same study reveals that no significant differences were observed between sexes and among racial/ethnic groups. Chlorpyrifos has been detected in serum samples of poisoned people (Drevenkar et al, 1993).

Toxicity in mammals

The lowest acute 50% Lethal Doses (LD_{50}) in rats and mice are 96 mg/kg and 100 mg/kg respectively (JMPR, 1999). Considering these acute toxicity levels, chlorpyrifos is classified as a moderately toxic insecticide under WHO Hazard Classification. The toxicity due to chlorpyrifos is caused by the inhibition of cholinesterase (ChE). The oxon of chlorpyrifos which is the active metabolite of chlorpyrifos inhibits ChE at higher rates than chlorpyrifos itself (Heilmair, 2008). The acute effects of chlorpyrifos include functional deficits arising from the inhibition of the ChE enzymes (Cochran et al, 2002). In rats, signs of inactivity, salivation, dyspnoea, flaccid paralysis, vomiting, piloerection, exophthalmia and diarrhoea have been observed due to acute intoxication with more sensitivity in females (JMPR, 1999).

An Acceptable Daily Intake (ADI) of 0.01 mg/kg and an Acute Reference Dose (ARfD) of 0.1 mg/kg have been established for chlorpyrifos exposure in humans (JMPR, 1999). These were based on the No Observable Effect Level (NOAEL) of ChE inhibition in rats, mice, dogs and human volunteers. The US Environmental Protection Agency (USEPA) ARfD and Chronic Reference Dose (CRfD) for chlorpyrifos are 0.005 mg/kg and 0.0003 mg/kg/day respectively. These are also based on the NOAEL of similar effects in rats and dogs (USEPA, 2000, pp. 1-25).

2.3.5 Dimethoate

Usage, chemical and physical properties

Dimethoate is an organophosphorus insecticide (CASRN 60-51-5) used for the control of agricultural insect and mite pests, house flies and insect pests in cattle (IPCS, 1989). It has been used in Sri Lanka for more than a decade for controlling insects in paddy, vegetable and fruit crops (Ministry of Agriculture and Lands, Sri Lanka, 1997, pp. 1-76). The chemical name of dimethoate is O, O- dimethyl S-methyl carbamoylmethyl phosphoro-dithioate (see Figure 2.3.3).

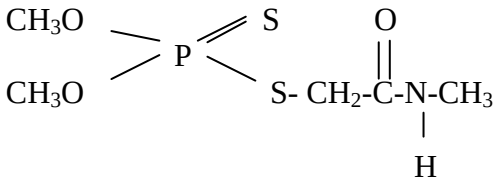

Figure 2.3.3 Chemical Structure of Dimethoate

The relative molecular mass of dimethoate is 229.2. The boiling point is 107^0 C at 0.05 mmHg and 86^0C at 0.01mmHg with a vapour pressure of 8.5 x 10^{-6} mmHg at 25^0C. The partition coefficient (n-octanol/water) is 5.959, having a solubility of up to 39 g/L in water at 21^0C. At pH 2-7 dimethoate is relatively stable in water whist at pH 9 its half life is 12 days. Dimethoate is highly soluble in organic solvents. The soil type, presence of microorganisms, pH, volume of pesticide used and the degree of evaporation may affect the accumulation and degradation of dimethoate in soil. In different plants, the half life varies

from 2-5 days. Rapid decomposition of dimethate takes place at increased temperatures (IPCS, 1989).

Metabolic degradation and excretion in mammals

Hydrolysis and oxidation are the main pathways of metabolism in insects and vertebrates. It undergoes oxidative desulfuration forming omethate, the major metabolite (IPCS, 1989). The ester and amide groups of dimethoate are cleaved in reactions that vary with the organism, this contributes to the selective toxicity of the compound. The metabolite dimethylthiophosphate (DMTP) is formed by the cleavage of the ester group during detoxification. DMTP can be oxidized to dimethylphosphates. Dimethyldithiophosphate (DMDTP) can also be formed by hydrolysis. Dimethoate is absorbed in the gut and excreted via urine and faeces90% of the compound is recovered in urine within 24 hours of administration in rats and humans (JMPR, 1997).

Toxicity in mammals

Dimethoate can be absorbed by the human body via ingestion, inhalation and skin contact. The signs of toxicity in mammals are generated by ChE inhibition which is common to the organophosphorus pesticides. The metabolite omethate is more toxic than dimethoate itself. Cholinestrase inhibition is the significant effect of exposure to dimethoate. Dimethoate also has been found to be mutagenic in bacterial cell cultures. The oral and dermal LD_{50} levels in rats are 150-400 mg/kg and 600 mg/kg respectively. Therefore dimethoate is classified as moderately toxic to mammals (IPCS, 1989).

The FAO and WHO jointly established an ARfD of 0.02 mg/kg for dimethoate which is based on the NOAEL values of ChE inhibition in rats and human volunteers (Pfeil, 2003). The acceptable daily intake (ADI) is 0-0.01 mg/kg (IPCS, 1989). The USEPA oral RfD of dimethoate is 0.0002 mg/kg/day and is based on the NOAEL of brain ChE inhibition in rats in a 2 year study (USEPA, 1990)

2.3.6 Diazinon

Usage, chemical and physical properties

Diazinon (CASRN 333-41-5) is a broad spectrum organophosphorus insecticide. It is used for the control of insects, acarines and spiders in agriculture, households and animals (IPCS, 1998). In Sri Lanka, it is recommended and registered for insect pest control in paddy and vegetable crops (Ministry of Agriculture & Lands, Sri Lanka, 1997, pp. 1-76). The IUPAC name of diazinon is O, O –diethyl O-(6-methyl-2-{1-methylethyl}-4-pirimidinyl) phosphorothioate (see Figure 2.3.4).

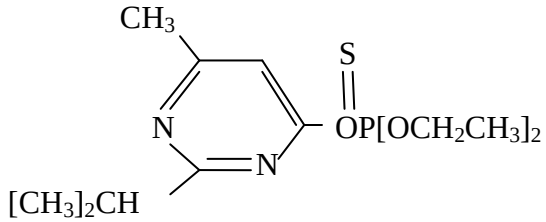

Figure 2.3.4 Chemical Structure of Diazinon

The relative molecular mass of diazinon is 304.35. Its density is 1.11 g/cm^3 at 20^{0}C. It is stable up to 100^{0}C and decomposes above 120^{0}C. It rapid hydrolyses in acidic media. Its

solubility in water is 60 mg/litre at 20^0C and it is completely soluble in common organic solvents (IPCS, 1998).

Diazinon is moderately mobile in soil. Organic matter and calcium carbonate content in soil influence its mobility. Degradation takes place mainly by biological activation. Thus, in sterile soil, the degradation half life is longer (118 days) than in normal soil (5 days). In water its half life is 5-15 days. Degradation occurs by chemical and biological processes. Uptake by aquatic organisms is rapid (IPCS, 1998).

Metabolic degradation and excretion in mammals

Diazinon can enter an organism via oral, dermal and inhalation pathways. Oxidation desulfuration takes place as a result of microsomal enzyme activity, leading to the formation ofthe metabolites of diazoxon, hydroxydiazoxon and hydroxydiazinon. Neither the parent molecule nor the metabolites accumulate in the body. Almost the entire oral uptake is likely to be excreted via urine within 7 days (IPCS, 1998).

Toxicity in mammals

Diazinon's toxicity is caused by ChE inhibition. Its metabolite, diazoxon, is 4000 times more active than its parent molecule in ChE inhibition (USEPA, 2005, pp. 1-78). Signs of acute toxicity include decreased spontaneous activity, sedation, dyspnoea, ataxia, tremors, muscle spasms, convulsions, lacrimation, diarrhoea and death (IPCS, 1998). However, these signs are reversible in those who survive. The oral LD_{50} in rats is $\geq$ 200 mg/kg and as

such, diazinnon is included in the moderately hazardous class of the WHO classification system (Marrs, 2001).The FAO/WHO ARfD for diazinon is 0.03 mg/kg bw which is based on a NOAEL of acute neurotoxicity in rats. The ADI of 0-0.002 mg/kg is based on a NOAEL of ChE inhibition in human volunteers observed in a one month study.

2.3.7 Profenofos

Usage, chemical and physical properties

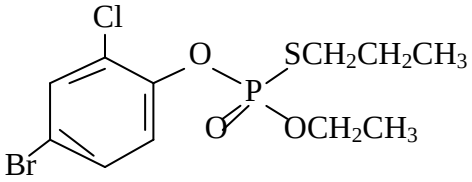

Figure 2.3.5 Chemical Structure of Profenofos

Profenofos (CASRN 41198-08-7) is a broad spectrum organo-thiophosphate insecticide recommended for insect and acarine pest control (USEPA, 2006, pp.1-100). It is recommended in insect pest control in vegetable and fruit crops in Sri Lanka (Ministry of Agriculture & Lands, Sri Lanka, 1997, p.1-76). Its IUPAC name is 0-4-bromo-2-chlorophenyl O-ethyl-S-propyl phosphorothioate. The relative molecular mass of profenofos is 373.6.

Metabolic degradation and excretion in mammals

Profenofos metabolises into 4-bromo-chlorophenol via two pathways, with the major pathway involving depropylation, desulfuration, phenyl-ester bond cleavage and conjugation in rats (Quest, 1990). It is classified as a moderately toxic chemical in the WHO classification of toxicity. ChE inhibition is the most sensitive effect of toxicity. Cholinergic signs were observed in rats after oral administration of profenofos. Signs of toxicity include sedation, salivation, discharge from eyes and nose, trismus, tremors, tonic-clonic convulsions, dyspnoea, exophthalmos, crooked body posture and ruffled fur. In rats, only small amount of orally administered profenofos is excreted through urine and faeces. In humans, fatal poisoning cases with profenofos' four major metabolites containing phosphorus have been identified (Gotoh et al., 2001). They are the despropylated profenofos and its isomer, desethylated profenofos, and des-S-propylated profenofos.

Toxicity in mammals

The lowest acute oral LD_{50} in rats is 298 mg/kg. Given the acute oral and dermal toxicity in rats, profenofos has been classified as moderately hazardous (Quest, 1990). The ADI of 0-0.01 mg/kg is based on a NOAEL in a multigenerational study in rats.

2.4 Human Health Risk Assessment Process

2.4.1 General methodology

Introduction

Human Health Risk Assessment is the characterisation of the magnitude of probable adverse impacts on human health, upon exposure to a particular toxic substance (Derelanko, 1995; Faustman et al., 2001; Connell, 2005). The risk assessment process consists of four major steps: *Hazard Identification*, *Exposure Assessment*, *Toxicity (Dose-Response) Assessment* and *Risk Characterisation* (see Figure 2.4.1). Completion of these steps results in assessment of the risk due to a particular exposure and can be followed by Risk Communication and Risk Management, but these steps are not considered in this thesis. These are concerned with the communication of risk and establishment of management of risk in specific situations. The steps of *Hazard Identification*, *Exposure Assessment*, *Toxicity Assessment* and *Risk Characterisation* are considered in detail in this section.

Hazard Identification

Hazard Identification is the initial step in the risk assessment process. The purpose of *Hazard Identification* is to determine whether a substance poses a hazard or has an adverse impact on human health. There are several methods used to evaluate whether a chemical is a health hazard to humans. One of the most convincing ways to identify a hazard is through the use of epidemiological data. These evaluations are usually the direct observations of

adverse effects in human populations obtained from an exposure to hazard substances (NRC, 1983; Faustman et al., 2001; Derelanko, 1995).

Bioassays on animals are useful for *Hazard Identification* in the absence of epidemiological data. Animal bioassay studies are helpful in identifying carcinogens (Ennever, 1987) and non-carcinogenic substances (Fenner-Crisp, 2003). For most bioassays, rats and mice are used. However, the differences in sensitivity in animals and humans to carcinogens are a major constraint.

Knowledge of the actions of similar structured substances is also used to identify hazardous chemicals (Faustman et al., 2001; Derelanko, 1995). This phenomenon is commonly used in research to evaluate the nature of a new chemical and is commonly described as Quantitative Structure Activity Relationships (QSAR).

The findings from *in vitro* assays and short term tests using microorganisms and animals are also used in the *Hazard Identification* process. These tests are regarded as less expensive methods. However, they are mostly used to identify carcinogens (Faustman et al., 2001).

Exposure Assessment

The estimation of the exposure to the hazard substance under different conditions is known as *Exposure Assessment* (Derelanko, 1995). Various parameters experienced by humans

associated with the exposure should be considered in the *Exposure Assessment* as described below.

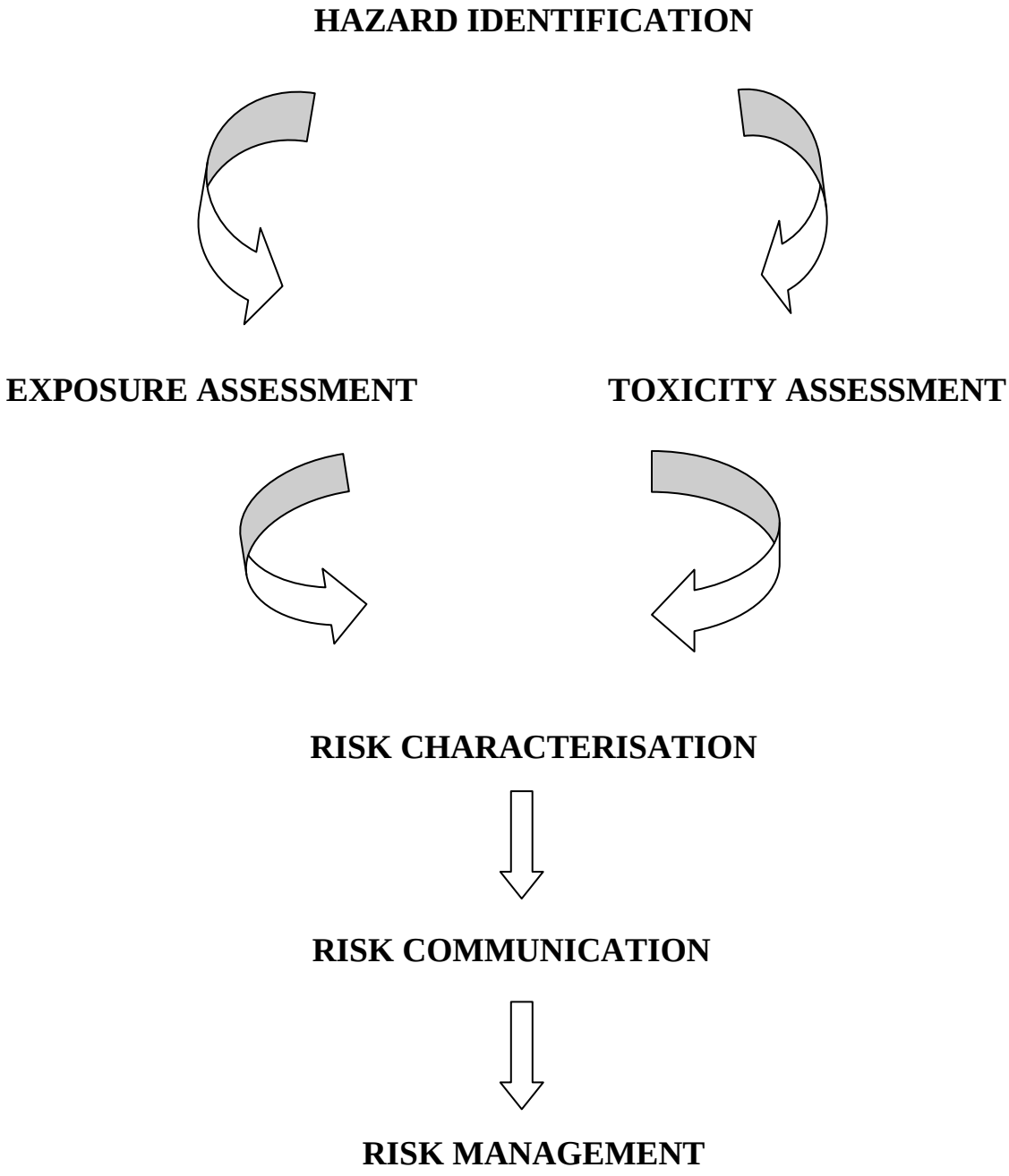

Figure 2.4.1 Schematic Diagram of the *Risk Assessment* & *Management Process*

The degree of exposure is usually measured as the dose and is determined by estimating the levels, frequency and the duration of exposure (Derelanko, 1995, Connell, 2005). In instances where the direct measure of exposure dose is difficult, alternative methods are used to measure the substance or its metabolites (used as biomarkers) in a body fluid. This method is used as a routine survey in estimating chemical exposure levels in the US population (CDC, 2005). Environmental concentrations are also used to estimate the dosage taken into the human body. For example, the concentration of a toxicant in breathing air is used to estimate the inhaled dose (Buck et al., 2001). The concentrations are converted to daily dosages for unit body weights.

The route or the pathway of exposure is important in assessing the exposure (Derelanko, 1995, Connell, 2005). Depending on the pathway the amount of absorbed dose can vary, i.e. Nolan et al. (1984) found that the level of chlorpyrifos absorbance by human gut is higher than the level absorbed through the skin (3%; Nolan et al., 1984). *Exposure Assessment* studies are often planned to assess the exposure that occurs via the major pathway (Cattani et al., 2001, Koch et al, 2001., Aponso et al., 2002). However, overall exposure can be assessed by adding exposure levels, contributed from each pathway (Buck et al, 2001).

Identifying the population at risk is another important factor in the *Exposure Assessment* (Derelanko, 1995), as people can be exposed to toxicants under different circumstances. *Exposure Assessment* studies are carried out to evaluate occupational (Hines, et al., 2001; Cattani et al., 2001; Aponso et al., 2002) and non-occupational (CDC, 2005; Adgate et al,

2001) exposure. Potential health risks may vary depending on the levels, frequencies and duration of exposure in each situation.

In *Exposure Assessment*, probability plots are used to represent the exposure levels in a population at different probability levels. The probability axis is a conversion of the cumulative frequency of exposure events in a particular exposed population. A probabilistic plot allows extrapolation of the data points to higher and lower exposure levels by fitting them to a straight line (Connell, 2005). Thus the probability of exposure at each exposure level can be obtained. Figure 2.4.2 illustrates a cumulative probability curve of exposure. In Figure 2.4.2, the 50% level of cumulative probability resembles the average exposure in the population.

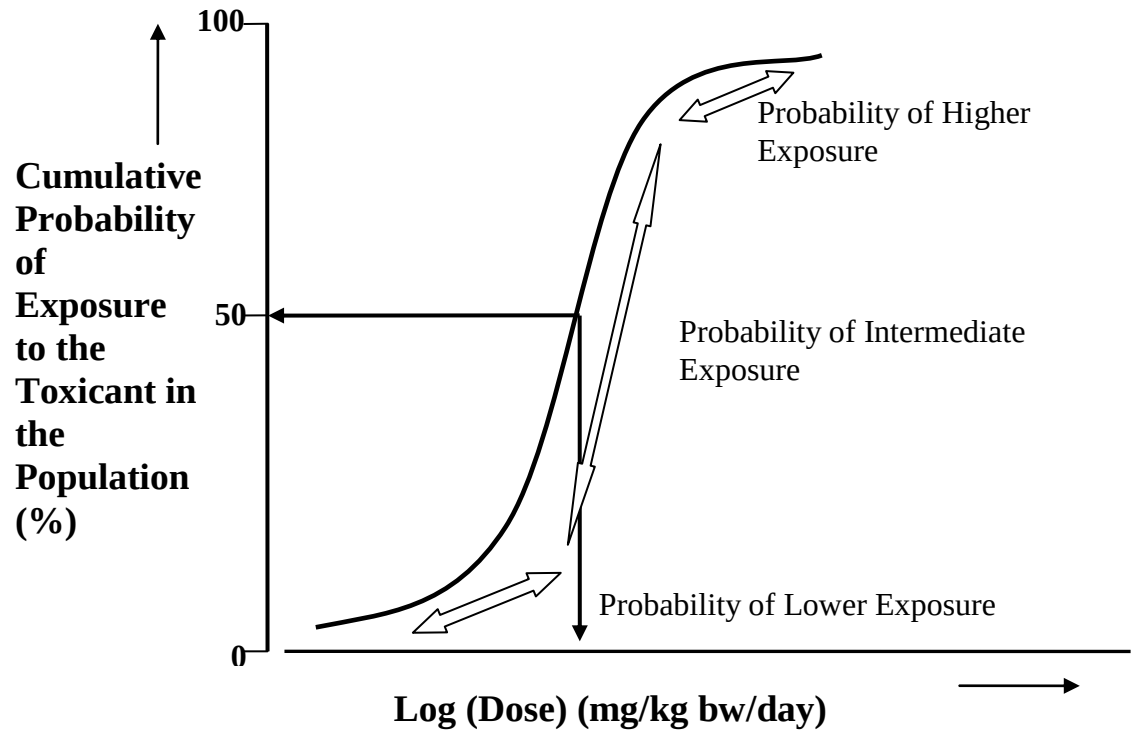

Figure 2.4.2 A Hypothetical Cumulative Distribution Plot for Exposure

Toxicity (Dose –Response) Assessment

The analysis of the relationship between the magnitude of the exposure and the expected associated effects is known as the *Toxicity (Dose-Response) Assessment* (Faustman et al., 2001; Derelanko, 1995). The biological responses of adverse effects shown by an organism upon exposure to a certain dose for a specific time are used to evaluate the toxicity of a substance (Connell, 2005).

Toxicity (Dose –Response) curves are used to represent the adverse biological effects that occur in response to the dose taken up (Derelanko, 1995). The probabilistic curves are commonly used to present toxicity if data is sufficiently available(Connell, 2005). These curves are approximate normal distributions plotted out on a linear-log basis, as shown in Figure 2.4.3. The plot is useful in finding the percent population that responds at a certain level of exposure. At the lowest dose levels, the most sensitive individuals show effects from the toxicant. With an increased dose, the number of the population showing effects increases, with the highest amount of people showing effects seen at the highest dose level (Connell, 2005).

Both animal and human response data are useful in the evaluation of the toxicity. Data from animal laboratory tests with Safety Factors (SF) or Uncertainty Factors (UF) is commonly used for the evaluation of adverse effects in the absence of human data (Connell, 2005). However, human epidemiological data is the most useful for the purpose of evaluating dose-response, as such information provides relevant and reliable toxicity analysis in a risk assessment process. Considering the differences that can prevail in similar exposure

situations between humans and test animals, the use of an SF or UF is required to make the animal toxicity data usable for the exposure situations faced by the humans. The application of a SF or UF with animal toxicity data will increase the level of toxicity, as it is applied to evaluate the safety. Thus, the use of an SF and UF not only allows for the increased sensitivity of humans compared to animals, but also accounts for factors such as intra-species variations, use of LOAEL (Lowest Observed Adverse Effect Level) in the absence of data for NOAEL (No Observed Adverse Dose Level) and for validating short term exposure data when assessing long term exposure.

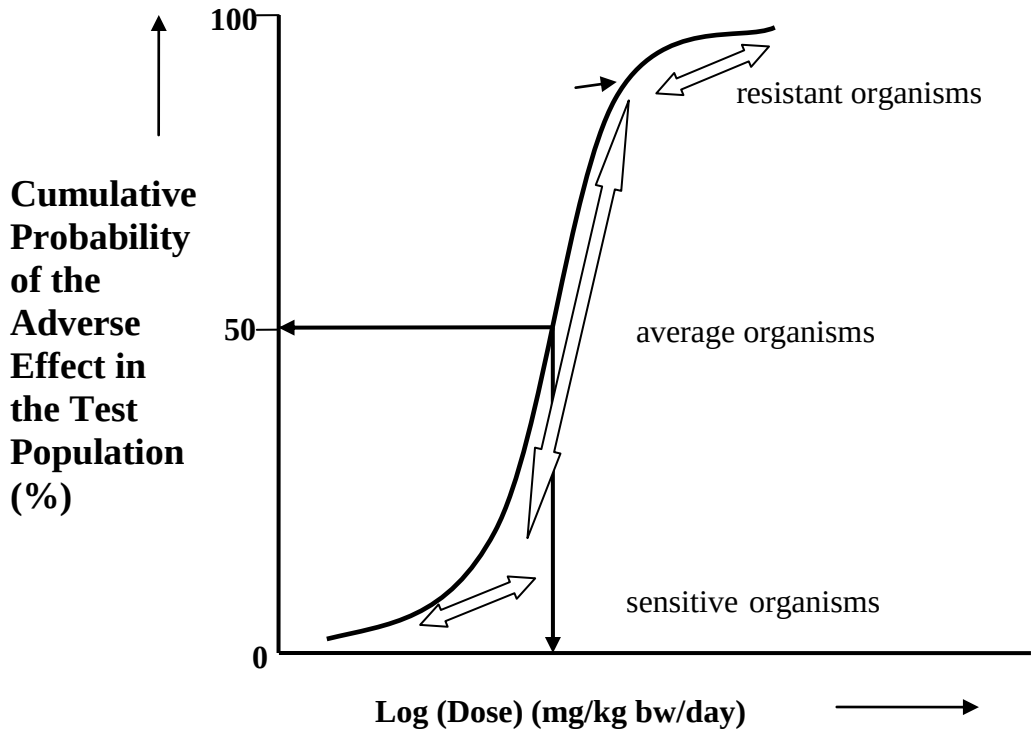

Figure 2.4.3 A Hypothetical Cumulative Distribution Plot for Dose-Response

The adverse effects considered in the *Toxicity Assessment* may vary according to the nature of the exposure event (Connell, 2005). Generally for 50% of tested organisms, Lethal Dose (LD_{50}) is one such adverse response shown by a population to a high dose level. The Lowest Observable Adverse Effect Level (LOAEL) and No Observable Adverse Effect Level (NOAEL) are some of the other response data (at the lowest dose showing a response and at the highest dose showing no response respectively) that can be used to evaluate the toxicity at low levels of exposure occurring for a long periods of time.

The Reference Doses (RfD in mg/kg BW/day) including the Acceptable Daily Intake (ADI in mg/kg BW/day) which are derived from the NOAEL or LOAEL of an adverse effect and an SF or UF can be used as a standard or benchmark to evaluate the adverse effect level of an exposure event (see Figure 2.4.4; USEPA, 1993; Connell, 2005).

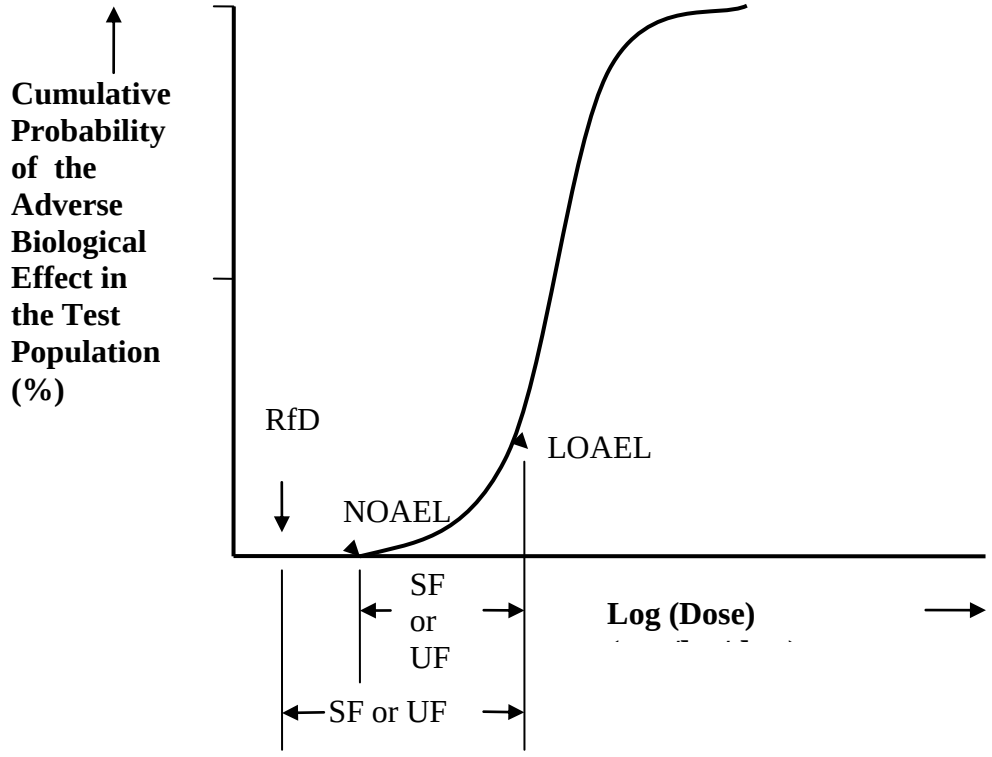

Figure 2.4.4 Illustration of Reference Doses in a Typical Dose-Response Curve

Risk Characterisation

The *Risk Assessment* process concludes with the final step of *Risk Characterisation*, providing a basis to initiate the *Risk Communication* and *Risk Management* process if necessary. At the *Risk Characterisation* step, the risk is quantitatively evaluated (Connell, 2005). For this purpose, the estimated Dose (mg/kg/day) in the *Exposure Assessment* process is compared with the RfD (mg/kg/day) and the ADI (mg/kg/day) and the outcome is described with a Hazard Quotient (HQ, see Equation 2.4.1) (Connell, 2005; USEPA, 1993).

$$HQ = \frac{Dose}{RfD\ or\ ADI} \qquad \text{Equation 2.4.1}$$

This *Risk Assessment* process is used by governmental and non-governmental agencies in order to make decisions on new and existing pesticides and other hazardous substances in regards to concerns on human health. The following are the decision making methods used by the various governmental and non-governmental regulatory agencies.

2.4.2 US Environmental Protection Agency (USEPA)

Reference Dose (RfD)

The Reference Dose (RfD) and the Uncertainty Factor (UF) concepts are used in the *Risk Assessment* process in the U.S. Environmental Protection Agency (USEPA, 1993). The RfD is derived from dividing the NOAEL gathered from laboratory animal tests, by the

Uncertainty Factor (UF). The NOAEL is the highest experimentally determined dose without a statistically or biologically significant adverse effect. The LOAEL is the lowest experimentally determined dose where an adverse effect is demonstrated.

Uncertainty Factors are used to reflect the uncertainty that may arise from animal and human studies when applied to human health risk assessments. In general, for interspecies variation a 10-fold factor is used for valid results of long term animal studies, while another 10-fold factor is applied to account for intra-species variations when extrapolating from prolonged studies with humans. An additional 10-fold factor is used when extrapolating the results obtained from short term studies in animals when long term or chronic results are not available. Also, another 10-fold factor is used when using the LOAEL instead of the NOAEL. In some cases an additional uncertainty factor, known as the modifying factor (MF), is used by the EPA. The MF is determined through professional judgement. MF is greater than 0 and less than or equal to 10. The RfD according to the USEPA is as in the Equation 2.4.2.

$$RfD = \frac{NOAEL}{UF \times MF} \qquad \text{Equation 2.4.2}$$

where RfD and the NOAEL are in mg/kg BW/day.

The definition of the RfD as described by USEPA (1993) is as "an estimation of a daily exposure to the human population that is likely to be without an appreciable risk of deleterious effects during a lifetime". A typical dose-response curve with representation of RfD, NOAEL and LOAEL is illustrated in Figure 2.4.4.

Margin of Exposure (MOE) or Margin of Safety (MOS)

Margin of Exposure (MOE) or Margin of Safety (MOS) is another method used to compare exposure and toxicity in the *Risk Characterisation* process by the USEPA (1993) (see Equation 2.4.3).

$$MOE\ or\ MOS = \frac{NOAEL}{EED} \qquad \text{Equation 2.4.3}$$

Where NOAEL is the experimental dose and EED is the Estimated Exposure Dose.

2.4.3 World Health Organization (WHO)

Acceptable Daily Intake

The *Risk Assessment* process in the World Health Organization (WHO) uses the Acceptable Daily Intake (ADI) to characterise the long-term risks posed by pesticides (WHO, 1997, pp. 1-33).

ADI is defined as "the estimate of the amount of a substance in food or drinking- water, expressed on a body-weight basis, that can be ingested daily over a lifetime without appreciable health risk to the consumer on the basis of all the known facts at the time of the evaluation" (WHO, 1997, pp. 1-33). ADI is expressed as mg/kg BW. ADI is calculated by using the NOAEL demonstrated in animal experiments and observations in humans with an

SF used to correct for uncertainties associated with the use of experimental data (see Equation 2.4.4).

The determination of an SF is mainly based on the differences in sensitivities between animals and humans and among the individuals within the human population (WHO, 1997, pp.1-33). Usually an SF of 100 is used for interspecies and intra-species variation. In addition, the type and severity of the effects suffered are considered when determining the ADI.

$$ADI(mg/kg\ BW) = \frac{NOAEL}{SF} \qquad \text{Equation 2.4.4}$$

Acute Reference Dose (ARfD)

Acute Reference Dose (ARfD) is "the estimate of the amount of a substance in food or drinking water, expressed on a body weight basis, that can be ingested over a short period of time, usually during one meal or one day, without appreciable health risk to the consumer on the basis of all the known facts at the time of the evaluation" (WHO, 1997, pp.1-33). ARfD is expressed in mg/kg body weight. For the derivation of ARfD (Equation 2.4.5) the NOAEL is obtained from studies for acute effects. The safety factors (SF) are similar to those described in ADI derivation in Equation 2.4.4.

$$ARfD = \frac{NOAEL}{SF} \qquad \text{Equation 2.4.5}$$

2.4.4 Risk assessments using probabilistic techniques

Risk assessments can be carried out by applying probabilistic techniques in the exposure and toxicity (dose-response) phases described previously and determine risk characterisation. According to the USEPA (2001) probabilistic risk assessment is a method using probability models to represent the likelihood of different risk levels in a population or to characterize uncertainty in risk estimates.

These methods for human and ecological risk assessment have been implemented by the USEPA (USEPA, 2001). The importance of the technique, in encountering uncertainties and variability, in exposure and dose-response assessments (Jager et al., 2001) and its many other uses (USEPA, 1997, pp. 1-33; Solomon et al., 2000; USEPA, 2001) have been described. The USEPA policy for human health risk assessment is, to limit the Monte Carlo and other probabilistic techniques as the main methods of assessing exposure. However in ecological risk assessments, these techniques are still valid for both exposure and toxicity (dose-response) assessments (USEPA, 1997; USEPA, 2001).

The USEPA describes the Monte Carlo technique as being the most widely used probabilistic method in probabilistic risk assessment and defines it as "a computer-based method of analysis, that uses statistical sampling techniques in obtaining a probabilistic approximation, to the solution of a mathematical equation or model" (USEPA, 1997). It is a technique used to characterise the uncertainty and variability in risk estimates by repeatedly sampling the probability distributions of the risk equation inputs and using these inputs to calculate a distribution of risk values (USEPA, 2001).

The applications of probabilistic technique can be found in many ecological and human health risk assessment studies assessing the risk of chemicals and agro chemicals (Connell, 2008; Djohan et al., 2007; Cooper et al., 2007; Smit et al., 2003; Lunchick, 2001, Solomon et al., 2000).

Unlike point estimate risk assessments which use point estimates for variables, probabilistic risk assessments use probability distributions for one or more variables (USEPA, 2001). Therefore, a pre-requisite of the application of probabilistic techniques is the availability of a comprehensive range of values for exposure and known dose-response endpoints. The method implemented by the USEPA, which is also adopted by Giesy et al. (1999) and Hall et al. (2000), is described in detail by Solomon et al. (2000).

In a probabilistic analysis the exposure data is plotted in an exposure-concentration/dose cumulative probability curve fitted to a log-normal distribution (see Figure 2.4.2). Likewise the toxicity (dose-response) data can also be plotted using the same axes used for exposure data. The data can be presented as Cumulative Probability Distributions (CPD) and can be used in characterisation of health risk (see Figure 2.4.3).

In the method used by Solomon et al. (2000) in ecological risk assessment, the toxicity (dose-response) data for all the species are combined in an effect-concentration distribution curve, fitted to a log-normal distribution. The exposure data is also plotted in the same axes as the effects data (Figure 2.4.5 A & B). The data is the presented as Cumulative Frequency Distributions to facilitate predicting the degree of risk expected. Thus, there are probability lines for both exposure and toxicity (dose-response), sharing a common horizontal axis

with the concentration of the toxicant, which helps determine the associated concentration for any effect level. As the final step in the probabilistic technique, Solomon et al. (2000) describe the generation of joint probability curves which describe the probability of exceeding the concentration associated with an effect level.

Although there are many common characteristics in ecological and human health risk assessments using probabilistic techniques, some differences can also be found. In human health risk assessments, the exposure and toxicity (dose-response) data are plotted against a dose axis fitted to a log-normal distribution. When presenting the effect, toxicity data from homogenous populations such as either rats or humans are used. A probabilistic scale can be used to convert the normal distribution into more linear plots. As the probability of 0 or 100 cannot be practically reached, the axis presents values from 1 to 99. The CPD curves are plotted with cumulative probability of exposure or toxicity (dose-response) against the log dose. In the step of risk characterisation, the effects of the probabilistic distributions of exposure are evaluated.

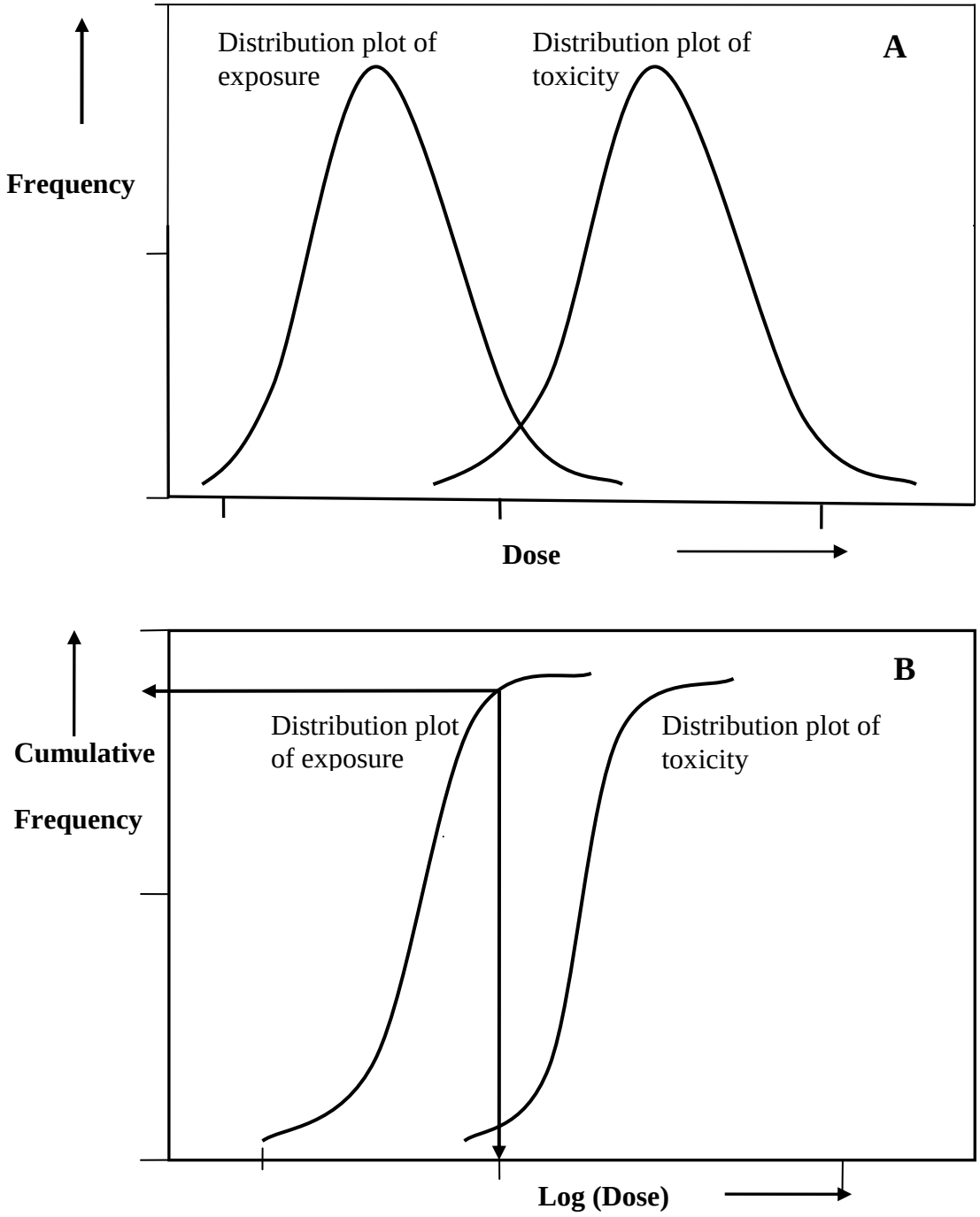

Figure 2.4.5 Exposure-Effect-Concentration Relationships Presented as Log-Normal (**A**) and Cumulative Log-normal distributions (**B**)

Source: Solomon et al., (2000)

3.0 RESEARCH METHODOLOGY

3.1 Strategy for *Risk Assessment* Used in This Study

The steps shown in the Figure 3.1.1 were carried out in the *Risk Assessment* process in this study. In the *Hazard Identification* step the amounts of OP pesticides used in Sri Lanka, the frequency of residue detection in food and water and the data available on exposure within the population was considered. Since this data resulted in the identification of chlorpyrifos as a hazard, the *Exposure Assessment* was carried out with reported data for chlorpyrifos. Probabilistic distributions were used to estimate the exposure using the Equivalent Chlorpyrifos Ingested Dose (ECID) and Dietary Chlorpyrifos Intake (DCI) described below. The Guideline Values established by the U.S. Environmental Protection Agency (USEPA), World Health Organization (WHO) and the Australian Department of Health and Ageing were used as measures of the dose- response in the *Toxicity Assessment.* The Hazard Quotient (HQ) values [HQ= Exposure/ Guideline Value (GV)] were used in the *Risk Characterisation* step.

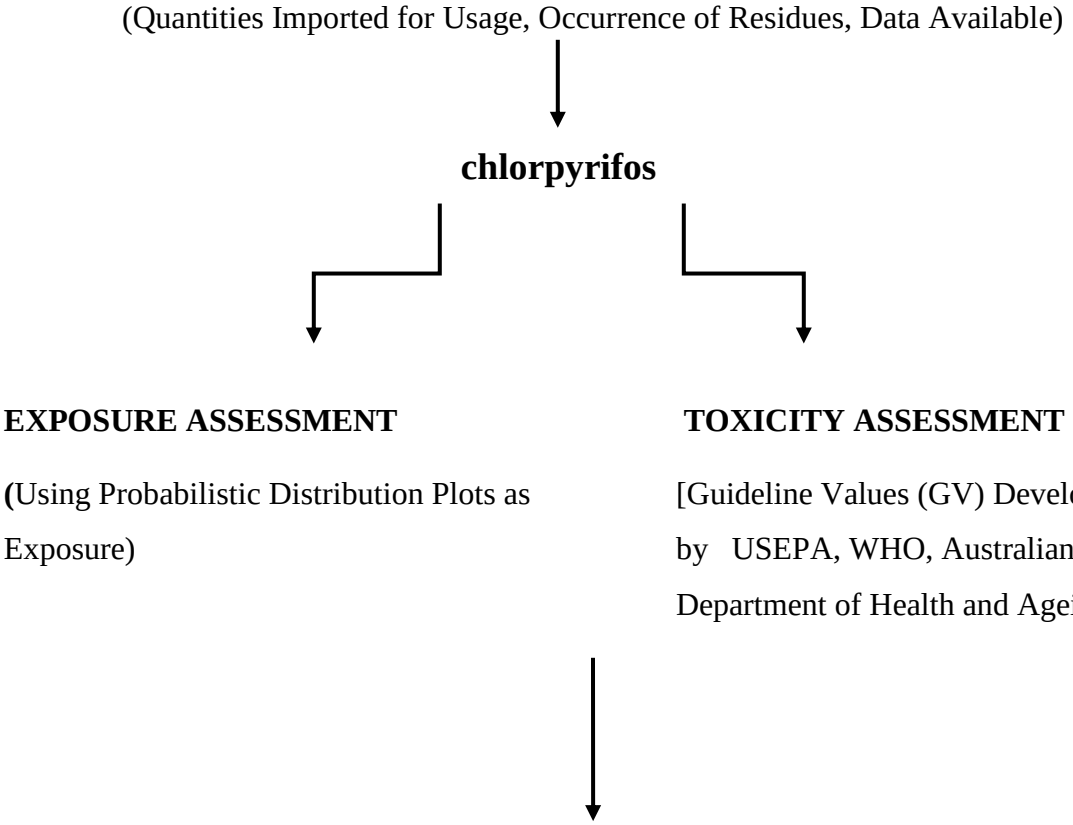

Figure 3.1.1 Schematic Diagram of the *Risk Assessment* Process Used in this Study

3.2 Sources of Data

A literature survey was carried out to search for reported data on organophosphate exposure and residues in Sri Lanka and internationally. Reported data on chlorpyrifos biomarker, 3, 5, 6 trichloro-2-pyridinol, in the urine of exposed populations, was collected for the exposure assessment. Also, data on OP residues reported in food items was collected. The sources of data from Sri Lanka included publications in international and Sri Lankan

journals, proceedings at international conferences, published data in books and reported data in government institutes. Reported data in Indian journals were used to find residue data on OPs. Internationally published journals were used to collect data on chlorpyrifos exposure to international populations. Similarly, the Guideline Values were collected from the literature survey mainly from library databases and also from other web sites.

3.3 Exposure Assessment using Probabilistic Technique

3.3.1 Equivalent Chlorpyrifos Ingested Dose (ECID) calculation and unit conversion

Creatinine adjustment from 3, 5, 6, trichloro-2-pyridinol (TCP) concentration

In this study, the reported data on creatinine (Cr) adjusted 3, 5, 6 trichloro-2-pyridinol (TCP) levels (µg/g Cr) (Aponso et al., 2002; Scher et al., 2008; Hill et al., 1995; Barr et al., 2005; CDC, 2005; Hines et al., 2001; Garabrant et al., 2008; Berkowitz et al., 2003; Aprea et al., 1999; Koch et al., 2001; Cattani, 2004; Panuwet et al., 2008; Panuwet et al., 2009), were used for the exposure dose (Equivalent Chlorpyrifos Ingested Dose) estimation of chlorpyrifos. TCP is mostly measured in units of µg/L urine or as µg/g creatinine. TCP analyses were based on the method of Gas Chromatography (GC) - Mass Spectrometry (MS). In all the studies internal standards were used for calibration, followed by hydrolysis, extraction, concentration and analysis. In some (Panuwet et al., 2009; Aponso et al., 2002), parallel analyses were carried out with samples fortified with TCP for more accuracy. Finally, creatinine corrected TCP concentrations were expressed using the Jaffe rate method in most cases.

When measured as a mass in the urine, TCP is subjected to the variation of daily volume of urine eliminated by the person. It is known that the volume of daily urine eliminated in a person varies with hydration status and hence may have an impact on the concentration level of excretion of the metabolite. Furthermore, creatinine is a by-product generated during the cellular metabolism process and is excreted mainly via the kidneys through urine (Mage et al., 2008). The daily mass of creatinine excreted in a person is considered approximately constant (CDC, 2005). Therefore it is assumed that the concentration with creatinine correction is a more reliable measurement, despite the limitations apparent with different age groups, ethnicities etc. (Mage et al., 2004; Mage et al., 2008).

Calculation of Equivalent Chlorpyrifos Ingested Dose (ECID)

The method used to estimate the daily doses by Garabrant et al., (2008), was modified to convert TCP into Equivalent Chlorpyrifos Ingested Doses (Equation 3.3.1).

$$ECID = TCP \times \frac{CPF_{MW}}{TCP_{MW}} \times CR \times 1.4 \times \frac{1}{BW} \qquad \text{Equation 3.3.1}$$

where ECID is the Equivalent Chlorpyrifos Ingested Dose in ng/kg body weight/day, TCP in ng/g Cr, CPF_{MW} and TCP_{MW} are the molecular weights of chlorpyrifos (350.6 g/mole) and 3, 5, 6 trichloro-2 pyridinol (198.4 g/mole), CR is the mass of creatinine excreted per day (g/day), BW is the body weight of the subject (kg) and 1.4 is a factor to correct for the total amount ingested considering 70% partial absorption of the oral intake (Nolan et al., 1984).

The following common assumptions were made in the ECID calculation.

- The reported TCP levels in urine resulted from chlorpyrifos exposure only.
- The main pathway of exposure was ingestion.
- All the absorbed doses of chlorpyrifos were excreted as TCP in urine.
- The spot or spontaneous urine samples reflected the exposure within previous 3 to 5 days (Nolan et al., 1984), given a 27 hour half life of TCP in humans and that the molecular ratio of chlorpyrifos to TCP is 1:1 (Nolan et al., 1984).
- The entire absorbed chlorpyrifos daily dose was recovered as TCP in urine within next 3-5 days.
- TCP levels were in a steady state.
- An average body weight of 70 kg was used unless otherwise specified.
- The average elimination rate of creatinine was considered as 2 g/day in general adults and pregnant mothers, assuming a mean concentration of 1.3 g/L creatinine was eliminated (CDC, 2005) in a daily average urine volume of 1.7 L/day from a healthy adult (Saieva et al., 2004) (1.3 g/L x 1.7 L/day = 2.2 g/day $\underset{\sim}{}$ 2 g/day).
- The average elimination rate of creatinine was considered as (1.3 g/L x 1 L/day = 1.3 g/day) $\underset{\sim}{}$ 1 g/day in farmers, pest control applicators and manufacturing workers, considering the potential low hydration status in a field working environment which could result in less urination.

Characterisation of Sri Lankan farmers

In order to compare the baseline and occupational exposure amongst Sri Lankan farmers, with the guideline values established by the regulatory agencies, which are based on oral intake, TCP levels reported in the individual farmers by Aponso et al. (2002) were converted into baseline and post application ECID, using *Equation 3.3.1*. The individual body weights reported for Sri Lankan farmers (Aponso et al., 2002) were used in the calculation.

Characterisation of farmers, general adults, pest control applicators, manufacturing workers and pregnant mothers in US

Scher et al. (2008) reported the chlorpyrifos mass (µg) in the exposed individual US farmers which was used to estimate the ECID, by dividing the mass with an average body weight of an adult (see Equation 3.3.2). The exposure was assumed to be a daily event.

$$ECID = CEM \times \frac{1}{Day} \times \frac{1}{BW} \qquad \text{Equation 3.3.2}$$

Where, CEM is the Chlorpyrifos Equivalent Mass in µg. The units of ECID in µg/kg body weight/day were converted into ng/kg bw/day (by multiplying with 1000) for the convenience of using standard units in this current investigation.

ECID levels were calculated for TCP levels reported for the 25^{th}, 50^{th}, 75^{th} and 95^{th} percentiles of US adults (Hill et al., 1995; Barr et al., 2005; CDC, 2005) and individual pest

control applicators (Hines et al., 2001), for the 5th, 50th and 95th percentiles of chlorpyrifos manufacturing workers (Garabrant et al., 2008) and, for 10th, 50th, 75th and 90th percentiles of pregnant mothers (Berkowitz et al., 2003) using Equation 3.3.1. The maximum TCP level reported by Hill et al. (1995) was converted to the nearest corresponding percentile using Equation 3.3.3 (Lane D, 2008). For manufacturing workers the reported average body weight of 88 kg was used in the calculation.

$$n = \frac{N}{100}P + \frac{1}{2} \qquad \text{Equation 3.3.3}$$

where, n is the rank of the participant, N is the number of participants and P is the percentile.

Characterisation of general adult population in Europe

ECIDs were calculated for TCP levels reported for Italian (Aprea et al., 1999) and German (Koch et al., 2001) adults (see Equation 3.3.1). Mean TCP values used in the calculation, for Italian adults were obtained from the ranges reported (by dividing the sum of upper and lower limits by two). Cumulative probability levels were assigned for mean TCP levels, using the frequency of observation data reported for each range of TCP levels. For German adults the reported minimum and maximum TCP levels were converted to the nearest corresponding percentiles, converting the to a common form (see Equation 3.3.3).

Characterisation of Australian pest control applicators

ECID levels were calculated from TCP concentrations reported for the 50^{th}, 75^{th}, 95^{th} percentiles and the minimum and maximum levels of Australian pest control applicators (Cattani, 2004), using Equation 3.3.1. The reported minimum and maximum TCP levels were converted to the nearest corresponding percentiles using Equation 3.3.3.

Characterisation of Thai farmers and children

TCP levels reported for the 25^{th}, 50^{th}, 75^{th}, 95^{th} percentiles and the maximum with Thai farmers (Panuwet et al., 2008) and for the 50^{th}, 95^{th} percentiles and the minimum and maximum levels of Thai school children (Panuwet et al., 2009), were converted to ECIDs (see Equation 3.3.1). The minimum and maximum levels were converted to nearest corresponding percentiles (see Equation 3.3.3). It was assumed that the average body weight of a child of age 12 to 13 was approximately 46 kg (Hollinger, 1995). The rate of creatinine elimination was assumed to be similar to that of a US child of the same age (0.8 g/day reported in Mage et al., 2008), since data on morphological characteristics or creatinine excretion in children of concern was not reported.

3.3.2 Construction of probability plots

In this study the Equivalent Chlorpyrifos Ingested Doses (ECID) were presented in cumulative probability distribution plots. For this, the estimated ECIDs were converted to log ECIDs and sorted in an ascending order (Griffith School of Public Health, 2007). Each

log ECID value was added to the next higher value to obtain a cumulative frequency distribution. The cumulative probability as a proportion or percentage scale was obtained by dividing each cumulative probability level by a number which was equal to '1 + total number of ECIDs'. The probability distributions were plotted using log ECIDs (for x axis) against the cumulative probability of the ECIDs (for y axis).

3.3.3 Calculation of Dietary Chlorpyrifos Intake (DCI), Total Dietary Chlorpyrifos Intake (TDCI) and Total Chlorpyrifos Intake (TCI)

Dietary Chlorpyrifos Intake (DCI) estimation with food and water

The Dietary Chlorpyrifos Intake (DCI) in both food and water intake was estimated using Equation 3.3.4

$$DCI = \frac{C \times CR}{BW} \qquad \text{Equation 3.3.4}$$

where, DCI is estimated in ng/kg/day, C is the concentration of chlorpyrifos in food (ng/kg) or water (ng/L); CR is the daily consumption rate of food (kg/day) or water (L/day) and, BW is the average body weight of an adult in kg.

Rice and vegetables of interest were assumed to be consumed daily by an average individual. Since data on residues in processed foods was not available for the study, it was assumed that there is no change in chlorpyrifos concentrations during processing activities.

Further, the other components of diet such as other vegetables and fruits were considered to have zero residue levels due to unavailability of data.

The chlorpyrifos concentrations in food and water reported in the units of mg/kg (Department of Agriculture, Sri Lanka, 2009; De Alwis et al., 2006; Aravinna et al., 2008), mg/l (or ppm) (Department of Agriculture, Sri Lanka, 2003; Wickramarachchi et al., 2005) and µg/L (Aravinna et al., 2005; Aponso et al., 2003), were converted to ng/kg (multiplying by 10^6) to ensure the data was expressed in consistent units throughout this study.

The daily consumption rates of the foods were calculated from the monthly per capita consumption rates reported under the 'Consumer finances and socio-economic survey' conducted in 2003 and 2004 (Central Bank of Sri Lanka, 2005). The respective per capita monthly consumption rates for rice (8.9 kg), beans (0.3 kg), cabbage (0.2 kg) and leafy mukunuwenna (0.2 kg) were divided by 30, to obtain the average daily consumption rates. The minimum daily consumption rate was considered as 10 g. The water consumption rate of an average Sri Lankan was assumed to be 2 L/day (USEPA, 2006). An average body weight of 70 kg was assumed in the DCI estimation.

Similarly DCI was calculated with rice and vegetables in India using the reported data (Kumari et al., 2004; Kumari et al., 2003; Mukherjee et al., 2003; Chalal et al., 1997; Singh et al., 2002; Deka et al., 2004), as minimum and maximum residue levels in µg/g or mg/kg. The residue levels were converted into DCI in ng/kg/day using Equation 3.3.4 and assumed that the consumption rates were similar to the rates reported in Sri Lanka (Central Bank of Sri Lanka, 2005). The respective per capita monthly consumption rates for egg plants (0.27

kg), tomatoes (0.06 kg), potatoes (0.3 kg), cucumber (0.04), bitter gourd (0. 07) and okra (0.1 kg) were used for the estimation of daily consumption rate. The minimum rate was considered as 10 g per day, including cauliflower, for which the consumption rate was not reported.

Chlorpyrifos Intake in Breathing Air (CI_A)

There were no reports available on chlorpyrifos concentrations in air samples in Sri Lanka. With the intention of estimating the Total Chlorpyrifos Intake (TCI) in an average person, the Chlorpyrifos Intake (CI_A) in breathing air (µg/kg/day) in the US (Buck et al., 2000) was extracted from a graph. It was assumed that the reported values are similar to the levels which could prevail indoors in Sri Lanka. The absorbed doses in air reported at each percentile (Buck et al., 2001) were plotted as a cumulative probability plot. The units were converted to ng/kg/day.

Total Dietary Chlorpyrifos Intake (TDCI) and Total Chlorpyrifos Intake (TCI)

The sum of DCIs in food (ng/kg/day) and water (ng/kg/day) was considered as the Total Dietary Chlorpyrifos Intake (TDCI) in an average adult in Sri Lanka (Equation 3.3.5).

$$TDCI = DCI_F + DCI_W \qquad \text{Equation 3.3.5}$$

where TDCI is presented in ng/kg/day. The sum of DCI in each food item was considered as the TDCI in an average Indian.

Probability distribution data for DCI levels was not available for most food items and water from the Sri Lankan data. Thus, the equations for trend line (Equation 3.3.6) of each DCI plot were used to calculate the respective DCIs at the probability levels of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 0.95 and 0.99. A similar method was used to calculate the respective DCIs for these probability levels with Indian data using the trend line equations of DCIs (Equation 3.3.6), plotted with available minimum and maximum residue data.

$$DCI_{FW} = m\ LOG(DCI_{FW}) + c \qquad \text{Equation 3.3.6}$$

Where, DCI_{FW} is the Dietary Chlorpyrifos Intake from food item or water, M and C are the respective slope and intercept of the trend lines. Plots of Log DCI against cumulative probability were used to present the distribution of TDCI. The sum of TDCI and Chlorpyrifos Intake (CI) in breathing air was considered as the Total Chorpyrifos Intake (TCI, see the Equation 3.3.7).

$$TCI = TDCI + CI_A \qquad \text{Equation 3.3.7}$$

Where, CI_A is the CI in breathing air in ng/kg/day. The TDCI and TCI are presented as cumulative probability distributions.

4.0 RESULTS AND DISCUSSION

4.1 Hazard Identification with Organophosphate Pesticides

Pesticides are mainly used for agricultural pest control in Sri Lanka**.** About 100 active ingredients are registered for use within the country, with several hundred formulations and brands. In 2006, a total mass of about 6000t of herbicides, insecticides, and fungicides was imported to the country, of which, half were herbicides and one third were insecticides. The highest toxicity level of pesticides currently in use or those of Hazard Class II of the WHO recommended classification (WHO, 2002). Most insecticides belong to this category, ten of which are organophosphates, including chlorpyrifos, dimethoate, profenofos and diazinon. These are popular among the farmers for their effectiveness in pest control. Chlorpyrifos is the most widely used. The total imported amount of chlorpyrifos, dimethoate, profenofos and diazinon in 2006 was 520t, which is 9% of the total amount of pesticides imported, and of this, around 200,000 kg was chlorpyrifos (Department of Agriculture, Sri Lanka, 2006).

The overall effectiveness of organophosphates has created concern regarding health risks to the population in Sri Lanka. Reportedly, thousands of lives were lost and thousands of others were admitted to hospitals, mainly due to intentional ingestion of organophosphates (Ministry of Healthcare & Nutrition, 2006, pp. 29-44). Intentional poisoning has been studied thoroughly for a long period of time (Jeyaratnam et al., 1982; Jeyaratnam, 1990; Fernando, 2002; Jeyaratnam et al., 1987; Eddleston et al., 2005) and this has resulted in several recommendations with the aim of reducing mortality and morbidity.

Occupational exposure is reported as one of the most common causes of poisoning in Sri Lanka, with most cases caused by organophosphates (Jeyaratnam et al., 1982; Smit et al., 2003; Aponso et al., 2002). However, many of the exposure incidents go unreported due to the lower prevalence and seriousness of the symptoms. Occupational exposure to organophosphate pesticides has been reported as having a negative impact on the health of farmers (Smit et al., 2003).

A study was carried out with a rural farming community in Southern Sri Lanka, to evaluate the health impacts amongst farmers due to exposure to organophosphate pesticides (Smit et al., 2003). The farmers showed AChE inhibition associated with exposure to organophosphate pesticides. In addition, according to a questionnaire answered by farmers, many of them showed acute symptoms significantly associated with AChE inhibition. Also the data indicated the presence of chronic symptoms associated with long term organophosphate exposure. Chlorpyrifos was reported as the most frequently used pesticide among the group.

Aponso et al. (2002) studied chlorpyrifos exposure among a group of farmers in Kandy district. Elevated levels of TCP (3, 5, 6 trichloro-2-pyridinol), the specific metabolite of chlorpyrifos, were detected in the urine of farmers who were involved in a chlorpyrifos spray event. The farmers apparently did not apply the pesticide for about 10 days prior to the spray event. However the metabolite was detected in urine obtained at the beginning of the spray event indicating that the exposure was due to sources other than agricultural pesticide spray.

Another study with pregnant mothers in a rural farming community in Southern Sri Lanka revealed health effects in two unborn children due to maternal exposure to low levels of organophosphates (Samarawickrema et al., 2008). The mothers (of the ages of 20 to 30 years) were living in a farming area during their pregnancy period, but were not directly exposed to pesticides. Chlorpyrifos was detected in maternal and placental cord blood in one mother while dimethoate was detected in the breast milk of another. However the metabolites of these pesticides were not analysed, although their occurrence is more likely than the parental molecules, due to their rapid metabolism (Nolan et al., 1984). In the study, significant inhibition of plasma butyl cholinesterase (BChE) levels in cord blood was found, indicating organophosphate exposure to the foetuses. In addition, significant DNA damage and oxidative stress was observed in the OP exposed foetuses.

There is a potential risk of exposure to organophosphates via food and water. Chlorpyrifos, profenofos, dimethoate and diazinon have been detected in edible portions of rice, vegetables and surface water in many regions in the country (Department of Agriculture, Sri Lanka, 2009; Aravinna et al., 2008; De Alwis et al., 2006; Department of Agriculture, Sri Lanka, 2009; Aponso et al., 2003; Aravinna, 2005; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002; Wickramarachchi et al., 2005). Chlorpyrifos was most frequently detected in food commodities and water. The general population is vulnerable to exposure via these foods, which are principle components of their diets. In this context, considering the quantities in use, the frequency of detection in food, water and in the population, there is a high potential for exposure and possible adverse effects on human health. Therefore it has been identified as a hazard in Sri Lanka.

4.2 Exposure Assessment with Organophosphate Pesticides in Sri Lanka

4.2.1 Sources and routes of exposure to the Sri Lankan population

The reports on monitoring organophosphate residues in food and water (Department of Agriculture, Sri Lanka, 2009; Aravinna et al., 2008; De Alwis et al., 2006; Department of Agriculture, Sri Lanka, 2008) indicated the presence of organophosphates in the environment in Sri Lanka. Since rice and vegetables are staple foods, there is a great potential of exposure via dietary ingestion. This is because these crops are vulnerable to pesticide treatments even at harvesting period. Water is also a possible source of exposure, with residues being detected in surface water, including drinking water wells (Aponso et al., 2003; Aravinna, 2005; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002; Wickramarachchi et al., 2005). No data was found to support indoor exposure as a source of OP exposure in Sri Lanka. However, Aponso (2002) reported that chlorpyrifos was not found in the dust collected from farm houses in Kandy district. Furthermore, it is no longer expected that there will be chlorpyrifos exposure via household pest control treatments as the use of chlorpyrifos for this purpose has been restricted (Office of the Registrar of Pesticides, Sri Lanka, 2004).

A specific group of people in farm families are expected to be exposed via sources resulting from farming operations including equipment, spray drifts, contaminated crops, soil, food and water. Evidence of occupational exposure in farmers and farm family members has been gathered (Jeyaratnam et al., 1982; Smit et al., 2003; Aponso et al., 2002; Samarawickrema et al., 2008). Considering the wide range of sources available for OP

exposure in a farming environment, it is assumed that all the main routes and pathways (dermal contact, inhalation and ingestion) are involved in exposure. For example, most commonly used knap-sac sprayers are operated just in front of the person in a way that the person is exposed to the pesticide continuously while walking across the treated area (Aponso et al., 2002). Furthermore, the low levels of use of personal protective equipment is believed to make the condition more severe (Aponso et al., 2002; Smit et al., 2003; Chandrasekara 1989). The habit of eating, drinking and smoking while spraying (Smit et al., 2003) creates additional exposure routes for the farmer.

4.2.2 Equivalent Chlorpyrifos Ingested Dose (ECID) in Sri Lankan farmers

Aponso et al. (2002) conducted a study to assess chlorpyrifos exposure in a group of farmers in Sri Lanka in 2000. The study monitored the change in concentration levels of 3, 5, 6 trichloro-2-pyridinol (TCP), a specific metabolite of chlorpyrifos, in the urine of farmers. Nineteen healthy male farmers, recruited from Kandy district, were asked not to apply chlorpyrifos within ten days prior to the study date. They supplied 100 ml urine samples just before commencing a typical chlorpyrifos spraying event (pre-application) and three other samples per day throughout five days after the spraying event (post-application). The urine samples were analysed for TCP by Gas Chromatography spiked with known concentrations of TCP. Standards were used in between every three sample injections and were compared with the chromatogram of 0.25 µg/ml TCP standard (Aponso et al., 2002; Aponso, 2002).

The post-application exposure was believed to have occurred during the spraying event as chlorpyrifos was applied to an overhead vegetable canopy. The change in TCP levels were calculated by subtracting baseline TCP levels detected in pre-application urine samples,

from the levels detected in post- application samples. TCP levels were used to estimate the post application internal doses in farmers. The method is described in detail by Aponso et al., (2002) and Aponso (2002). However, a detailed assessment was not made on baseline exposure in farmers.

The reported TCP data by Aponso et al. (2002) was converted to a common measure of Equivalent Chlorpyrifos Ingested Dose which represented the exposure (ECID, see the Methodology in Section 3.3.1). ECID levels in farmers in baseline and post application situations were compared with established Guideline Values (GV) and with exposure levels (ECID) monitored in other international groups. The GVs for chlorpyrifos were based on the studies of oral administration of chlorpyrifos to animals or humans (USEPA, 2000; JMPR, 1999; Australian Department of Health and Ageing, 2008). The respective baseline and post application ECID levels are presented in Table 4.2.1 and Figure 4.2.1.

Based on the half life and excretion rate of TCP in humans (Nolan et al., 1984) it is assumed that a continuous daily exposure to chlorpyrifos for 3-5 days results in a steady state concentration of TCP, which is reflected in urinary TCP levels on a typical day (Mage et al., 2004; Garabrant, et al., 2008). Accordingly, creatinine corrected baseline TCP levels were reported for every farmer except one who had levels below the detection limit of 6 µg/L (Aponso et al., 2002). Reasons for variations of baseline TCP in farmers were not reported. In this situation, the farmers had not used chlorpyrifos for at least ten days prior to the date of study and therefore the baseline TCP in farmers indicate the entry of chlorpyrifos within the pre-application period from other routes. Hence, it was assumed that the ingestion of contaminated food & water, dermal contact with contaminated soil and

plants by entering into treated fields, and inhalation of contaminated air were the possible causes of baseline exposure.

Table 4.2.1 Equivalent Chlorpyrifos Ingested Doses (ECID) in Sri Lankan Farmers (Source: Aponso et al., 2002)

Baseline ECID in Individual Farmers Calculated from TCP Analysis in Urine (ng/kg/day)	Post application ECID in the Same Individual Calculated from TCP in Urine (ng/kg/day)
-	8400
1.0	6800
80	10000
90	9400
140	5500
170	2900
220	11000
250	2500
250	6200
310	8900
350	4800
350	2900
350	5000
490	9600
540	10000
550	4700
730	6300
730	11000
1600	7300
Mean = 379	Mean = 7010

It is noteworthy that the lowest baseline ECID was about 1.0 ng/kg/day (0.0 on log scale, see Figure 4.2.1) which is 100 fold lower than the next dose observed. All the other doses

were between 80.0 ng/kg/day (1.9 on log scale; see Figure 4.2.1) and 1600 ng/kg/day (3.2 on log scale; see Figure 4.2.1). The mean ECID was 379 ng/kg/day (2.6 on log scale; see Figure 4.2.1). The slope of the distribution plot was 1.3. The variations of the levels observed between individual farmers were thought to be due to possible differences in exposure levels, metabolism and/or analytical uncertainties.

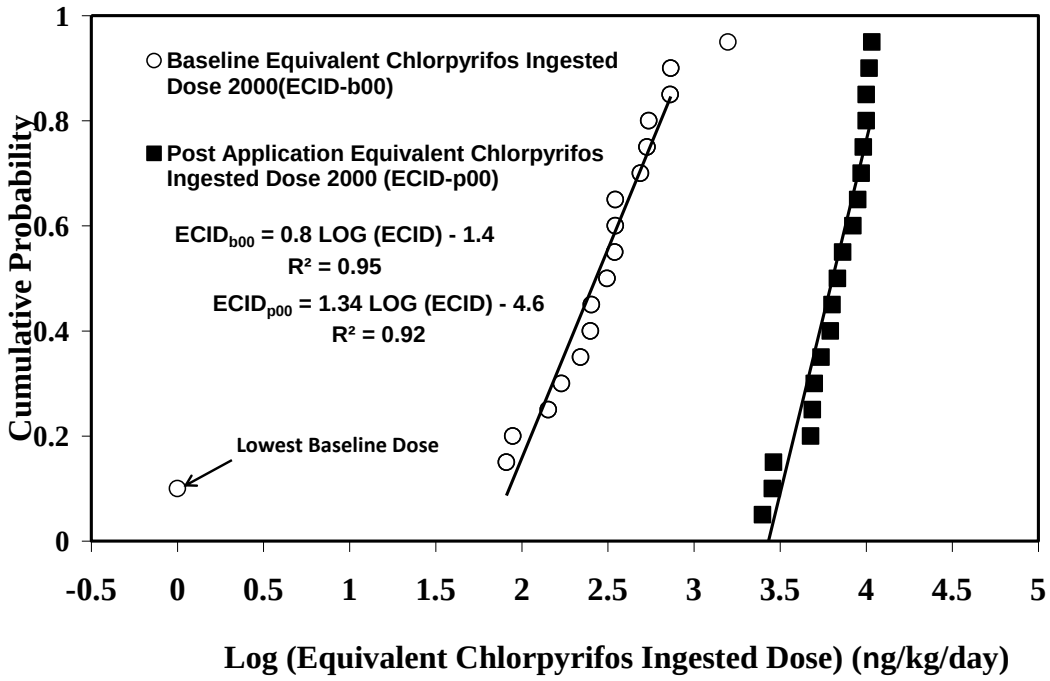

Figure 4.2.1 Equivalent Chlorpyrifos Ingested Doses (ECID) in Sri Lankan Farmers during 2000 (Source: Aponso et al., 2002)

The post application ECID levels were distributed between 2500 and 11000 ng/kg/day (3.4 and 4.0 on log scale; see Figure 4.2.1). There was a four fold difference between the minimum and the maximum values which is comparatively narrower than the distribution of baseline doses. The slope of the dose distribution plot was 0.8. All the farmers having levels above the mean (7010 ng/kg/day or 3.8 on log scale; see Figure 4.2.1) were reported to spray comparatively a larger volume of chlorpyrifos for a longer time. It was also

reported that 30% of the farmers used more than the recommended rates and a similar proportion used leaking knapsack sprayers. Seventeen out of the nineteen farmers consumed alcohol daily, and twelve were smokers in their everyday life. However, the behaviour of the farmers during the application event was not revealed.

4.2.3 Dietary, water and air exposure to pesticides in Sri Lanka

Organophosphate residues in food commodities

Chlorpyrifos residues have been reported in raw rice, vegetables and water sources in Sri Lanka (see Tables 4.2.2, 4.2.3). Despite the large number of sample analyses carried out in many studies, only a few samples can be found positive for chlorpyrifos. Most of this data was either insufficient or unsuitable for a dietary exposure analysis. Thus, only the data reported in rice (Department of Agriculture, Sri Lanka, 2009), cabbage (Aravinna et al., 2008), beans (Aravinna et al., 2008; Department of Agriculture, 2009), mukunuwenna (*Alternanthera sissilis*, a leafy vegetable grown in Sri Lanka) (De Alwis et al., 2006) and water (Aponso et al., 2003; Aravinna, 2005; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002) were considered in the dietary exposure analysis.

All the considered studies on residue analysis in vegetables and rice were reported to be carried out from 2001 to 2009. Sample collections were made in many parts of the country, from vegetable growing areas, markets or from research fields at harvesting. The sampling plans of the studies were reported to be statistically designed covering several agricultural instructional divisions or/and 'grama niladhari divisions' (GND) composed of several

villages. The cabbage and bean samples were obtained from up country vegetable growing areas in Nuwara-eliya, Badulla and Kandy districts while mukunuwenna samples were taken from four Assistant Government Divisions in the Colombo district, representing twenty four GNDs. Rice samples were collected from research plots of the Department of Agriculture in Gannoruwa in the Kandy district. Residue data reported for water (Aponso et al., 2003; Aravinna, 2005; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002; Wickramarachchi et al., 2005) came from various sources in intensive agricultural areas in the dry and wet zones in the country. They represented tanks, protected wells and unprotected wells which were used for drinking, bathing and irrigation.

The residue analyses for rice and vegetables were carried out in different laboratories. However, these studies (De Alwis, et al., 2006; Aravinna et al., 2008; Department of Agriculture, Sri Lanka, 2009; C. Magamage, Research Officer, 2009, pers. Comm.) were reported to have followed standard methods. The methods included preparation of samples, filtration, extraction, concentration, calibration with standards, recovery by spiking, analysis with GC/MS and GC/ECD (Electron Capture Detector) and blanks. Similarly, standard methods were used for analysing water samples (Aponso et al., 2003; Aravinna, 2005; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002; Wickramarachchi et al., 2005). Sample analysis was performed in GC with ECD and NPD (Nitrogen Phosphorous Detector). The methods of sampling were described as statistically designed with cluster sampling (Aravinna et al., 2003), periodically from representative sampling points with replicates (Aponso et al., 2003; Department of Agriculture, Sri Lanka, 2003) and with replicates from several sources (Eramudugolla, 2002). Wickramarachchi et al. (2005) collected samples from five locations, however, no further details were given.

Sampling was followed by extraction (liquid/liquid or solid phase), recovery studies with spikes, and calibration with standards. However, detection limits were not reported in some.

The data was presented as individual figures (De Alwis et al., 2006; Department of Agriculture, Sri Lanka, 2009; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002; Wickramarachchi et al., 2005), ranges (Aravinna et al, 2008) or graphs (Aponso et al., 2003) and in different units; mg/kg, mg/L and µg/L. The limits of quantification of chlorpyrifos in each considered dietary component are given in Table 4.2.2. The percentage of detection of residues in cabbage, beans, mukunuwenna and rice were 20%, 13%, 15% and 80% respectively (see Table 4.2.2). Rice samples showed higher proportions of detection compared to the others. The chlorpyrifos detection levels in water ranged between 10^1 to 10^6 ng/L (see Table 4.2.3). The detection limits for water analyses were not available. Only 22 samples were reported positive for chlorpyrifos out of 635 samples analysed in the studies, indicating a 3.5% contamination rate of the respective water sources.

It was reported that four out of twenty two detections in leafy mukunuwenna exceeded the Maximum Residue Limit (MRL) of $5x10^5$ ng/kg, which is set by the Sri Lanka Standard Institution (De Alwis et al., 2006; see Figure 4.2.2). Four of the cabbage samples and four of the bean samples alsoexceeded the respective MRLs of $1x10^6$ ng/kg and $1x10^4$ ng/kg established by the Codex Alimentarius Committee (Aravinna et al., 2008; see Figure 4.2.2). None of the rice samples exceeded the Codex MRL (Joint FAO/WHO Codex Alimentarius Commission, 1995) of $5x10^6$ ng/kg (see Figure 4.2.2). Three of the twenty-two water samples with detected residues exceeded the WHO Guideline Value (GV) for drinking

water (See Table 4.2.3). These three values were removed from Dietary Chlorpyrifos Intake (DCI) calculation as well as from Total Dietary Chlorpyrifos Intake (TDCI) calculations.

Table 4.2.2 Chlorpyrifos Residues in Rice and Vegetables

Dietary component (No.detected / No. analysed)	Chlorpyrifos-Range of detections (Minimum and Maximum) (10^3 ng/kg)	LOQ (10^3 ng/kg)	Reference
Rice (12/15)	29 -417	20	**, 2009
Mukunuwenna (22/144)	14-1942	10	De Alwis, et al., 2006
Cabbage (18/90)	10-5000	10	Aravinna et al., 2008
Beans (7/54)	3.3-100	#4, ##N/A	Aravinna et al., 2008#; **, 2009##
Lettuce (1/30)	10-50	4	Aravinna et al., 2008
Leek (2/129)	100-500	10	Aravinna et al., 2008
Egg plant (1/2)	102	N/A	**, 2009
Green chilli (1/3)	2.6	N/A	**, 2009
Snake gourd (3/3)	5-101	N/A	**, 2009
Green chilli* (8/42)	0.8-12	0.005	**, 2008
Beans* (12/52)	0.4-14.7	0.005	**, 2008
Cabbage* (3/48)	0.2-1.2	0.005	**, 2008
Snake gourd*(7/28)	0.1-1	0.005	**, 2008
Egg plant*(2/41)	0.9-1.4	0.005	**, 2008

N/A- Not available; LOQ- Limit of Quantification; * Detected in surface washings of the food commodity; **Department of Agriculture, Sri Lanka; #LOQ reported; ##LOQ not reported

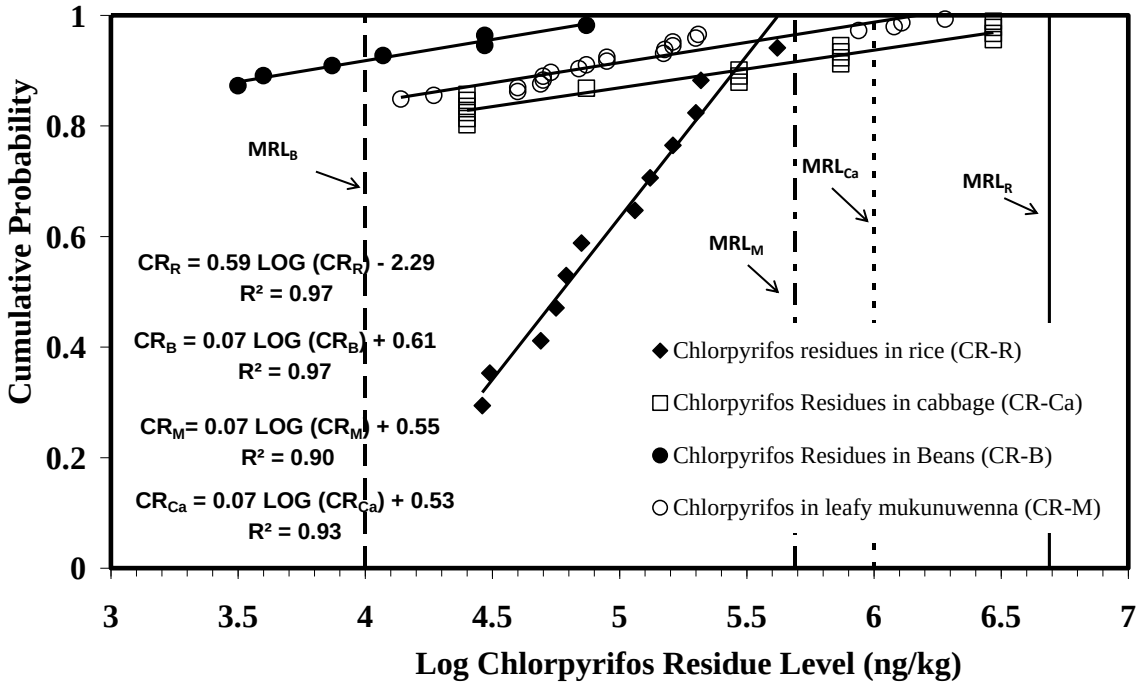

Figure 4.2.2 Chlorpyrifos Residues in Dietary Components in Sri Lanka

No reported data on air contamination from chlorpyrifos in Sri Lanka could be found. In order to assess the Total Chlorpyrifos Intake (TCI) levels in Sri Lankans, air contamination data from a closely related scenario reported by Buck et al. (2001) was adopted. The data was generated in Arizona in U.S.A from outdoor air samples in households which did not have chlorpyrifos treatment in the previous year of the study, but may have had such treatment prior to this. This was the most comparable exposure scenario to air intake to Sri Lankans found from the literature. Since indoor treatment using chlorpyrifos in Sri Lanka is not practiced, the adoption of data from Buck et al. (2001) was assumed to be appropriate. Chlorpyrifos usage for household pest control was only legal in Sri Lanka until 2004 (Registrar of Pesticides, Sri Lanka, 2004).

Table 4.2.3 Chlorpyrifos Residues in Water

Source of water	Chlorpyrifos- Range of detections (10^3 ng/L) (No detected/No analysed)	Reference	Guideline Value (10^3 ng/L)
Tanks (DZ)	0.03-0.1 (3/544)	Aponso et al., 2003	30.0 (WHO, 2004)
Tanks (WZ)	0.02-0.03(3/12)	Department of Agriculture, Sri Lanka, 2003	
Wells (DZ)	0.04-6.4 (12/14)	Eramudugolla, 2002	
Wells (WZ)	$0.7^{\#}$ (1/60)	Aravinna et al.,2005	
Tanks (DZ)	2800-6770 (3/5)	Wickramarachchi et al., 2005	

DZ-Dry zone, WZ-Wet zone; $^{\#}$ LOQ 0.04 x 10^3 ng/L

Residues of profenofos, diazinon and dimethoate have been detected in various raw dietary components in Sri Lanka (see Tables 4.2.4 & 4.2.5). Profenofos is the second highest in frequency of detection. However, few detections were reported, out of many samples analysed, and hence the data was not sufficient for a dietary exposure analysis. Profenofos also showed a wider detection range from 5000 (excluding surface washings) to 5 x10^6 ng/kg. Many of the diazinon detections were reported in surface washings of food commodities. Dimethoate was the least detected OP insecticide.

Table 4.2.4 Profenofos, Diazinon and Dimethoate Residues in Rice and Vegetables

Pesticide	Dietary component (No. detected / No. analysed)	Range (10^3 ng/kg)	LOQ (10^3 ng/kg)	Reference
Profenofos	Mukunuwenna(5/144)	11-50	10	De Alwis et al., 2006
	Beans (3/51)	5-50	8	Aravinna et al., 2008
	Lettuce (3/30)	500-5000	16	Aravinna et al., 2008
	Cabbage(3/90)	10-5000	20	Aravinna et al., 2008
	Leek (2/129)	50-100	20	Aravinna et al., 2008
	Green chilli* (2/48)	0.1-12	N/A	**, 2008
	Beans* (2/52)	1.2-5	N/A	**, 2008
Diazinon	Rice (7/16)	12-103	10	**, 2009
	Mukunuwenna(4/144)	12-90	10	De Alwis et al., 2006
	Green chilli* (1/42)	2	N/A	**, 2008
	Beans* (3/52)	1.2-1.6	N/A	**, 2008
	Snake gourd* (1/28)	0.8	N/A	**, 2008
	Egg plant* (4/41)	0.8-1.7	N/A	**, 2008
Dimethoate	Beans* (1/52)	0.8	N/A	**, 2008
	Snake gourd* (1/28)	0.5	N/A	**, 2008

* Detected in surface washings of the food commodity; N/A- Not available; ** Department of Agriculture, Sri Lanka

Table 4.2.5 Profenofos, Diazinon and Dimethoate Residues in Water

Pesticide	Source of water	Range in water (ng/L) (No detected/No analysed)	Reference
Profenofos	Tanks	3.6 – 73 (7/12)	Department of Agriculture, Sri Lanka, 2003
	Wells	10 (1/60)	Aravinna et al.,2005
Diazinon	Tanks	12- 150 (4/544)	Aponso et al., 2003
Dimethoate	Tanks	14 - 52 (1/544)	Aponso et al., 2003

Dietary Chlorpyrifos Intake (DCI), Total Dietary Chlorpyrifos Intake (TDCI) and Total Chlorpyrifos Intake (TCI) in Sri Lanka

The Dietary Chlorpyrifos Intakes (DCI) were calculated (see Section 3.3.3) in rice, cabbage, beans and mukunuwenna using the reported residue concentrations (see Table 4.2.2) and daily per capita consumption rates (see Table 4.2.6). Rice and vegetables are the staple foods in Sri Lanka. The estimated per capita consumption of rice of an average person is about one hundred kg per year (Central Bank of Sri Lanka, 2005). A survey conducted by the Central Bank of Sri Lanka in 2003/ 2004 (Central Bank of Sri Lanka, 2005) reported that beans, cabbage and mukunuwenna were among the most commonly consumed vegetables in Sri Lanka. However, it was noted that the average daily consumption of vegetables is very low (see Table 4.2.6). This might be a result of the availability of numerous varieties of vegetables in the country, which limits daily

consumption to a few types. The DCI via water was also calculated (see Section 3.3.3) using available data (see Table 4.2.3). Since daily average consumption volumes of water were not estimated for Sri Lanka, an average volume of 2 L/day (USEPA, 2006) was used for the calculation.

Table 4.2.6 Dietary Chlorpyrifos Intake (DCI) in Rice and Vegetables in Sri Lanka

Dietary component	Amount in a diet of an average person per day	Dietary Chlorpyrifos Intake (DCI) in each dietary component (ng/kg/day)		Limit of Quantification (LOQ) or Detection Limit (DL) in (ng/kg/day)***
		Min	Max	
Rice	300 g*	120	1800	86.0
Cabbage	10 g*	4	430	1.4
Beans	10 g*	0.5	10	N/A
Mukunuwenna	10 g*	2	280	1.4
Water	2 L**	0.6	180	N/A

Source: * Consumer finances and socio-economic survey 2003/04 (Central Bank of Sri Lanka, 2005); ** USEPA Drinking Water Health Advisories RfD (USEPA, 2006); N/A- Not Available; ***Respective DL of the residue chlorpyrifos in rice, cabbage and mukunuwenna are given in the Table 4.2.2.

The minimum and maximum DCI values in an average person calculated in each dietary component are presented in the Table 4.2.6. Figures 4.2.3 and 4.2.4 present the cumulative probability distributions of DCI in each food item and water respectively.

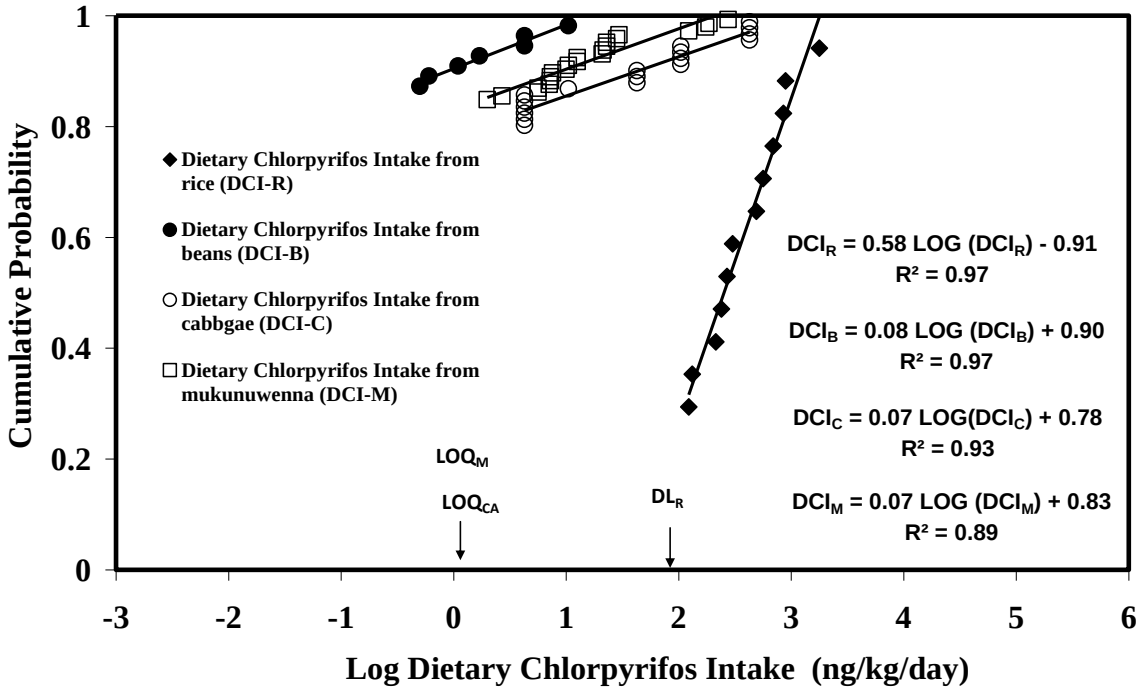

Figure 4.2.3 Dietary Chlorpyrifos Intake (DCI) in Rice and Vegetables in Sri Lanka

DL_R –Detection Limit in rice; LOQ_{Ca} and LOQ_M – Limits of Quantification in cabbage and mukunuwenna

The probability distribution plots of cabbage, mukunuwenna and beans were comparable. The plots of all the vegetables were observed to be above the cumulative probability level of 0.8. Lower levels were not observed because of respective Limits of Quantification (LOQ) and Detection Limits (DL) (see Table 4.2.6). Vegetables showed a wide range of DCI distribution (slope 0.07 to 0.08; see Figure 4.2.3) within a limited range of probability between 0.80 to 0.99 compared to distribution of DCI in rice. The distribution range for

cabbage was plotted using mean values of the reported residue ranges. Therefore the actual range of dose distribution should be a little wider than what is shown in Figure 4.2.3.

Wider distribution ranges are reflections of variations in detection levels occurring. One reason is the possible differences in agricultural practices carried out in the sampled areas. For example, the method, frequency and the concentration of pesticide application could be different from one farmer to another, especially with fewer adherences to the pesticide recommendations. This is an obvious variable in detecting the residues in cabbage and mukunuwenna, for which chlorpyrifos is not recommended in pest control in Sri Lanka. Another reason for the variation in the residue levels is the time spent between the last application and the chlorpyrifos analysis, which is unknown. Moreover, analytical differences could have affected the residue levels.

Comparatively, DCI in rice is distributed in a narrower range (slope 0.6; see Figure 4.2.3). Since most of the samples were detected with chlorpyrifos (see Table 4.2.2) a broad probability distribution from 0.3 to 0.94 was observed (see Figure 4.2.3). The DCI in rice was calculated using chlorpyrifos residues reported in a study carried out for special research purposes (Department of Agriculture, Sri Lanka, 2009). In the research study chlorpyrifos treatments were carried out at the same rate, although with different frequencies and time intervals for each replicated rice plot. Due to this reason, there is a possibility for higher frequency of detection of residues within a narrow range of concentrations (10^4-10^5 ng/kg; see Table 4.2.2). Furthermore, lack of reported residue data from farmer fields or markets was a limitation within the study.

The DCI in water is presented in Figure 4.2.4. The distribution of DCI in water is comparatively wider (slope 0.01; see Figure 4.2.4) and is distributed in a narrow cumulative probability range of 0.96 to 0.99. This reflects the wide variation among residue detections in the samples. The samples were obtained from different sources and sites of the wet zone and dry zone in the country (see Table 4.2.3). Depending on the severity of pesticide usage in the area, the resulting residue levels in water bodies can vary. Eramudugolla (2002) and Aravinna et al. (2008) reported that sampling was carried out in protected and unprotected wells within intensive agricultural areas. The other sampling sources were large tanks near agricultural areas (Aponso et al., 2003; Department of Agriculture, 2003; Wickramarachchi et al., 2005).

Unusually high detection levels (see Table 4.2.3) were reported in some of the tanks (Wickramarachchi et al., 2005). The respective DCIs of these residue levels ranged from 10^4 to 10^5 ng/kg body weight/day (4.6 to 5.3 on log scale; see Figure 4.2.4), which is more than 140 times higher than the USEPA Drinking Water Health Advisories Reference Dose (USEPA, 2006) of 300 ng/kg/day (2.47 on log scale; see Figure 4.2.4). These samples were reported to be collected from catchment areas of tanks in an agricultural area with a heavy use of pesticides. However, this data was considered unsuitable for the Total Dietary Chlorpyrifos Intake (TDCI) estimation, because these levels exceeded the limit of solubility of chlorpyrifos in water (JMPR, 1972). None of the other DCI levels in water exceeded the USEPA Reference Dose (see Figure 4.2.4).

Buck et al. (2001) reported estimated Chlorpyrifos Intake in breathing air (CI_A) samples which were assumed to be similar to levels in Sri Lanka. The rate of inhalation of an adult,

exposure duration, concentration of chlorpyrifos in the air and body weight was considered in the estimation of CI_A. The levels ranged between 10^{-2} and 10^{0} ng/kg/day (-2.3 and 0.8 on log scale; see Figure 4.2.4 and Table 4.2.8) from 0.1 to 0.99 probability levels. The maximum CI_A is 7.0 ng/kg/day. This level is considerably smaller compared to the DCI in vegetables and water (see Table 4.2.6). The range of distribution in terms of CI_A and probability is wide. This is likely due to the higher frequency of detection and to the personal differences in indoor chlorpyrifos usage indoors as reported in Buck et al. (2001).

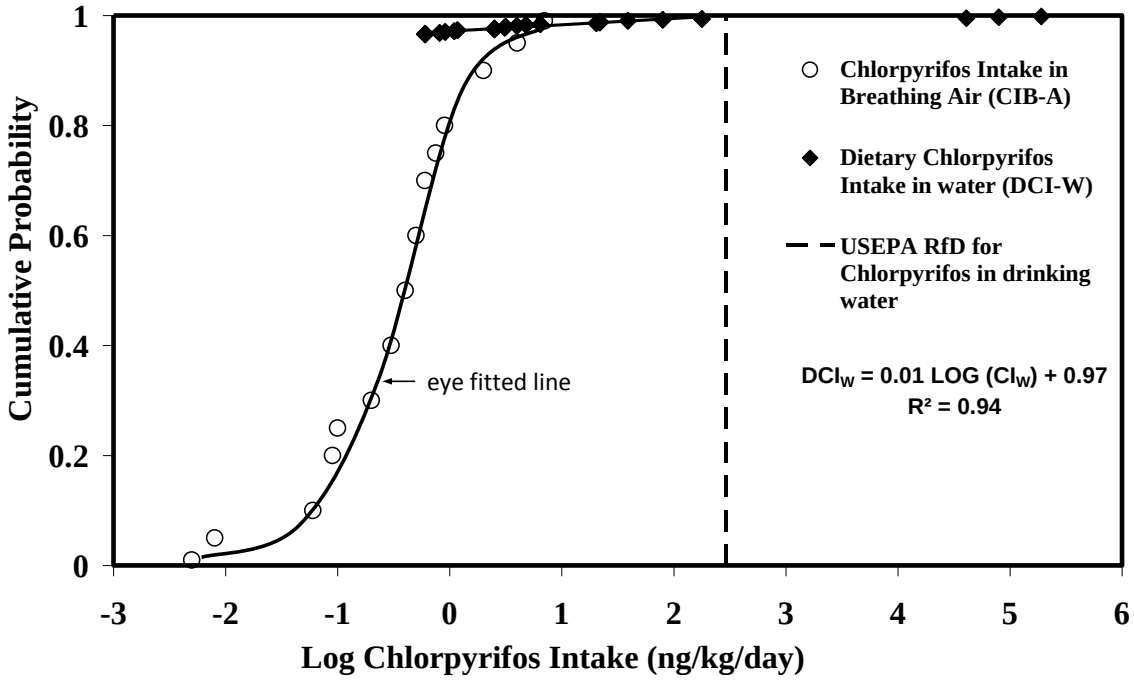

Figure 4.2.4 Dietary Chlorpyrifos Intake (DCI) in Drinking Water and Chlorpyrifos Intake in Breathing Air (CI_A)

The Total Dietary Chlorpyrifos Intake (TDCI) in an average Sri Lankan was calculated using the DCI levels in rice, cabbage, mukunuwenna, beans and water and is presented in Figure 4.2.5. The TDCI was calculated for the cumulative probability levels of 0.1, 0.2, 0.3,

0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 0.95 and 0.99 using respective DCIs estimated from the trend line equations of DCI plots (see Section 3.3.3). The contributions of chlorpyrifos from rice, vegetables and water to TDCI at each probability level are presented in Table 4.2.7.

Table 4.2.7 Percent Contribution of Dietary Chlorpyrifos Intake (DCI) to Total Dietary Chlorpyrifos Intake (TDCI)

Cumulative probability	% Contribution to Total Dietary Chlorpyrifos Intake (TDCI)				
	Rice	Cabbage	Mukunuwenna	Beans	Water
0.1	100 (50)	-	-	-	-
0.5	100 (260)	-	-	-	-
0.8	99.7 (850)	0.2 (2)	-	-	-
0.9	95.2 (1300)	3.8 (50)	1.0 (10)	-	-
0.95	82.6 (1500)	14.4 (260)	2.8 (50)	0.2 (4)	-
0.99	57.7 (1800)	32.5 (1000)	6.2 (190)	0.4 (13)	3.2 (35)

Note: The Dietary Chlorpyrifos Intake levels (ng/kg/day) calculated from the trend-line equations of Figures 4.2.3 and 4.2.4 at respective probability levels are given in parentheses next to the percentage contribution value.

At the 0.95 probability, DCI in rice contributed to 83% (see Table 4.2.7) of the TDCI. At lower probability levels below 0.9, almost all TDCI was due to the DCI in rice. This was because of the higher frequency of detection of chlorpyrifos in the rice samples (see Table 4.2.2). The higher consumption rate of rice has made its contribution to TDCI prominent even at higher probabilities above 0.9, where higher levels of chlropyrifos residues were detected in vegetables than in rice (see the maximum residue levels in Table 4.2.2).

Average daily consumption of rice in an average person in Sri Lanka was ten times higher than the total vegetable consumption (see the daily consumption rates in Table 4.2.6).

One of the limitations with residue data on rice is that, it does not represent the levels in farmer fields or markets, due to sampling being limited to only research fields (Department of Agriculture, Sri Lanka, 2009). Although a difference in levels may exist between the samples used in this study and those from farmer fields and markets, it cannot be elicited due to the lack of data.

Furthermore, it was reported that rice sampling was carried out at the time of harvesting of the crop. It can be expected that residue levels would still be high during the harvesting period. Therefore, the levels observed may somewhat differ from the levels that may be present in processed rice. Rice is mainly consumed after processing with sun-drying, storage for a period of time, par boiling and polishing, although exceptions are found where it is consumed just after sun drying. Par boiling and polishing could reduce chlorpyrifos residue levels (Deka et al., 2004). Storage may also reduce residue levels, but no reports showing this were found. These limitations could have meant that the contribution from rice to TDCI was different than what was estimated in this study. However, further research is needed, supported by residue analyses, to investigate this situation

At the 0.95 probability level, the contribution to TDCI from DCI in vegetables is 17% with the highest estimated in cabbage (see Table 4.2.7). Although the daily rate of consumption of cabbage is low (10 g; see Table 4.2.6), the higher residue detections at 0.95 probability levels (see Figure 4.2.2) increased its DCI. The least contribution to TDCI was observed

from DCI in beans (3%; see Table 4.2.7). Both the rate of consumption (10 g; see Table 4.2.6), and low residue detections (see Figure 4.2.2) contributed to this. The DCI in the leafy vegetable mukunuwena contributed 3% of the TDCI (see Table 4.2.7) as a result of its residue levels (see Figure 4.2.2) and the low daily consumption rate.

Water added a small portion (3%; see Table 4.2.7) to the TDCI, even at the 0.99 level. The census and statistics survey carried out in 2001 (Department of Census and Statistics, Sri Lanka, 2006) reported 9.9% of households in Sri Lanka drink water from unprotected wells, while more than 5% use river, tank or stream water for their drinking water. About 50% of households obtain water from protected wells. However, the percentage contribution of chlorpyrifos in water (3%) to TDCI provides an indication of the low proportions of the average population which can be exposed to chlorpyrifos through water.

The probability distribution of Total Chlorpyrifos Intake (TCI) is presented in the Figure 4.2.5. TCI was calculated from adding TDCI (see Figure 4.2.5 and Table 4.2.7) and CI_A (see Figure 4.2.4) values together, at all the probability levels (see Section 3.3.3). Figure 4.2.5 shows that the TDCI and TCI are mostly similar at all the probability levels with 99% TDCI contribution at the 0.95 probability level. This indicates less contribution from inhalation. With these study results it can be considered that the TCI is similar to TDCI in Sri Lanka. However, local data is necessary to confirm the actual CI_A levels.

Table 4.2.8 Total Dietary Chlorpyrifos Intake (TDCI) and Chlorpyrifos Intake in Breathing Air (CI_A)

Cumulative Probability	*Total Dietary Chlorpyrifos Intake (TDCI) (ng/kg/day)	**Chlorpyrifos Intake in Air (CI_A) ng/kg/day
0.1	50	0.1
0.2	80	0.1
0.3	120	0.2
0.4	170	0.3
0.5	260	0.4
0.6	380	0.5
0.7	560	0.6
0.8	850	0.9
0.9	1300	2.0
0.95	1800	4.0
0.99	3100	7.0

Sources: * Department of Agriculture, Sri Lanka, 2009; Aravinna et al., 2008; Aravinna et al., 2008; De Alwis et al., 2006; Aponso et al., 2003; Aravinna, 2005; Department of Agriculture, Sri Lanka, 2003; Eramudugolla, 2002; ** Buck et al., 2001

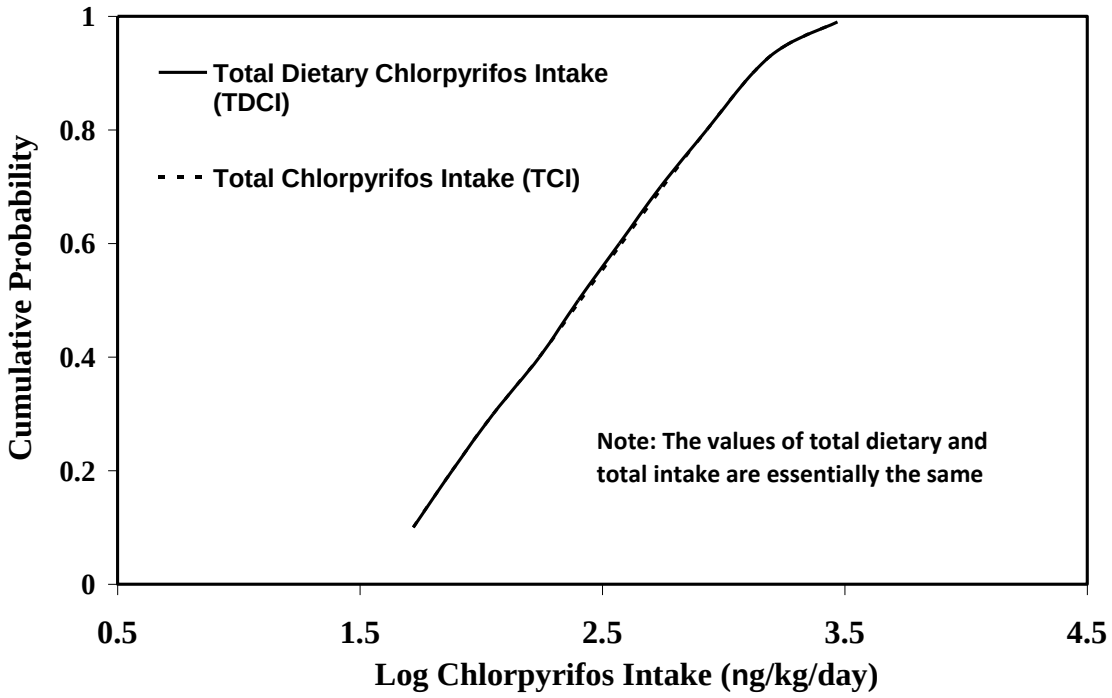

Figure 4.2.5 Total Dietary Chlorpyrifos Intake (TDCI) and Total Chlorpyrifos Intake (TCI) in Sri Lanka

The study estimated the Total Dietary Chlorpyrifos Intake (TDCI) of an average person in Sri Lanka using available reported data. There was a limitation in selecting dietary components due to the unavailability of residue data reported in Sri Lanka. The total weight of the daily diet was decided as 330g excluding water, using the only available report to obtain consumption rates, a survey conducted by the Central Bank of Sri Lanka in 2003/ 2004 (Central Bank of Sri Lanka, 2005). This report produced data as monthly consumption rates and hence, was converted to daily rates. Also, the consumption of considered vegetables was assumed to be a daily event, even though these vegetables are consumed several times per month and may in fact have a higher consumption rate.

As discussed in previous paragraphs, the DCIs were estimated from data reported in unprocessed food samples. Deka et al. (2004) reported that the residue levels detected in polished and parboiled rice were lower than the levels detected in unpolished and non-parboiled samples. Furthermore, chlorpyrifos residues were detected in the surface washings of some vegetables (see Table 4.2.2, Department of Agriculture, Sri Lanka, 2008). This data indicates that the TDCI levels in processed foods can expected to be lower than the estimated levels in this study. However, data from processed samples of a similar diet is needed to verify this.

4.3 Exposure Assessment of Populations Internationally

4.3.1 Equivalent Chlorpyrifos Ingested Doses (ECID) in farmers, general adults, pest control applicators, manufacturing workers and pregnant mothers in the US

ECID in farmers

Scher et al. (2008) reported equivalent chlorpyrifos mass (µg) absorbed during a spraying event in twelve farmers in South Carolina and Minnesota in USA. The participants were randomly selected licensed pesticide applicators, recruited in a survey known as Farm Family Exposure Study, conducted during 2000 and 2001. The chlorpyrifos exposure was compared with a model estimation in the study. The farmers applied chlorpyrifos to a land area of one acre and supplied 24 hour urine samples after the application event for four consecutive dates. Pre-exposure urine samples were also collected from the farmers on the day prior to the application event.

In Scher et al. (2008), the urine samples were analysed for TCP metabolite, which was then converted into equivalent chlorpyrifos masses, using the total post application TCP excretion rates (μg/hour) over 96 hours. The TCP levels were also adjusted for incomplete recovery in urine and molecular ratio of chlorpyrifos to TCP. TCP levels were also corrected for the baseline exposure by subtracting pre-exposure levels from post-application TCP levels. Although TCP excretion rates were used for the calculations in the study, throughout the study period creatinine excretion was also monitored to maintain linearity with urine volumes.

The chlorpyrifos masses reported by Scher et al. (2008) were converted to ECIDs and are presented in Figure 4.3.1 (see Section 3.3.1). Of twelve farmers, only ten were included in the ECID estimation since the others were reported to have had two application events during the study period. The ECID levels were distributed between 400.0 and 7300.0 ng/kg/day (2.6 and 3.9 on log scale) with a slope of 0.7, which is a relatively narrow distribution.

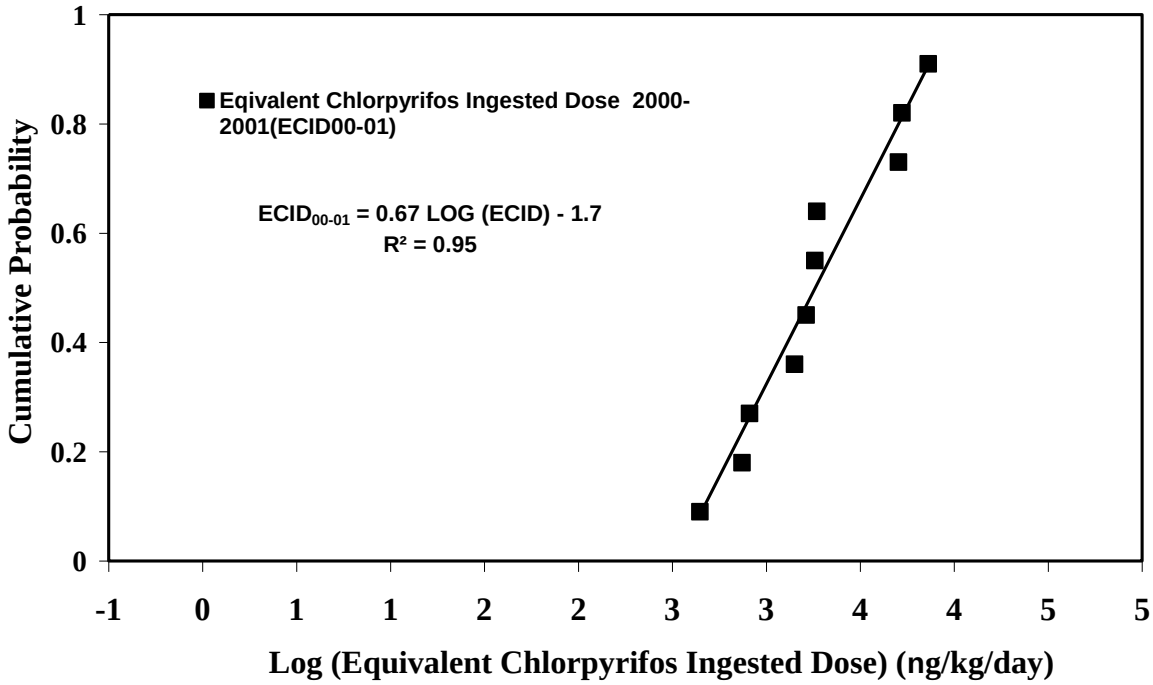

Figure 4.3.1 Equivalent Chlorpyrifos Ingested Doses (ECID) in US farmers during 2000 to 2001

Considering the large extent of farm land cultivated by US farmers, it is obvious that their pesticide application cannot be carried out by hand-operated equipment. They were reported to use ground booms and tractor-drawn spreaders. This method of application is less likely to result in direct contact with the pesticide, unless the farmer is not wearing protective gear during the preparation and handling of the mixtures. Scher et al. (2008) reported that some farmers were excluded from the study involved as they did not observe any exposure, as a result of being in an enclosed cab whilst spraying the pesticide. Furthermore, they mentioned that the use of granular formulations resulted in less exposure.

ECID in general adult population

Biological monitoring of selected chemicals and their metabolites in urine samples of the US population has been carried out annually as a routine process (CDC, 2005) via the National Health and Nutrition Examination Survey (NHANES) and is conducted by the Centers for Disease Control and Prevention in USA. The main purpose of this survey is to study the exposure levels to some chemicals, including chlorpyrifos, in the general population, and to serve as a data base for comparison with other exposure situations. The participants are males and females in different age categories residing in different areas in the country.

For the analysis of chemicals including TCP, a 'spot' urine sample is obtained from each volunteer. Mage et al. (2004) defines a 'spot' urine sample as a 'void without a record of the volume, or elapsed time in hours from the previous void'. A spot urine sample adjusted for daily creatinine excretion rate can be used to estimate the daily excretion rate of TCP, which is assumed to be in a steady state, resulting from a continuous previous exposure.

The TCP concentrations of nearly 1000 participants were reported at the 5^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th}, 99^{th} and the 100^{th} percentiles in the 1988-1994 survey (Hill et al., 1995). The participants were randomly selected males and females from many parts of the country, who were between the ages of 20 to 59 years and represented several ethnicities. 82% of the participants were reported to be positive for chlorpyrifos exposure. In the 1999-2000 survey average TCP concentrations of 832 randomly selected adults between 20 to 59 years were reported at the 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th} and the 95^{th} percentiles (Barr et al., 2005). The

participants were recruited from 26 locations throughout the US, with broad demographic variations. The frequency of detection was 89% above the detection limit (400 ng/L) and lower than that of the 1988-1994 survey (1000 ng/L). In the 2000-2001 survey, the average TCP levels of 1113 were reported for the 50^{th}, 75^{th}, 90^{th} and the 95^{th} percentiles (CDC, 2005). These participantsalso followed similar criteria to those of previous surveys. The percent frequency of detections was not reported for each particular age group. Also, in the two latter surveys, the TCP levels pertaining to the maximum percentiles were not reported.

The TCP levels were converted into ECIDs (see the methodology in Section 3.3.1) in order to evaluate the exposure in US adults (refer to Table 4.3.1 and Figure 4.3.2). The ECID levels during 1988-1994 are distributed between 100.0 ng/kg/day to 1200.0 ng/kg/day (2.0 to 3.4 on log scale; see Figure 4.3.2) within the 0.25 to 0.99 cumulative probabilities. The maximum ECID level (2500 ng/kg/day or 3.4 on log scale) at the 1.0 probability level (100^{th} percentile) is twice as high as the level at the 0.99 probability level (99^{th} percentile). Few differences were observed among the dose distributions in the three surveys, reflected by the slopes of 0.9, 0.8 and 0.7 in 1988-94, 1999-2000 and 2001-2002 respectively. Overall the highest ECID levels were observed during the 1988-94 period and the lowest in 1999-2000. The ECID detected at the 0.90 probability level in the populations in the 1988-94 survey resembled the level at the 0.95 level of probability in the 1999-2000 survey, but was between these percentiles in 2001-2002 (see Table 4.3.1) indicating a decrease in the ECID levels followed by a slight increase in the last survey.

Table 4.3.1 Equivalent Chlorpyrifos Ingested Doses (ECID in ng/kg/day) in US adults

Cumulative Probability	1988-1994	1999-2000	2001-2002
0.25	100.0	60.0	-
0.50	160.0	100.0	120.0
0.75	260.0	180.0	230.0
0.90	470.0	320.0	400.0
0.95	620.0	480.0	550.0
0.99	1200.0	-	-
1.0	2500.0		

Indoor exposure was assumed to be one of the major pathways of exposure in the general population in the USA (Hill et al., 1995; Barr et al., 2005; Morgan et al., 2005; Berkowitz, 2003). Heavy usage of chlorpyrifos in the USA was recorded in the late Nineties, estimated at 9-14 million kg for agricultural and non-agricultural pest control purposes (Hines et al., 2001). It was reduced to five million kg in early 2000 (CDC, 2005). The reduction of chlorpyrifos usage was reflected in the dose distributions from 1988-94 onwards. Chlorpyrifos was introduced as an alternative to chlordane for indoor pest control during the period of 1988-94, resulting in higher frequencies of exposure (Hill et al., 1995; Hines et al., 2001).

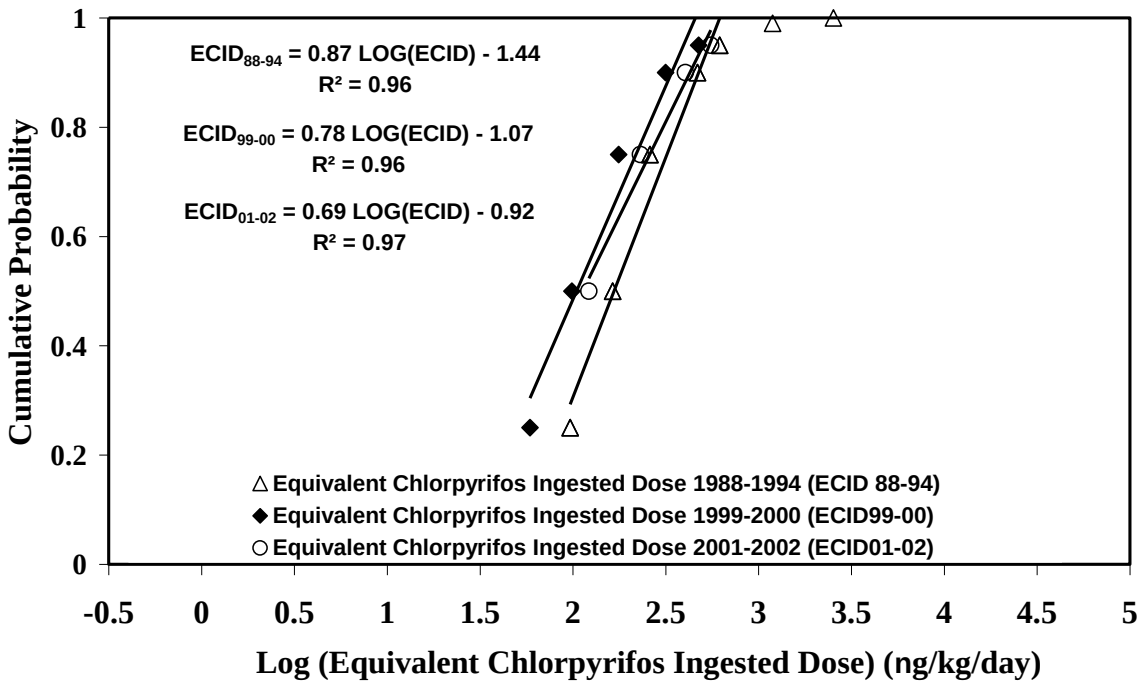

Figure 4.3.2 Equivalent Chlorpyrifos Ingested Doses (ECID) in US adults during 1988 to 2002

The reasons for a lower frequency of detection in NHANES 1999-2000 were discussed in the study of Barr et al. (2005). Major changes occurred with the reassessment of regulations related to chlorpyrifos. This has resulted in reductions in food tolerances in certain foods, and thereby less contamination and less detections. Also voluntary reduction of the use of OPs, including chlorpyrifos, has also contributed to the lower frequency of detections as compared to 1988-94. Regulatory decisions were made by USEPA to reduce indoor treatment with chlorpyrifos except for ant and roach baits (USEPA, 2002). Pre- and post-construction termite control was prohibited by the end of 2005 with a successive phasing out over the years. This may have decreased the frequency of exposure among the general

public. However, the presence of comparatively higher ECID levels during 2001-2002 than during 99-00 is inexplicable. The small time gap masked the trend of the exposure compared to the 1988-94 survey which has been carried out for seven consecutive years.

In the present study, it was assumed that all TCP excreted in urine was an outcome of exposure to chlorpyrifos. However TCP is also one of the main metabolites of chlorpyrifos methyl which is used as an insecticide in agriculture. The annual usage of chlorpyrifos methyl in the USA is much lower when compared to chlorpyrifos usage (chlorpyrifos: chlorpyrifos methyl ratio of 125:1; CDC, 2005). Therefore it can be assumed that chlorpyrifos methyl is unlikely to result in significant exposure in the general population.

ECID in pest control applicators

Chlorpyrifos exposure has been assessed in a group of pest control (termiticide) applicators in the Piedmont region of North Carolina, USA (Hines et al., 2001). A model assisted with measurements of chlorpyrifos in their breathing air samples and TCP levels in urine samples were used to assess the exposure. The participants included 35 volunteers between 18-54 years of age, representing a number of companies, who worked full time (8 hours a day and 5 days a week) as licensed applicators. The study was conducted in 1998 during a busy work period with workers treating crawl spaces in houses. The job included drilling and digging trenches or holes in concrete slabs, followed by a treatment with a flow of chlorpyrifos and covering the trenches and holes with mortar. The study describes all the job types carried out by the workers during the study period in detail, the details of

chlorpyrifos usage by duration, extent of treated area and the amounts and concentrations of chlorpyrifos in breathing air samples.

Hines et al. (2001) monitored the work pattern of the applicators along with the personal air samples for chlorpyrifos and urine for TCP, for a maximum of five days. The first morning void urine samples of each day, collected from the workers over five working days, were analysed for TCP and were presented as creatinine adjusted mean levels in the form of a graph. However, the TCP levels were not corrected for background exposure from sources other than those involving occupational exposure.

In this study, the TCP levels were converted to ECID (see Section 3.3.1) in order to assess occupational exposure compared to Guideline Values.

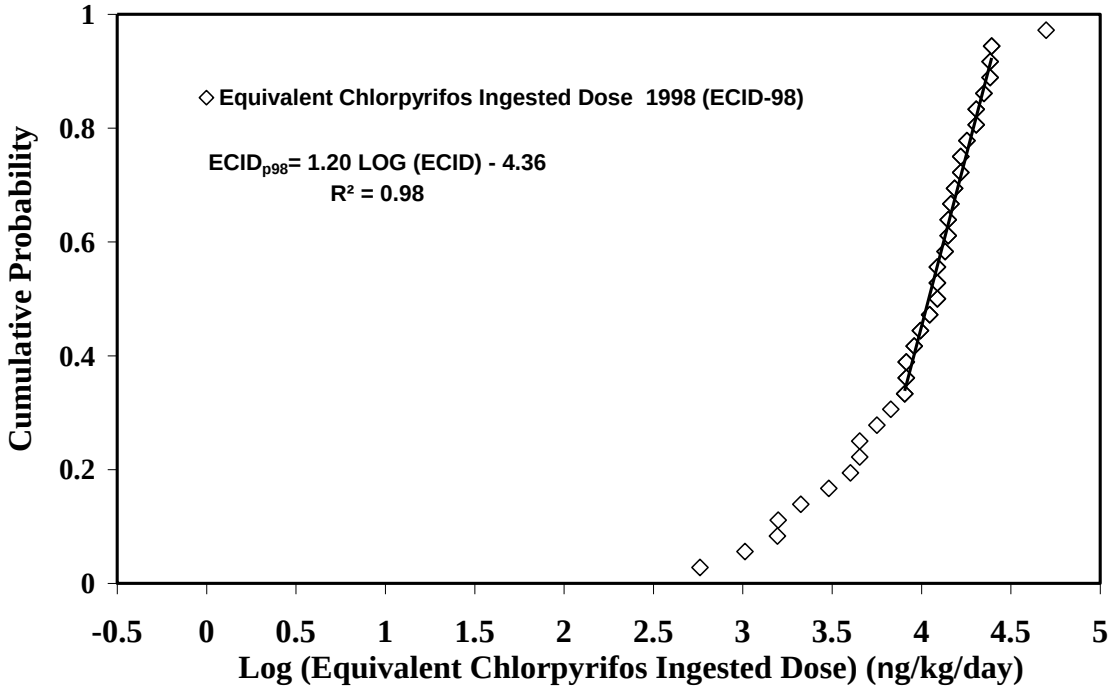

Figure 4.3.3 Equivalent Chlorpyrifos Ingested Doses (ECID) in US pest control applicators during 1998

The ECID levels were distributed between 580.0 ng/kg/day (2.8 on log scale; see Figure 4.3.3) and 50000.0 ng/kg/day (4.7 on log scale; see Figure 4.3.3). The maximum level observed was 86 times higher than the minimum. The slope of the dose distribution plot in the linear range was 1.2 (3.9 to 4.3 on log scale; see Figure 4.3.3). However, a broader distribution was observed below the linear range (2.7 to 3.8 on log scale; see Figure 4.3.3). The total exposure was assumed to be as a result of work-related chlorpyrifos exposure. The workers were in close contact with the application equipment which would possibly result in more exposure (Hines et al., 2001). However, each of the applicators differed in the nature of their application activities in terms of protective measures taken, the duration spent applying chlorpyrifos and the volumes of chlorpyrifos used. For example, many treated crawl spaces, while others treated basements or slabs. Also, some used gloves, respirators, boots etc., while others had little protection.

Depending on these circumstances the exposure could vary from person to person, and this was was reflected in the ECID levels. In the study of Hines et al. (2001), the applicators were not examined for any baseline exposure. However, it has been revealed (Hill et al., 1995; Barr et al., 2005) in surveys carried out in the US during 1988-94 and 1999-2000 respectively, that 82% and 89% of the general population have reported the presence of urinary TCP, the biomarker of chlorpyrifos, representing baseline exposure. In this context, the post-application Equivalent Ingested Doses which were presented in Figure 4.3.3 are somewhat higher than the actual amounts.

ECID in manufacturing workers

The urinary TCP measurements were used to evaluate the impact of occupational chlorpyrifos exposure on ChE levels in workers at a chlorpyrifos manufacturing company in USA (Garabrant et al., 2008). ChE levels in blood were analysed together with TCP levels in morning void urine obtained from the workers on four occasions between 1999 and 2000 (one sampling during September-November in 1999, one sampling during March-May in 2000 and two samplings during September-November in 2000). The sampling seasons resembled characteristics of the work carried out by the workers. For example, the period from March to May was considered to provide exposure data from sources outside the work place, such as agriculture, and was considered to be a non-occupational situation. One of the samplings during September to November in 2000 involved a maintenance period in the factory which was assumed to provide unusual exposure. The exposures at two other sampling periods from September to November in 1999 and 2000 were not discussed in detail by the authors, but were described as exposure during non maintenance work, therefore assumed as periods of occupational exposure. The individual TCP levels, corrected for the daily creatinine excretion were not reported. The data in the monitoring periods was reported for the $5^{th,}$ 50^{th} and 95^{th} percentiles.

These TCP levels were converted to the ECID levels (see Section 3.3.1) and are presented in Table 4.3.2 and Figure 4.3.4. The ECIDs, in each of the sampling periods were represented by 50 to 53 workers. The ECID levels in the workers during different sampling periods varied at the 0.05, 0.50 and 0.95 probability levels within the ranges of 1.5×10^2 to

2.9 x 10^2 ng/kg/day, 1.1 x 10^3 to 1.7 x 10^3 ng/kg/day and 1.0 x 10^4 to 2.1 x 10^5 ng/kg/day respectively. Thus, a considerable difference in the levels can be seen at the 0.95 probability level. The highest ECID was observed in the period of exposure involving factory maintenance work ($ECID_{MWE00}$ 210000 ng/kg/day or 5.3 on log scale; see Table 4.3.2 and Figure 4.3.4). This was 21 times higher than the lowest ECID observed at the same probability level. Also in this period, an increase in the ECID levels was observed from the 0.50 to the 0.95 probability level (120 times), compared to the differences in the other periods (the largest difference was 19 times). This may be due to the type of activities that could be expected, such as cleaning and repairing of machines which may have exposed the workers to highly contaminated environments.

Table 4.3.2 Equivalent Chlorpyrifos Ingested Doses (ECID in ng/kg/day) in US Manufacturing Workers

Sampling Period	0.05 Cumulative Probability Level	0.50 Cumulative Probability Level	0.95 Cumulative Probability Level
Occupational exposure 1999	200	1100	13000
Outside Occupational Exposure (2000)	150	1200	10000
Occupational exposure 2000	260	1500	29000
Exposure from factory maintenance Work (2000)	290	1700	210000

The lowest ECID at the 0.95 probability level was estimated in the period of exposure from sources outside the occupational environment ($ECID_{OOE00}$10000 ng/kg/day or 4.0 on log scale; see Table 4.3.2 and Figure 4.3.4). However, the ECID levels at the 0.05, 0.50 and 0.95 probability levels did not reflect an additional exposure compared to the occupational exposure ($ECID_{OE99}$ and $ECID_{OE00}$; see Table 4.3.2 and Figure 4.3.4). Similar distribution patterns (slope 0.5) were observed in the periods of occupational exposure ($ECID_{OE99}$; see Table 4.3.2 and Figure 4.3.4) and from sources outside the occupational environment ($ECID_{OOE00}$; see Table 4.3.2 and Figure 4.3.4) and were not largely different from the occupational exposure period in 2000 ($ECID_{OEOO}$; slope 0.4; see Figure 4.3.4). Overall, the ECID levels indicate that exposure at the higher probability levels (Ex: 0.95 level) during the maintenance period increased markedly over levels during the other periods.

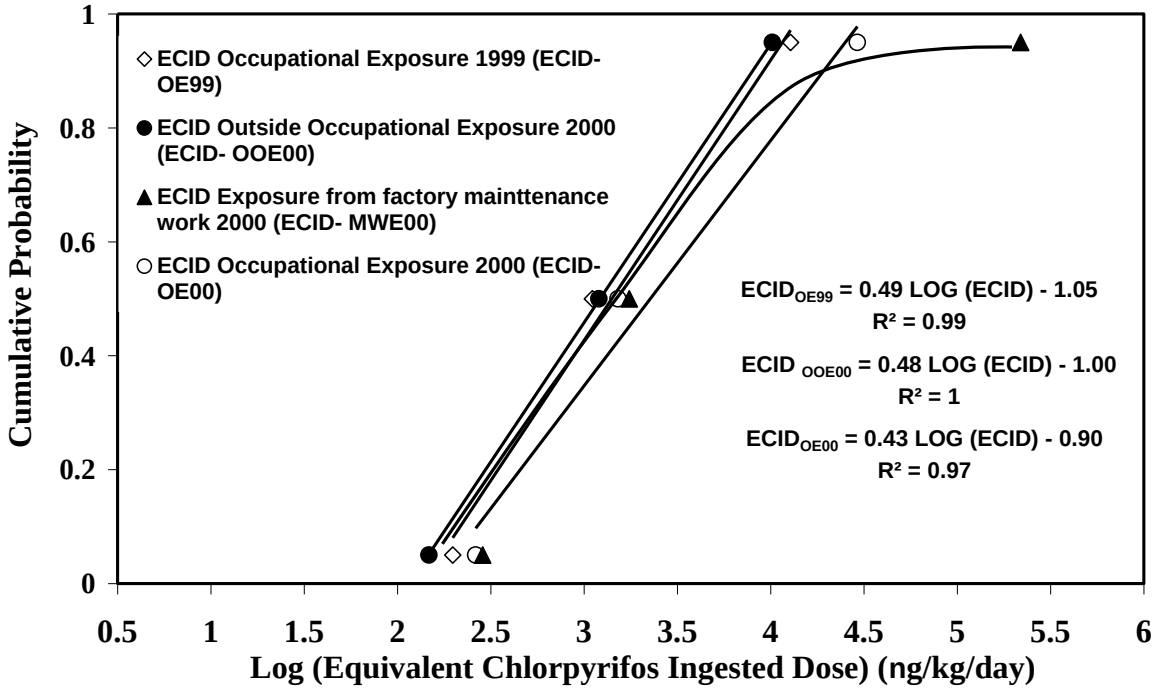

Figure 4.3.4 Equivalent Chlorpyrifos Ingested Doses (ECID) in US Manufacturing Workers during 1999 to 2000

ECID in pregnant mothers

Maternal exposure to pesticides has been assessed in healthy pregnant mothers registered at maternity clinics at Mount Sinai Hospital in New York from 1998 to 2001 (Berkowitz et al., 2003). The mothers were recruited whilst in their early pregnancy period. Mothers with drug or alcohol addiction or pregnancy complications were not recruited for the study. The participants were a group of 365, between 20 and 30 years of age, with diverse differences in ethnicities and educational backgrounds.

They were administered a questionnaire based on environmental exposure to pesticides. Spot urine samples were obtained from the mothers during their last months of pregnancy for TCP analysis. Individual TCP levels were not reported. The creatinine adjusted TCP levels reported at 10^{th}, 25^{th}, 50^{th}, 75^{th} and the 90^{th} percentiles were converted to ECID levels (see Section 3.3.1) and are presented in Figure 4.3.5.

The Equivalent Ingested Doses were distributed in a wide range from 30 to 5200 ng/kg/day (1.5 to 3.7 on log scale; see Figure 4.3.5) with a slope of 0.4 (see Figure 4.3.5). At the 90% probability level, the highest dose was 170 fold higher than the lowest dose calculated at the 10% level of probability.

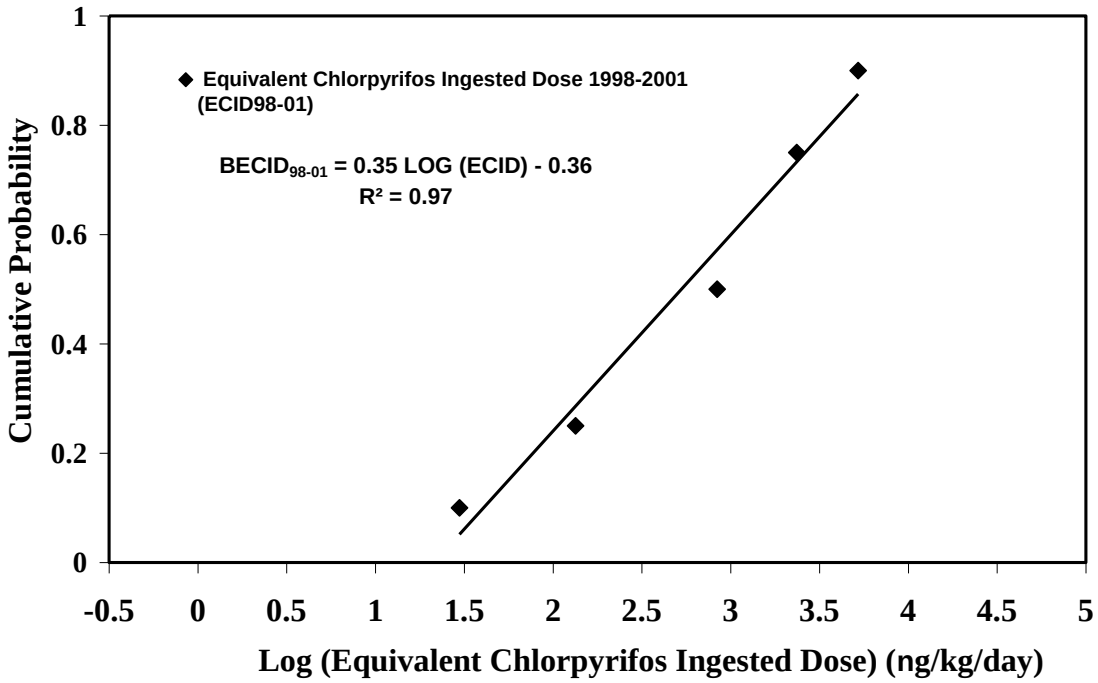

Figure 4.3.5 Equivalent Chlorpyrifos Ingested Doses (ECID) of Chlorpyrifos in US Pregnant Mothers during 1998 to 2001

Indoor pesticide usage was assumed to be the most common source of chlorpyrifos exposure, according to a questionnaire answered by participants (Berkowitz et al., 2003). Indoor pesticide usage in bait traps, can sprays, gels, boric acid, sticky traps and pest bombs was reported by 72% of the 365 mothers. At other times, pesticide treatment was carried out by another household member, an exterminator, building staff member or a fumigator. Although the group of pesticides used were not mentioned, the study focus was mainly on chlorpyrifos usage. It was revealed that the more highly educated (at least high school education) mothers had the highest TCP levels in their urine samples. However, none of the other socio-demographic factors had any consistent relationship with TCP level. In addition, the study objectives were directed to indoor pesticide exposure and therefore the

potential exposure from other sources such as diet, work place and the outdoor environment was not assessed.

Overview of chlorpyrifos exposure in the US population

The ECID levels in the USA varied in a range from 600 to 210000 ng/kg/day at the 0.95 level of cumulative probability (see Table 4.3.3). The lowest levels were observed in adults from the general population who were reported to have non-occupational exposure. The highest dose represented an unusual exposure situation to an occupational environment, in manufacturing workers. Other occupational exposure situations, such as farmaing and pest control application yielded levels between these dose levels.

The exposure levels in the manufacturing workers in normal working environments were comparable with those of the farmers. Applicators showed higher ECIDs than those in the farmers reflecting their greater involvement with continuous activities related to pesticides. Pregnant mothers showed higher dose levels than those observed in general adults, suggesting an unusually higher exposure, from a non-occupational environment. However the physiological changes that may occur during pregnancy may also have an effect on the rate of creatinine excretion in pregnant mothers and, if so, could affect the creatinine adjustment of the chlorpyrifos biomarker (TCP). The distribution patterns of the exposure are described by the slopes, intercept and the linear correlation coefficient values of the plots (see Table 4.3.3).

Table 4.3.3 Equivalent Chlorpyrifos Ingested Doses (ECID in ng/kg/day) in US populations

Population	0.95 Cumulative Probability	ECID distribution plot*		
		Slope	Intercept	R^2
Farmers (2000-01)	8400.0	0.7	-1.7	0.95
General adults				
1988-94	600.0	0.9	-1.4	0.97
1999-00	500.0	0.8	-1.1	0.96
2000-01	600.0	0.7	-0.9	0.98
Pest control applicators (1998)	26000.0	1.2	-4.3	0.98
Manufacturing workers (1999-00)				
Low exposure	10000.0	0.5	-1.0	1.0
High exposure	210000.0	N/A	N/A	N/A
Pregnant mothers (1998-2001)	5000.0	0.4	-0.4	0.97

*(ECID) = (slope) (log ECID) + intercept; N/A –Not Available

4.3.2 Equivalent Chlorpyrifos Ingested Doses (ECID) with general adult population in Europe

ECID in the Italian general adult population

Aprea et al. (1999) assessed TCP levels in a group of 42 Italian adults in relation to their food habits. The study objectives were to provide a picture of pesticide exposure via the pathways of wine drinking and food intake among the general population. The study assumed that TCP could result from exposure to chlorpyrifos, chlorpyrifos methyl or TCP as a degradation product in the environment. A low amount of TCP (up to 14% w/w) could be present in commercial chlorpyrifos formulations (Aprea et al., 1999). However, the

statistics of the amounts of chlorpyrifos and chlorpyrifos methyl usage in Italy were not given.

The participants were healthy males and females in the aged between 20 and 60 years, from the Pavia, Siena and Trento regions in Italy and had no reported history of chlorpyrifos exposure. As a rule of the study, they were not supposed to exceed consumption of more than 250 mL wine orsmoke more than 5 cigarettes a day. It was assumed that exceeding this level of alcohol consumption would affect the regulation of enzymes in the human body. High smoking was considered to increase the exposure from the residues left in treated tobacco.

Spot urine samples were obtained from the 42 participants during 1997 and were analysed for TCP. TCP was detected in 88% of the participants, including all the men (21) and wine drinkers (17) in the study population. The creatinine adjusted TCP concentrations were presented as classes (ranges) in the form of a bar chart.

The ECID levels calculated from the mean TCP levels (see Section 3.3.1) are presented in Figure 4.3.6. It was assumed that the exposure from other sources was negligible with respect to the TCP levels present in the participants. The levels were distributed in a range from 120 ng/kg/day (2.1 on log scale; see Figure 4.3.6) to 900 ng/kg/day (3.0 on log scale; see Figure 4.3.6) with a slope of 0.7. The mean level was 260 ng/kg/day (2.4 on log scale).

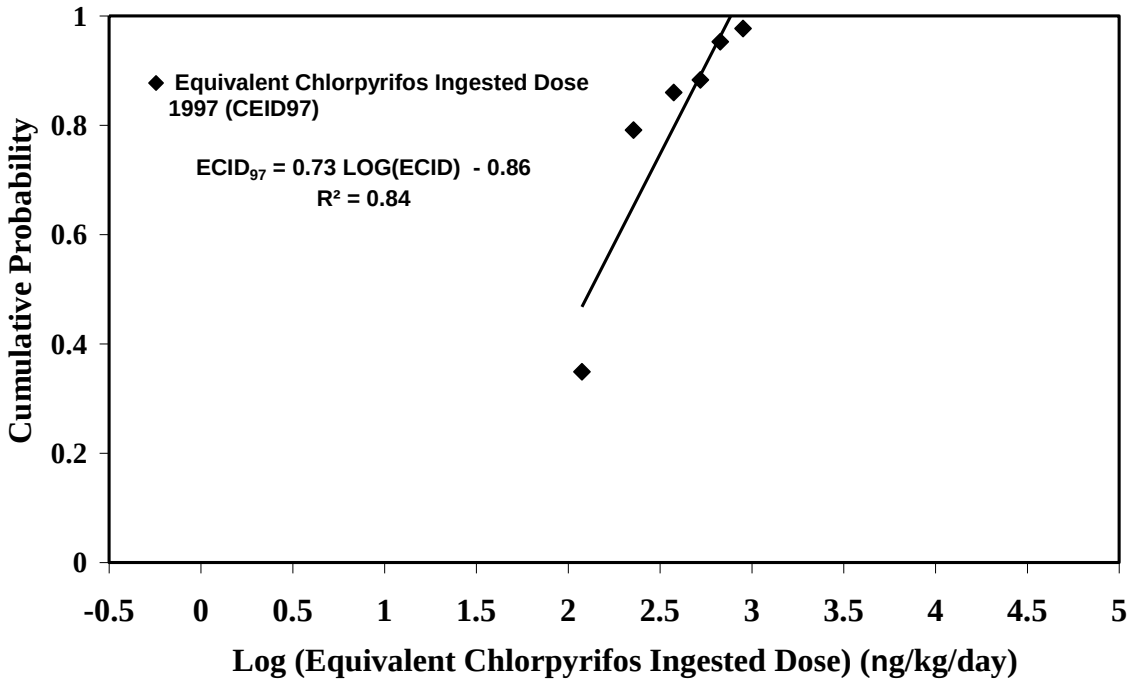

Figure 4.3.6 Equivalent Chlorpyrifos Ingested Doses (ECID) in Italian General Population during 1997

It is noteworthy that the ECID levels in Figure 4.3.6 were calculated from the mean values of the reported TCP classes.

A similar study was carried out by Saieva et al. (2004) with 69 participants from two other regions (Florence and Ragusa) in Italy during 1998 (the ECID levels are not presented in the graphs). The participants, who had no history of chlorpyrifos exposure, supplied 24 hour urine samples for the TCP analysis. The minimum, maximum and mean creatinine adjusted TCP levels were reported in the study. The respective ECID levels for the minimum, maximum and mean TCP levels were 60 ng/kg/day, 1300 ng/kg/day and 270 ng/kg/day (1.8, 3.1 and 2.4 on log scale- data not plotted). These levels are comparable with the ECIDs calculated for the participants in the study of Aprea et al. (1999) (see Figure 4.3.6).

In both studies, it was suggested that exposure most likely occured via the dietary intake pathway. In addition, Aprea et al. (1999) revealed that wine drinking had a significant effect on TCP levels in urine, which also was reflected in the ECID levels. Saieva et al. (2004) found a relationship between smoking and high TCP levels in the study group. However, none of the studies suggest exposure via indoor treatments, since it was less likely to be practiced in Italy.

ECID in the German general adult population

Koch et al. (2001) assessed TCP levels in the urine of 50 general adults in Meklenburg-Vorpommern in Germany. It was assumed that the TCP levels resulted from the intake of food treated with chlorpyrifos and chlorpyrifos methyl pesticides. However, the statistical details of the usage of these pesticides in Germany were not revealed. The year of the study was not reported. The participants, who supplied spontaneous urine samples for the analysis, were men and women aged 22 to 57 years, and had never been occupationally exposed to organophosphates. In the study, all the urine samples contained TCP. The creatinine adjusted minimum and maximum TCP levels together with the levels for the median and 95^{th} percentile were reported.

The TCP levels were converted to ECID and assumed that exposure from sources other than chlorpyrifos was negligible (see Section 3.3.1). The respective ECID levels are presented in Figure 4.3.7. They ranged from 0.8 to 2100 ng/kg/day (0.9 to 3.3 on log scale; see Figure 4.3.7) with a slope of 0.4. The mean dose was 160 ng/kg/day (2.2 on log scale).

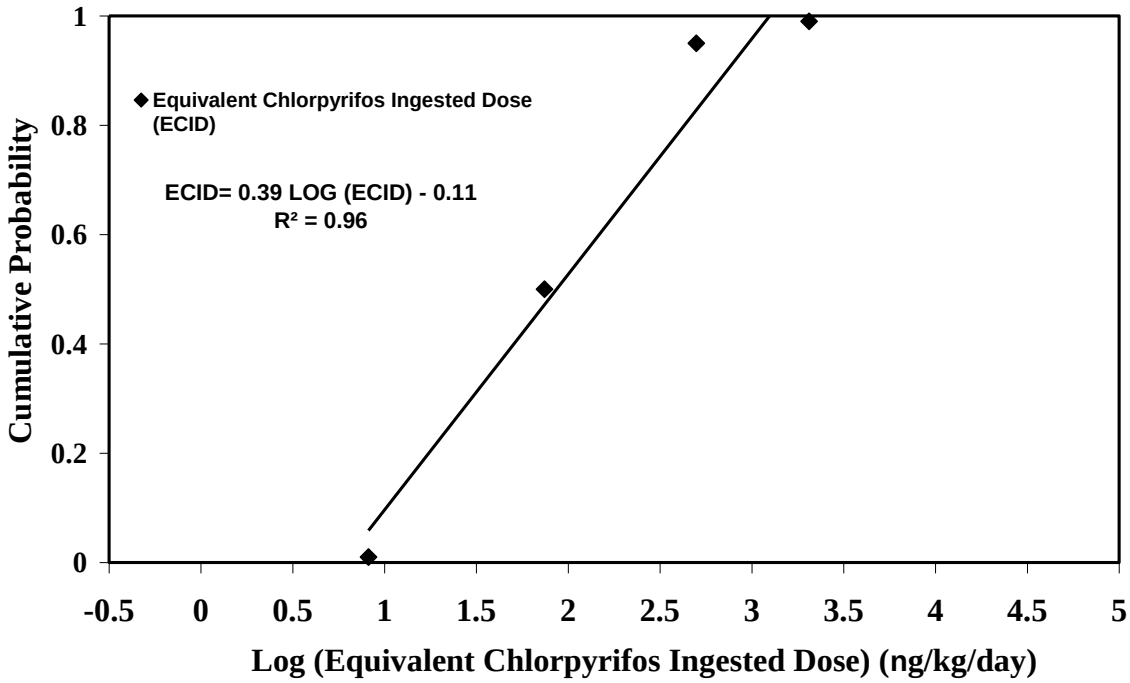

Figure 4.3.7 Equivalent Chlorpyrifos Ingested Doses (ECID) in German General Population (published in 2001)

4.3.3 Equivalent Chlorpyrifos Ingested Doses (ECID) in Australian pest control applicators

A survey was conducted during 1998 and 1999 to evaluate work place exposure to chlorpyrifos in a group of pesticide workers around Perth in Australia (Cattani, 2004). The participants represented 10% of the termite control work force in Western Australia, were from a number of licensed pest control companies and had volunteered for the survey. Some of the workers used chlorpyrifos and bifenthrin for termite control purposes, while the others used only chlorpyrifos. All were involved in pre-construction, post-construction or under-floor treatments of buildings with similar operating equipment. A questionnaire was administered to the workers to assess their background knowledge in relation to protective measures, work practices and health condition.

Chorpyrifos levels were measured in breathing air and surface wipe samples, together with urinary TCP and blood ChE levels. The urine samples were collected from nineteen workers before and after a chlorpyrifos application event and were analysed for TCP. TCP levels for individual applicators were not reported. The creatinine adjusted TCP concentrations were reported for the minimum, maximum, median, 75^{th} and the 95^{th} percentiles in thirteen workers. However, the levels were not different between the pre- and post-application samples.

The post-application TCP levels were converted to ECID levels (see Section 3.3.1) and are presented in the Figure 4.3.8. The levels ranged from 1100 to 37000 ng/kg/day (3.0 to 4.6 on log scale; see Figure 4.3.8) with a slope of 0.4. The highest estimated ECID was 33 times greater than the lowest.

The ECID levels represented 5% of the termite control work force in Western Australia although 10% participated in the survey. Most of the workers were reported to be ineffective at protecting themselves from exposure to chlorpyrifos, resulting high levels of exposure. Most of them were reported to spill or splash the insecticide at work. Some of them were reported to eat or smoke while at work, with contaminated clothes and gloves on, even without washing themselves.

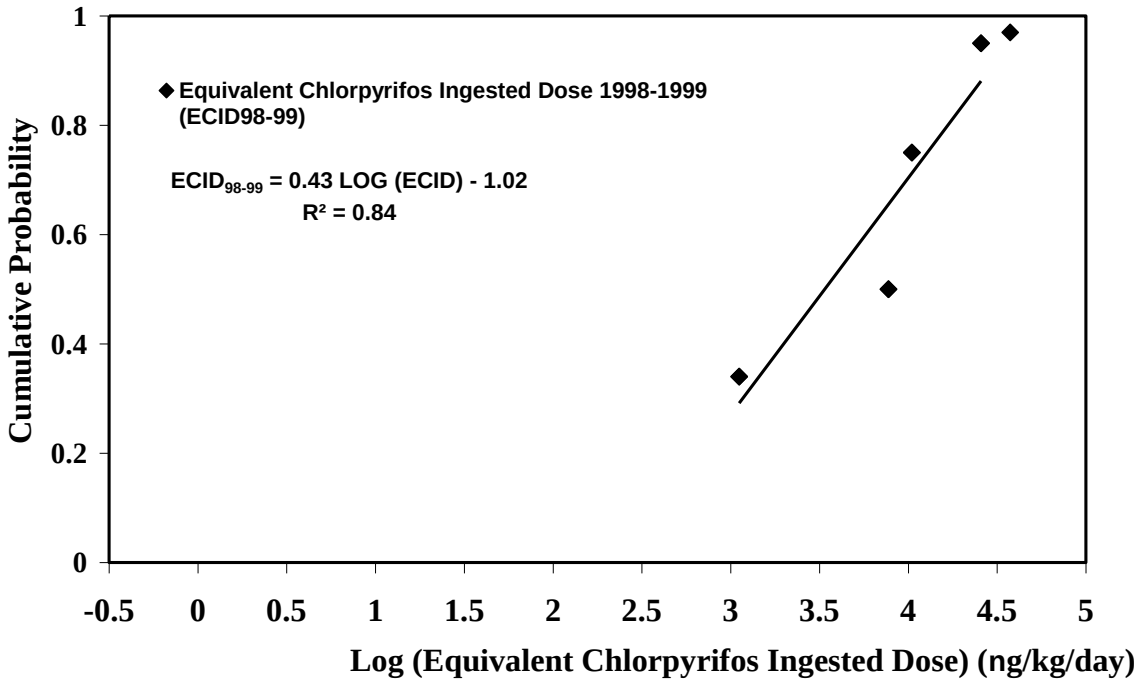

Figure 4.3.8 Equivalent Chlorpyrifos Ingested Doses (ECID) in Australian pest control applicators during 1998 to1999

4.3.4 Equivalent Chlorpyrifos Ingested Doses (ECID) in Thai farmers and children

ECID in farmers

A total of 136 farmers from two Thai farming communities participated in a pesticide exposure evaluation study during a farming season in 2006 (Panuwet et al., 2008). They were males between the ages of 20 to 65 years from the Pong Yaeng (67 participants) and Inthakhin (69 participants) regions in Chaing Mai province. They were known to work every day on the farm, which may have lead to a steady state excretion of pesticides or metabolites in their urine as a result of the associated exposure.

The farming areas were located apart from one another but both communities were engaged in mixed crop cultivation. However, some differences were observed in the selection of crops and pesticides. A number of pesticides were used during the three months prior to the study, with chlorpyrifos being one of the most frequently used by Pong Yaeng farmers. All the farmers applied pesticides by themselves with motor pumps and back pack hand pumps.

The farmers were administered a questionnaire on personal details, farming practices, experience and pesticide usage, followed by a urine collection. A morning void urine sample was collected from each farmer during the study period, which was then subjected to TCP analysis. The creatinine adjusted TCP concentrations were reported for the maximum, 25^{th}, 50^{th}, 75^{th} and the 95^{th} percentiles separately for both farming groups and for all the farmers participating in the study. In total, about 77 % of the farmers reported detectable TCP. The TCP levels were converted into ECIDs (see Secction 3.3.1) and are presented in Table 4.3.4 and Figure 4.3.9.

Table 4.3.4 Equivalent Chlorpyrifos Ingested Doses (ECID in ng/kg/day) in Thai Farmer Groups

Cumulative Probability	Pong Yaeng farmers	Inthakhin farmers	Total farmers
0.25	-	20.0	20.0
0.50	70.0	40.0	50.0
0.75	200	100	130
0.95	700	1300	800
Maximum	1800	4600	4600

The ECID in Pong Yaeng and Inthakhin farmers ranged from 70.0 to 1800 ng/kg/day (1.9 to 3.3 on log scale; see Figure 4.3.9) and 20.0 to 4600 ng/kg/day (1.2 to 3.7 on log scale; see Figure 4.3.9). The respective slopes of the plots are 0.5 and 0.4 showing a comparatively wider distribution of doses among the Inthakhin farmers. At the 0.95 cumulative probability level, the farmers from Inthakhin region showed higher levels of ECID than the farmers from Pong Yaeng.

Chlorpyrifos was one of the frequently used pesticides by Pong Yaeng farmers (72%) within the 3 months prior to the study, but was not used frequently by Inthakhin farmers (81%). Nonetheless, it was reported that the differences in the TCP concentrations among the two groups were not significant. This indicates both farmers were exposed to chlorpyrifos either from their working environment or from non-occupational sources such as diet.

Panuwet et al. (2008) reported that the cropping pattern selected by the farmer has an influence on exposure, since the farmers involved in single crop farming were observed to have significantly higher exposure, compared to farmers involved in multiple crop farming. However, this is reasonable if only a single crop situation consumes more chlorpyrifos, than a number of crops cultivated in a similar extent of land area. Also it was suggested that higher exposure levels in the farmers may have resulted from their spray schedules.

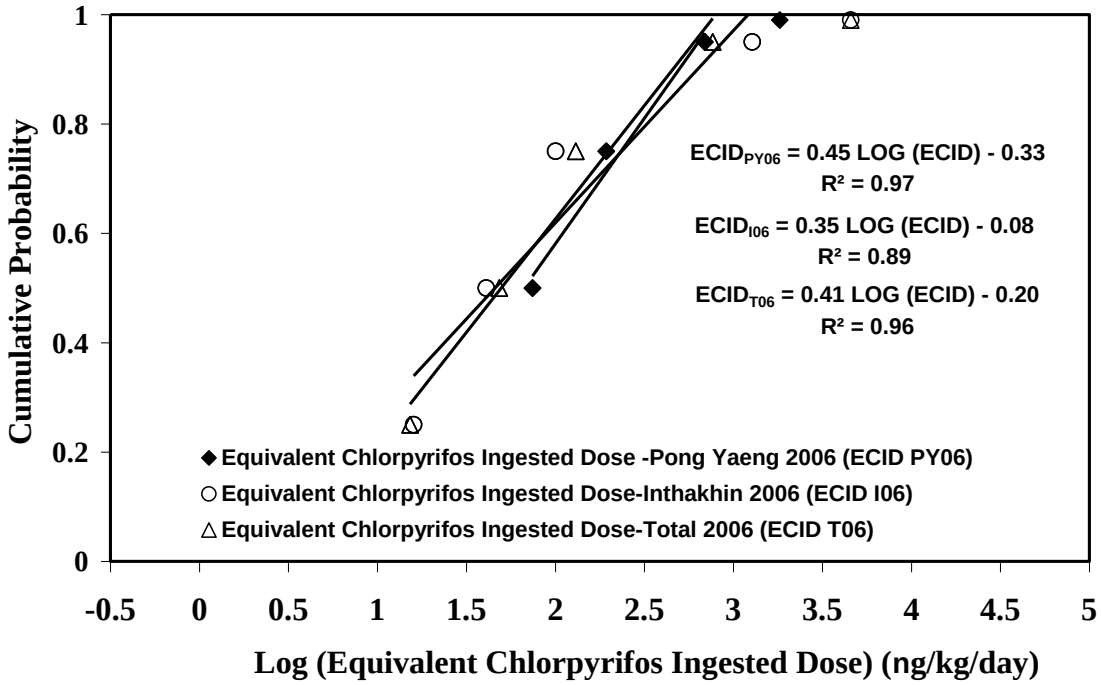

Figure 4.3.9 Equivalent Chlorpyrifos Ingested Doses (ECID) in Thai Farmers during 2006

ECID in children

Panuwet et al., (2009) evaluated the urine samples of a group of Thai school children for certain pesticide metabolites, considering the higher potential of exposure due to the heavy use of pesticides in Thailand. The year of the study was not reported. The children were selected from a school in Chiang Mai province, where they represented a higher geographic and socioeconomic profile prevailing in the society. They were aged between 12 to 13 years and were identified as having either agricultural or non-agricultural family backgrounds.

The first morning void urine samples were collected from 207 children and were analysed for TCP. 92% of the students reported urinary TCP. The creatinine adjusted TCP levels were reported for the minimum, maximum, median and the 95th percentile. In the present study, TCP levels were converted to ECIDs (see Section 3.3.1) and are presented in Figure 4.3.10.

The ECIDs ranged from 30.0 to 1800 ng/kg/day (1.4 to 3.2 on log scale; see Figure 4.3.10) with a mean of 170 ng/kg/day (2.2 on log scale; see Figure 4.3.10). The slope of the dose distribution plot was 0.5. The students having the highest ECID (1800 ng/kg/day, see Figure 4.3.10) were from an agricultural background.

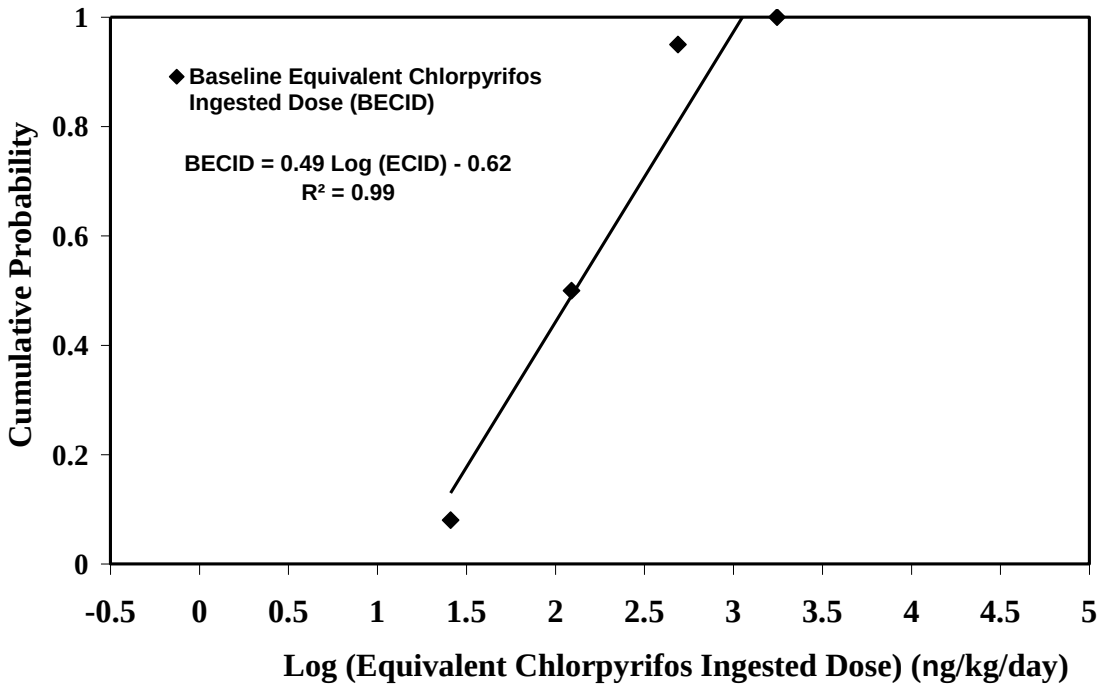

Figure 4.3.10 Equivalent Chlorpyrifos Ingested Doses (ECID) in Thai Children from Panuwet et al., (2009)

Parental occupations were examined in the study of Panuwet et al. (2009) with respect to chlorpyrifos exposure in children, since exposure is likely to be associated with , parental occupational environments especially agriculture. The parents of the children were identified as farmers, traders, labourers and office employees. According to Panuwet et al. (2009), there is no significant difference in mean urinary TCP levels and hence in mean chlorpyrifos exposure between children from agricultural and non-agricultural families. The reported higher proportion (92%) of chlorpyrifos exposure reported among the children shows that an agricultural background is not the dominant pathway of exposure. Furthermore, dietary exposure was assumed to be a major pathway of exposure, with chlorpyrifos being monitored frequently in dietary components in Thailand (Panuwet et al., 2009).

4.3.5 Dietary exposure to organophosphates in India

Organophosphate residues in food commodities

Chlorpyrifos residues have been reported in rice, vegetables and water in Hisar, Jaipur, Delhi, Assam, Ludhiana, Tamilnadu, Kanpur, Gujrat and Punjab in India (Kumari et al., 2004; Kumari et al., 2003; Mukherjee et al., 2003; Chalal et al., 1997; Singh et al., 2002; Deka et al., 2004). The majority of studies were part of the programme of the All India Coordinated Research Project (AICRP) on Pesticide Residues. All the studies were carried out from 1994 to 2002.

Since there were many non-detected results reported, the chlorpyrifos levels are presented in Table 4.3.5 together with the number detected, for comparison with chlorpyrifos levels detected in food commodities in Sri Lanka. Table 4.3.6 presents the residue range of chlorpyrifos detected in water bodies in India. None of this reported data presented the individual residue levels in crops, but instead reported the minimum and maximum levels or average values (see Tables 4.3.5 and 4.5.6). Therefore probability plots were developed using only minimum and maximum residue levels given in Tables 4.3.5 and 4.3.6 and the marker points in Figure 4.3.11 represent the corresponding log values. Lower cut off levels of the probability plots can be seen due to the unavailability of residue detections below the minimum detection limits.

Chlorpyrifos in rice and vegetables varied between 4.0×10^2 and 1.0×10^6 ng/kg (see Table 4.3.5). One of the possible reasons for such variation is the different usage patterns of pesticides in different sampling areas throughout India. When and whether the pesticides were sprayed are important factors of usage patterns. Also, the analytical differences and different LODs contribute to variations in strengths and frequencies of detections, to some extent. The climatic differences prevailing during the pesticide application periods may also have contributed. The vegetables were reported to have been collected from a number of regions all over in India, with some of them grown in winter (Kumari et al., 2003) while others were grown in semi-arid (Singh et al., 2002) or sunny (Singh et al., 2003) conditions. Pesticide usage in different areas could vary with concentrations and frequencies of application. Moreover, climatic conditions such as rain, wintry or sunny weather could affect the persistence of residues in vegetables. For example, rain can, to some extent, wash pesticides off the surface of the crop, while sunny weather could possibly reduce the

residue content by evaporation. The different analytical methods and the sensitivity of analytical equipment could also vary the detection levels.

Table 4.3.5 Chlorpyrifos Residues in Rice and Vegetables in India

Diet component (Number detected/ Number analysed)	Minimum (10^3 ng/kg)	Maximum (10^3 ng/kg)	Maximum Residue Limit (MRL) 10^3 (ng/kg)	Reference
Rice (10/23)	5	20	500*	Deka et al., (2004); Singh et al., (2003)
Cauliflower (21/50)	1	45	50*;200**	Kumari et al., (2004); Mukherjee et al., (2003); Kumari et al., (2003); Chalal et al., (1997)
Cabbage (18/33)	6	120	1000*$^{+}$; 200**	Kumari et al., (2004); Mukherjee et al., (2003); Kumari et al., (2003); Chalal et al., (1997)
Tomato (32/72)	6	200	500* 200**	Kumari et al., (2002); Singh et al., (2002); Kumari et al., (2003); Mukherjee et al., (2003); Chalal et al., (1997)
Okra (11/33)	20	40	200**	Kumari et al., (2003); Singh et al., (2002); Mukherjee et al., (2003); Chalal et al., (1997)
Egg plant (17/58)	0.4	38	200**	Chalal et al., (1997); Kumari et al., (2002); Kumari et al., (2003)
Potato (7/12)	10	101	2000*	Kumari et al., (2003); Kumari et al., (2004)
Bittergourd (26/34)	5	40	200**	Kumari et al., (2002); Singh et al., (2002)
Cucumber (14/22)	7	1000	200**	Kumari et al., (2002); Singh et al. , (2002)

*Codex Alimentarius MRL (FAO, 2009); $^{+}$ USEPA tolerance (USEPA, 2008); ** MRL in India (Agnihotri, 1999 cited in Mukherjee, 2002)

The residue concentrations exceeded the Maximum Residue Limits (MRL) in none of the vegetables, except cucumber (See Table 4.3.5). The detected levels of chlorpyrifos in water did not exceed the Guideline Values (See Table 4.2.6).

Table 4.3.6 Chlorpyrifos Residues in Water Sources in India

Dietary component	Range (ng/L)	Reference	Guideline Value (ng/L)
Water (tube wells, open wells, lakes)	420-6870	Singh et al., 2002	30000*

*WHO, 2004; *Note: The number of detections was not reported*

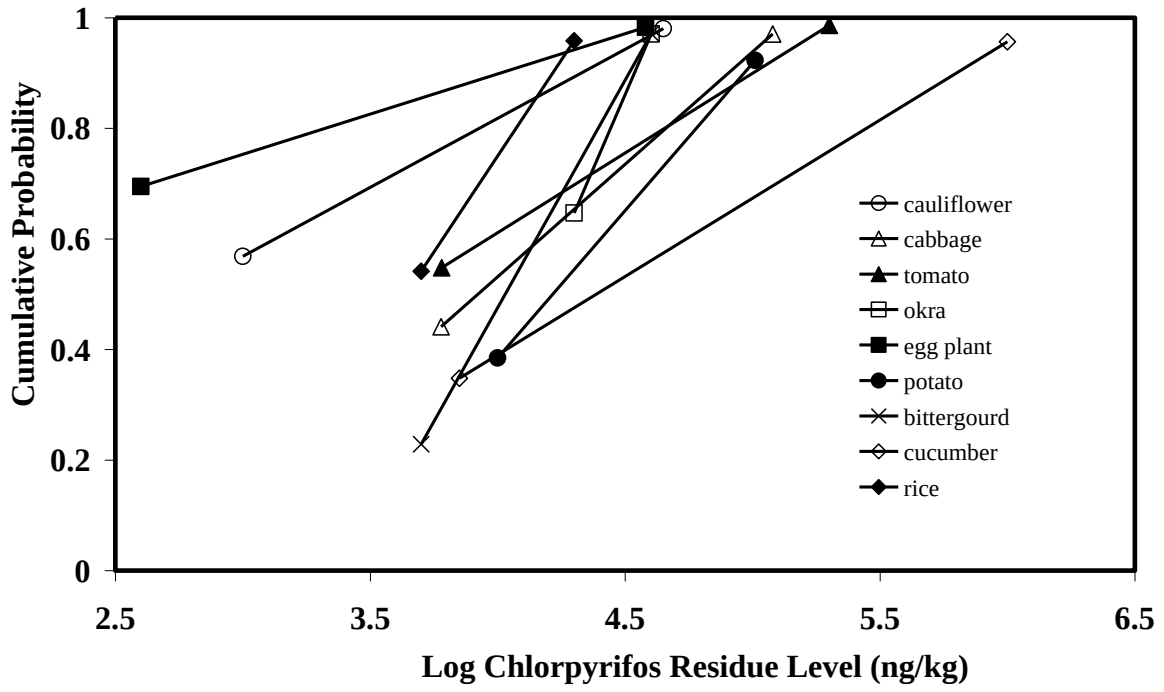

Figure 4.3.11 Chlorpyrifos Residues in rice and vegetables in India

Note: The marker points in probability plots represent reported minimum and maximum levels of residues in each food commodity

Among the other organophosphates, monocrotophos, quinalphos, malathion and dimethoate were frequently reported in India (see Table 4.3.7; Kumari et al., 2002; Kumari et al., 2001; Singh et al., 2002; Parihar et al., 1997; Shah et al., 2000; Gupta et al., 1998; Kumari et al., 2002b; Chalal et al., 1997; Mukherjee et al., 2002).

The organophosphates listed in Table 4.3.7 were reported from Hisar, Jaipur, Delhi, Assam, Ludhiana, Tamilnadu, Kanpur, Gujrat and Punjab in India. The studies were part of the All India Coordinated Research Project (AICRP) on pesticide residues. The detections were reported most frequently in egg plants, cauliflower, okra, tomato and cabbage. Individual residue levels in the crops were not reported, but were reported as minimum and maximum values. All the pesticides varied in a comparable range from 2×10^3 to 2×10^6 ng/kg (see Table 4.3.7). The same reasons discussed in the variation of chlorpyrifos levels (see Section 4.3.5), such as differences in the characteristics of pesticide application, including recommended rates, frequency and time of application, climatic changes in the crop growing areas and analytical differences of the residues, can be expected to vary the residue levels in these pesticides listed in Table 4.3.7.

Table 4.3.7 Monocrotophos, Quinalphos, Malathion and Dimethoate Residues in Vegetables in India

Pesticide	Vegetable (No. contaminated/ No. analysed)	Detection Range (10^3 ng/kg)	Reference
Monocrotophos	Egg plant (50/188)	19-900	Kumari et al., (2003); Kumari et al., (2002); Singh et al., (2002);Parihar et al., (1997); Shah et al., (2000)
	Okra (30/45)	33-851	Kumari et al., (2003); Kumari et al., (2002); Shah et al., (2000)
	Cauliflower (25/105)	5-1500	Kumari et al., (2002); Kumari et al., (2003); Gupta et al., (1998); Shah et al., (2000); Chalal et al., (1997)
	Tomato (28/57)	33-247	Kumari et al., (2001); Singh et al.,2002; Kumari et al., (2004); Shah et al., (2000)
	Cabbage (13/61)	48-1700	Kumari et al., (2003); Gupta et al., 1998; Shah et al., (2000); Chalal et al., (1997)
Malathion	Egg plant (12/122)	8-2000	Kumari et al., (2002); Mukherjee et al., (2002); Kumari et al., (2004); Parihar et al., (1997)
	Cauliflower (5/17)	16-60	Mukherjee et al., (2002); Kumari et al., (2003)
	Okra (22/49)	103-249	Kumari et al., (2002); Kumari et al., (2004); Mukherjee et al., (2002); Chalal et al., (1997)
	Tomato (4/32)	30-70	Mukherjee et al., (2002); Chalal et al., (1997)
	Cabbage (7/23)	7-590	Mukherjee et al., (2002); Kumari et al., (2002); Chalal et al., (1997)
Quinalphos	Brinjal (39/236)	3-1100	Kumari et al., (2002); Kumari et al., (2003); Singh et al., (2002); Kumari et al., (2004); Parihar et al., (1997); Shah et al., (2000); Chalal et al., (1997)
	Cauliflower (22/112)	7-178	Kumari et al., (2002); Mukherjee et al., (2003); Kumari et al., (2004); Gupta et al., (1998); Shah et al., (2000); Chalal et al., (1997)
	Okra (3/27)	6-99	Shah et al., (2000); Chalal et al., (1997)
	Tomato (7/42)	9-104	Mukherjee et al., (2002); Kumari et al., (2002); Chalal et al., (1997)

	Cabbage (12/52)	18-2000	Singh et al., (2002); Mukherjee et al., (2002); Gupta et al., (1998); Shah et al., (2000)
Dimethoate	Cauliflower (12/42)	99-107	Kumari et al., (2002); Shah et al., (2000)
	Brinjal (16/141)	25-1500	Kumari et al., (2002); Parihar et al., (1997); Shah et al., (2000)
	Tomato (7/25)	2-52	Kumari et al., (2002); Shah et al., (2000)
	Cabbage (10/58)	29-1200	Kumari et al., (2002); Gupta et al., (1998); Shah et al., (2000)

Dietary Chlorpyrifos Intake (DCI) and Total Dietary Chlorpyrifos Intake (TDCI)

The minimum and maximum levels of chlorpyrifos residues in dietary components of an average person in India (see Table 4.3.5) were converted to Dietary Chlorpyrifos Intakes (DCI) in ng/kg/day (see Section 3.3.3). In the absence of published work on the consumption rates of the food items considered, it was assumed that the per capita food consumption rates in India were similar to those of Sri Lanka. Furthermore, rice and vegetables are staple food items in India (Deka et al., 2004; Mukherjee, 2003) resembling a similar situation to Sri Lanka.

The adopted daily food consumption rates were converted from the monthly per capita consumption rates (see Section 3.3.3) and are given in Table 4.3.8. Since the number of residue detections in water was not reported (see Table 4.3.6), data was not used for the estimation of DCI due to the difficulty in assigning probability levels. The estimated DCI from each diet component is presented in Table 4.3.8 and Figure 4.3.12. They are the corresponding levels of chlorpyrifos residues presented in Figure 4.3.11. The DCIs ranged in from 0.1 to 140.0 ng/kg/day (-1.0 to 2.1 on log scale). The highest maximum DCI was

observed in cucumber despite its low consumption rate (see Table 4.3.8). This is a result of its higher level of residue detections (see Table 4.3.5). Although the consumption rate of rice was high compared to cucumber (see Table 4.3.8) the comparatively low level of residue detections has resulted in a lower maximum DCI in rice (Maximum DCI in rice and cucumber in Table 4.3.8). The DCIs in all other vegetables ranged from 10^{-1} to 10^{0} ng/kg/day (see Table 4.3.8) which was lower than the DCIs in cucumber and rice.

Table 4.3.8 Dietary Chlorpyrifos Intake (DCI) in India

Dietary component	Amount in a diet of an average person per day(g)*	Dietary Chlorpyrifos Intake (DCI) (ng/kg/day)	
		Min	Max
Rice	300	20	90
Cabbage	10	1.0	20
Egg plant	10	0.1	5
Tomato	10	1.0	30
Okra	10	3.0	6
Potato	10	1.0	10
Biter gourd	10	0.1	6
Cucumber	10	1.0	140
Cauliflower	10	0.1	6

*Source: Consumer finances and socio-economic survey 2003/04 (Central Bank of Sri Lanka, 2005)

The Total Dietary Chlorpyrifos Intake (TDCI) for an average Indian person was calculated using the DCI levels in rice and vegetables (see Section 3.3.3). The trend line equations of each of the plots in Figure 4.3.12 were used to obtain the respective DCIs at 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 0.95 and 0.99 (see Section 3.3.3). The percentage contributions to TDCI from the DCIs in rice and vegetables at several probability levels are listed in Table 4.3.9. The TDCIs are presented in the Figure 4.3.13.

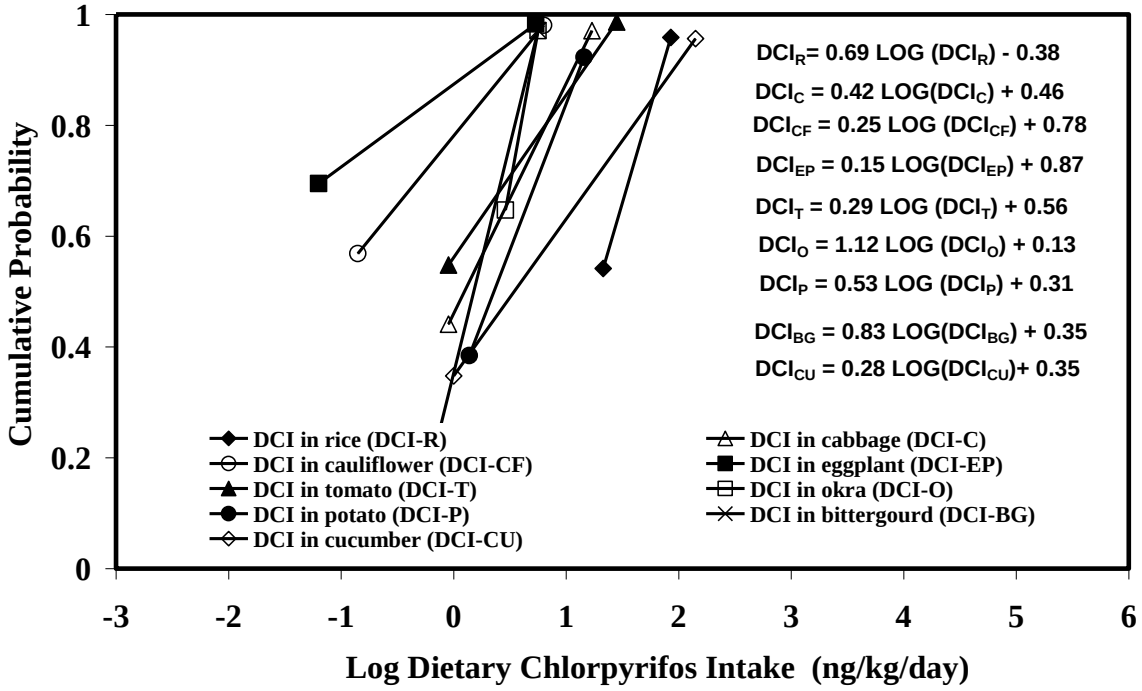

Figure 4.3.12 Dietary Chlorpyrifos Intake (DCI) in India

Note: The marker points in probability plots represent estimated minimum and maximum Dietary Intake levels in each food commodity

The TDCIs in India ranged from 7.0 ng/kg/day to 380.0 ng/kg/day (0.8 to 2.5 on log scale; see Figure 4.3.13). The DCI via water was not included in the calculation of TDCI due to unavailability of residue detection frequencies. TDCI in India were calculated in rice and

few vegetables assuming similar per capita daily consumption rates to Sri Lanka. The total weight of the considered diet was 380 g with only 80 g of it containing vegetables (see Table 4.3.8). However, it was reported that an average daily Indian diet contains 150 g to 250 g of vegetables (Mukherjee, 2003). Therefore it is expected that the average dietary exposure from a diest consisting of these vegetables (see Table 4.3.8) could be higher than what was calculated.

Table 4.3.9 Percent Contribution of Chlorpyrifos in the Diet Components to Total Dietary Chlorpyrifos Intake (TDCI)

Cumulative probability	% Contribution to Total Dietary Chlorpyrifos Intake (TDCI)	
	Rice	Vegetables
0.1	71.4 (5.0)	28.6 (2.0)
0.5	57.5 (18.6)	42.5 (13.7)
0.95	28.4 (83.2)	71.6 (208.9)
0.99	25.2 (95.5)	74.8 (282.8)

Note: The Dietary Chlorpyrifos Intake levels (ng/kg/day) calculated from the trend-line equations of the plots in Figure 4.3.12 at respective probability level are given in the parentheses next to the percentage contribution value

However, DCIs and TDCIs were calculated using raw food samples which were not processed for cooking. It has been suggested that processing mechanisms such as polishing and parboiling rice and washing vegetables may reduce residue levels in food samples (Deka et al., 2004; Department of Agriculture, Sri Lanka, 2008). However, this should be

confirmed by further research on the DCIs in these dietary components in a processing situation. Furthermore, vegetables that are consumed without cooking, such as cucumber, may still have the potential of contributing to a higher DCI, especially when since they were detected with comparatively higher residue levels.

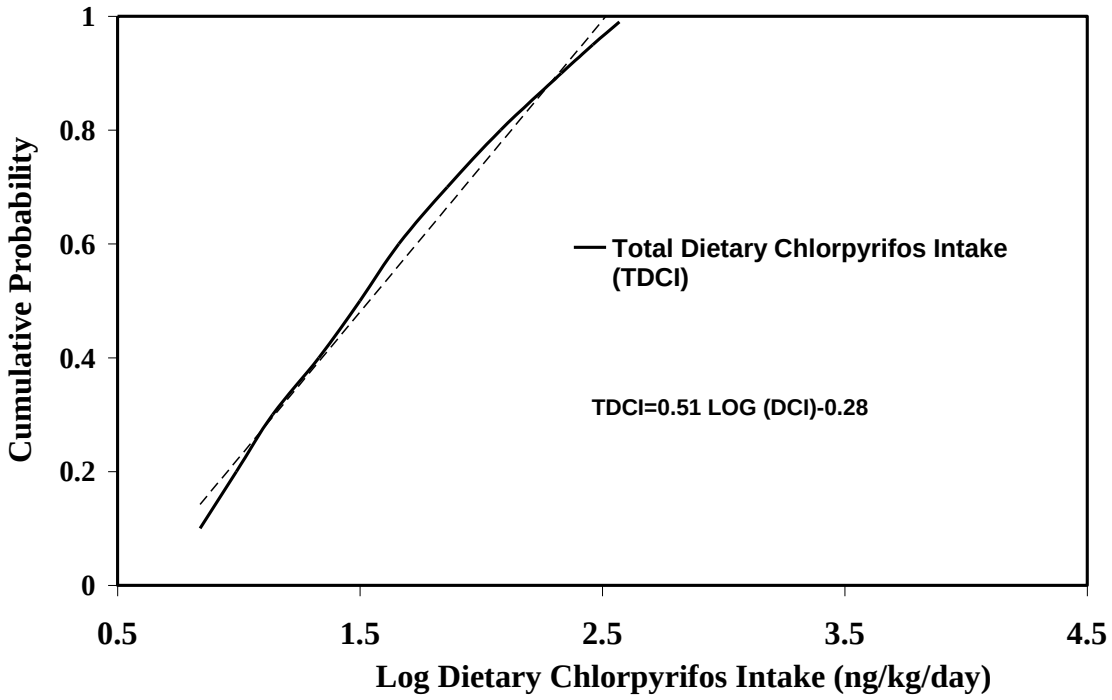

Figure 4.3.13 Total Dietary Chlorpyrifos Intake (TDCI) in India

Note: Total Dietary Chlorpyrifos Intake (TDCI) in India excludes DCI in water

4.4 Comparison of chlorpyrifos exposure in different international populations and Risk Characterisation

The Equivalent Chlorpyrifos Ingested Doses (ECID) of Sri Lankan farmers were compared with the levels observed with selected international populations, categorised according to the reported similarities with exposure. Also, the Total Dietary Chlorpyrifos Intake (TDCI)

levels estimated in diets were compared with baseline ECID of Sri Lankan farmers, whilst considering the similarities in those variables. For example, TDCI represents the chlorpyrifos dose entering a human body through food consumption and similarly, this dose is estimated, just as baseline ECID is estimated, using urinary TCP, the specific metabolite of chlorpyrifos. The ECID and TDCI levels were also compared with guideline values established for risk characterisation, by regulatory agencies. These comparisons were made at the 0.50 and 0.95 probability levels, to compare the respective levels and to characterise the risk at median and high exposure situations in 50% and 5% of the considered populations, respectively.

4.4.1 Comparison of Sri Lankan farmers with the international groups of interest

A comparison of farmers from Sri Lanka, Thailand and the USA

The Equivalent Chlorpyrifos Ingested Dose (ECID) levels estimated for Sri Lankan farmers were compared with the levels of other farmer groups from Thailand and the USA who were likely to be exposed to chlorpyrifos during farming activities. These levels were compared at the median (0.50 probability) and high exposure (0.95 probability) levels (see Table 4.4.1). In Sri Lankan farmers the baseline and post-application ECID were also compared. It is noteworthy that the post-application levels of ECID showed a major increase (x7 to x22) over the baseline levels, estimated immediately before chlorpyrifos application. The baseline levels were not directly related to pesticide application since the farmers were reported to have avoided chlorpyrifos spraying for ten days prior to the study

(Aponso et al., 2002) and were assumed to be from other sources including diet, contaminated plants and soil and farming equipment.

Table 4.4.1 Equivalent Chlorpyrifos Ingested Doses (ECID) in the Farmers Internationally

Cumulative Probability Level	***Sri Lankan Farmer-Baseline (2000) (10^3 ng/kg/day)**	***Sri Lankan Farmer-Post-Application (2000) (10^3 ng/kg/day)**	****Thai Farmer (2006) (10^3 ng/kg/day)**	*****US Farmer (2000-2001) (10^3 ng/kg/day)**
0.50	0.3 (log 2.5)	6.8 (log 3.8)	0.05 (log 1.7)	2.0 (log 3.3)
0.95	1.6 (log 3.2)	11 (log 4.0)	4.6 (log 3.6)	8.4 (log 3.9)

* See Figure 4.2.1; **See Figure 4.3.9; ***See Figure 4.3.1

Note: The log ECID levels are given in the parenthesis next to each ECID

Considering the ECID levels at the high exposure situation (0.95 probability), Sri Lankan farmers had the highest dose of 11.0 x 10^3 ng/kg/day (see Table 4.4.1; Figure 4.2.1) at post-application whilst, Thai farmers had the lowest dose (4.6 x 10^3 ng/kg/day; see Table 4.4.1; Figure 4.3.9). The difference was observed to be more than twice that of the dose received by Thai farmers. The ECID in US farmers was 8.4 x 10^3 ng/kg/day (see Table 4.4.1; Figure 4.3.1). At median exposure levels, the highest ECID was found in Sri Lankan farmers, and was estimated to be 6.8 x 10^3 ng/kg/day, post-application. Thai farmers showed the lowest dose of 0.05 x 10^3 ng/kg/day while US farmers were estimated to have received 2.0 x 10^3 ng/kg/day. The possible reasons for these differences are analysed below.

The post-application ECIDs found in Sri Lankan farmers were directly related to chlorpyrifos exposure received from a planned application event (Aponso et al., 2002). The farmers were spraying cholorpyrifos over an average of 0.25 acres of overhead canopy, using personal individual knap-sac sprayers (Aponso et al., 2002). Most of them were not wearing personal protective equipment and had a high potential for exposure to chlorpyrifos due to their less protective methodology of pesticide application. Moreover, 30% of the farmers were reported to use volumes of pesticides over the recommended application rates and a similar number were using leaking sprayers (Aponso et al., 2002). These factors are difficult to quantify in the post-application ECID levels, but are factors influencing the observed ECID levels.

The ECIDs in US farmers, were also estimated at the time of completing a spray session. The extent of land area sprayed by a US farmer was 40 times higher than the area covered by a Sri Lankan farmer. Although the exposure would be expected to be higher in US farmers due to the use of a higher volume of chlorpyrifos to cover a larger area, this was not reflected in the ECID levels. In fact, the ECIDs in US farmers were somewhat lower than the levels found with Sri Lankan farmers. One possible reason for this difference could be the comparatively protected way of pesticide application by US farmers. US farmers used ground booms and tractor mounted spreaders for pesticide spraying (Scher et al., 2008). This method of pesticide spraying provides a higher level of protection to the applicator, a factor that was reflected in the ECID levels.

The chlorpyrifos exposure in Thai farmers was not specified as a course of direct spraying (Panuwet et al., 2008). The farmers were reported to use chlorpyrifos in farming, but not

that frequently. ECID was a reflection of the exposures from various sources including, exposure encountered during their everyday farming activities (Panuwet et al., 2008). This might represent exposure from spraying, although this was not specified. Hence, the ECID in Thai farmers can be compared with post-application as well as, baseline ECID levels in Sri Lankan farmers. Accordingly, in the high exposure situation (0.95 probability), the ECID of the Thai farmer was nearly 3 times higher than the baseline level ECID of Sri Lankan farmers and about 2 times lower than the post-application levels.

A comparison of Sri Lankan farmers with pest control applicators and manufacturing workers in Australia and USA

The post-application ECIDs in Sri Lankan farmers absorbed from chlorpyrifos spraying were compared with the levels estimated in pest control applicators in Australia and the US, and also with manufacturing workers in the US. The work related exposure was compared herein. In general, the manufacturing workers and pest control applicators were full time (8 hours a day, five days a week) workers who were involved in pesticide application as an occupation. In contrast, the farmers in Sri Lanka applied pesticides occasionally however; the exposure data used in the study were work related (Aponso et al., 2002).

Comparing the post-application ECID levels of 11.0 x 10^3 ng/kg/day (see Table 4.4.2; Figure 4.3.4), estimated in Sri Lankan farmers at high exposure (0.95 probability), they were mostly similar to the levels found in US manufacturing workers estimated outside occupational exposure (10.0 x 10^3 ng/kg/day in OOE; see Table 4.4.2; Figure 4.3.4). The manufacturing workers were expected to receive exposure from sources in agricultural

environments during this period (Garabrant et al., 2008). Although this indicates that the US workers were involved in chlorpyrifos related activities in agriculture, one can expect that not all the workers were involved in such activities. This is because, at the median exposure level (0.50 probability), the ECID of 50% of the manufacturing workers (1.2 x 10^3 ng/kg/day; see Table 4.4.2 and Figure 4.3.4) was much less (five fold), than the post application ECID estimated in Sri Lankan farmers (6.8 x 10^3 ng/kg/day; see Table 4.4.2; Figure 4.2.1). However, if all the workers practiced pesticide related activities during this period, low levels of ECID can still be expected, due to the use of suitable protective wear and safe handling of pesticides.

US manufacturing workers exposed in an occupational environment had an estimated ECID of 210 x 10^3 ng/kg/day (see $^{\#\#}$OE in Table 4.4.2; Figure 4.3.4), at the high exposure level (0.95 probability). This exposure was reported to be as a result of maintenance work during the factory shut down period and was considered to be atypical. Compared to the post application ECID in Sri Lankan farmers, this value is 19 times higher. However, the ECID in 50% of the workers at median exposure situation (0.50 probability), was 1.8 x 10^3 ng/kg/day (see $^{\#\#}$OE in Table 4.4.2; Figure 4.3.4) and was very low compared to levels estimated at high exposure. Also, this was not much different from the levels estimated for them during time outside the occupational exposure period (1.2 x 10^3 ng/kg/day; OOE in Table 4.4.2; Figure 4.3.4) and, was less than the ECID (4 fold) calculated in Sri Lankan farmers post-application. It seems that although atypical exposure may occur in 5% of the manufacturing workers, another 50% avoided higher exposure either by adhering to protective measures or by working in factory environments where exposure was minimal. The ECID in US workers due to typical occupational exposure was estimated to range from

13.0 x 10^3 ng/kg/day to 29.0 x 10^3 ng/kg/day (see #OE in Table 4.4.2; and Figure 4.3.4) at high exposure (0.95 probability). This is a variance of up to 2.5 fold in contrast to post-application levels in Sri Lankan farmers (11.0 x 10^3 ng/kg/day). Considering the nature of the occupation of the US workers, which is full time work for five days a week, it could be expected that the ECID at high exposure (0.95 probability) qould be higher, given a half life of 27 hours for TCP excretion in humans, which indicates that the exposure occurred within the 3 to 5 days prior to a spot urine sample (Nolan et al., 1984). However, the lower ECID levels in 50% of the workers (at 0.50 probability) compared to that of the Sri Lankan farmers, reflect the stringent regulations on personal protection for workers.

Comparable levels of ECID were found only in the median exposure situation (0.50 probability), between Sri Lankan farmers at post-application (6.8 x 10^3 ng/kg/day) and Australian pest control applicators (7.8 ng/kg/day; see Table 4.4.2; Figure 4.3.8). At the same probability level, the difference between farmers (6.8 x 10^3 ng/kg/day; see Table 4.4.2) and US pest control applicators (12.0 x 10^3 ng/kg/day; see Table 4.4.2; Figure 4.3.3) was 1.5 times. The dose of 26.0 x 10^3 ng/kg/day estimated for applicators from both countries (see Table 4.4.2; Figure 4.3.3; Figure 4.3.8) at high exposure situation (0.95 probability), was about 4 fold higher than the dose calculated for Sri Lankan farmers (11.0 x 10^3 ng/kg/day; see Table 4.4.2).

Pest control applicators from both countries were reported to be involved in termite control work, using chlorpyrifos as the insecticide of choice (Hines et al., 2001; Cattani, 2004). Termiticide application is a full time occupation carried out on work days during a week, and necessitates frequent handling of pesticides. For example, US applicators were reported

to work for more than five days a week during busy periods (Hines et al., 2001). In addition, most of the applicators were treating enclosed crawl spaces which were supposedly provided less ventilation. Under these circumstances, there is a higher potential for exposure to pesticides unless necessary protective measures are taken. Cattani (2004) explained that most of the protective measures taken by the applicators were not sufficient to minimise exposure.

Table 4.4.2 Equivalent Chlorpyrifos Ingested Doses (ECID) in the Pest Control Applicators and the Manufacturing Workers Internationally

Cumulative Probability Level	***Sri Lankan Farmer (2000) (10^3 ng/kg/day)**	****US Pest Control Applicators (1998) (10^3ng/kg/day)**	**US Manufacturing Workers (1999-2000) (10^3 ng/kg/day)**			****Australian Pest Control Applicators (1998-1999) (10^3 ng/kg/day)**
	PA#		**OOE**	**OE#**	**OE ##**	
0.50	6.8 (log 3.8)	12.0 (log 4.1)	1.2 (log 3.07)	1.1-1.5 (log 3.04-log 3.2)	1.8 (log 3.2)	7.8 (log 3.9)
0.95	11.0 (log 4.0)	26.0 (log 4.4)	10.0 (log 4.0)	13.0-29.0 (log 4.1-log 4.5)	210.0 (log 5.3)	26.0 (log 4.4)

PA#-Post Application; OE#-Typical Occupational Exposure (See Figure 4.3.4 for $ECID_{OE99}$ and $ECID_{OE00}$); OE##-Atypical Occupational Exposure (See Figure 4.3.4 for $ECID_{MWE00}$,); OOE-Outside Occupational Exposure (See Figure 4.3.4 for $ECID_{OOE00}$); * See Figure 4.2.1; **See Figure 4.3.3; ***See Figure 4.3.8

Note: The log ECID levels are given in the parenthesis next to each ECID

Alternatively, the farmers were exposed to pesticides during a spraying event with no exposure for ten days prior to the event (Aponso et al., 2002). It would be expected that the duration of contact with pesticides was less in farmers, compared to the continuous occupational exposure of a pest control applicator, which has already been discussed. Thus, farming is an integrated event associated with many activities other than pesticide application.

Furthermore, the concentrations and volumes of chlorpyrifos used by farmers vary from those used by pest control applicators. These differences could also contribute to the differences observed in ECID levels in farmers, as well as in applicators. For example, Sri Lankan farmers used a maximum of 100L of diluted mixture throughout their spraying event (Aponso et al., 2002) while the applicators used greater volumes (Hines et al., 2001; Cattani, 2004). Consequently, one can expect the exposure levels with farmers to be less than the levels in pesticide applicators if the exposure is proportionate to the volume of pesticide handled, and the duration for which it was handled..

A comparison of Sri Lankan farmers with general populations in Italy, Germany, Thailand and USA

The baseline ECID for Sri Lankan farmers were compared to the levels estimated for general populations of adults from the US, Italy, Germany, pregnant mothers in the US and children from Thailand. All these populations were considered to have more or less similar types of sources for exposure.

It is interesting to find that in the median exposure situation (0.5 probability), the baseline ECID of 0.3 x 10^3 ng/kg/day (see Table 4.4.3; Figure 4.2.1) in 50% of the farmers was comparable with the respective levels of 0.1 x 10^3 ng/kg/day, 0.13 x 10^3 ng/kg/day and 0.07 x 10^3 ng/kg/day (see Table 4.4.3), estimated with adults from the USA (see Table 4.3.1, Figure 4.3.2), Italy (see Figure 4.3.6) and, Germany (see Figure 4.3.7). Also, in the high exposure situation (0.95 probability), similar results were found with a dose of 1.6 x 10^3 ng/kg/day for farmers (see Table 4.4.3; Figure 4.3.2), 0.6 x 10^3 ng/kg/day for the US adults (see Table 4.4.3; Table 4.3.1; Figure 4.3.2), 0.63 x 10^3 ng/kg/day for Italian adults (see Table 4.4.3; Figure 4.3.6) and, 0.5 x 10^3 ng/kg/day for German adults (see Table 4.4.3; Figure 4.3.7). The difference could be attributed to a higher dietary exposure, additional exposure from working in treated fields or handling of contaminated farming equipment by farmers. The ECIDs with adults in three countries were similar at both probability levels. The adults in the US would be expected to be exposed mainly from indoor treated environments for household pests and their diet (Hill et al., 1995; Barr et al., 2005), while in Italian and German populations the exposure was believed to be as a result of diet (Aprea et al., 1999; Koch et al., 2001). None of the adults were known to have occupational or any other known exposure to pesticides.

A similar situation was observed with the ECID levels in Sri Lankan farmers and Thai children. The respective baseline levels of farmers (0.3 x 10^3 ng/kg/day; 1.6 x 10^3 ng/kg/day), were comparable to the levels of 0.1 x 10^3 ng/kg/day and 0.5 x 10^3 ng/kg/day in Thai children at the 0.5 and 0.95 probability levels (see Table 4.4.3; Figure 4.3.10). It is noteworthy that in the estimation of ECID in children, common physiological characteristics (average body weight and average daily creatinine excretion rate; see Section 3.3.1) were adopted, which were believed to be appropriate for the age group.

Table 4.4.3 Equivalent Chlorpyrifos Ingested Doses (ECID) in the General Population Internationally

Cumulative Probability Level	***Sri Lankan Farmer (2000) (10^3ng/kg/ day)**	****US General Population (2001-2002)**	*****General Population in Europe (10^3 ng/kg/day)**		**+US Pregnant Mothers (1998-2001) (10^3 ng/kg /day)**	**++Thai Children (Published in 2009) (10^3 ng/kg/ day)**
	BL#	**(10^3ng/kg/ day)**	**Italy (1997)**	**Germany (Published in 2001)**		
0.50	0.3 (log 2.5)	0.1 (log 2.0)	0.13 (log 2.1)	0.07 (log 1.9)	0.8 (log 2.9)	0.12 (log 2.0)
0.95	1.6 (log 3.2)	0.6 (log 2.8)	0.63 (log 2.8)	0.5 (log 2.7)	4.7 (log 3.7)	0.47 (log 2.7)

BL#-Baseline; ** See Figure 4.2.1; ** See Figure 4.3.2; *** See Figures 4.3.6 (Italy) & 4.3.7 (Germany); + See Figure 4.3.5; ++See Figure 4.3.10

Note: The log ECID levels are given in the parenthesis next to the each ECID; For ECID values at 0.50 and 0.95 probability levels Trend line values were used, only when reported TCP levels were not found to estimate ECID)

Out of 207 Thai children, 92% had been exposed to chlopyrifos (Panuwet et al., 2009). The children represented both agricultural (101 children) and non-agricultural (106 children) families in Thailand. Thus, exposure by means other than agriculture could also be expected. Given the frequent detection of chlorpyrifos in food commodities (Panuwet et al., 2009), the most common pathway of exposure was considered to be through diet,yet,

the maximum exposure level in children with an agricultural background was twofold higher than the maximum level found in non-agricultural community. The ECID level in the high exposure situation (0.95 probability) (0.47×10^3 ng/kg/day; see Table 4.4.3; Figure 4.3.10) may also resemble the associated exposure from an agricultural environment.

The ECIDs in pregnant mothers from the US (see Table 4.4.3; Figure 4.3.5), were found to be higher than the levels found in other general adults in the US (see Table 4.4.3). Also, these levels (0.8×10^3 ng/kg/day; 5.0×10^3 ng/kg/day) were higher than the respective baseline ECIDs (approximately 3 times) observed in Sri Lankan farmers (0.3×10^3 ng/kg/day; 1.6×10^3 ng/kg/day; see Table 4.4.3), in both the median (0.50 probability) and high exposure (0.95 probability) situations.

Most of the mothers, were believed to have been exposed through indoor use of household pesticides (Berkowitz et al., 2003), although the use of chlorpyrifos was not specified. Out of a group of 365 mothers, 72% revealed their presence at home while different types of pest control activities were carried out (Berkowitz et al., 2003). Other than indoor exposure, contributions from dietary and other pathways would also be expected. Considering the pathways of exposure among the US general population, which are expected to be mostly the same (Barr et al., 2005), the levels found in the mothers are unusual. However, their involvement with the pesticide at an occupational level was not revealed. In addition to this, the differences in metabolism during pregnancy may also have affected ECID levels in mothers, possibly by changing excretion rates of creatinine (see Section 3.3.1).

4.4.2 Comparison of Total Dietary Chlorpyrifos Intake (TDCI) in Sri Lanka with the Total Dietary Chlorpyrifos Intake (TDCI) in India and the baseline Equivalent Chlorpyrifos Ingested Dose (ECID) in Sri Lankan farmers

Total Dietary Chlorpyrifos Intakes (TDCI) in Sri Lanka and India

The Total Dietary Chlorpyrifos Intake (TDCI) in an average diet composed of rice and vegetables was estimated using the Dietary Chlorpyrifos Intakes (DCI) for each dietary component, calculated from the residue data reported in Sri Lanka and India (see Section 3.3.3). The trend line equations of the DCI plots, plotted with the available data of each dietary component were used to calculate the TDCI at each probability level.

The TDCI levels of both countries were compared at the high exposure (0.95 probability) and median (0.50 probability) situations (see Table 4.4.4; Figures 4.2.5 for Sri Lanka; Figure 4.3.13 for India). The TDCI of Sri Lanka at the 0.95 probability level was 1.8×10^3 ng/kg/day in the diet, six times greater than the level of 0.3×10^3 ng/kg/day calculated in the Indian diet. The difference between the TDCI levels at the 0.50 level was 10 times between the diets in Sri Lanka and India, having TDCIs of 0.3×10^3 ng/kg/day and 0.03×10^3 ng/kg/day respectively. At both these levels, DCI in water did not contribute to any of these diets. Furthermore, DCI in water contributed only at the 99% cumulative probability level to the TDCI in the Sri Lankan diet (see Table 4.2.7).

At the 0.95 probability level, the respective DCI levels of 1500 ng/kg/day and 314 ng/kg/day (see Table 4.2.7) in rice and vegetables in Sri Lanka were higher than the

respective levels of 83.2 ng/kg/day and 208.9 ng/kg/day in India (see Table 4.3.9). Further, at this level of probability, rice contributed the highest proportion of 83 % (see Table 4.2.7) of the TDCI, with vegetables making up the remainder (see Table 4.2.7) in the Sri Lankan diet. In contrast, rice contributed to a lesser proportion of 28% (see Table 4.3.9) of the TDCI in the Indian diet with the highest contribution of 72% coming from vegetables (see Table 4.3.9). At the 0.50 level of probability, only rice contributed to the TDCI with a DCI of 0.3 x 10^3 ng/kg/day (see Table 4.2.7) in the Sri Lankan diet, whist in the Indian diet a DCI of 0.02 x 10^3 ng/kg/day in rice (see Table 4.3.9) and 0.01 x 10^3 ng/kg/day of vegetables (see Table 4.3.9) contributed in comparable proportions of 57% and 43% respectively. The DCI in water did not contribute at any of these probability levels in both diets. Further, water contributed only at the 0.99 probability level, contributing 3.2 % of the TDCI in the Sri Lankan diet (see Table 4.2.7).

In this study, the maximum and minimum chlorpyrifos residue levels reported in rice in Sri Lanka (420 x10^3 ng/kg/day and 29.0 x 10^3 ng/kg/day; see Table 4.2.2) were 21 fold and 6 fold higher than the levels reported in rice in India (20.0 x 10^3 ng/kg/day; 5.0 x 10^3 ng/kg/day; see Table 4.3.5). In addition, rice was calculated with the highest rate of daily consumption in the considered diets with 300g per day (see Table 4.2.6; Table 4.3.8). This resulted in higher DCIs from rice in the Sri Lankan diet compared to India. Furthermore, the DCI was calculated assuming similar daily consumption rates in all the dietary components and a common average body weight for an average person in the two countries (see Section 3.3.3). Factors affecting the DCI likely include the concentration of residues in the food commodities. The higher concentration of residues in Sri Lankan rice together with a higher consumption rate multiplied the DCI level and hence the TDCI. Moreover,

even though the residue levels in vegetables were higher, low consumption rates reduced the DCI (see Table 4.2.6).

Table 4.4.4 Total Dietary Chlorpyrifos Intakes (TDCI) in Sri Lanka, India and Equivalent Chlorpyrifos Ingested Dose (ECID) in Sri Lankan Farmers

Cumulative Probability Level	**Total Dietary Chlorpyrifos Intake (TDCI)**		**Equivalent Chlorpyrifos Ingested Dose (ECID)- Baseline Sri Lankan Farmer (2002) (10^3 ng/kg/day)**
	Sri Lanka* (2001-2009) (10^3 ng/kg/day)	**India** (1994-2002) (10^3 ng/kg/day)**	
0.50	0.3 (log 2.5)	0.03 (log 1.5)	0.3 (log 2.5)
0.95	1.8 (log 3.2)	0.3 (log 2.5)	1.6 (log 3.2)

*See Figure 4.2.5; **See Figure 4.3.13

Note: The respective log levels are given in the parenthesis next to each TDCI and ECID

Chlorpyrifos was one of the most frequently monitored and reported pesticide residues in all food commodities in Sri Lanka (Alwis et al., 2006; Aravinna et al., 2008; Department of Agriculture, Sri Lanka, 2009). In rice, the residue data was obtained from only one investigation for Sri Lanka (Department of Agriculture, Sri Lanka, 2009) and two investigations for India (Singh et al., 2003; Deka et al., 2004). In all the studies, the samples were obtained from special research rice culture plots. Thus, there is a chance that differences in residue levels could exist between samples from research fields and farmer fields. However, this needs to be verified with data. Furthermore, in Sri Lanka the residue data was reported to be analysed in samples collected at harvesting time of the rice crop (Department of Agriculture, Sri Lanka, 2009), which may have resulted in higher residue

levels. Although the same method was carried out by Singh et al., 2003, the rice grain in India was polished before the analysis. Thus, the polished rice contains a lesser concentration of residues than the unpolished rice (Deka et al., 2004). The status of the rice grain in the Sri Lankan study was not reported, but is expected to be unpolished.

Deka et al. (2004) reported that chlorpyrifos was above an average LOD of 0.001 µg/g was rarely detected in rice in India (two out of fifteen samples). Above the same LOD, the most detected residues were endosulfan (80%) and some other organochlorines (HCH -100% and DDT-60%). The higher frequency of detection of these pesticides indicates their wide use in rice pest control as compared to chlorpyrifos. This might be one of the reasons for low level of detections of chlorpyrifos in India. India also reported detection of other insecticides more frequently than chlorpyrifos in vegetables (Kumari et al., 2004; Singh et al., 2002; Mukherjee et al., 2003; Kumari et al., 2003). This further shows a lower usage of chlorpyrifos compared to other insecticides in India. However, the factors such as frequency and rate of pesticide application, whether and when the spraying was carried out and, agricultural practices are vital in detecting residues, but were not reported in the studies. Moreover, the diverse climatic conditions prevailing throughout different regions in India, could also affect the types and rate of application of pesticides and thus, the residue levels in food commodities.

There was a limitation in the study with selecting dietary components for the TDCI estimation. Therefore, few vegetables were considered in the diets together with rice due to the availability of the reported residue data. The vegetables were assumed to be consumed every day at a minimum consumption rate of 10 g/day (see Section 3.3.3; Central Bank of

Sri Lanka, 2005). Although this is a comparatively low rate compared to the average daily rate of vegetables consumed by a person (Mukherjee, 2003), it was considered justifiable since daily consumption includes a variety of vegetables in some of which residues may not have been detected.

DCIs and TDCIs were calculated in unprocessed food in both countries. It is believed that processed food may contain lower amounts of residues. For example, usually rice is consumed after storing for few days to months followed by sun drying which would be expected to decrease the residue concentration. In some instances, the rice grain is parboiled prior to dehusking and polishing. The residue levels in polished and parboiled rice were found to be lower than levels in unpolished and non-parboiled rice (Deka et al., 2004). Similarly, washing and cooking may reduce the levels of residues in food. This was shown by detection of residues in surface washings of the vegetables reported by Department of Agriculture of Sri Lanka (2008) (see Table 4.2.2). Therefore, the same amount of processed foods of the considered diets may contribute to lower TDCI than what was estimated in the study. However this needs to be verified by further research.

Total Dietary Chlorpyrifos Intake (TDCI) and Equivalent Chlorpyrifos Ingested Dose (ECID) in Sri Lanka

The Total Dietary Chlorpyrifos Intake (TDCI) levels calculated in the average daily diet in Sri Lanka were compared at median (0.50 probability) and high exposure (0.95 probability) situations, with Equivalent Chlorpyrifos Ingested Dose (ECID) in Sri Lankan farmers at a baseline exposure. The ECIDs were calculated from the urinary chlorpyrifos metabolite,

TCP, and represent chlorpyrifos intake in the diet in the same units of ng/kg/day as the TDCI. At 0.95 cumulative probability, the TDCI of 1.8 x 10^3 ng/kg/day (see Table 4.4.4) was comparable with the baseline ECID of 1.6 x 10^3 ng/kg/day in the farmers (see Table 4.4.4). Also at the 0.50 level, the TDCI of 0.3 x 10^3 ng/kg/day was equivalent to the ECID of 0.3 x 10^3 ng/kg/day (see Table 4.4.4). This suggests dietary exposure could be expected to be a main pathway of baseline exposure in farmers. However, the TDCI was estimated in unprocessed food components and hence could be expected to have higher DCI levels than in processed and cooked food. Therefore, further research is needed for TDCI estimation in processed foods since the farmers are also likely to be exposed by entering treated fields, and contact with contaminated farming equipment.

4.4.3 Comparison of Ingested Doses and Dietary Intakes with Guideline Values

Guideline Values (GVs) on the critical levels for exposure to chlorpyrifos have been established by the U.S. Environmental Protection Agency (USEPA, 2000), the World Health Organization (WHO) (JMPR, 1999) and the Government of Australia (Australian Department of Health and Ageing, 2008), and are presented in the Table 4.4.5. Since these values are expressed in the same units and based on oral intakes, they may be compared with the Equivalent Chlorpyrifos Ingested Doses (ECID) calculated in this study. Each of these Guideline Values (GV) are based on the No Observed Adverse Effect Levels (NOAEL) of plasma or red blood cell (RBC) Cholinesterase (ChE) inhibition in animal species (rats, dogs and mice) and humans.

The NOAEL (see Table 4.4.5) is divided by a recommended Safety Factor (SF) or Uncertainty Factor (UF). The uncertainty factor of 10 is used when the data is derived with humans, and it is 100, when the dose is derived from other species to set the GV. In addition, the Food Quality Protection Act (FQPA) Safety Factor Committee (SFC) in the USA has recommended an SF of 10 to establish the Acute and Chronic Population Adjusted Doses (APAD and CPAD) of USEPA for chlorpyrifos, based on the increased sensitivity and susceptibility at high (acute) and repeated (chronic) doses, given the potential adverse effects, including developmental neurotoxicity (USEPA, 2000). Thus, the FQPA SF is applicable for populations of females (13 to 50 years), infants and children (see Table 4.4.5).

Plasma and RBC ChE inhibition are the endpoints for the establishment of the GVs (see Table 4.4.5). ChE inhibition is the most sensitive effect in humans and animals observed with chlorpyrifos exposure (USEPA, 2000). Thus plasma and RBC ChE inhibition occur below the levels of exposure needed to inhibit brain ChE. Brain ChE inhibition is associated with neurotoxicological effects. RBC inhibition is considered as an early precursor to the inhibition of brain ChE (Garabrant et al., 2008).

The Acute Reference Dose (ARfD) and the APAD (see Table 4.4.5) are based on a NOAEL from studies in rats that were orally dosed with 1 x 10^6 ng/kg and 1.5 x10^6 ng/kg/day chlorpyrifos, with the respective observations of significant inhibition of plasma (28-40%) and RBC (30%) cholinesterase (ChE) (USEPA, 2000). The Chronic RfD (CRfD) and CPAD (see Table 4.4.5) are based on the NOAELs from four toxicological studies in rats and dogs ranging from 90 day to 2 years. The adverse effects observed included

significant plasma and RBC ChE inhibition from 2.2 x 10^5 to 3.0 x 10^5 ng/kg/day dose levels (USEPA, 2000). A NOAEL based in a developmental neurotoxicity study with pregnant rats carried out for 2 weeks in which the pups of the exposed rats were observed to have experienced toxic effects was also considered in determining the CRfD and CPAD.

The WHO GVs of Acceptable Daily Intake (ADI) is based on the NOAEL of 1 x 10^5 ng/kg/day of erythrocyte ChE activity inhibition in human volunteers in a 9 day study (see Table 4.4.5). This was supported by the NOAELs of four more studies in rats and dogs with no inhibition of brain ChE shown at a dose of 1 x 10^6 ng/kg/day (JMPR, 1999). The ADI established by the Department of Health and Ageing in Australia (see Table 4.4.5) is based on the NOAEL of plasma ChE in a 28 day human volunteer study (Australian Government, 2008).

The ECIDs in the international populations in median (0.50 probability) and high exposure (0.95 probability) situations were compared with the GVs with relation to their exposure situations. Accordingly, the baseline ECIDs in Sri Lankan farmers and the ECID in Thai farmers were compared with the CRfD (0.3 x 10^3 ng/kg/day; see Table 4.4.5), the ADI set by WHO (10 x 10^3 ng/kg/day; see Table 4.4.5) and the Australian Department of Health and Ageing (3 x 10^3 ng/kg/day; see Table 4.4.5). In the median exposure situation, the ECID in Sri Lankan farmers (0.3 x 10^3 ng/kg/day; see Table 4.4.1) was equal to the CRfD, while Thai farmers had levels below the CRfD. With both groups of farmers the ECID (1.6 x 10^3 ng/kg/day; 4.6 x 10^3 ng/kg/day; see Table 4.4.1) exceeded the CRfD with high exposure (0.95 probability). In none of the farmers did the levels exceed the ADI of WHO and in only 5% of the Thai farmers did the levels exceed the ADI set by Australia.

Similarly, the ECID in the general population (adults) of the USA, Italy and Germany were compared with the CRfD (0.3 x 10^3 ng/kg/day; see Table 4.4.5), ADIs of the WHO (10 x 10^3 ng/kg/day; see Table 4.4.5) and the Australian Department of the Health and Ageing (3 x 10^3 ng/kg/day; see Table 4.4.5). With all the populations, the levels (0.5 x 10^3 to 0.63 x 10^3 ng/kg/day; see Table 4.4.3) exceeded the CRfD only at high exposure (0.95 probability). None of the levels exceeded the ADI values.

The ECIDs of US pregnant mothers and Thai children were compared with the CPAD (0.03 x 10^3 ng/kg/day; see Table 4.4.5) and the ADI values set by WHO (10 x 10^3 ng/kg/day; see Table 4.4.5) and the Australian Department of Health and Ageing (3 x 10^3 ng/kg/day; see Table 4.4.5). In 50% of both populations, the levels (0.8 x 10^3 ng/kg/day and 0.1 x 10^3 ng/kg/day; see Table 4.4.3) exceeded the CPAD at median exposure (0.50 probability). The ECID of mothers (4.7 x 10^3 ng/kg/day; see Table 4.4.3) was higher than the ADI of Australia at 0.95 probability. However, the ADI set by the WHO was not exceeded by the mothers at any probability level. None of the ADIs were exceeded by the levels in children.

After comparing the post application ECID for Sri Lankan farmers and occupationally exposed populations with ARfD (5.0 x 10^3 ng/kg/day; see Table 4.4.5) following observations were made. The levels of Sri Lankan farmers (6.8 x 10^3 ng/kg/day; see Table 4.4.1) and pest control operators in Australia (7.8 x 10^3 ng/kg/day; see Table 4.4.2) and the USA (12.0 x 10^3 ng/kg/day; see Table 4.4.2) at 0.50 probability level, were higher than the ARfD. In US farmers (8.4 x 10^3 ng/kg/day; see Table 4.4.1) and manufacturing workers in occupational and outside occupational exposure situations (10.0 x10^3 ng/kg/day to 210 x

10^3 ng/kg/day; see Table 4.4.2) the levels exceeded the ARfD only at high exposure situation (0.95 probability).

Table 4.4.5 Guideline Values (GV) for Intake of Chlorpyrifos

Guideline Value	**Dose (10^3 ng/kg/day)**	**End Point**	**NOAEL (10^3 ng/kg/day)**	**Reference**
ARfD (USEPA)	5.0	Inhibition of Plasma (3-6 hours post exposure) and RBC ChE in rats (4 hours post exposure)	500 (UF= 100)	USEPA, 2000
APAD (children and females13-50 yrs)* (USEPA)	0.5		500 (UF=100, *FQPA= 10)	
CRfD (USEPA)	0.3	Inhibition of Plasma and RBC ChE in rats (2 year, 90 day and developmental at 2 weeks)and dogs (2 year and 90 day)	30 (UF= 100)	
CPAD(children and females 13-50 yrs)* (USEPA)	0.03		30 (UF= 100, *FQPA=10)	
ADI (WHO)	10	Inhibition of Erythrocyte ChE in humans (9 day oral)	100 (SF=10)	JMPR, 1999
		Inhibition of Brain ChE in rats (2 year, dietary and reproduction study) , mice (developmental study) and dogs (2 year dietary study)	1000 (SF=100)	
ADI (Australian Government)	3	Inhibition of Plasma ChE in humans (28 days)	30 (UF=10)	Australian Department of Health and Ageing, 2008

ARfD-Acute Reference Dose; APAD –Acute Population Adjusted Dose; CRfD-Chronic Reference Dose; CPAD-Chronic Population Adjusted Dose; ADI- Acceptable Daily Intake

**Note: FQPA(Food Quality Protection Act) Safety Factor Committee in US established a safety factor of 10 for chlorpyrifos in females 13-50 yrs, infants and children based on the sensitivity and susceptibility to high dosages (USEPA, 2000)*

Likewise, Guideline Values of ADI set by WHO (10 x 10^3 ng/kg/day; see Table 4.4.5) and the Australian Department of Health and Ageing (3 x 10^3 ng/kg/day; see Table 4.4.5) and the CRfD (0.3 x 10^3 ng/kg/day; see Table 4.4.5) were used to compare the Total Dietary Chlorpyrifos Intakes (TDCI) in Sri Lanka and India. In the median exposure situation (0.5 probability), the TDCI of the Sri Lankan population (0.3 x 10^3 ng/kg/day; see Table 4.4.4) was equal to the CRfD and exceeded it (TDCI 1.8 x 10^3 ng/kg/day; see Table 4.4.4) at the 0.95 probability level. The TDCI of the Indian population was equal to the CRfD at the 0.95 level of probability. None of the TDCI levels exceeded the ADIs set by the WHO and Australia.

4.4.4 Risk Characterization using Hazard Quotients (HQ)

There are specific guideline values, developed by certain regulatory organizations which can be used to evaluate risk to health, by calculation of a Hazard Quotient ($Exposure\ Dose/Guideline\ Value$). These guideline values (GV; see Table 4.4.5) used to calculate HQ, are estimated using a No Observed Adverse Effect Level (NOAEL) for certain toxicological endpoints, together with an uncertainty factor. Also, Equivalent Chlorpyrifos Ingested Dose (ECID) and Total Dietary Chlorpyrifos Intake (TDCI) used as exposure doses in this study were estimated using methods to convert exposure observed by other means such as a metabolite or residues in food. Therefore, in both these measures experimental uncertainties could be reflected to some extent. For this reason, just exceeding the GV to estimate a marginal HQ above unity would not be expected to cause adverse effects, but still can be used as a cautionary measure to prevent potential risks. Thus, only relatively higher HQ values can be expected to pose a risk of adverse effects.

The USEPA Acute Reference Dose (ARfD; see Table 4.4.5) is used for risk evaluation of high level short term exposure in occupational and similar situations. The Chronic Reference Dose (CRfD; see Table 4.4.5) is applicable to low level repeated exposure ,usually associated with non-occupational situations. The Chronic Population Adjusted Dose (CPAD; see Table 4.4.5) for chlorpyrifos, has been developed to evaluate the HQ, with special attention paid to sensitive populations such as women of child bearing age, infants and children (USEPA, 2000) and is concerned with the adverse effects associated with repeated exposure. Since, the value for CPAD (0.03×10^3 ng/kg/day) is set below the level of the CRfD (0.3×10^3 ng/kg/day), the HQs would be comparatively higher. The GVs are in units of ng/kg/day and represent the dose ingested with food per day. The ECID (Equivalent Chlorpyrifos Ingested Dose) which represents chlorpyrifos exposure was calculated from the urinary level of the metabolite TCP as shown in Section 3.3.1 and represents the ingested dose in the same units as the GVs.

Hazard Quotients (HQ) calculated using the US Environmental Protection Agency Guideline Values (GV)

The Hazard Quotients (HQ), were calculated for the estimated ECIDs at the high exposure (0.95 probability; $HQ_{0.95}$) and median exposure (0.50 probability, $HQ_{0.50}$) levels in the occupationally exposed populations, listed in Table 4.4.6 using the Acute Reference Dose (ARfD) of the USEPA (see Table 4.4.5). The HQs ranged from 0.2 to 2.4 at the 0.50 level of probability and from 1.7 to 42, at the 0.95 level for the considered groups (see Table 4.4.6). The highest risk of potential adverse effects was observed in US manufacturing workers with a $HQ_{0.95}$ of 42, at the 0.95 cumulative probability level. The estimated ECID

at this level resulted from an atypical exposure at the work place. The $HQ_{0.50}$ for workers was acceptable with a HQ less than 1 (see Table 4.4.6). Sri Lankan farmers and pest control applicators in the US and Australia were at marginal risk at the 0.50 probability level, with $HQ_{0.50}$ values of 1.3, 2.4 and 1.5 respectively (see Table 4.4.6). As discussed previously, a HQ value which shows a marginal risk (~1), would not be expected to cause adverse effects, given the method of establishing a GV using a NOAEL and a safety factor. A much higher HQ was observed for farmers and pest control applicators at the 0.95 probability level (see Table 4.4.6). US farmers were only at a marginal risk even at the 0.95 probability level, with a $HQ_{0.95}$ of 1.7 (see Table 4.4.6). The $HQ_{0.50}$ of US farmers was 0.4, which was acceptable given the GVs.

Table 4.4.6 Hazard Quotients (HQ) based on the Acute Reference Dose (ARfD) of USEPA*

Cumulative Probability	Hazard Quotients (HQ)						
	[1]Sri Lankan farmer-Post Application	[1]US farmer	[2]US pest control applicator	[2]US manufacturing worker			[2]Australian pest control applicator
				OOE	**OE[#]**	**OE [##]**	
0.50	1.3	**0.4**	2.4	**0.2**	**0.2-0.3**	**0.3**	1.5
0.95	2.2	1.7	5.2	2.6	2.6-5.8	42	5.2

*See Table 4.4.5; [1]see ECID in Table 4.4.1; [2]see ECID in Table 4.4.2; HQ values below 1.0 (acceptable risk levels) are in bold; OOE-Outside Occupational Exposure; OE[#]-Typical Occupational Exposure; OE[##]-Atypical Occupational Exposure

The HQs were calculated at the 0.95 ($HQ_{0.95}$) and 0.50 ($HQ_{0.50}$) probability levels using the USEPA chronic Reference Dose (CRfD; see Table 4.4.5) and the ECIDs of the non-occupationally exposed populations. At the median exposure (0.50 probability) level, populations of Sri Lankan farmers, Thai farmers and general adults of the USA, Italy and Germany had an acceptable risk with a HQ of one or less (see Table 4.4.7). However, Thai farmers were at comparatively higher risk of suffering adverse effects, at the 0.95 probability level with a $HQ_{0.95}$ of 15.3 (see Table 4.4.7). Marginal risk was observed at the 0.95 probability level, in general populations of the USA, Italy and Germany with $HQ_{0.95}$ from 1.6 to 2.0 (see Table 4.4.7). Sri Lankan farmers at baseline exposure had a potential risk, with $HQ_{0.95}$ of 5.3 at the 0.95 probability level.

Table 4.4.7 Hazard Quotients calculated with the Chronic Reference Dose (CRfD) for the USEPA*

Cumulative Probability	Hazard Quotients (HQ)		
	[1]Sri Lankan farmer-Baseline	[1]Thai farmer	[2]General Populations (Adults) in the Germany, USA and Italy
0.50	**1.0**	**0.1**	**0.2 to 0.4**
0.95	5.3	15.3	1.6 to 2.0

*See Table 4.4.5; [1]see ECID in Table 4.4.1; [2]see ECID in Table 4.4.3; HQ values below 1.0 (acceptable risk levels) are in bold

Table 4.4.8 Hazard Quotients (HQ) calculated with the Chronic Population Adjusted Dose (CPAD) of USEPA*

Cumulative Probability	Hazard Quotients (HQ)	
	[1]US Pregnant Mothers	[1]Thai Children
0.50	28	4.0
0.95	157	15.7

*See Table 4.4.5; [1]see the ECID at the Table 4.4.3

The HQs (see Table 4.4.3), were calculated at the high exposure (0.95 probability; $HQ_{0.95}$) and median exposure (0.50 probability; $HQ_{0.50}$) situations, with Chronic Population Adjusted Dose (CPAD; see Table 4.4.5) for more sensitive and susceptible groups of pregnant females and children, with repeated exposure. The US mothers were at high risk, having the highest observed HQ at the 0.95 probability level of $HQ_{0.95}$ of 157 (see Table 4.4.3). This resulted from the low value of the GV used, due to use of an additional safety factor, given the sensitivity of pregnant mothers and children. The mothers were still at a potentially high risk at the 0.50 probability level with $HQ_{0.50}$ of 28. Thai children had a lower risk ($HQ_{0.50}$ of 4.0 at the 0.50 probability level) compared with the higher risk at the 0.95 level of probability (HQ 15.7).

Hazard Quotients (HQ) calculated using Acceptable Daily Intake (ADI) of the World Health Organization (WHO)

The GV of Acceptable Daily Intake (ADI) of the World Health Organization (WHO), which is based on ChE inhibition in humans, rats and dogs, has been set to characterize the long term risk posed by pesticides. The HQ was calculated from the equation of $'HQ = Exposure\ Dose/Guideline\ Value'$. Both the Exposure Dose and the Guideline Value are in the same units of ng/kg/day and were assumed to represent chlorpyrifos intake by ingestion.

Table 4.4.9 Hazard Quotients (HQ) calculated with the Acceptable Daily Intake (ADI) of the World Health Organization (WHO)*

Hazard Quotients (HQ)	Cumulative Probability	
	0.05	**0.95**
[1]Sri Lankan Farmer- Baseline	**0.03**	**0.1**
[1]Thai Farmer	**0.005**	**0.4**
[3]General Populations (Adults) in Germany, USA and Italy	**0.01**	**0.05-0.06**
[3]US Pregnant Mothers	**0.08**	**0.5**
[3]Thai Children	**0.01**	**0.05**

*See Table 4.4.5; [1]see ECID in Table 4.4.1; [2]see ECID in Table 4.4.2; [3]see ECID in Table 4.4.3; HQ values below 1.0 (acceptable risk levels) are in bold

HQs were calculated using the Acceptable Daily Intake (ADI) set by the World Health Organization (see Table 4.4.5) for GV and ECIDs, of non-occupationally exposed groups, in long term exposure situations. Thai farmers were observed as having an acceptable risk at the median exposure situation (0.50 probability), with a $HQ_{0.50}$ of 0.005 (see Table 4.4.9). At the same level of probability, Sri Lankan farmers at baseline, general populations in the USA, Italy and Germany, US pregnant mothers and Thai children also had acceptable risk levels ($HQ_{0.50}$ values of 0.03, 0.01, 0.08 and 0.01 respectively) (see Table 4.4.9). At the high exposure situation (0.95 level), farmer groups from Sri Lanka and Thailand and, the US mothers were still at lower risk with respective HQs of 0.1, 0.4 and 0.5, although they were higher than the $HQ_{0.95}$ of general adult populations ($HQ_{0.95}$ from 0.05 to 0.06; see Table 4.4.9) and children ($HQ_{0.95}$ 0.05; see Table 4.4.9).

Hazard Quotients calculated using Acceptable Daily Intake (ADI) of the Australian Department of Health and Ageing

The Australian Government (Department of Health and Ageing), has set an Acceptable Daily Intake (ADI) of 3×10^3 ng/kg/day, which is in the same units and represent ingestion of chlorpyrifos via food and water, as do the Equivalent Chlorpyrifos Ingested Doses (ECID). The ADI consider long term exposure. This value for ADI is somewhat lower than the ADI set by the WHO (10×10^3 ng/kg/day; see Table 4.4.5) and higher than the USEPA CRfD (0.3×10^3 ng/kg/day; see Table 4.4.5). Therefore HQs calculated could be expected to lie between the HQs calculated using the GVs of ADI (WHO) and USEPA CRfD.

The HQs were calculated with the Acceptable Daily Intake (ADI) of Australian Department of Health and Ageing (see Table 4.4.5), for non-occupationally exposed groups with long

term exposure. At the 0.50 probability level, Sri Lankan farmers at baseline exposure, Thai farmers, the general adult populations of the USA, Italy and Germany, US mothers and Thai children had HQs below one ($HQ_{0.50}$ 0.1, 0.01, 0.03, 0.2 and 0.03 respectively; see Table 4.4.10), indicating the risk to be acceptable. Even at the 0.95 probability levels Sri Lankan farmers, Thai children and the general adult populations of the USA, Italy and Germany were at acceptable risk levels with a $HQ_{0.95}$ of 0.5, 0.1 and 0.1-0.2 (see Table 4.4.10). Thai farmers and US mothers were at a marginal risk with a $HQ_{0.95}$ of 1.5 and 1.7 at the 0.95 probability level (see Table 4.4.10).

Table 4.4.10 Hazard Quotients (HQ) calculated with the Acceptable Daily Intake (ADI) of Australian Department of Health and Ageing*

Hazard Quotients (HQ)	Cumulative Probability	
	0.50	0.95
[1]Sri Lankan Farmer- Baseline	**0.1**	**0.5**
[1]Thai Farmer	**0.01**	1.5
[3]General Populations (Adults) in the Germany, USA and Italy	**0.03**	**0.1-0.2**
[3]US Pregnant Mothers	**0.2**	1.7
[3]Thai Children	**0.03**	**0.1**

*See Table 4.4.5; [1]see the ECID at the Table 4.4.1; [2]see the ECID at the Table 4.4.2; [3]see the ECID at the Table 4.4.3; HQ values below 1.0 (acceptable risk levels) are in bold

Hazard Quotients calculated using the Guideline Values (GV) for Total Dietary Chlorpyrifos Intake (TDCI) in Sri Lanka and India

The previously discussed HQs were calculated using the Equivalent Chlorpyrifos Ingested Doses (ECIDs) derived from analyses of the urinary metabolite of chlorpyrifos, TCP (3, 5, 6 trichloro-2-pyridinol). An alternative method of estimating HQs is, to use the ingested doses, calculated from chlorpyrifos content of each dietary component and drinking water (TDCI), as the exposure dose ($HQ = Exposure\ Dose/Guideline\ Value$). Accordingly, HQs were calculated at the 0.50 and 0.95 cumulative probability levels. It is noteworthy that, trend line equations from each plot of Dietary Chlorpyrifos (DCI) Intake, were used to calculate TDCI, at each probability level. At both these levels, the Dietary Chlorpyrifos Intake (DCI) in Sri Lanka and India represent the intake only in food components. Furthermore, the contribution from water to TDCI was observed only at the 0.99 level of cumulative probability in the Sri Lankan diet.

HQs ($TDCI/GV$) were calculated for the median (0.50 probability) and high exposure (0.95 probability) situations (see Table 4.4.11),using the Total Dietary Chlorpyrifos Intakes (TDCI) in Sri Lanka and India (see Table 4.4.4), and the Guideline Values (GV) for ADIs from the WHO and Australian Department of Health and Ageing and the USEPA CRfD. These HQ levels for Sri Lankan TDCI, were comparable with previously discussed HQ levels for Equivalent Chlorpyrifos Ingested Dose (ECID), in Sri Lankan farmers atbaseline exposure (see Table 4.4.9; Table 4.4.10; Table 4.4.7).

Table 4.4.11 Hazard Quotients (HQ) calculated with the Guideline Values (GV) for Total Dietary Chlorpyrifos Intake (TDCI)

Hazard Quotients (HQ) calculated with the Guideline Values (GV)*	0.50 Cumulative Probability		0.95 Cumulative Probability	
	[1]Sri Lanka	[2]India	[1]Sri Lanka	[2]India
Acceptable Daily Intake (ADI, WHO)	**0.03**	**0.003**	**0.1**	**0.03**
Acceptable Daily Intake (ADI, Australia)	**0.1**	**0.01**	**0.6**	**0.1**
Chronic Reference Dose (CRfD, USEPA)	**1.0**	**0.1**	6.0	**1.0**

*See Table 4.4.5; [1]see the TDCI at the Table 4.4.4; [2]see the TDCI at the Table 4.4.4; HQ values below 1.0 (acceptable risk levels) are in bold

The HQs using the ADI from the WHO for Sri Lanka, with a $HQ_{0.50}$ of 0.03 and $HQ_{0.95}$ of 0.1, were at acceptable risk levels, whilst for India, the HQs were even lower ($HQ_{0.50}$ of 0.003 and $HQ_{0.95}$ of 0.03). HQs with ADI of Australian Department of Health and Ageing, were also acceptable for both countries, with $HQ_{0.50}$ values from 0.01 to 0.1 (see Table 4.4.11) and $HQ_{0.95}$ from 0.1 - 0.6 (see Table 4.4.11). HQs using CRfD were still acceptable for Sri Lanka at the 0.50 probability level, with a $HQ_{0.50}$ of one and for India at both exposure situations, with $HQ_{0.50}$ of 0.1 and $HQ_{0.95}$ of 1.0. At the 0.95 probability level, there was a slightly higher risk for 5% of the Sri Lankans with a $HQ_{0.95}$ of 6.0 (see Table 4.4.11), using the diet considered in the study.

5. CONCLUSIONS

5.1 Chlorpyrifos and Other Organophosphate Pesticides in Food and Drinking Water in Sri Lanka

Chlorpyrifos, profenofos and diazinon were the most frequently detected organophosphates in rice and vegetables in Sri Lanka with concentrations in the range of 2.6×10^3 to 5.0×10^6 ng/kg, 5.0×10^3 to 5.0×10^6 ng/kg and 1.2×10^4 to 1.0×10^5 ng/kg respectively. Dimethoate was not reported, except in the surface washings of vegetables. In sources of water, chlorpyrifos ranged from 20 to 6400 ng/L although a few unusually high levels of up to 10^6 ng/L were reported up to. Few detections of profenofos (3.6 to 73.3 ng/L) and diazinon (12 to 150 ng/L) were also reported. However, chlorpyrifos was the only OP which could be used for a probabilistic assessment of Dietary Intake, considering the data reported.

According to the study results, rice was the major contributor of chlorpyrifos (100% at 0.50 and 83% to 0.95 probability levels) to the TDCI (50 ng/kg/day to 3000 ng/kg/day) in an average diet in Sri Lanka. Vegetables contributed about 17% TDCI, at the 0.95 level of probability (310 ng/kg/day). The contribution from water was negligible and was observed only at the 0.99 level of probability, with 3% TDCI. However, one of the major limitations of the study was with availability of data. For instance, the DCI for rice was estimated using data obtained from only one study that was carried out as a research trial. Therefore, the TDCI estimated with these available data, was considered to be useful as a preliminary

result or rather, as the worst residue situation, particularly given the data for rice. Furthermore, it is noteworthy that this study on estimating TDCI was conducted with unprocessed dietary components and may vary from a diet with processed components.

Low exposure to chlorpyrifos in breathing air was indicated by assuming that, the atmospheric concentrations present in Sri Lanka were the same as in US outdoor air (0.4 ng/kg/day at 0.50 and 4.0 ng/kg/day, at 0.95 probability levels). However, this should be confirmed by monitoring air samples for chlorpyrifos in Sri Lanka.

At the high exposure situations (0.95 probability), TDCI in the Sri Lankan diet (1800 ng/kg/day) was about 6 times higher than the levels found in a similar diet in India (300 ng/kg/day). The difference between the average TDCI levels, calculated at the 0.50 probability level, was 10 fold. However, the time periods of the residue analyses were different for the two countries, with those in Sri Lanka dating from 2001 to 2009 and those in India conducted from 1994 to 2002. Also, the Indian analyses resulted in detection mostly of pesticides other than chlorpyrifos (monocrotophos, endosulfan, DDT, HCH). This may be as a result of a low level and lesser frequency of chlorpyrifos usage in India.

5.2 Health Implications for Sri Lankan farmers (Baseline situation) and the General Population

The baseline Equivalent Chlorpyrifos Ingested Doses (ECIDs, 300 ng/kg/day at 0.5 and 1600 ng/kg/day at 0.95 probability levels) calculated from TCP in urine from Sri Lankan farmers, were in good agreement with the Total Dietary Chlorpyrifos Intake levels calculated in an average vegetarian diet (TDCI, 300 ng/kg/day at 0.5 probability and 3000 ng/kg/day at 0.95 probability levels), in Sri Lanka. These levels were also comparable with the general levels found in adults in the US, Italy and Germany and Thai children at median (0.50 probability) and high exposure (0.95 probability). However, the levels were below those estimated in US pregnant mothers and Thai farmers, at the 0.95 probability level. Therefore, it can be concluded that the baseline levels of ECIDs for farmers, at the 0.50 and 0.95 probability levels, were comparable with the levels found with other populations exposed in non-occupational situations and also with the TDCI in an average person's diet in Sri Lanka.

Baseline ECID at medium exposure situation (0.50 probability) suggested that the long term health risks in 50% of Sri Lankan farmers were at an acceptable level with a $HQ_{0.50}$ of one, using the regulatory Guideline Value of US Environmental Protection Agency (USEPA) Chronic Reference Dose (CRfD). However, there was a slightly higher health risk to 5% of farmers, with a $HQ_{0.95}$ of 5.3. The GV, (CRfD), is based on the long term adverse effects of plasma and RBC ChE inhibition in rats. The health implications were similar for TDCI levels calculated in Sri Lankan diet, with a $HQ_{0.50}$ of 1.0 and a $HQ_{0.95}$ of 6.0, using the USEPA CRfD.

5.3 Health Implications for Sri Lankan farmers (Post Application Situation)

Post-application ECID in Sri Lankan farmers, in median (at 0.50 probability) and high exposure (at 0.95 probability) situations were 6800 ng/kg/day and 11000 ng/kg/day respectively. These levels were somewhat higher than those found in US farmers (8400 ng/kg/day), but were lower than the levels in pest control applicators in the US (26000 ng/kg/day) and Australia (26000 ng/kg/day) at 0.95 probability levels. They were comparable with the levels found with Australian applicators (7800 ng/kg/day), at 0.50 level of probability and with US manufacturing workers in a non-occupational exposure period (10000 ng/kg/day), at 0.95 level of probability. However, they were considerably lower (19 fold) than the occupational exposure levels found with manufacturing workers in atypical conditions (210000 ng/kg/day) and somewhat lower at typical conditions (13000-29000 ng/kg/day).

In both median and high exposure situations, Sri Lankan farmers were at a marginal risk for exceeding the USEPA Acute Reference Dose, with a $HQ_{0.50}$ of 1.3 and $HQ_{0.95}$ of 2.2. The GV of USEPA ARfD, is based on the NOAEL of adverse effects of plasma and RBC cholinesterase inhibition observed in surrogate animals and a safety factor. Therefore, it is noteworthy that the HQs used for risk characterisation resulted from estimated values of GVs and exposure doses of ECIDs, using indirect measures. Accordingly, potential for health implications, may not be expected given a marginal excess of the GV.

5.4 Health Implications for International Populations

Thai farmers in high exposure situations (0.95 probability), showed a relatively high potential risk of adverse effects with a $HQ_{0.95}$ of 15.3, using the USEPA CRfD and a marginal risk of 1.5, using ADI (Australian Department of Health and Ageing). Thai children also had a relatively high potential risk of adverse effects with a $HQ_{0.95}$ of 16.6 using the CRfD.

ECID levels in the high exposure group (5%) of general adults in the USA exceeded CRfD marginally, with a $HQ_{0.95}$ of 2.0. The potential risk to pregnant mothers at median exposure was relatively high with a $HQ_{0.50}$ of 26.6, using the CPAD. Only a marginal risk, exceeding ARfD, was apparent in high exposure groups (5%) of occupationally exposed populations of farmers ($HQ_{0.95}$ 1.7) and pest control applicators in Australia and the USA ($HQ_{0.95}$ 5.2). The risk varied from a $HQ_{0.95}$ of 2.6 to 42.0, in US manufacturing workers, with a high risk potential for adverse effects during atypical exposure periods.

5.5 Further Research

The study focused mainly on risk assessment of the OP pesticide, chlorpyrifos. This was due to the limitation of residue data for other pesticides. However, other than chlorpyrifos, profenofos also was detected in many vegetable crops albeit less frequently. There was no data reported on profenofos residues in rice, which is the major dietary component in a Sri Lankan diet. Although the levels reported for profenofos assisted with detections below LOD could have been used to assess the risk with reported vegetables, major attention was

focused on assessing chlorpyrifos exposure with a complete diet. Furthermore, chlorpyrifos was the most frequently used pesticide among the considered OPs. However, this does not indicate that exposure to other pesticides such as profenofos, is unimportant. Assessing these pesticides with available data, and further research on residue analyses in other crops is suggested as well.

As discussed in the previous sections, the major limitation of the study was the availability of data. This was apparent when data on residues in rice was not reported from farmer fields or markets. Also, reported data was rare for many vegetables. Due to these limitations, the study was compelled to be designed with the available data and these limitations may have been reflected in the results obtained. Therefore, it is suggested that well designed residue studies are further required on market samples of rice and vegetables, to assist with risk assessments of pesticides in Sri Lanka. This is important not only because the usage of pesticides is high, but also the reported pesticide misuses can lead to unnecessary levels of residues. Furthermore, in this study a large effort was expended to estimate the Dietary Chlorpyrifos Intake in an average Sri Lankan diet. However, due to unavailability of reported data in processed food items, ultimately the DCI was expressed for an unprocessed diet only. This may perhaps overestimate the actual DCI if processing could reduce the levels of residues. Therefore, further studies are required on residue analyses in processed food samples. In addition, further knowledge is needed on other exposure pathways such as water, air, and dust, particularly in farming areas.

As a whole, the study assessed chlorpyrifos exposure in a group of farmers post-application and, baseline exposure with connection to the exposure via an average diet in Sri Lanka.

However, there could be other groups of interest such as children, pregnant mothers, family members of farmers who are vulnerable to high levels of exposure to pesticides. Although few published works are available on such groups, further research is important to expand the data base. This should include analyses on any of the hazardous pesticides, including chlorpyrifos.

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